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Stress Urinary Incontinence Therapeutic Approach in the Emergency County Clinical Hospital Saint Andrew the Apostle Constanta

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Abstract

Transobturator tape (TOT) gives an excellent outcome in the treatment of stress urinary incontinence. Midurethral sling surgeries in the form of TOT surgery are the recommended treatment for stress urinary incontinence. A retrospective study was performed for a period of 5 years (2017-2021) on patients admitted to the Clinical Emergency Hospital Saint. Andrew the Apostle Constanta, on the two departments of Obstetrics- Gynecology OG I and OG II. The study was aimed to find how many of total interventions were performed using transobturator tape for stress urinary incontinence. The patients were followed according to the following criteria: age, origin, symptoms.

Keywords: Transobturator Tape, Stress Urinary Incontinence, Urogynecology

Introduction

Stress urinary incontinence is the unintentional passing of urine when the body is in distress such as cough or laugh. It is a problem that affect millions of women (System, 2001).

In the United States approximately 13 million people suffer from this kind of dysfunction, stress urinary incontinence being less prevalent in men than in women (Luber, 2004).

Some authors state that stress urinary incontinence (SUI) prevalence is variably estimated between 4% and 35% of adult women (Thom, 1998).

The International Continence Society's tried to create a standardization of terminology for lower urinary tract dysfunction in order to make possible a future calculation of real prevalence for this kind of disease (Abrams et. al., 2003).

The main sign and symptom of stress urinary incontinence is described as "the complaint of involuntary leakage on effort or exertion, or on sneezing or coughing" (Abrams et. al., 2003).

Stress urinary incontinence may also be associated with depression and anxiety, particularly in the elderly patients with an urge component but also in young people (Dugan et. al, 2000).

Principal risk factors for stress urinary incontinence are represented by aging, the dysfunction becoming more relevant after the installation of menopause, obesity, the increased Body Mass Index, resulting in an increased intra-abdominal pressure and leading to weakening of the pelvic floor innervation and musculature failure and smoking whereas the roles of pregnancy and childbirth remaining controversial (Luber, 2004), (Osborn et. al. 2013).

Other risk factors may include estrogens depletion, delirium, stroke, medication, such as diuretics, Beta- or Alpha-adrenergic agonists, Caffeine or alcohol (Hannestad et. al., 2000).

For the diagnosis of stress urinary incontinence, there are some urodynamic analyses that should be performed, like the stress pad test, when the wears a urinary pad and performs some activities that could trigger urinary leakage. The test is considered positive when there is 1ml of urine after one hour or 4 ml of urine after 24 hours (Krhut et. al., 2014).

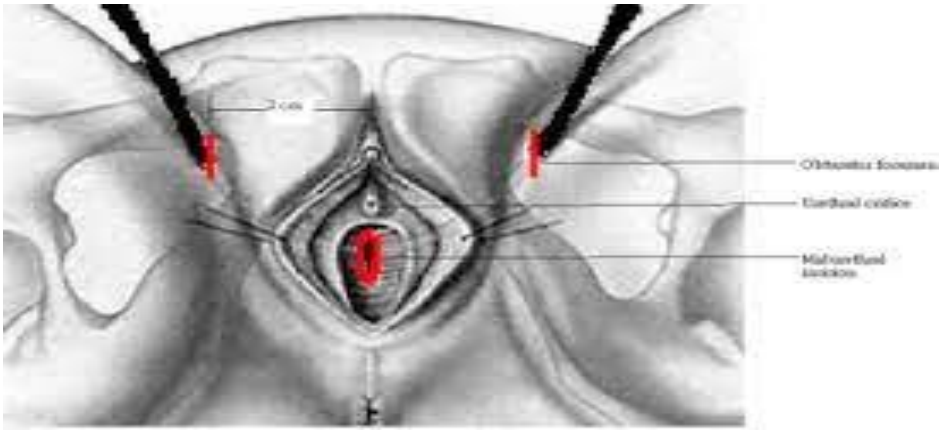
Although urodynamics has been regarded as a valuable test in elucidating the underlying mechanism of urinary incontinence, findings must be correlated with the patients' symptoms (Powell et. al., 1981).

A urinalysis should be performed on all patients with incontinence, from the midurine, to rule out pyuria (infection), hematuria (infection, stones, or cancer), proteinuria (renal disease), and glycosuria (diabetes) (Deutchman et. al., 2005).

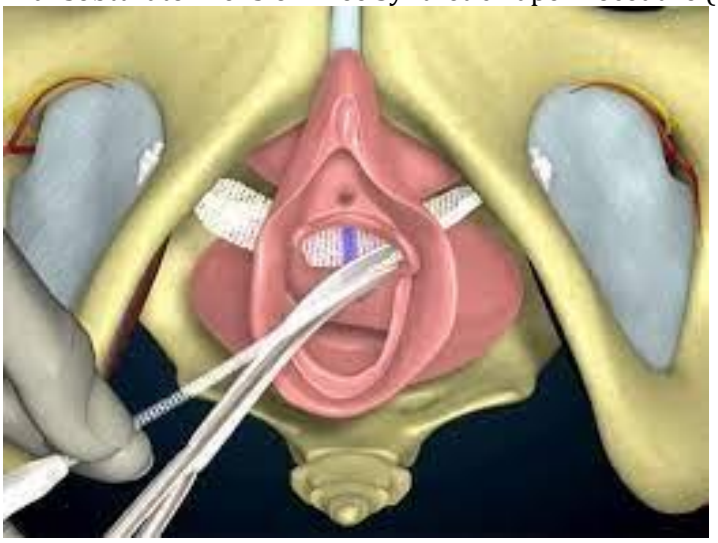
The treatment for stress urinary incontinence may be medical at the beginning, including topical estrogens, behavioral therapy, Alpha- adrenergic or anticholinergic medication (Kershen et. al., 2004).

Non-surgical mechanical treatments include pessaries that elevate the mid urethra, urethral occlusive devices, weighted vaginal cones that provides sensory feedback during pelvic floor muscle exercise like Kegel exercises (Godman, 2014), (Ward et.al., 2002).

The surgical treatment includes plenty of methods for the management of Stress Urinary Incontinence, from the Burch colposuspension, to midurethral sling using autologous materials, transvaginal tension-free synthetic tape (TVT) and Transobturator tension free synthetic tape (TOT) (Ward et.al., 2002), (Latthe et. al., 2007).



Transobturator Tension Free Synthetic Tape Procedure (Wang et. al., 2016)



Transvaginal Tension Free Synthetic Tape Procedure (Braga et. al., 2018)

Transvaginal Tension- Free Tape and Trans-obturator Tension Free Tape are the most cost-effective primary procedures, retaining the success and cure rates associated with colposuspension but with decreased morbidity, shorter hospital stay and quicker return to work (Ward et. al., 2008).

Material and Method

The present study was aimed to analyze the incidence of stress urinary incontinence and the Trans-obturator Tension Free Tape using interventions in the Clinical Emergency Hospital Saint Andrew the Apostle Constanta within the Obstetrics-Gynecology I and II departments.

The study was a retrospective one, over a period of 5 years, between 01.01.2017 and 31.12.2021, and the data were collected from the observation sheets and from the operative protocols of the two departments.

Between 01.01.2017 and 31.12.2021, a total number of 14,250 patients were admitted to the Obstetrics-Gynecology I and Obstetrics-Gynecology II departments, 3746 patients on the gynecology department

The total number of patients included in the study was 93, all of whom presented to the hospital for symptoms mainly related to the symptoms of stress urinary incontinence.

The incidence of stress urinary incontinence in the period presented was **2.48%** of all hospitalizations in the two departments of Obstetrics-Gynecology.

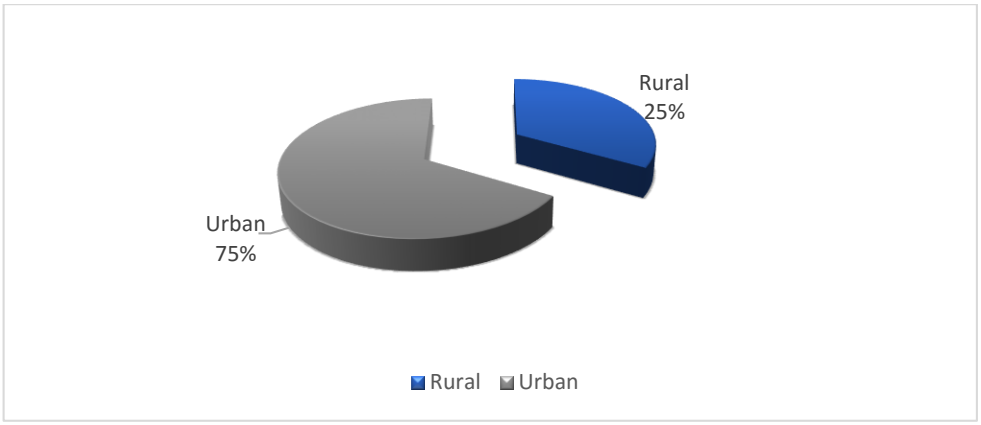
Out of 3746 patients admitted on the gynecology department, 93 were diagnosed with stress urinary incontinence.

Distribution of the studied batch by provenance environment

The studied batch of patients was divided into rural and urban environments.

Table 1. Distribution of the studied group by provenance environment

	Frequency	Procent
Rural	23	25%
Urban	70	75%
Total	93	100%



Graphic 1. Distribution of the studied group by provenance environment

Both from the table above and from the graphic representation, a higher incidence of stress urinary incontinence can be observed in the urban population. Urban population incidence is 75%, compared to the rural population, which is only 25% of cases. These results can be explained by the low addressability of rural women to the gynecologist compared to urban women.

Distribution of the studied group by smoking habit

The studied over the five years was classified into groups of smokers and non-smokers.

Table 2. Distribution of the studied group by smoking habit

A	Number of Patients	Incidence
Smokers	80	86 %
Non- Smokers	13	14 %
Total	93	100%

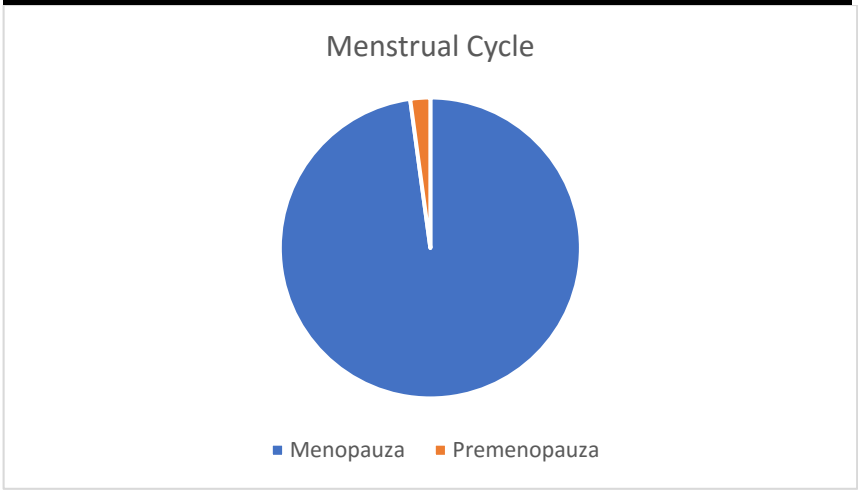
Graphic 2. Distribution of the studied group by smoking habit

It can be seen from the graphic analysis above that the highest incidence of symptoms related to stress urinary incontinence is in **the smokers group**.

Distribution of the studied group by menstrual period

Table 2. Distribution of the studied group by menstrual period

A	Number of Patients	Incidence
Menopause	91	97.85 %
Pre- Menopause	2	2,15 %
Total	93	100%



Graphic 2. Distribution of the studied group by menstrual period

It can be seen from the graphic analysis above that the highest incidence of symptoms related to stress urinary incontinence is in **the menopaused patients group**, most of the time, in this age period overlapping both the associated symptoms of estrogen absence, and that associated with menopause atrophy.

Discussions

Stress Urinary Incontinence occupies a very well-defined place in gynecological practice. The incidence of this kind of pathology in the Emergency County Clinical Hospital "Saint Andrew the Apostle" Constanta was **2.48%.** Some authors state that stress urinary incontinence (SUI) prevalence is variably estimated between **4% and 35%** of adult women [1]. Probably the low incidence from our study is due to CO-VID 19 pandemic and to low addressability of patients regarding this kind of pathology

It can be seen from the graphic analysis above that the highest incidence of symptoms related to stress urinary incontinence is in **the menopaused patients group**, most of the time, in this age period overlapping both the associated symptoms of estrogen absence, and that associated with menopause atrophy.

It can be seen from the graphic analysis above that the highest incidence of symptoms related to stress urinary incontinence is in **the smokers group.** Studies suggest a strong statistical relationship between current and former cigarette smoking and both stress and motor urinary incontinence in women (Bump et. al., 1992).

Conclusions

Preferred surgical intervention for the stress urinary incontinence in the Emergency Clinical Hospital " Saint Andrew the Apostle " Constanta was Transobturator Tension Free Synthetic Tape Procedure.

The procedure needs special skills of urogynaecology in order to be performed and a special type of tape, but its outcome is the best surgical way for solving this kind of disfunction.

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Current Status of Ethnobotany in Albania

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Abstract

Traditional Ecological Knowledge (TEK) concerning the use of plants for different purposes had survival value, are embedded in culture and considered adaptive responses to environmental challenges. Albania is known for its rich linguistic, cultural and biological diversity. Albanian flora has a high considerably number of medicinal plants and they have been extensively used albeit expressed in folk medicinal knowledge and practices. Several ethnobotanical studies and extensive fieldwork have been conducted in Albania both by local and foreign scientists. In addition, ethnobotany is experiencing a theoretical and conceptual diversification. The history of ethnobotany can be at least can be traced back in 19th century. This article aims to provide an historical and theoretical review of ethnobotany in Albania and outlines possibilities for future advancements.

Keywords: plants, traditional ecological knowledge, ethnobotany, Albania, Balkans

Introduction

Traditional ecological knowledge can be defined as a cumulative body of knowledge, practice and belief evolving by adaptive processes and handed down through generations by cultural transmissions, about the relationship of living beings (including humans) with one another and with their environment (Berkes, 1999). Stated differently, TEK are cultural responses to solve the many adaptive problems humans faced in their evolutionary past and still face today. The TEK concept is most closely associated with the field of ethnoecology and together with subdisciplines of ethnobotany and ethnozoology, composes the broader area of ethnobiology (Anderson, 2011). As Anderson points out (2011) ethnobiology as a scholar endeavor and an interdisciplinary field which has established relationships with various other disciplines such as biology, anthropology, cognitive psychology, ethnology, it is most closely associated with studies focused on local classification systems for biological species. Ethnoecology, in turn, is associated with local ways of understanding the relationships between humans and their natural environment, which includes ecological aspects such as soil, climate, ecological communities and other environmental factors in addition to the species themselves (Hunn, 2007). The

history of ethnobiology can be traced back in 19th century. The first period, which we might call the "preclassical," began in the last century when the foundations of the discipline were laid and its various branches, e.g., ethnobotany and ethnozoology, first designated and defined (Clement, 1998). In 1874, S. Powers coined the term “aboriginal botany” (1875) and J. W. Harsheberger (1896) used the term ethnobotany as “plants used by primitive and aboriginal people” (1896). The first studies were conducted among “aboriginal” or” primitive” people and their botanical knowledge were not considered valid, in comparison to Western Science development and use of systematic nomenclature. According to Hunn (2007) in the second phase, ethnobiology was elaborated in the cognitive/linguistic anthropology of the 1960s and the institutionalization of ethnobiology coincided with the emergence of the cognitive sciences and was entangled with more general ambitions of cognitive anthropology and ethnoscience. The main assumptions and guiding principle relied on the conception of the “psychic unity of humankind” *alias* irrespective of their cultural background, all humans have at their disposal the same cognitive toolkit (Bender & Beller, 2011). The works of B. Berlin and P. Kay (1969) and B. Berlin (1992) supported this assumption. In this framework, the evolved computational programs in the human mind are assumed to be responsible for producing a universal (that is, species typical) human nature (Tooby & Cosmides, 2005). In contrast, the influence of culture in the formation of cognitive processes is related to the organization of the brain by experience and the fact that the experience is organized by culture (Bender et al., 2010). That is, the human mind does not consist of pre-specified programs but is built via a constant interplay between the individual and its environment (Karmiloff-Smith 2009). From this view, traditional ecological knowledge is embedded in culture and considered adaptive responses to environmental challenges.

The role of learning: Accumulation and transmission of TEK

The wealth of knowledge about the local environment has developed over thousands of years and been passed down through a multitude of generations in oral teachings (Berkes, Colding & Folke, 2000). Topics common to ethnobiology studies are the modes of transmission (D’Andrade, 1981) and distribution of local knowledge or TEK in a certain society (Romney and Moore 1998). Modes of transmission are enabled by social learning which includes a wide array of behaviors such as imitation, observational learning of novel foraging techniques, peer or parental influences on individual preferences, as well as outright teaching (Gariepy et al., 2014). The capacity to learn from others enables humans to gradually accumulate information across generations and develop well-adapted tools, beliefs, and practices that are too complex for any single individual to invent during their lifetime (Boyd, Richerson & Heinrich, 2011). In animals, there is accruing evidence for systematic individual variation in social learning within species and reliance on cultural knowledge to solve a novel task (Mesoudi et al., 2016; Gruber et al., 2009). Close to 50 cultural variants have been reported, including subsistence behavior, tool-use, communication signals,

and grooming patterns (Horner & De Waal, 2009). Understanding when, how and why individuals learn from others is a significant challenge (Rendell et al*.,* 2011). To make good use of learning from others (social learning), we need to learn from the right others; from agents who know better than we do (Heyes, 2016).

In addition, cultural transmission refers to the process of acquired cultural information through modes of learning, including symbolic learning. It occurs through at least three different, non-mutually exclusive paths: (1) from parents (vertical); (2) from age peers (horizontal); and (3) from older generations (oblique) (Reyes-Garcia et al., 2009). In this context, long-term pair bonds, kin recognition, exogamy, and multi-locality create ties between unrelated families, facilitating the transmission of medicinal knowledge and its fitness implications (Salali et al*.,* 2016). Mechanisms for the intergenerational transmission of knowledge are embedded in social systems (Berkes, Colding & Folke, 2000). Many cognitive and motivational systems that originally evolved to solve non-social problems have been co-opted by evolution to contend with social challenges (Gould & Lewontin, 1979). Complementing these general-purpose mechanisms are a small set of brain areas for which there is tantalizing evidence of uniquely specialized social functions, which may have evolved in only a limited number of species that have confronted the most complex social environments (Gariepy et al., 2016).

Cultural values are an essential component of every society, and they act as checks and balances in the management of natural resources (Verschuuren et al., 2010). They are integrated and are part of the socio-cultural systems, which involve the socio-ecological system. The latest refers to the interplay between members of society and traditional ecological knowledge which are responsible for the construction of the cultural niche in that humans uniquely developed ability to learn which is crucial for human ecological success i.e adaptations to their natural habitat (Boyd et al., 2011). The advocates and the proposers of the cognitive niche hypothesis, Tooby and De Vore (1987), do not take fully in consideration the ability to learn from others, or social learning. According to Boyd et al., (2011) despite the cognitive basis for cognitive niche construction, the cultural niche construction assumes that cultural learning is cumulative, which enforce adaptations and maladaptation's. In this context, the cultural niche construction is related to environmental modification to solve the adaptive problems a society face and sometimes responses, can be as well as maladaptive. The evolutionary perspective is essential to the growth of ethnobiology as a science (Santoro et al*.,* 2018; Bajrami and Qirjo 2019a; Bajrami and Qirjo 2019b; Bajrami, 2022).

Methods

For the short review presented in this paper, we searched for papers cited in the Scopus, PubMed, and Web of Science. The search was performed using combination of keywords like Albania, ethnobotany, and the Balkans. A total number of 16 publications were recorded in the databases for the period 2000 to 2022. In addition,

we conducted a bibliographic search from the year 1945 to 1990 to find materials, articles and books, that have botanical data and ethnobotanical knowledge, including folk botanical names.

Ethnobotanical Studies in Albania

The geographical and ecological specificity along with cultural diversity of the Balkan region has resulted in the development of a distinct diversity not only of medicinal plants but also knowledge, transmission, and use of them (Jaric et al 2018). Over the past decades several ethnobotanical studies and extensive fieldwork in the Balkan region has been conducted, including Albania.

Albania geographical position in Mediterranean and in the Balkan peninsula results in many different types of landscapes and includes 3 250 species belonging to 165 families and 910 genera of those 30 are endemic and about 180 sub-endemic (Paparisto et al., 1988; Vangjeli et al., 1995). Albania is rich in biological and landscape diversity and has a high considerably number of medicinal and aromatics plants, specifically, 310 species which belong to 62 family (Papathopulli, 1976). Albanian traditional medicine is created and developed almost like traditional medicine found in other socio-cultural systems. The use of medicinal plants and the emergence of medical system it is related not only to their own tradition but also their being part for over five centuries of the Ottoman Empire. More specifically, between 1479 and 1912, Albania was part of the Ottoman Empire.

During the medieval and early modern period in the Ottoman Empire, the medical hierarchy had three official distinguishable positions: physicians (known as *hekims* or *tabibs*), surgeons (*cerrahs*), and ophthalmologists (*kehhals*) (Shefer-Mossensohn, 2011). *Cerrahs* in Albania were specialized in one or several body organs or medical techniques and they used different parts of plants like *Sanbucus nigra, Hedera helix, Iris dalmatica, Hypericus perforatum, Urtica dioca, Artemisia absinthum, Papaver somniferum* etc. during their work (Minga, 2009). In addition, a pioneer study by Saraçi and Damo (2021) based on a review of 39 texts from 23 authors that include travelers, explorers, missionaries, naturalists, anthropologists, botanists, etc. who had written about Albania from the end of the 18th century (1796) to the first decades of the 20th century (1940) highlighted the ethnobotanical knowledge on their texts. They have collected traditional knowledge on plant uses related with magic, rites, folk, beliefs, medicine, and food (Saraçi and Damo 2021).

Traditional ecological knowledge in Albanian culture is expressed in people's perceptions and cultural practices in relation to nature. More specifically, in their perceptions and cultural practices regarding mountains, rivers, *Orët* (*The Hours*). vegetations etc. (Tirta, 2004). Even after the improvement of sanitation, healthcare and building of the hospitals before and during communism period in Albania, most of the population counted on traditional medicine and traditional healers. Mainly, ethnobotanical studies were conducted by researchers working at the Institute of Folk Medicine, for the identification and study of traditional receipts and traditional

practices (Kokalari et al., 1980). Data and sources on traditional use of plants during communism can be found on the works of several Albanians botanists and ethnobotanists (Mitrushi 1952, 1953a, 1953b, 1955; Demiri 1958; Lako 1965;).

After the fall of communism, a major and rapid cultural transition was associated with the loss of long-held traditions in relation to nature, including dietary habits (Bajrami, 2019c). Additionally, the migration to major urban areas caused the further loss of medicinal plant uses and practices. Today those practices are found in somewhat isolated rural areas and the need for their conservation and sustainability is of crucial economic importance. Albania is ranked 24th World MAP exporter in 2014 and sage (*Salvia officinalis*) dominates the medicinal crops in Albania, even though, there is an observed reduced supply of wild MAPs, due to both damaged MPAs resources and a reduced labor force in mountainous areas (Imami et al. 2015).

After 2000s, there have been conducted several ethnobotanical field studies in Albania. These studies have been important in documenting traditional ecological knowledge and ethnobotanical knowledge in Albania. They were conducted mostly in north, north-eastern, east, south, and south-eastern Albania (Dinga et al. 2001; Pieroni et al., 2005; Pieroni, 2008; Pieroni, 2010; Pieroni et al., 2014a; Quave & Pieroni, 2014; Pieroni & Quave, 2014; Papajani et al. 2014; Pieroni et al., 2015; Peçi, Proko & Mullaj, 2016; Bussmann et al., 2016; Pieroni, 2017; Pieroni & Soukand, 2017; Stillo, Içka & Damo, 2018; Tomasini & Thelaide 2019a; Tomasini & Thelaide 2019b).

Conclusions

Traditional ecological knowledge is continually evolving, are socially transmitted, and are considered as components of a particular socio-ecological system, which is included in a socio-cultural system. TEK among Albanians are expressed in their classification, perceptions and cultural practices in relation to nature. These perceptions and behaviors are responsible for the construction of the socio-ecological system as a whole. Both wild and locally cultivated plants for different purposes are still used in some part of Albania, especially in isolated and rural areas, to meet people's needs. As noted, ethnobotanical knowledge is generally under-documented for minorities such as Roma, Greek minorities and Çam population, Albanians living in the southern part of Albania and Greece. Albania represents a great potential for ethnobotanists, to help documenting and conserving the rich biocultural heritage of the entire Balkans. In the future, ethnobotanical studies among Albanians should be focused in deep south of Albania, where exists a vast amount of cultural diversity and minorities, using an evolutionary approach.

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A Significant Hidden Truth Concerning the Leaky Gut Syndrome: It Might Be a Small Intestinal Enteropathy Rather than a Gluten-Induced Intestinal Dehiscence

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Abstract

Aim: Demonstration of a hidden fact concerning the leaky gut (LG) challenge due to a natural gut bacterium misbehavior. **Background:** Great scientific efforts are dealing with the topic of the LG challenge; many are unsupported by true etiologic evidences, some are indirectly close the real truth while few are touching near the roots of this truth. The truth might date since 1985 and 1986 where a biological bacterium *(Helicobacter pylori)* has been forced outside the stomach with consequent disease flare up. The traces of this bacterium while in the stomach helps digestion, absorption and intestinal motility. If it migrates and occupies the small intestine for nutrition, its products in profuse amounts would definitely cause indigestion, malabsorption and intestinal delay with subsequent excess fermentation, even putrefaction, excess production and absorption of many toxins that could explain the adverse symptoms encountered in the LG syndrome. **Methods**: A prospective study included 9 male patients known with LG disease. They were given a side dish of chickpea flour béchamel or puree during or in between the attacks of symptoms. **Results:** All patients demonstrated marked improvement and decreased frequency of symptoms. **Conclusion:** The chickpea flour is a good fluid absorbent helping to turn the gut fluid contents into semi-formed pasty matter which is less fermetable and moving better in the gut resulting in less production and less absorption of toxins. Scientific efforts should be better directed towards control of environmental chemicals and the antibiotic abuse which could lead to misbehavior of some natural gut microbiota.

Keywords: antibiotic abuse, chickpea flour, date's fibers, enteropathy, gluten sensitivity, gut barrier, intestinal permeability, Helicobacter pylori, leaky gut, microbiota

Introduction

Most of the world's scientific efforts dealing with the hot topic of the leaky gut (LG) challenge are locked upon repair of gut permeability due to a chronic inflammatory disease, damage of intestinal barrier due to non-inflammatory stress-associated conditions, gluten and gluten sensitivity, intestinal dysbiosis and auto-immunity, misbehavior of gut microbiota and endorsing dietary exclusion; most of them are indefinite and unsupported by truly clear evidences [1-6]. Those investigators who are searching for a link between the LG syndrome and a microbiome-related potential intestinal inflammatory states, the link of the syndrome with microbiota and Alzheimer disease, a combined link between LG disease with microbiota and autism even those who are suggesting an association with colorectal cancer are possibly approaching indirectly very close to a real truth as concerns this conflicting medical challenge [1,7-10]. Employment of a probiotic cocktail though is not sufficiently decisive per its own yet it could be an intelligent idea enough to touching the roots of this truth [11]. The journey of this truth might have a bit long history since nearly 170 years before with sinificant stops before nearly 90 years, 30 years later and further 20 years after where an investigator has reported in 1853 that there is ammonia that exists in gastric lumen, in 1930s it was reported that the source of ammonia in the stomach is due to the activity of a urease enzyme, in 1960s a scientist has confirmed that the urease activity in the stomach is not a property of the stomach but of a bacterial origin and as early as the beginning of 1980s where it was illustrated that the amounts of ammonia existing in the stomach are not toxic but even beneficial [12]. That is until 1985 and 1986 where a biological bacterium (*Helicobacter pylori*) has been forced via antibiotic aggression to migrate outside the stomach with an associated world's disease flare up; the LG challenge could be among these diseases. *H. pylori* while in the stomach could function to protect from acid reflux, significantly it also helps to protect the gastric wall from its acid if it goes in excess and protects from absence of the acid during abscece of food [12-14]. Its traces while in the stomach helps digestion, absorption and intestinal motility. If it is forced to migrate from its natural habitat and occupies the small intestine for nutrition during the process of digestion, its products in profuse amounts would definitely cause indigestion, malabsorption and intestinal delay with subsequent excess fermentation, even putrefaction and production of toxins [14]. Absorption of these toxins could explain the adverse symptoms encountered in the LG syndrome.

Aim

Demonstration of a hidden fact concerning the LG challenge due to a natural gut bacterium non-intentional misbehavior.

Motive of Study

In spite of all the extensive therapeutic efforts a successful achievement for the management of the LG disease is indefinite. Although some investigators emphasized an aging-related LG disorder [11], yet newly-developed gluten allergy betwwen 60-

70 years of age was not enough convincing. The successful trials to develop a happy gut via dietary exclusion of some elements of food for some temporary periods then returning to them infrequently without developing any gut problems might signify that a permamant gut pathology is not a constant cell damage related to the disease but it could be a sort of constitutional dysfunction. These observational findings were sufficiently motivating this study to search for a temporary definite patho-physiological dysfunction that could explain the symptoms encountered in the LG syndrome.

Design

A prospective multiple-case clinical study has been done in Zaitona medical cupping center during 2019-2021 in Medina, Saudi Arabia.

Methods

Nine male patients known with LG disease on symptomatic medications were included in the study, they were in three age groups, each group included three patints and the age range was 16-25, 34-50 and 61-72 years. Their symptoms varied from mild to moderate while one of them aged 40 years used to develop sometimes severe symptoms. They were given a side dish of chickpea flour béchamel or puree during or between the attacks of symptoms for 6-9 weeks. They were also given a dried dates powder as an alternative sweetener when required when they feel craving for sweets. They tolerated both stuffs without problems as concerns their disease condition and they liked both of them. A specific test for existence of *H. pylori* in the colon (*H. pylori* fecal antigen) was done for all patients [12,14]. All patients were allowed and instructed to employ their own symptomatic medications when required.

Results

All patients were found positive for existence of colonic *H. pylori* strains. All patients have tolerated both food stuffs used in the study and they mostly preferred and enjoyed the chickpea béchamel or puree. All patients demonstrated obvious improvement and decreased frequency of symptoms even most of them did not find any need to use their own symptomatic medications during the period of study. Follow up of patients for further six months showed similar observations.

Ethical Considerations

All patients were re-assured about safety of the food stuffs used in the study as concerns their disease condition and it is just a dietary stuff. Patients were allowed to lead their own style of life and they were free to quit the study whenever they like. An informed signed consent was taken from all patients.

Discussion

The challenge of the LG is a hot world's topic that has been extensively studied, great scientific and psophisticated efforts have been dealing with this problem but without definite cure outcomes. The literature reports include attempts to cure disorders in gut permeability barrier related to chronic inflammatory or stress conditions [1,2], management of gluten/food sensitivity and auto-immunity via dietary exclusion [3-6], and further efforts to rectify dysbiosis whether it is abnormal existence or misbehavior of natural microbiomes within its natural habitat [4,7,8]. However, all these great efforts were unsupported by clear evidences. Those investigators who are searching for a link of the syndrome with microbiota and Alzheimer disease, a combined link between LG disease with microbiota and autism and even those who are suggesting an association with colorectal cancer are possibly approaching indirectly very close to a real truth as concerns this conflicting medical challenge as all these pathologies could be a result of the same reason which is translocation or mal-existence of a natural microbiome where it does the proper good function in an improper site [7-10,15-17]. Employment of a probiotic cocktail though is not sufficiently decisive per its own yet it could be an intelligent idea touching the roots of this truth which could be dysbiosis [11].

The interest of the investigator of this study with the LG challenge started since 2017 through suggesting meals for LG disease patients as alternatives for wheat, milk products and sugars. Whereas his attention towards the hot world's topic of *H. pylori* began as early since 2003; whether *H. pylori* is guilty, not guilty or innocent; whether it is biologic or pathologic; whether its antibiotic eradication is necessary and possible or un-necsssary because impossible; whether the antibiotic eradication therapies are effective or ineffective; whether *H. pylori* is eradicated or forced to migrate and should we fight and kill or save *H. pylori*!! It has been found that *H. pylori* colonized the stomach since an immemorial time as if both the gastric wall and the bacterium used to live together in peace harmless to each other, it has been also reported that recurrence of *H. pylori* in the stomach is unavoidable and it was further emphasized that *H. pylori* has got huge defense talents for survival within the hell fire of the gastric acid [12,14,17]. Could these criteria altogether suggest that *H. pylori* might be a natural bacterium!!

Physiological intelligence has been praised for juxta-mucosal ammonia of the stomach as the ammonia adjacent to the gastric mucosa is responsible for the endothelial-derived nitric oxide (NO) liberation from micro-capillaries of gastric mucosa via a shear stress effect whereas NO is entitled for the control of mucus secretion from gastric mucosa and mcus thickening; hence ammonia and NO are responsible for the formation of the thick viscid alkaline gastric mucus layer that constitutes the main gastric wall protection from its strong acid meanwhile *H. pylori* is lying safe under this mucus shield and protected by a sheath of ammonia at its immediate vicinity which helps to buffer any acidity that penetrates the mucus shield

[12,14,18,19]. Then what is the nutrition of *H. pylori* and how it could gain it!! *H. pylori* eats organic urea to produce its ammonia and pyruvate in order to gain energy, it picks up its food from the remnants of gastric lumen contents in a blink after travel of the meal and drop of the acid to low residual level but still protected by a jacket of ammonia thus leaving before returning traces of ammonia in the gastric lumen that excites back the acid secretion [12,14]. Accordingly, *H. pylori* helps to protect the gastric wall from its acid if it goes in excess and helps to protect the gut and the human body from absence of the acid during absence of food as the gastric acid is the major defense line against bacteria invading the gut with food and drinks. This biological competitive buffering phemomena between ammonia of *H. pylori* and the gastric acid is constant leaving all the time residual traces of ammonia in gastric lumen that assists to maintain the integrity of the gastro-esophageal sphincter as ammonia is smooth muscle tonic helping in turn to protect from acid reflux [13,20-23]. If *H. pylori* is natural it should have a function, and if it plays these wonderful functions in only one area of the gut it should be natural and hugely biologic. It has been emphasized that *H. pylori* is not essentially pathologic in attitude by its own but it is mostly forced to its pathologic sequels either due to misbehavior in food habits or the antibiotic violence towards it. It has been further realized that misconception and misbehavior towards *H. pylori* was leading to major spread of illness during the latest three decades [14,17]; the leaky gut disease could be among these diseases.

NO is a cure and poison in the meantime; that is in normal levels it is cure while in overdoses it is toxic. As ammonia in the gut liberates NO via a shear stress effect, accordingly; ammonia in the gut is a cure and poison at the same time meaning that ammonia in low residual levels is healthy whereas in profuse amounts it could be toxic and pathologic [18,19,24]. Therefore; while *H. pylori* exists in the stomach, travel of few traces of its ammonia from gastric lumen to the small intestine is supposed to assist digestion, absorption and intestinal motility. If *H. pylori* is forced to migrate from the stomach and it comes to occupy the small intestinal mucosa for nutrition, it would definitely cause indigestion, malabsorption and intestinal delay with excess fermentation in turn, even putrefaction and production of toxins [14]. Absorption of these toxins could explain the adverse symptoms related to the LG syndrome without existence of a damage in gut barrier or constant pathologic change in intestinal permeability.

The chickpea flour béchamel was selected in this study for satiety as an alternative for wheat products while the dried date's powder was chosen as a sweetener alternative for sugars and both of them are also suitable for the patient's disease condition. It was interesting to observe apparent improvement and decreased frequency of symptoms among all patients upon using these two food stuffs even during the symptom attacks. It has been realized that the chickpea flour and the dried fibers contained in the date's powder are known fluid absorbents and bulk formatives that could turn the liquid indigested gut contents into formed stuff which is less fermetable and travels better in the gut resulting in less production and less

absorption of toxins. This could explain the improvement of symptoms among patients of this study upon adding the chickpea flour recepies and the dried date's fibers to their diet. Further investigators have also emphasized that dietary fibers could impact a protective effect on gut barrier integrity being poorly fermented by gut microbes and likely promote the gut transit rate thus reduce the time available for bacterial fermentation of non-digested food stuff [25].

It was not scientifically sound then to suggest that any of these two food stuffs employed in this study would instantly correct a permanent pathologic dehiscence in the gut barrier. It is also scientifically silly to imagine that the gut bacteria change its behavior to cause anaerobic fermentation of the gut contents. It is better logic to consider that the fault in the LG disease is not a permanent gut permeability damage but it could simply be a potential inflammatory error. As all patients were found positive for *H. pylori* strains, thus; the assumption that the migrating *H. pylori* strains could come to occupy the mucosa of small intestine simply for nutrition seems logic whereas its produced ammonia which would be entrapped within the gut mucosa in excess amounts in this situation as being unbuffered by any acidity would be then toxic leading to indigestion, malabsorption and intestinal delay with excess fermentation particularly for fermentable food products containing gluten. Hence; could the challenge of the LG disease be a potential small intestinal enteropathy rather than it is a gluten-induced intestinal dehiscence!! Could a big compromise be as simple as such!! Could the challenge of the LG syndrome be just small intestinal enteropathy rather than it is true gut barrier damage!! Could the matter be a non-intentional misbehavior of a natural bacterium due to the antibiotic violence towards it and would correction of the antibiotic use alleviate the problem!!

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Conflict of interest

No conflict of interest is existing.

Conclusion

The challenge of the LG syndrome might be a small intestinal enteropathy rather than it is a gluten-induced intestinal dehiscence. Scientific efforts should be better directed towards control of environmental chemicals and the antibiotic abuse which could lead to misbehavior of natural gut microbiota. Natural specific potent measures should be employed to correct abnormal behavior/existence of gut microbiota.

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The Pareto Method - A Beneficial Management Method for Increasing Profitability in the Drugs Market

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Abstract

The management methods represent the multitude of means and procedures with the help of which the management influences the approach to the elements of the driven system in order to obtain the established objectives. Contemporary organizations management can no longer be achieved without the use of scientific methods that allow the appreciation and efficient use of objective economic laws, the efficient and rational use of resources, the stimulation and use of creativity of employees and managers and the correct appreciation of results. Pareto analysis is a modern management method, very valuable to increase the profitability of companies and increase the efficiency of an organization. This paper aims to select the best ranked pharmaceuticals using Pareto analysis. The paper studies the values from 10 different community pharmacies in the city of Constanta, over a period of 12

months. In respect to the localization criteria, the pharmacies were selected from all regions of the city, from the center to the more external neighbourhoods. We highlighted the importance of the Pareto method in the selection of the most valuable preparations in the community pharmacies in Constanta. The obtained results indicate that the Pareto analysis is an important tool that can be used with great effect by the pharmacy manager.

Keywords: Pareto method, management, drugs market

Introduction

Management methods represent the multitude of means and procedures with the help of which the management influences the elements approach of the driven system in order to obtain the established objectives. Contemporary organizations management can no longer be achieved without the use of scientific methods that allow the appreciation and efficient use of objective economic laws, efficient and rational use of resources, stimulating and using the creativity of employees and managers and correct appreciation of results [1]. The first part of the paper shows the Pareto analysis, which is a modern management method, very valuable in order to increase the profitability of companies and increase the efficiency of the organization in question. Decision-making aspects are also improved, as they are crucial elements of management, with decisions developed and implemented being an important basis for the quality level of management [2]. This paper aims to select the best valued preparations with the help of the Pareto analysis.

The Pareto method was used to establish the most vital medicines released from the pharmacy in terms of sales made and in the process of supplying community pharmacies. The importance of applying the Pareto method to the process was highlighted by selecting the most important prescriptions and elaborations of pharmacy preparations. Modern management methods have been applied to improve the system and reduce errors in the community pharmacy.

Pharmaceutical management activities

Management is given a special place in any organization or company. In many cases, a pharmacy operates on principles similar to those of an ordinary company. Thus, the pharmaceutical management has the following roles:

- An important role in decision making and establishing the pharmacy policy is the setting of objectives by the manager, in order to streamline all the processors that will follow. The manager must set a group of main, basic goals that have a rather philosophical role, and then he must set a group of specialized, well-defined goals, such as achieving a certain turnover, on a

certain period of time. The manager must continuously check and improve objectives, and must be adaptable to market alterations.

- Human and material resources largely depend on goal setting. In the case of pharmacies, it is often the case that the same person performs both functions at the same time, which is not feasible in the long run and leads to a decrease in efficiency. Management aims to establish organizational structures and coordinate them in order to increase workplace efficiency as much as possible.
- Planning and controlling the current and upcoming activities is very important. The manager devotes a large part of his time from one day to the control of daily activities, this often leading to altering the time allocated for future activities. In this regard, routine activities should be delegated to other people, so that managers are allowed a better allocation of their own time.

Pareto analysis

Pareto analysis, also known as the Pareto law or the 80/20 rule, is one of the modern methods of management. This allows users to choose the important elements of a business or activity. This model was discovered by Vilfredo Pareto, an Italian economist, in 1897, which is where the name of this analysis comes from. From this analysis it was concluded that 80% of the effects or results come from 20% of causes or sometimes from a much smaller portion of strong forces [3].

Rule 80/20 is not a strict formula and shows us that in any activity, some things are probably more important than others. In some cases the ratio of 70/30 between results and causes is much more plausible than the 80/20, but in very few cases 50% of cases lead to 50% results [4]. The 80/20 analysis can show us that a minority of causes generate in most cases a majority of results.

Pareto analysis is used in most cases to alter the relationships they approach in order to use them in a higher percentage.

Company management is constantly facing many difficulties that must be solved in the shortest possible time and at the best possible cost. A crucial element of management is the decision, which is influenced by various methods used. The use of a modern method is usually due to the high complexity of the problems encountered, the novelty of the problems, the time required to solve the problems, etc. [5].

Research regarding the value of community pharmacies preparations from Constanta, Romania

The paper studies the values from 10 different community pharmacies from the city Constanta, over a period of 12 months. The materials studied were taken from the 10 community pharmacies preparation books, from 01.05.2021-01.05.2022. In order to respect the localization criteria, the pharmacies were selected from all regions of the city, from the center to the more external neighbourhoods.

For every pharmacy included in the study, the following data has been taken into consideration: the date, the compounding act number, the preparation, its value and its prince in RON (lei) [6, 7].

Table 1 below shows the preparation values from the 10 pharmacies taken into the study, reffered to F1 to F10.

From the results of Table 1 it can be noticed that the total number of preparations taken into this study was 10. The total values in RON vary a lot from 20548 to 1296 lei. Three formulations can be highlighted that appear in all the pharmacies, the oxygenated water, the Petrini paste and the rivanol solution. Other preparations that are also present in most pharmacies are diluted alcohol, borax glycerine, tincture of iodine and ichtiol ointment. A classification of the total value of the preparations has been made (Table 2).

Table 1. The preparations values in RON, from the 10 pharmacies, in the period

01.05.2021 – 01.05.2022

No	Preparations	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	Boricated Alcohol 4%	125	-	-	-	330	26	383	-	-	-
2	Borax Glycerine 10%	1980	22	-	122	313	178	414	77	98	49
3	Menthol Mixture	1780	-	580	-	878	212	1038	77	49	277
4	Rivanol Solution 1‰	2660	543	490	467	980	260	980	55	88	244
5	Ichtiol Ointment 10%	760	-	160	243	150	88	150	14	113	123
6	Salicylic Ointment 5%	-	-	-	-	-	55	-	24	-	-
7	Petrini Paste	8900	480	880	1450	9800	1655	1713	440	650	4210
8	Tincture of Iodine 2%	513	-	388	855	-	88	180	-	66	513
9	Oxygenated Water 3%	2800	488	513	330	980	177	1090	22	133	190

10	Diluted Alcohol	1030	680	-	880	-	390	855	113	99	590
	Total	20548	2213	3011	4347	13431	3129	6803	822	1296	6196

Table 2. Total classification of the total value in RON and the percentage from the total value of the formulations

No.	Preparations	Total value of the preparations in RON	% of the total value of the preparations
1	Boricated Alcohol 4%	864	1.39
2	Borax Glycerine 10%	3253	5.26
3	Menthol Mixture	4891	7.91
4	Rivanol Solution 1‰	6767	10.95
5	Ichtiol Ointment 10%	1801	2.91
6	Salicylic Ointment 5%	79	0.12
7	Petrini Paste	30178	48.83
8	Tincture of Iodine 2%	2603	4.21
9	Oxygenated Water 3%	6723	10.87
10	Diluted Alcohol	4637	7.5
	Total	61796	100

From Table 2 there can be observed that the Petrini Paste represents the most valuable preparation with 48.83% from the total value of the formulations.

Conclusions

The study has been conducted on 10 community pharmacies from Constanta, in a period of 12 months, from 01.05.2021 to 01.05.2022.

We highlighted the importance of the Pareto method in selecting the most valuable preparations in community pharmacies in the city of Constanta. The results obtained validates the Pareto method, 5 of the 10 formulations taken into the study gave an apromixately 80% of the total value of the pharmaceutical formulations.

The obtained results indicate the fact that the Pareto analysis represents an important tool that can be used to great effect by the pharmacy manager.

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Consumption of PPI Drugs in Primary Health Care in Albania During 2010-2020

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Abstract

The aim of the study was to estimate the out-of hospital Proton-pump inhibitors use in Albania (national level) during 2010-2020. All data were collected from Health Insurance Institute (HII) and analyzed reflecting the ambulatory and outpatient use for the period 2010-2020. The data about the consumption of drugs were expressed as a number of Defined Daily Dose (DDDs) /1000 inhabitants/day. For all the period under study 2010-2020, there were collected and analyzed data of import and domestic production of drugs, which represent the real consumption of drugs in the country. These data were subsequently included in a comparative analysis with the utilization data according to the Health Insurance Institute. Furthermore, it becomes visible the poor coverage by the scheme of the necessary alternative cures of the ulcerous disease. The reimbursement scheme offers only omeprazole. However, the consumption of omeprazole under the scheme is in much lower levels compared to the real data of omeprazole consumption coming from import figures, which shows its excessive utilization without medical prescription.

Keywords: Drug utilization, DDD/1000 inhabitants/day, PPI drugs

Introduction

Proton pump inhibitors (PPIs) are essentially H^+-K^+-ATPase inhibitors suppressing gastric acid secretion. These drugs tend to be used for the management of acid-related diseases, such as peptic ulcer disease (PUD), gastro-esophageal reflux disease (GORD), gastrointestinal (GI) bleeding and *Helicobacter pylori* infection, or the prevention of gastric ulcers in patients who are taking non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids (GCs), antiplatelet and anticoagulants.(1)

PPIs are one of the most commonly prescribed drug class worldwide, and off-label use is widespread (2).

The currently marketed main PPIs include omeprazole, esomeprazole, lansoprazole, pantoprazole and rabeprazole. PPI usage has dramatically increased since the

introduction in the late 1980s. Nowadays, they have become one of the most commonly prescribed and used drugs in the world(3). For instance, in the UK, nearly 59 million PPIs were dispensed annually, and the total usage doubled since 2007.(4) In one of the largest teaching hospitals in the southwest of China, an appreciable increase in PPI utilization was observed rising about 10.4-fold between 2004 and 2013.(5) Meanwhile, urgent concern about the overutilization of PPIs has been growing. It has been estimated that between 25% and 70% of the PPI prescriptions in the USA have no appropriate indication (3 6)

These facts alert the increasing worries regarding the cost and also safety, especially for long-term use.

I. Materials and Methods

The data were obtained from the Health Insurance Institute (HII) (7). All data were collected and analyzed reflecting the ambulatory and outpatient use for the period 2010-2020. The analysis included the total number of prescriptions, and quantities of drugs. The data about the population were obtained from the Institute of Statistics (INSTAT)(8). The data about the consumption of drugs were expressed as a number of Defined Daily Dose (DDDs)/1000inhabitants/day. All drugs were classified by groups of Anatomic Therapeutic Chemical Classification (ATC).

Data on real consumption (import and domestic production)

For all the period under study 2010-2020 there were collected and analyzed data from the import and domestic production of the drugs,(9) which represent the real consumption of drugs in the country. It was noted that the increase in consumption from one year to another were small, e.g. the consumption from 2018 to 2020 (i.e. 3 years) was increased by only 2.58%. Consequently, in order to obtain an updated study, there were chosen the data of import and domestic consumption only for the last three years, 2018, 2019,2020, and those were involved in a comparative analysis with the equivalent consumption data according to HII. In order to minimize the effect of variations consumption-inventory balances from one year to another, it was calculated and put to analysis the annual average value of the three chosen years (on one hand that of the import and domestic consumption, and on the other hand that of HII).

II. Results

The only proton pomp inhibitor included in the reimbursement list during these years is omeprasol. The other PPI registered in our country are esomeprazole, lansoprazole, pantoprazole and rabeprazole. But their consumption flows out of the reimbursement system.

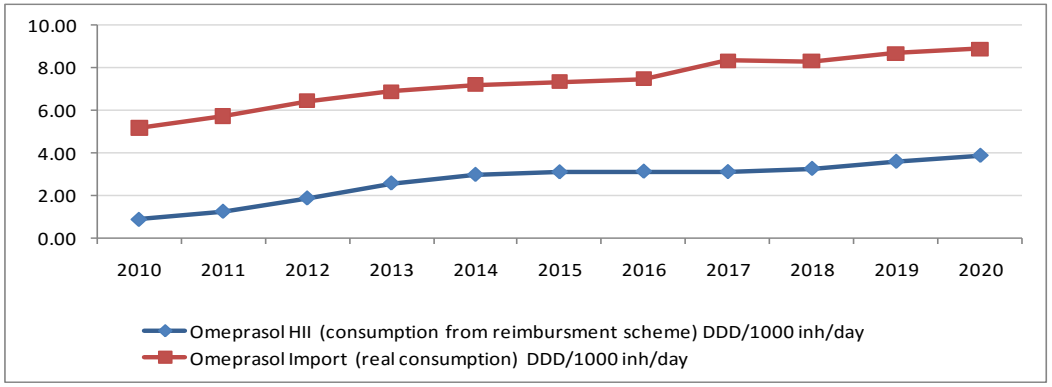

Figure 1 Annual average value of consumption of Omeprazole: consumption based on import (real consumption) [*] versus consumption based on HII.

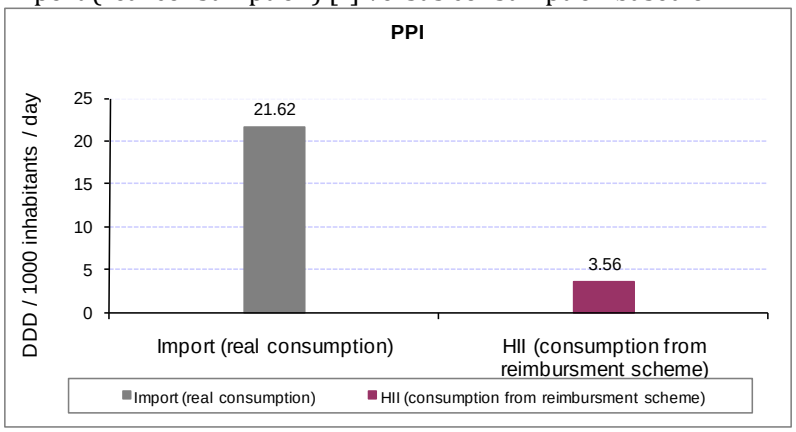

Figure 2 Annual average value of consumption of Proton-pump inhibitors class: consumption based on import (real consumption) [*] versus consumption based on HII.

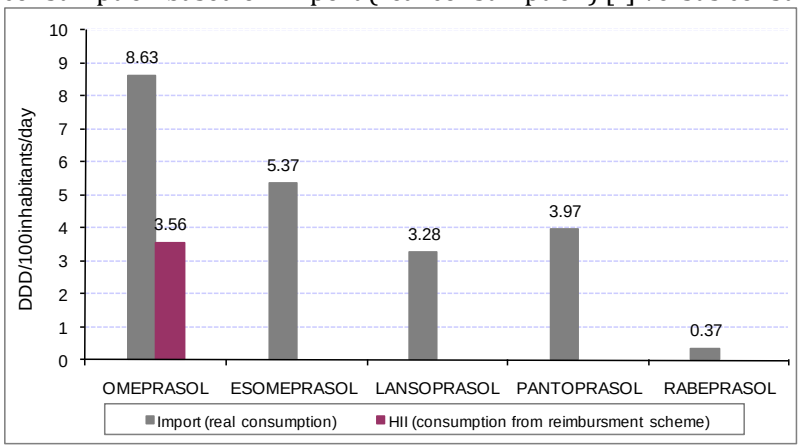

Figure 3 Annual average value of consumption of each Proton-pump inhibitor: consumption based on import (real consumption) [*] versus consumption based on HII.

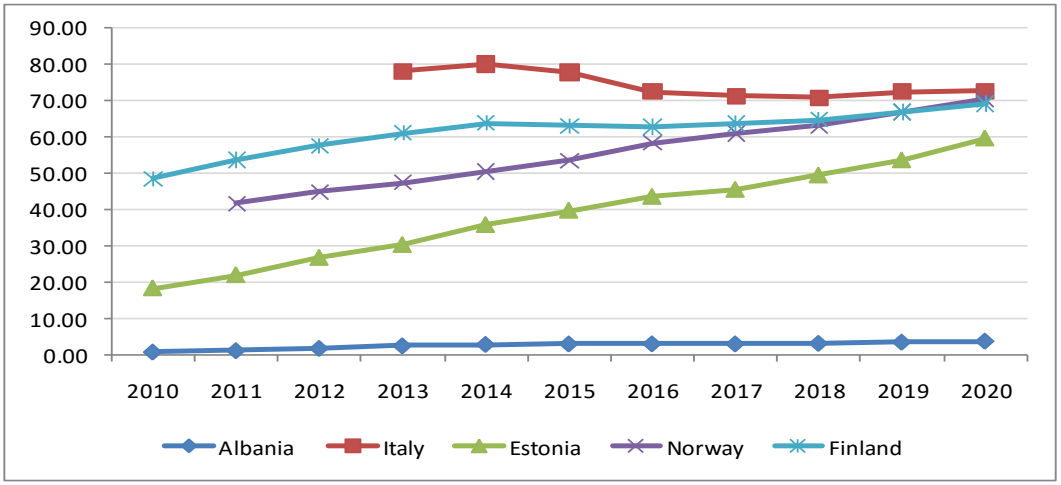

Figure 4 International comparison in the consumption of Proton-pump inhibitors drugs class (DDD/1000 inhabitants/day): Albania, Italy [10], Estonia [11], Norway [12-15], Finland [16-19]

III. Discussion

Due to their efficacy and tolerability, utilization of proton pump inhibitors (PPI) has significantly increased worldwide. Parallel to the clinical benefits, potential long-term side effects have been observed.

Figures 2 and 3 put emphasis on the poor coverage by the scheme of the necessary alternatives in the cure of peptic morbidity. The reimbursements scheme offers only omeprazole. Another issue which can be raised by analyzing these graphics is why the consumption of omeprazole under the scheme is such in lower values compared to the real consumption of omeprazole. This indicates that even this alternative, although covered by the scheme, is actually taken in large scale without prescription.

According to HII, omeprazole is reimbursed only for ulcerous disease and gastroesophageal reflux disease certified through endoscopic examination and the duration of the treatment is 4-6 weeks. After 4-6 weeks, the patient should reperform the endoscopy in order for the family doctor to have the right to repeat the prescription. It is comprehensible that in a similar situation, the patient is almost conditioned to obtain the drug directly in the pharmacy by avoiding the consultation with the family doctor.

In previous studies performed some years earlier (20), a common finding was that there is consumed a lot more ranitidine rather than omeprazole, while from the pharmacological perspective, PPI are superior compared to antiH2 in the cure of ulcerous morbidity (21). Beginning from 2008 and onwarts, there can be noted a shift in consumption, with decrease antiH2 receptors drugs and an increase of PPI, which

is reasonable considering that PPI have the highest efficacy in the reduction of gastric hyperacidity.

Omeprazole was the most widely used, at around 75%, although the rate should approach 100% as it is the first choice agent based on specific recommendations (22). In spite of this, pantoprazole is reported as the most widely used PPI in other countries such as the US (23). The most frequent indication for PPI use was GERD followed by NSAID ulcer prophylaxis which is in contrast to other studies in which the predominant indication for PPI use was NSAID ulcer prophylaxis (24-26).

PPIs are, in most cases, safe and well tolerated (a factor that explains their widespread usage) but they are not harmless. Mild reactions such as headaches, nausea or abdominal pain have been reported, as well as some other less frequent but more serious events such as an increase in infections (pneumonia, C. difficile diarrhea), acid reflux, increased bone fracture risk, hypomagnesemia and acute interstitial nephritis.

Measures should be taken in order to achieve a better PPI use, such as improving the distribution of therapeutic recommendation guidelines. Studies have demonstrated its association with an improvement in the appropriateness of PPI prescription, paired with a decrease in interactions and adverse effects and a reduction in pharmaceutical spending (27, 28).

International Comparison of Consumption

As shown in Figure 4, the consumption of PPI drugs in Albania, as compared to other countries, is very low (consumption values presented for all countries, including Albania, are the official values as referred by the respective reimbursement systems).

In France, studies performed (29) suggest PPI overuse, not always in line with the French guidelines. In particular, inappropriate co-prescription with NSAID was frequent.(29)

The same results outcome from another similar study conducted in China (30)

In Hungary the prevalence of proton pump inhibitor use was between from 41.9 to 50.4 DDD per 1,000 inhabitants and per day between 2014 and 2018. Pantoprazole was the most frequently used active ingredient, both in the nationwide data and in the patient-level surveys.(31)

In Hungary (as in Denmark), pantoprazole was the most frequently prescribed and dispensed PPI, while in Iceland, omeprazole and esomeprazole were the most frequently used PPIs (32;33). The dominance of pantoprazole in Hungary can be explained by the high number of generic products and their consequent lower price compared to other PPI agents.

In another study conducted in Spain, in a district of Basque health service, PPI prescription increased by 23.75% (from 78.14 DHD in 2009 to 96.70 DHD in 2014). Their use was much higher than that of other European countries. In the same period,

omeprazole relative prescription compared to other PPIs decreased by 4.56% (omeprazole % Defined daily dose (DDD) went from 74.67% in 2009 to 70.11% in 2014).(34**)**

IV. Conclusions

The consumption values of PPI drugs in Albania are comparatively low. An important part of the PPI drugs flows out from the reimbursement scheme. A comparative analysis in the consumption of PPI between Albania and other countries suggested also important differences in the overall consumption values. We need to perform further studies in the future to get deeper information about this topic.

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The Control of Vital Parameters and Their Importance in Soccer Players of the Women's National A in Albania

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Abstract

Vital parameters or otherwise vital signs are the measurements of the most basic functions of the body**.**They are the main pillars with which we determine the general physical condition of the athletes.It is important to first review vital signs assessment. Monitoring vital signs in athletes, during training, is highly important in order to avoid overtraining and to be careful at the same time in monitoring their health condition.The data for this study was collected during the preparatory training phase of the Women's National A in Montenegro in February 2021.Part of this study were 20 female athletes according to different age groups who were subjected to the measurement of vital parameters.The measurements were performed before the beginning and after the end of the exercise in order to understand which it would be specifically these values, also referring to their current physical and health condition.From the obtained data it was evident that the pulse is the vital parameter which changes as a result of the overload received during the training process performed by the athletes in relation to other parameters.In three of the athletes,a fluctuation of the values at the level of the respiratory apparatus was observed,which was related to their previous state of health.The measurement of vital parameters during exercise is a good indicator to assess general well being physical and health of the athlete.Also,the importance of measuring these parameters before,during and after the sports activity is essential to avoid various problems that can even lead to fatality for the athlete.

Keywords: Vital parametres, prevention, athletes, measurements, health

1. Introduction

Vital parameters or otherwise vital signs are the measurements of the most basic functions of the body. They are the main pillars with which we determine the general physical condition of the athletes. It is important to first review vital signs assessment.[1] Heart rate (HR), blood pressure (BP), respirations, skin and body temperature assessment, and pupil assessment are considered the five basic vital signs,in many areas, pulse oximetry is added to this list as a sixth vital sign.[2]

Monitoring vital signs in athletes, during training, is highly important in order to avoid overtraining and to be careful at the same time in monitoring their health condition.In order to detect overtraining, the training load of each athlete needs to be monitored and individualized.Training load is the product of training volume times the training intensity, where training volume usually refers to the duration of training and training intensity refers to how hard someone is training and how this preparation at a high level of performance can affect their physical and health condition. Exercise causes a series of immediate responses from the body as it tries to adapt to sudden changes in its state of balance. When these increases come imposed on a regular basis training, the body responds by settling on new basic conditions that make it capable of more effective performance[8].The intensity of training can be objectively measured via vital signs and specialized indexes, such as heart rate, oxygen consumption, weight lifted, power output, blood lactate concentration,and hormonal levels [3,4]. Another noninvasive measure of training load, often used, is maximal oxygen consumption (VO2max).More specifically, studied the effect of normal and overload interval training at VO2 max on aerobic parameters and overtraining markers such as subjective ratings of fatigue and muscle soreness [5].There is general agreement in modern medicine on the fundamental importance of regular physical and sporting activity in individuals of all ages, including children, for maintaining the efficiency of the organism and for the primary and secondary prevention of cardiovascular pathologies.The achievement of a slower and more regular heart pulse, a physiological cardiac hypertrophy that ensures a circulatory system adequate to the effort, the control of arterial tension values.The positive effect includes a favorable action on the parameters: carbohydrates (diabetes mellitus) lipid (higher HDL cholesterol, lower LDL, triglyceridemia within the limits) on the control of body weight, obesity, osteoporosis and in all pathologies linked to a sedentary lifestyle. Some clinicians may also be less familiar with pulse oximetry. Pulse oximetry provides a measure of the percentage of oxygen within the blood, obtained through use of an electronic fi nger sensor. Under normal conditions, the pulse oximetry reading will generally be between 96% and 100%, with patients exhibiting a reading of 90% usually requiring treatment.[6] However, it is important to note, that the pulse oximetry reading obtained should be correlated closely with the athletes signs and symptoms, and treatment should not be based on the oximetry reading alone.[7] In this context, the main goal is the classification of possible symptoms during their exercise by means of these vital parameters, which in some cases may also refer to an overfatigue or collapse as a result of an increased exercise load. The main causes of sudden non-cardiovascular death include hyperthermia, rhabdomyolysis and asthma.[9] Non-cardiovascular causes of sudden death are very real risks facing today's athletes.[10] Fortunately, these conditions they are often recognized by their clinical manifestations and symptoms,by the physician thus avoiding potentially life-threatening situations.The four main vital signs routinely checked by healthcare providers include body temperature,pulse rate,breathing rate (respiration),blood pressure, along with some other specific examinations based on

the medical analysis protocol of each athlete.As well as the normal values of the vital parameters are shown in table.1 as follow.

Common causes of collapse during activity

- Non-serious causes:
- Exhaustion
- Dehydration
- Lowering of blood pressure when standing
- Muscle cramps
- Serious causes
- Low blood sodium level (hyponatremia)
- Heat stroke
- Low blood sugar level (hypoglycemia)
- Low body temperature (hypothermia)
- Cardiac arrest
- Other clinical situations such as stroke,cerebral haemorrhage and diabetic coma.

Vital Sign	**Normal Value**
Body Temperature	36.1 to 37.9
Pulse	60 – 100 beats/minute
Respiration/Breathing	12 – 18 breaths per minute
Blood Presure	90/60 to 120/80

Table 1

2. Methodology

The data for this study was collected during the preparatory training phase of the Women's National A in Montenegro in February 2021. Part of this study were 20 female athletes according to different age groups who were subjected to the measurement of vital parameters such as pulse, SPO2, temperature, arterial pressure during an exercise session.To perform these measurements were used, a pulse oximeter, thermometer, and a device for measuring arterial pressure.The measurements were performed before the beginning and after the end of the exercise in order to understand which it would be specifically these values, also referring to their current physical and health condition. All this by first referring you to a general anamnesis which helped to clearly understand the entire physical and health status of each of them, before the measurement in such a way that the obtained reference values of the vital parameters were correct, excluding errors possible. In this way,

each of the girls was asked separately about their physical condition, which refers to any possible damage during the exercise of their sports activity, or any possible current or past pathology that could affect in their performance during intensive training.

3. Results

From the obtained data it was evident that the pulse is the vital parameter which changes as a result of the overload received during the training process performed by the athletes in relation to other parameters. In three of the athletes, a fluctuation of the values at the level of the respiratory apparatus was observed, which was related to their previous state of health. As for the body temperature values, only one of the girls showed a slight increase that was accompanied by fatigue and what did not allow the continuation of physical activity at the moment it started and the increase in exercise load. Arterial pressure also showed no changes for any of the athletes, referring to its normal values.These measurements were performed during four training sessions on two different days to understand if any possible changes in these parameters would appear.These values before and after training are all referenced in table.2 below.

Age	Body Temperature Before/After	SPO2 Before/After	Pulse Before/After	Bloode Pressure Before/After
25 years old	36.3 / 36.4	98 / 97	82 / 124	120/80 mmHg;110/75 mmHg
25	36.5 / 36.5	98 / 96	80 / 125	130/80 mmHg;115/70mm Hg
29	36.2 / 36.3	97 / 98	76 / 120	100/65 mm Hg;105/65mm Hg
25	36.1 / 36.4	96 / 99	74 / 118	110/80 mm Hg;95/60 mm Hg
26	36.1 / 36.2	96 / 98	78 / 121	120/70 mmHg;110/65 mm Hg
27	36.4 / 36.4	97 / 98	68 / 118	130/75mm Hg;120/70 mm Hg
25	36.6 / 36.5	97 / 98	70 / 122	125/80mm Hg;115/80 mm Hg
20	36.3 /36.4	96 / 97	72 / 130	100/60 mm Hg;95/60mm Hg
23	36.2 / 36.2	98 / 97	80 / 126	120/70mm Hg;110/65 mm Hg
25	36.5 /36.5	98 / 96	82 / 131	110/70mm Hg;100/60 mm Hg

27	36.7 / 37.5	97 / 96	74 / 120	130/80mm Hg;125/80 mm Hg
19	36.2 / 36.3	97 / 96	76 / 122	115/80mm Hg;115/75 mm Hg
21	36.4 / 36.2	96 / 98	81 / 125	120/75mm Hg;110/75 mm Hg
21	36.3 / 36.4	98 / 98	68 / 128	120/70mm Hg;120/65 mm Hg
18	36.5 / 36.4	98 / 97	70 / 130	100/65mm Hg;96/60 mm Hg
19	36.1 / 36.2	96 / 97	80 / 125	125/80mm Hg;120/80 mm Hg
18	36.3 / 36.3	98 / 97	82 / 128	110/70mm Hg;110/75 mm Hg
20	36.4 / 36.5	97 / 98	76 / 124	130/75mm Hg;125/75 mm Hg
17	36.5 / 36.5	96 / 99	78 / 132	100/65mm Hg;110/65 mm Hg
19	36.2 / 36.4	97 / 99	75 / 125	115/70mm Hg;110/70 mm Hg

Table .2

4. Discussion

It is also worth discussing the fact that for each athlete, all medical examinations must be carried out in detail before the start of each competition to rule out the possibility of any possible pathology which could turn out to be dangerous if not detected in time. Also the medical staff as well as the athletic trainer of the team are the central component of the sports medicine team, ensuring that athletes experiencing injuries or acute illnesses receive appropriate evaluation, management, and referral as needed. It is not necessary for the medical staff to derive the precise diagnosis of an athlete's condition; however, it is critical for the medical staff to be able to recognize the need for immediate referral to a hospital's for a more specialized treatment as well as for the realization of the relevant more detailed examinations.

5. Conclusion

In conclusion, the measurement of vital parameters during exercise is a good indicator to assess general well being physical and health of the athlete. Also, the importance of measuring these parameters before, during and after the sports activity is essential to avoid various problems that can even lead to fatality for the athlete.From all the data and results of the table above, we see that football, the change in the values of the vital parameters comes as a result of the physical activity and the overload that occurs during the training session,and to improve in this way the physical performance.The changes of these values are at a normal level both for

the type of sports activity and for the age of the athletes, and do not pose a risk to the athlete's life.

6. Recommendations

Based on these data, the role of the doctor in the team should always be taken into account to prevent various pathological situations from the mildest to the most dangerous situations.This should be possible through teamwork between the doctor, the physiotherapist and the athletic trainer in order to achieve maximum results in training and in different competitions by the athletes, avoiding in this way any possible damage.

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Considerations on the Liability for Intentional Personal Injury of the Surgeon Who Carries Out Arbitrary Medical-Surgical Treatment: The Italian Case

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Abstract

The criminal liability of surgeons is one of the most complex and engaging issues in contemporary criminal doctrine and jurisprudence. This study focuses on the surgeon's liability for personal injury for providing medical-surgical treatment without the patient's informed consent. Over the years, Italian doctrine and jurisprudence have recognized that medical-surgical treatment conducted without the patient's informed consent or in the presence of invalid informed consent constitutes a criminal offence, even though the latter is not expressly provided for by Italian Criminal Law. According to the Italian Court of Cassation, medical-surgical treatment integrates the objective and subjective elements of some criminal offences already provided by the Italian Criminal Code, such as intentional personal injury (Article 582 of the Italian Criminal Code), unintentional homicide (Article 584 of the Italian Criminal Code), or private violence (Article 610 of the Italian Criminal Code). The conflicting jurisprudential solutions proposed over the years on the issue generate a series of perplexities about the medical professional's activities, uncertainty about whether the doctor must intervene in particular cases, and, most crucially, which criminal offence should be applied if he intervenes.

Keywords: Medical-surgical treatment, informed consent, criminal liability, personal injury, Italian Criminal Code

Introduction

Arbitrary medical-surgical treatment, carried out in the absence of the prior acquisition of the informed consent of the adult and capable patient or the presence of his conscious dissent, has been considered by doctrine and jurisprudence as criminally relevant. The question is an often-disputed topic in Italian doctrine and jurisprudence, and it is a problem that demands special consideration according to

the specific elements it raises, particularly the importance attributed to informed consent in the medical field.

The patient's right to informed consent requires the patient to be fully informed about his health conditions, such as diagnosis, prognosis, benefits, and risks of the treatment, as well as alternative therapies and the consequences of the refusal[1] (See Furramani & Bushati, 2021, p. 266; Furramani, 2017, p. 364).

However, it is necessary to analyse if the violation of this right may result in criminal consequences, given that criminal law does not provide for the absence of informed consent to medical-surgical treatment. The doctrine considers informed consent a cause of the lawfulness of medical treatment (Antolisei, 1969, p. 240; Vassalli, 1973, p. 81), and failure to inform the patient and obtain his consent inevitably generates criminal illegitimacy because medical treatment violates the patient's right to self-determination (Omodei, 2020, p. 81). The only situation in which the doctor can intervene without first obtaining the patient's informed consent is that of necessity and urgency, as defined in Article 54 of the Italian Criminal Code, in the presence of specific conditions that justify a doctor's intervention to protect the patient's health or life (See Furramani, 2014, p. 114).

Currently, the criminal relevance of medical treatment is assessed through reference to general offences and the occurrence of harmful events (Brusco, 2006, p. 4262). Regarding arbitrary medical treatment, the Italian Court of Cassation's jurisprudence has specifically considered the offence of intentional personal injury under Article 582 of the Italian Criminal Code. The idea that arbitrary medical-surgical treatment may be criminally relevant implies the need for a preliminary examination of the Supreme Court's rulings in this regard.

Literature Review

Medical-surgical treatment refers to a wide range of medical treatments, including the medical treatment of cosmetic surgery. According to the doctrine, the concept of medical-surgical treatment refers to "*the activity aimed at eliminating or attenuating or making it possible in any case to eliminate or attenuate an abnormal state of the body or mind, that is the improvement of the external appearance of the person*" (Crespi, 1955, p. 6). Therefore, the opportunity arises to broaden the scope of medical-surgical treatment as it is not only related to activities aimed at treating or freeing the organism from a disorder or disease but also to activities that have the aim of decreasing, even if they do not entirely eliminate, physical suffering (Crespi, 1955, p. 6).

Doctrine (Bilancetti & Bilancetti, 2013, p. 706; Eusebi, 1995, p. 728; Giraldi, 1993, p. 149; Manna, 2004, p. 460; Rodriguez, 1991, p. 1153; Viganò, 2004, p. 150; De Lia,

[1] Article 1, para. 3, Law No. 219, 22 December 2017, *Rules on informed consent and advance treatment provisions*, in the Italian Official Gazette, No.12 of 16-01-2018.

2000, p. 48; Iadecola, 2002, p. 2041; Iadecola, 2002, p. 517) and jurisprudence consider that medical-surgical treatment carried out in the absence of informed consent or the presence of invalid informed consent is criminally relevant, attributing to the surgeon the responsibility for injury or death even when the latter carries out the treatment according to the medical art rules[1] (Iadecola, 1993, p. 163; Furramani & Bushati, 2021, p. 283).

According to the different approaches on the topic, each medical-surgical treatment, in principle, integrates the objective and subjective elements of some criminal offences already provided for in the Italian Criminal Code. The jurisprudence of the Italian Supreme Court has confirmed this orientation in a series of decisions[2] (Viganò, 2004, p. 141; Giamaria, 1991, p. 1123), which oscillate between a first and widespread orientation, which identifies the offence of intentional personal injury under Article 582 of the Italian Criminal Code[3] (Iadecola, 1998, p. 240; Cfr. Centonze, 2012, pp. 59 et seq.); and if this injury results in death, which is causally attributable to the surgery, the surgeon will be liable for unintentional homicide under Article 584 of the Italian Criminal Code[4] (Gribaudi, 2012, p. 55; Di Pentima, 2013, p. 131; Ciauri, 2009, p. 1102; Mellillo, 1993, p. 63). The latter orientation causes numerous perplexities and does not appear to be acceptable. A second orientation invokes the private violence offence under Article 610 of the Italian Criminal Code in the case of a surgeon acting in the absence of the patient's informed consent[5], even if the treatment is performed following the *leges artis,* regardless of the outcome of the treatment (See Canestrari, 2006, p. 676; Arrigoni, 2004, 1264; Fiandaca, 2009, p. 307).

In this regard, it is necessary to highlight another different opinion, which excludes the intentional nature of medical conduct. Noting, in the first place, that medical treatment is intended to improve a person's health conditions (Crespi, 1995, p. 6), and precisely for this reason, medical behavior differs from criminal behavior that affects the subject's psychophysical integrity (Gribaudi, 2012, p. 56; Furramani & Bushati, 2021, p. 283; Furramani, 2017, p. 167). Nevertheless, this peculiar nature of the medical act is insufficient to justify medical conduct carried out without informed consent. Consequently, arbitrary medical-surgical treatment has often been considered criminally relevant. Even today, there are no univocal orientations in doctrine and jurisprudence.

Part of the doctrine (Eusebi, 1995, p. 728; Rodriguez, 1991, p. 1153; Passacantando, 2005, p. 241) argues that medical-surgical activity affects the bodily integrity of the patient and that the surgeon is exempted from criminal liability only if the patient has

[1] Ass. Firenze, 8 November 1990, *cit.* p. 163.; Cass. Pen., Sez. IV, 11 July 2001, no. 1572, *cit*., p. 2041.
[2] Ass. Firenze, 8 November 1990, *cit.*; Cass. Pen., Sez. IV, 11 July 2001, no. 1572, *cit.*, p. 2041.; Trib. Roma, 25 May 2000, in *Giust. pen.,* 2000, *cit.*, p. 49.
[3] Cass. Sez. Un., 21 January 2009, no. 2437, in *Dir. pen. proc*, 2009, IV, p. 447.
[4] Cass. Pen., 21 April 1992, in *Cass. Pen.,* 1993, pp. 63 et seq.
[5] Cass. Pen. Sez. I, no. 3122, 29 May 2002, Volterrani.; Cass. Pen., Sez. IV, 11 July 2001, no. 1572, in *Riv. it. med. leg*., 2002, p. 867.

given his informed consent (See Furramani & Bushati, 2021, p. 283). In this case, the patient's informed consent serves as a foundation for justifying the medical treatment (Bilancetti & Bilancetti, p. 272).

The literature examined for this study focuses on various perspectives that doctrine and jurisprudence have on the surgeon's criminal liability. The jurisprudential solutions proposed over the years on the criminal relevance of arbitrary medical-surgical treatment are divergent and conflicting and consequently entail a series of uncertainties on the criminal offence to apply in case of violation of the patient's informed consent. The same fluctuations are registered in the doctrinal viewpoints. These perplexities generate doubts about the medical professional's activities, uncertainty about whether the doctor must intervene in certain situations, and, most crucially, which offence should be applied if he intervenes.

Research Method

The purpose of this study is to explore the various doctrinal and jurisprudential viewpoints on criminal liability for arbitrary medical-surgical treatment. This elaboration is composed of two parts: the first examines the criminal relevance of arbitrary medical-surgical treatment characterised by therapeutic purposes and the configuration of the objective and subjective elements of the criminal offence of intentional personal injury, according to Article 582 of the Italian Criminal Code. The second focuses on an in-depth analysis of the criminal relevance of non-therapeutic medical-surgical treatment and the various perspectives concerning the latter.

This elaboration uses qualitative research methods to analyse the criminal liability of the surgeon for performing the medical treatment without the patient's informed consent. Furthermore, our research aims to highlight the Italian Court of Cassation's contrasting jurisprudence regarding the issue.

The criminal liability for personal injury under Article 582 of the Italian Criminal Code: the definition of “desease”

The liability for personal injury provided for by Article 582 of the Italian Criminal Code in the case of arbitrary medical-surgical treatment has been confirmed several times by the Italian Supreme Court, according to which the absence or the invalidity of the patient's informed consent makes the medical-surgical treatment criminally relevant as it violates the patient's free self-determination (Omodei, 2020, p. 81).

In this context, it is relevant to analyse Article 582 of the Italian Criminal Code, which in the first paragraph outlines: *"Whoever causes a personal injury to anyone, from which a disease of the body or mind derives, shall suffer the penalty of imprisonment from three months to three years".* It is necessary to highlight that the mental element that characterizes the conduct envisaged by this criminal offence is the conscience and intention of causing anyone an injury from which a disease of the body or mind derives.

It is easy to understand that to configure the objective element of the offence of intentional personal injury (Article 582 of the Italian Criminal Code), we should refer to the definition of disease. The latter represents an issue much discussed in doctrine and jurisprudence.

Thinking back to the preparatory works of the Italian Criminal Code, the notion of "disease" was attributable to a much broader concept, as it included *any anatomical or functional impairment of the organism*[1] (Iadecola, 2006, p. 484; Fanelli, 2006, p. 960). This notion, which differs from the definition provided by medical science, has been the subject of conflicting orientations in the Supreme Court jurisprudence, divided into two different currents; a first jurisprudential orientation that embraced the definition of disease as *any anatomical and functional impairment of the organism*[2] (See Brusco, 2006, p. 4268; Iadecola, 2007, p. 179; Lattanzi & Lupo, 2010, pp. 208 et seq.; Cfr. Massaro, 2006, pp. 2453 et seq.; Fiori, 2009, pp. 519 et seq.; Baima Bollone & Zagrebelsky, 1975, pp. 18 et seq.). Based on these considerations, even if the surgeon carries out a therapeutic treatment aimed at improving health or even when the patient benefits from the treatment, he still must answer for the crime of intentional personal injury according to Article 582 of the Italian Criminal Code. And a second orientation based on medical-legal science, which in our opinion, seems more acceptable, according to which the term "*disease*" refers to a functional or appreciable impairment of the organism (Rodriguez, 1993, p. 153 et seq.; Turillazzi, 2009, p. 1086; Vigano, 2004, pp. 178 et seq.). In this context, those impairments that don't provoke an anatomical or functional alteration cannot be considered a disease, according to Article 582 of the Italian Criminal Code[3].

Both doctrine and jurisprudence generally accept the last viewpoint. Considering this approach, the Supreme Court's jurisprudence held that if the patient received surgical treatment that improved his health, the latter could not have caused the "*disease"*[4] (Turillazzi et al., 2009, p. 1063).

It is worth recalling, here, the position of the Italian Supreme Court in the famous Massimo[5] sentence and also the jurisprudential orientation before 1992[6], which qualified the arbitrary medical-surgical treatment that resulted in a lesion of the

[1] Cass., Sez. V, 2 February 1984, no. 5258.; Cass., Sez. V, 14 November 1979, no. 2650; Cass., Sez. I, 30 November 1976, no. 7254; Cass., Sez. I, 11 October 1976, no. 2904.; Cfr. Cass., Sez. Un., 21 January 2009, no. 2437, in *Dir. pen. proc.*, 2009, IV, p. 447.; Cass., Sez. IV, 19 March 2008, no. 17505.; Cass. Pen., Sez. IV, 28 October 2004, no. 3448.; Cass., Sez. V, 15 October 1998, no. 714.; Cass. Pen., Sez. IV, 14 November 1996, no. 10643.

[2] Cfr. Trib. Ferrara, 3 March 1977, Beltrame, in *Foro it.*, 1977, II, p. 302.; In this sense Cass., Sez. V, 16 March 2010, no. 16271, in *CED Cassazione*, no. 247259.

[3] Cfr. Cass., Sez. V, 16 March 2010, no. 16271, *cit*.

[4] Cass., Sez. Un., 18 December 2008 - 21 January 2009, no. 2437.

[5] Cass. Pen., 21 April 1992, no. 5639, Massimo, in *Cass. pen*., 1993, p. 63.

[6] Cass. Pen., 2 February 1984, in *Giust. pen.,* 1985, II, p. 32.; Cass., Pen., 11 November 1976, in *Riv. pen.,* 1977, p. 473.; Cass. Pen., 14 November 1979, in *Cass. pen*, 1981, p. 545.; Cass. Pen., 21 April 1992, *cit.*, p. 63.

patient's tissues as intentional personal injury according to Article 582 of the Italian Criminal Code, considering "*disease*" not only *"the functional alteration"* but *"any anatomical alteration of the organism"* (Gribaudi, 2012, pp. 55-56; Pellissero, 2005, pp. 464 et seq.).

It is clear that the notion of disease used is suitable for covering all consequences of medical-surgical treatment, including the mere incision of the tissues, which constitutes a minor anatomical alteration (Viganò, 2004, p. 171), and also scars, bruises, contusions, and states of shock, even when they do not affect the general organic conditions (Bilancetti & Bilancetti, 2013, p. 284).

It is necessary to note that the definition of disease as any anatomical alteration is doubtful and is not acceptable for some reasons. In the first place, from the medical point of view, the simple changes of the organism do not integrate the concept of disease[1] (See Baima Bollone & Zagrebelsky, 1975, pp. 20 et seq.; Galiani, 1974, pp. 144 et seq.; Gallisai, 1993, p. 392). Secondly, this definition considers criminally relevant even medical-surgical treatment aimed at beneficial purposes or followed by an auspicious outcome.

This orientation of the Court has been the subject of numerous criticisms by the criminal law and medico-legal doctrine, which considers *"disease"* the *"process that determines an appreciable functional impairment of the organism"*[2] (See Mantovani, 1995, p. 192; Antolisei, 2008, p. 77; Iadecola, 2007, p. 179; Fucci et al., 2011, p. 273; Casciaro & Santese, 2012, p. 337; Coratella, 2006, p. 104). This definition coincides with the medico-legal definition of disease as an evolutionary pathological process unfailingly accompanied by significant impairment of the organism's functions. Logically, the simple anatomical alteration of the organism that does not interfere with the organism's functionality should be excluded[3] (Iadecola, 2007, p. 185; Brusco, 2006, p. 4268; Turillazzi, 2009, p. 1095; Massaro, 2006, p. 2454).

Medical behaviour: "typical" or "atypical" conduct of the offence of intentional personal injury?

Concerning the objective element of the criminal offence of intentional personal injury (Article 582 of the Criminal Code), the United Sections of the Italian Court of Cassation intervened in 2008[4]. In this ruling, the Court considered the surgeon's criminal irresponsibility for providing a treatment not authorized by the patient, executed under the protocols and *leges artis* that improved the patient's health conditions. According to the Court, medical behaviour does not fall under the

[1] Cass. Pen., 26 May 2010, (dep. 23 September 2010), no. 34521,
[2] Cass. Pen., 26 May 2010, no. 34521, *cit*.
[3] Cass. Pen., 28 June 2011 (dep. 6 September 2011).; Cass. Pen., 26 May 2010, no. 34521, *cit*.
[4] Cass. Pen., Sez. Un., 18 December 2008, no. 2437.

provisions of Articles 582 (Pietra, 2009, p. 70), 584[1] or 610 of the Italian Criminal Code[2] (Eusebi, 1995, p. 728; Furramani & Bushati, 2021, pp. 281-282).

The orientation is also embraced by the doctrine, according to which medical-surgical therapeutic treatment performed without the patient's informed consent but under the *leges artis* and followed by a beneficial result is criminally irrelevant[3] (Salerno, 2014, p. 953; Barni, 2010, pp. 747 et seq.), because the causal efficacy concerning the disease event is lacking in this case (Salerno, 2014, p. 953; Barni, 2010, pp. 747 et seq.; Giunta, 2001, pp. 377 et seq.).

The issues raised are all centred on the type of medical treatment performed on the patient. Doctrine and jurisprudence highlight that arbitrary non-therapeutic medical treatment can involve different criminal offences. The point deserves particular attention since the doctrine brings therapeutic activity back to the area of lawful activity, but it does not constitute a cause for the exclusion of criminal liability, rather it represents a non-codified cause of justification (Antolisei, 1969, p. 240; Vassalli, 1973, p. 81).

In this context, it is necessary to distinguish between therapeutic medical treatment carried out in compliance with the *leges artis* and medical treatment in violation of the latter.

There is no doubt that therapeutic treatment carried out following the standards of medical art (*leges artis*) and the existence of a beneficial outcome[4] for the patient cannot constitute criminal behaviour. Compliance with protocols and medical art rules aims to remove or attribute risks connected with medical treatment to fortuitous events only (Marinucci, 1991, pp. 22 et seq.). As a result, it is crucial to emphasize that not every arbitrary medical-surgical treatment can aggravate the patient's health conditions or cause *"disease"*. Furthermore, the medical behaviour is not characterized by intention to cause injuries, as required by the personal injury offence under Article 582 of the Italian Criminal Code[5] (Gliatta, 2010, p. 464; Barni,

[1] According to Eusebi, the medical act in the absence of the patient's informed consent should not be considered lawful only because it has been performed *leges artis* but also considering the purpose of such conduct, which is to combat the disease. Therefore, it does not constitute the offence of intentional personal injury according to Article 582 of the Italian Criminal Code, regardless of the outcome (Eusebi, 1995).

[2] Cass. Pen., Sez. Un., 18 December 2008, no. 2437, *cit*.

[3] Cass. Pen., Sez. I, 26 March – 12 June 2014, no. 24918; Cass. Pen., 8 June 2010, no. 21799.

[4] See Cass. Pen., Sez. Un., 18 December 2008 – 21 January 2009, no. 2437. In this direction see App. Bari, Sez. III, 20 September 2011.

[5] In this regard App. Bari, Sez. III, 20 September 2011, (in: www.giurisprudenzabarese.it); Cass. Pen., Sez. V, 21 April 2016, no. 16678.; Cass., Sez. Un., 18 December 2008, no. 2437; Cass. Pen., Sez. IV, 14 March 2008, no. 11335, in *Dir. pen. proc.*, 2009, I, p. 70.; Cass. Pen., 21 January 2009, no. 2437.; Cass. Pen., Sez. I, 29 May 2002, no. 528, in *Studium iuris*, 2003, p. 511.; Cass. Pen., Sez. I, 29 May 2002, no. 26446, in *Riv. It. dir. proc. pen*., 2003, p. 604.; Cass., Sez. IV, 9 March 2001, Barese, in *Cass. pen*., 2002, p. 517.; Cass. Civ., Sez. III, 15 January 1997, *Scarpetta c. Ospedale civile Umberto I Ancona*, in *Foro it*., 1997, I, p. 771.; Cass. Civ., Sez. III, 6 October 1997, *Musumeci v. Finocchiaro*, in *Giur. it*., 1998, p. 1816.; Cass. Civ., Sez. III, 16

2002, p. 613; Iadecola, 1991, p. 165; Manna, 2007, p. 611; Turillazzi et al., 2009, p. 1088; Pietra, 2009, p. 70; Furramani & Bushati, 2021, p. 282). On the other hand, from the point of view of the objective element, it is excluded that arbitrary medical treatment followed by a favorable outcome may cause the "disease", in the sense of appreciable health damage resulting in functional impairment of the patient's body, as required by Articles 582 and 584 of the Italian Criminal Code (Manna, 2007, p. 611; Polvani, 1993, p. 736; Furramani & Bushati, 2021, pp. 281-282).

Nevertheless, the risks associated with medical-surgical treatment cannot be removed since medical-surgical treatment can cause harm to the patient's health or endanger his life, regardless of compliance with the medical art rules or following precautionary rules of medical diligence (Giunta, 2001, p. 402). Consequently, the surgeon should obtain the patient's informed consent.

Given the various solutions proposed by doctrine and jurisprudence, it is also necessary to consider decision No. 11335 of 2008 of the Italian Court of Cassation[1], which excludes the configuration of the crime of personal injury under article 582 of the Italian Criminal Code. In this case, the Court considers that the sole lack of the patient's informed consent cannot establish the criminal liability of the surgeon[2] (Pietra, 2009, p. 75; Furramani & Bushati, 2021, p. 283).

The above considerations are valid for therapeutic medical-surgical treatment performed in compliance with the protocols and medical art rules and followed by an auspicious outcome. However, the criminal relevance of arbitrary medical treatment for non-therapeutic purposes remains to be analyzed. Consider, for example, cosmetic surgery, which involves operations aimed at improving a person's exterior appearance.

Brief considerations on arbitrary medical-surgical treatment followed by an unfavourable outcome

In such an interpretative context, it seems reasonable to investigate the criminal relevance of the arbitrary medical-surgical treatment that results in an unfavourable outcome. After the profound and radical changes recorded in jurisprudence concerning the latter hypothesis, the Court of Cassation excludes the configuration of the objective element of the offence of intentional personal injury according to Article 582 of the Italian Criminal Code, even when the arbitrary medical treatment is

October 2007, no. 21748, in *Fam. dir*., 2007, p. 1162.; Cfr. Cass., Sez. III, 14 March 2006, no. 5444, in *Mass. giur. it*, 2006; Cass. Pen., Sez. IV, 21 April 1992, *Massimo*, in *Cass. pen*., 1993, p. 63.; Cass., Sez. IV, 27 March 2001, Cicarelli, in *Riv. it. med. leg*., 2002, p. 574.; Cass., 11 July 2001, Firenziani, in *Cass. pen*., 2002, p. 2041.

[1] Cass. Pen., Sez. IV, 14 March 2008, n. 11335.

[2] Cass. Pen., 29 May 2002, *cit*., p. 604 s.

followed by a worsening of the patient's health conditions, in consideration of the therapeutic purpose that characterizes medical conduct[1] (Giunta, 2001, p. 403).

The Supreme Court (Decision No. 21799/2010) confirmed this viewpoint, recognizing that: "*in the case of an intervention followed by an unfortunate outcome, it could be discussed the responsibility for voluntary injuries or unintentional homicide in the case of death, in the presence of absolutely anomalous and distorted behaviour of the doctor, and in any case dissonant concerning the curative purpose that must characterize one's therapeutic approach."* In this case, it must be ascertained that the surgeon *"acted even though he was conscious that his intervention, which would later cause harm or death of the patient, would have produced an unnecessary impairment of the patient's physical or mental integrity"*[2] (concrete predictability of the event). Following the reasoning of the Supreme Court, the medical intervention that causes an unnecessary impairment of the individual's bodily integrity, characterized by non-therapeutic purposes, is suitable for integrating the offence of intentional personal injury under Article 582 of the Italian Criminal Code (Furramani & Bushati, 2021, p. 284). Eventually, if death occurs, it is configurable the crime of unintentional homicide, according to Article 584 of the Italian Criminal Code[3] (Fucci et al., 2011, p. 265; Papi, 2011, p. 697; Bilancetti & Bilancetti, 2013, pp. 751 et seq.), both from an objective and a subjective point of view (Beulke & Diebner, 2013, pp. 839 et seq.)

Even in the latter case, it emerges that Supreme Court jurisprudence has overcome the traditional elaboration, which tended to bring arbitrary medical-surgical treatment back into the criminally relevant area, even though performed in compliance with protocols and medical art rules.

Based on this orientation, even the medical-surgical treatment carried out according to *leges artis* but followed by an unfortunate outcome cannot configure the offence of personal injury (Article 582 of the Italian Criminal Code)[4] (Cfr. Passacantando, 1993, pp. 107-109; Manna, 2007, p. 611; Manna, 1984, pp. 3 et seq.) since the latter necessarily requires the mental element of intention[5] (Fiori et al., 2002, p. 881; Cfr. Nannini, 1989, p. 77; Lattanzi & Lupo, p. 22) in addition to the presence of the objective element. In this particular hypothesis, the worsening of the patient's health conditions is suitable for configuring the "disease" under Article 582 of the Italian Criminal Code (Cfr. Polvani, 1993, p. 736; Polvani, 1996, p. 193), but in line with the orientation of the Court of Cassation, it lacks the mental element of the crime, and

[1] Cass. Pen., Sez. IV, 24 June 2008, no. 37077.
[2] Cass. Pen., Sez. IV, 8 June 2010, no. 21799, in *Riv. it. med. leg*., 2010, 747, with critical notes by M. Barni; Cass. Pen., Sez. Un., 18 December 2008, no. 2437.; Cass. Pen., Sez. IV, 23 September 2010, no. 34521.; Cass. Pen., Sez. V, 6 September 2011, no. 33136.
[3] Cass. Pen., 26 May 2010, no. 34521, *cit*.
[4] In this sense Trib. Palermo, the ordinance of 31 January 2000, GIP Massa, in *Foro it.,* 2000, III, p. 441.
[5] The mental element required by the criminal offence of personal injury under Article 582 of the Italian Criminal Code is intention. In these terms Cass. Pen., Sez. IV, 9 March 2001, no. 28132, Barese, in *Cass. pen.,* 2002, p. 517.; Cass. Pen., Sez. IV, 9 March 2001, no. 585, in *Juris Data, Sentenze Cassazione Penale*.

therefore, the intention of voluntary injuries (Article 582 of the Criminal Code), which is incompatible with medical activity[1] (Iadecola, 2010, pp. 1050 et seq.; Casciaro & Santese, 2012, pp. 338 et seq.).

On the contrary, in the arbitrary medical treatment performed in violation of medical art rules, it is possible to notice the presence of an intention to cause injuries. It is therefore evident, according to the Supreme Court jurisprudence, to recognize intention as a mental element necessary for configuring the offence of personal injury, the behaviour of the doctor must be absolutely anomalous and distorted and, in any case, dissonant with the curative purpose that characterizes therapeutic medical treatment. Therefore, medical conduct must be abnormal and much more serious than lack of skill, negligence, or imprudence[2].

The last issue to address is identifying the mental element of the arbitrary medical treatment performed in violation of the patient's expressed dissent. The jurisprudence[3] has unequivocally outlined the configurability of the crime of intentional personal injury (Article 582 of the Italian Criminal Code) in the case of medical treatment performed in violation of the patient's dissent, even if indirectly expressed (Cfr. Manna, 2004, p. 460; Viganò, 2004, pp. 150 et seq.). In this case, medical conduct can be placed on the same level as the conduct that damages the person's bodily integrity, thus configuring the criminal offence of intentional personal injury according to Article 582 of the Italian Criminal Code.

To clarify, the Court of Cassation has correctly held that "*the conduct of the doctor who intervenes with an inauspicious outcome on a patient who has expressed disagreement with the type of surgery represented to him must be qualified intentional and not negligent.*[4]*"* In this case, the mental element of the crime is evident, the presence of intention and conscience in carrying out an intervention that will certainly cause a worsening of the patient's clinical situation. Consequently, the intention is recognizable in the behaviour of the doctor who acts with the awareness of a useless intervention, whose risks are prevalent to the benefits[5] (Pietra, 2009, p. 72).

To conclude, the approach that recognizes that any arbitrary medical treatment might constitute the offence of intentional personal injury, even if performed following medical art rules (*leges artis*) and with a favourable outcome, is not acceptable[6].

The Italian Supreme Court emphasizes that in circumstances where a surgeon performs a medical treatment without the patient's informed consent if he has operated on the conviction of the presence of consent due to carelessness or lack of

[1] Cass. Pen., 8 June 2010, no. 21799.
[2] *Ibidem*.
[3] Cass. Pen., 26 May 2010, no. 34521, *cit*.
[4] *Ibidem.*
[5] Cass. Pen., Sez. IV, 14 March 2008, no. 11335.
[6] Cass. Pen., 11 July 2001, no. 1572, *cit.*: *"Since this activity implies the completion of acts which in their materiality manifest the objective element of the crime, damaging the bodily integrity of the subject*".

skills, he must be held liable for negligence[1] (Di Pirro, 2013, p. 97). Therefore, remains open the possibility of configuring the crime of negligent personal injury (Article 590 of the Italian Criminal Code)[2] or manslaughter (Article 589 of the Italian Criminal Code), where, because of the doctor's inexperience or negligence, the death of the patient occurs[3] (Eusebi, 1995, p. 728; Iadecola, 2002, p. 2041; Viganò, 2004, pp. 162 et seq.).

Reflections on non-therapeutic medical-surgical treatment

According to the doctrine, non-therapeutic medical-surgical treatment comprises both the objective and subjective elements that define the offence of personal injury under Article 582 of the Italian Criminal Code (Beulke & Diebner, 2013, p. 839). From the point of view of the objective element, non-therapeutic medical conduct, which does not improve the patient's health and is carried out without the patient's informed consent, can cause the disease as required by Article 582 of the Italian Criminal Code (Furramani & Bushati, 2021, p. 284).

And from a subjective point of view, the surgeon acts intending to damage the patient's physical or psychological integrity as required by the offence of personal injury (Furramani & Bushati, 2021, p. 284). Logically, we should also accept the configuration of unintentional homicide under Article 584 of the Italian Criminal Code if the non-therapeutic medical treatment causes the patient's death, which is causally related to personal injuries.

And what if the doctor performs the treatment in violation of the medical art rules, with completely abnormal and distorted behaviour that is not aimed at the patient's cure? In this regard, an appropriate solution appears to be the one offered by the Court of Cassation when it argues that: *"the doctor who subordinates the patient to an event (which then results in death) will answer for unintentional homicide (...), in the absence of any therapeutic purpose, for purposes dissimilar from the protection of the patient's health, such as when it consciously causes unnecessary mutilation or acts for purposes different from the patient's health protection.*[4]"

The decision of the Court clarifies the point of the situation regarding the criminal relevance of non-therapeutic medical treatment carried out in the absence or the presence of invalid informed consent of the patient. And therefore, it is necessary for criminally relevant conduct to identify the therapeutic purpose of the treatment, the existence of informed consent, and compliance with the medical art rules. In

[1] Cass. Pen., Sez. Un., 21 January 2009, in *Cass. Pen*., 2009, p. 1806.
[2] Cass. Pen., Sez. V, 21 April 2016, no. 16678.
[3] Cass. Pen., Sez. IV, 14 March 2008, no. 11335, *cit*.
[4] Cass. Pen., Sez. IV, 23 September 2010, no. 34521.; Cass. Pen., 8 June 2010, no. 21799, *cit.;* Trib. di Milano, 21 July 2000, has recognized the responsibility of the doctor under Article 582 of the Italian Criminal Code for the administration of an insulin-based therapy for anti-abortion purposes without the patient's informed consent, applied in the absence of the protocols accepted by the scientific community, which resulted in hypoglycaemic crises and consequent temporary disabilities.

particular, the purpose of the treatment is considered necessary for determining the presence of intention in medical conduct[1] (Fiori et al., 2011, pp. 258 et seq.; See Fucci et al., 2011, p. 269).

Even if it must be admitted that this distinction is not the only criteria to be considered in identifying the mental element, given that intention must also be found in the therapeutic medical act performed against the patient's will, in violation of his explicit dissent.

Currently, the position embraced by the Italian Supreme Court concerning the offence of personal injury is that which coincides with the concept of disease as an "*evolutionary pathological process, necessarily accompanied by a more or less significant impairment of the functional structure of the organism."*[2] Therefore, to configure the crime of personal injury, the medical conduct must naturally cause a harmful event connected to a functional impairment suitable for configuring the notion of disease outlined above, as well as being performed in violation of medical *leges artis* (Salerno, 2014, p. 961).

In this regard, it is necessary to distinguish between the hypotheses of medical-surgical treatment carried out in the total absence of the patient's informed consent or cases of invalid consent and medical treatment carried out in violation of the patient's explicit refusal[3] to undergo the treatment (Canestrari, 2015, p. 67; Canestrari, 2014, pp. 79 et seq.; Barni, 2002, p. 613; Fiori & Marchetti, 2009, p. 229; Fiori et al., 2002, pp. 891 et seq.). In the last case, it is possible to notice the mental element of the personal injury offence, the intention, required by article 582 of the Italian Criminal Code since the doctor consciously acts on a patient who explicitly refuses medical treatment after being adequately informed.

Final conclusions

The previous approach, which proposed the configurability of the crime of intentional personal injury (Article 582 of the Italian Criminal Code) or unintentional homicide (Article 584 of the Italian Criminal Code) in the hypothesis of arbitrary medical-surgical treatment, now appears to be outdated. It is crucial to highlight, at this point, that medical behaviour should not be confused with activity intended to inflict injury (Cfr. Vergallo et al., 2010, pp. 21 et seq.). Instead, the mental element required by Article 582 of the Italian Criminal Code as specific intent will be configurable in the hypothesis in which: *"(...) the surgeon, or doctor, even if motivated by therapeutic intentions, is aware that his intervention will produce an unnecessary impairment to the*

[1] Cass. Pen., 8 June 2010, no. 21799, *cit*.
[2] Cass. Pen., 28 June 2011 (dep. 6 September 2011).; Cass. Pen., 26 May 2010, no. 34521, *cit*.
[3] Cass. Pen., Sez. IV, 20 April 2010, no. 21799; Cass. Sez. Un., 21 January 2009, no. 2437, in *Dir. pen. proc.*, 2009, IV, p. 447; Cass. Pen., Sez. IV, 23 January 2008, no. 16375.; Cass. Pen., Sez. I, 29 May – 11 July 2002, in *Riv. it. dir. proc. pen*., 2003, I, p. 604; Cass. Pen., Sez. IV, 11 July 2001, no. 1572, in *Riv. it. med. leg*., 2002, p. 867.; Trib. Palermo, the ordinance of 31 January 2000, GIP Massa, in *Foro it.,* 2000, III, p. 441.

physical or psychological integrity of the patient[1]" (Cfr. Barni, 2002, p. 615; Fiori, 2009).

Consequently, cases in which the surgeon is guided by non-therapeutic purposes should be considered differently, such as cases of scientific research or experimentation or other purposes different from the protection of the patient's health. In this case, the medical conduct can cause an impairment to the patient's safety and the mental element coincides with the intention of personal injury (Article 582 of the Italian Criminal Code) (Cfr. Manna, 2004, p. 463).

In conclusion, the significance of informed consent in all medical-surgical treatments must be acknowledged, as it serves as a necessary prerequisite for the lawfulness of medical treatment and as a fundamental right of freedom; but it is also true that a lack of informed consent does not automatically constitute the offence of personal injury (Article 582 of the Italian Criminal Code) or unintentional homicide (Article 584 of the Italian Criminal Code)[2]. Considering arbitrary therapeutical medical-surgical treatment as intentional personal injury or unintentional homicide when there is no specific legislation on the subject means violating the principle of legality of criminal law, which can harm legal certainty.

In this context, the intervention of the legislator is necessary. Consequently, we had to wait for a univocal jurisprudential position or legislative intervention to establish the boundaries of criminal relevance of arbitrary medical-surgical treatment.

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Why Blood-Let Out Cupping Therapy is a Highly Biological Clinical Procedure

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Abstract

Aim: Demonstration of the high biological value of blood-let out (BLO) cupping therapy. **Review:** BLO cupping therapy is defined as withdrawal of blood trapped within the tissues together with the inflammatory toxic mediators which are believed to be functionally obliged to this blood via superficial skin scratching and suction for the purpose of cure and prophylaxis. A fundamental fact in cupping therapy that has been constantly documented is the source of the removed blood during cupping procedures which is the interstitial space not the circulation meaning that it is functionless as the blood functions inside the circulation; in turn cupping therapy should include no harm, it is mandatory even for a healthy individual and that the healthy benefit of cupping therapy is definite. The principal biological benefits of cupping are sero-clearance or clearance of circulation from its undesired elements with protection towards vascular events and withdrawal of the toxic mediators thus guarding against chronic illness; both sero-clearance and withdrawal of toxic mediators are challenges which could not be achieved via any clinical measure. The mechanism in cupping is basically mediated via histamine release due to skin scratching attracting the circulation towards the cupping area and nitric oxide liberation via a shear stress effect due to repeated suction leading both to a highly selective pooling of the whole circulation within a localized sector of the capillary bed over a limited interval. **Conclusion:** BLO cupping therapy is a clinical procedure with huge biological benefits that could assist the outcomes of medical therapy.

Keywords: blood-let out cupping therapy, cupping therapy, histamine release, nitric oxide, pooling of circulation, sero-clearance, skin scratching, skin suction, toxic mediators

Introduction

Definition: Blood-let out (BLO) cupping therapy is an ancient clinical procedure and in spite of its simplicity it includes huge biological benefits (Nasrat et al., 2015f; Nasrat et al., 2015c; Nasrat, 2017). It is defined as withdrawal of blood trapped within the tissues together with the inflammatory toxic mediators which are believed to be functionally obliged to this blood via superficial skin scratching and repeated suction for the purpose of cure and prophylaxis. The term ''functionally obliged'' signifies that these mediators which are acidic function to keep this trapped blood in liquid state whatever long it stays within the tissues like the citrates in the blood donation bag thus this trapped blood could be revealed out if cupping is ever done and unlike the blood within tissues of the muscles caused by trauma which if left could clot and get organized. The term ''are believed'' means that there is no single reference to support this obligatory relation between the trapped blood and these mediators except the behavior of the blood removed during the process of cupping therapy; that it never clots inside the body whatever it stays but it clots fast and strong when it is let-out same as the obligatory relation in hyperglycemia where fluis and electrolytes are lost with the excess blood glucose in urine as being osmotically obliged to it leading in turn to the metabolic sequels encountered in uncontrolled diabetes (Nasrat et al., 2015f; Nasrat, 2017).

Cupping therapy procedure in brief steps: The cupping procedure starts by placing suction cups on the required areas of the skin for 3-5 minutes. The value of these suction cups is attraction of the undesired elements from deep important strctures in the body to some less important areas towards the skin. Cups are removed and tiny superficial scratchings are done on the skin then cups are re-applied and repeat suction is employed with accumulation of blood inside the cups in turn. The source of this let out blood is not from the circulation but from within the tissues as proved by the observational finding that the cupping procedure reaches a point where blood-letting out stops whatever the suction is going on meaning that it is derived from a limited space not from an open circulation otherwise let out of blood would never stop so long the suction goes on. Therefore; cleaning the cups from blood is done and repeat placing them with repeat suction until blood letting-out stops. The blood upon letting out is seen first liquid but it clots inside the cup faster and stronger than any other blood as being trapped blood that has left the circulation earlier before some long time not freshly leaving the circulation. After reaching stop of blood-lettig out, waiting two hours, one night or one day then repeat suction without further scratching, there would be blood-letting out again, what is the source of this new blood that has accumulated in the tissues again!! No source of blood except the circulation as if the circulation is sacrificing some of its blood elements; why!! Because undesired old cells; actually microscopic examination reveals that it is all old red blood cells. This new blood freshly leaving the circulation to the tissues appears more liquid, apparently less dark and clots slower; that is the blood which is sacrificed by the circulation shortly after and in response to the cupping procedure thus it is the

blood that would be trapped within the tissues and is supposed to be withdrawn during the future cupping procedure (Nasrat, 2017).

The following figure (Fig. 1) shows a deep thigh hematoma around 12 inches depth visualized by MRI (left), its response towards the suction on the skin (middle) and its near disappearance after skin scratching and repeat suction (right). It is worthy to pay the attention that this hematoma travelled across the thigh towards the skin suction in transverse direction meaning that it is not contained inside a blood vessels as the vessels in the thigh are longitudinal (Nasrat, 2017).

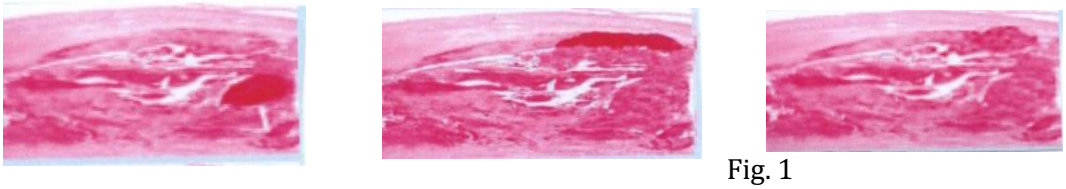


Fig. 1

The following figures demondstrate the tiny skin scratching in cupping therapy which should be around 1 mm. in length and around 0.1 mm. in depth (Fig. 2) and the sufficient blood which is let out from these tiny scratches (Fig. 3).

Fig. 2

Fig. 3

The following figures illustrate a cup filled with blood (Fig. 4) and a strong clot staying stable unsupported on the skin (Fig. 5).

Fig. 4

Fig. 5

Fig. 6

Fig. 7

The above figures (Fig. 6& 7) demonstrate that the cupping procedure reaches a step of NO blood-let out in spite of continued suction

The following figures (Fig. 8& 9) show clot inside a cup and the inflammatory mediators in the form of clear fluid on top and the other near the end of a cupping procedure where the inflammatory mediators appear as clear fluid drops.

Fig. 8

Fig. 9

Figure 10 shows the digital color view of the venous blood samples taken from patients with hepatitis C virus before and the morning after the cupping session that clearly illustrate the high biological value related to the cupping procedure in sero-clearance which is an integral health target (Nasrat, 2017).

Bfore After

Fig. 10

These observational findings and illustration figures ar solid and constant facts in all cupping therapy procedures (Nasrat et al., 2015c; Nasrat, 2017).

A Fundamental fact in cupping therapy: A fundamental fact in cupping therapy that has been constantly documented in all cupping procedures is the source of the removed blood during cupping which is the interstitial space that is from within the tissues not the circulation meaning that the removed blood is functionless as the blood functions inside the circulation; in turn cupping therapy first should include no harm as the blood which is lost is useless, secondly it is mandatory even for a healthy individual as any normal individual would include trapped blood within his tissues particularly of the upper back thus if cupping is done for a healthy individual would reveal blood out therefore what is the purpose of leaving blood to accumulate within the tissues so long its normal existence is inside the circulation and thirdly the healthy benefit of cupping is definite due elimination of harmful useless material from the body (Nasrat, 2017).

The definite criteria indicating from where blood is let out during cupping therapy or the source of blood in BLO cupping therapy: The source of blood which is derived out during blood-letting out cupping therapy is definitely from within the tissues in the interstitial space and is not from the circulation even not from very tiny micro-capillaries under the skin as proved by solid constant observational/experimental findings in all cupping procedures.

These integral observational findings which are charachteristic of cupping therapy are solid and constant in all cupping procedures, it could be emphasized and confirmed via some experimental clear facts.

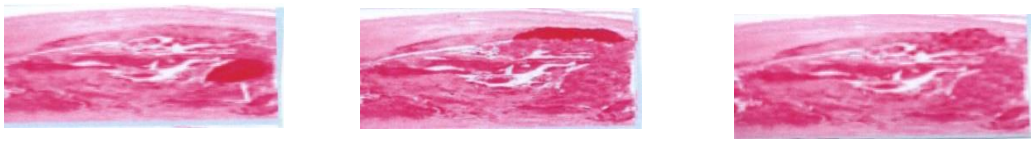
Blood-letting out in cupping therapy reaches a point where the let out of blood stops whatever the suction is meaning that it is derived from a limited space not from an open circulation or else blood-letting out would never stop so long the suction goes on even it is coming from tiny micro-capillaries (Fig. 6& 7).

After cleaning the cups from blood, re-applying them on the skin and revision of suction, the blood which is let out later is getting every time darker in color and faster in clotting inside the cup meaning that the blood is arranged in layers so that the blood that has left the circulation earlier is deeper and older hence it is darker and clots faster; the blood could exist in layers within the tisuues not inside the circulation and this is definitely a good document.

Some elderly people who are on anticoagulants for some cerebral or cardiac reason might need to undergoe cupping therapy for any therapeutic purpose such as sprung of the back or a joint, those people do not need to interrupt their anticoagulants as these drugs are critical that should not be interrupted or delayed and furthermore these drugs run and function inside the circulation while the blood which is let out in cupping therapy comes from outside the circulation hence there sould be no relation between them; that what actually is happenning as the blood which is let out in those patients clots fast rather in 5 minutes and strong as if these anticoagulants are not there as the blood under anticoagulation should clot 3-4 times slower than the nomal

blood i.e. in 21-33 minutes at least; this should be a definite decisive strong document about the source of blood in cupping therapy.

The following figure which is the previous figure 1 that shows a deep thigh hematoma visualized by MRI, picture (a); its response towards the suction on the skin, picture (b) and its almost disappearance after skin scratching and repeating suction, picture (c) also confirms the same finding about the source of blood from where it is being derived out in cupping therapy.



(a) (b) (c)

The blood which is let out during cupping therapy clots fast and stong in rather 3-5 minutes at first then in 1-3 minutes for the next deep layer then even in less than one minute for the next deeper layers and that is because this blood has left the circulation earlier unlike the fresh venous blood sample that clots in 7-11 minutes. These hard clots if left for a short while, they dissolve again as shown in figure 11 that is simply because these clots are composed of red blood cells only lacking the constituents of a proper clot which are red cells, platelets and fibrinogen, the latter two components are responsible for stability of the clot, getting thrombosed and contracted (Nasrat, 2017).

Fig. 11

The above figure (Fig. 11) shows a picture of a hard clot in place unsupported and dissolving (left) while the other picture on the right shows how blood clots fast, strong and dissolves

This striking observational finding together with the documented microscopic examination of the blood which is let out during cupping therapy being composed only of old red blood cells confirms the integral fact that the blood which is let out during cupping therapy is not derived from the circulatin even not from tiny micro-capillaries under the skin otherwise it would be a mixture of the whole blood elements (Nasrat et al., 2015f; Nasrat, 2017).

The scientific theory in cupping therapy (mechanism of function in cupping therapy); the highly selective pooling of the whole circulation within a localized sector of the capillary bed over a limited interval: Figure 12 shows the side view of the biconcave normal red blood cells (in red) and the spherical old red cells (in blue).

Fig. 12

The following figure (Fig. 13) demonstrates an imaginary diagram of the micro-capillary arterio-venous junction.

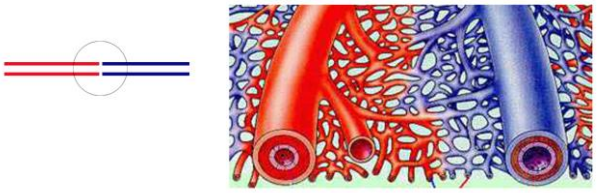


Fig. 13

The following figure (Fig. 14) demonstrates an imaginary diagram for the micro-capillary arterio-venous junction at normal situations (left) and during micro-capillary dilatation (right).

Fig. 14

The biologic circulatory activity which takes place within a short while after the cupping procedure could be described as “A highly selective pooling of the whole circulation within a localized sector of the capillary bed over a limited interval”. The

pooling of the circulation is related to the effect of histamine released due to skin scratching while falling of the undesired spherical red blood cells outside the circulation is due to the influence of the endothelial-derived nitric oxide liberated via the shear stress effect due to the act of repeated suction leading to micro-capillary dilatation. In normal situations, the biconcave healthy red cells circulate through the micro-capillary bed smoothly from the arterial to the venous side while the spherical unhealthy red cells have to get squeezed to the size of micro-capillaries in order to go through the narrow capillary bed under the influence of blood pressure. These cells recoil or regain their spherical shape after passing beyond the narrow vessels. In case of micro-capillary dilation, the matter is not much different for the healthy biconcave red cells whereas the unhealthy red cells getting squeezed to an ovoid oblong shape recoil and gain a blunt-shaped distal end while situated within the dilated micro-capillary arterio-venous potential junction hence getting stuck and restoring most of their spherical shape thus becoming unable to proceed through the venous side of the micro-capillaries and therefore are lost within the interstitial space constituting the blood of the future cupping session (Nasrat et al., 2015f; Nasrat et al., 2015c; Nasrat, 2017).

The following diagram (Fig. 15) demonstrates the imaginary flow of normal red blood cells within the capillary bed from the arterial to venous side.

Fig. 15

Figure 16 demonstrates the imaginary flow of the old spherical red cells in the capillary bed during normal situations where the cell gets compressed to an oblong shape then recoils and regains its spherical shape upon leaving the narrow vessels.

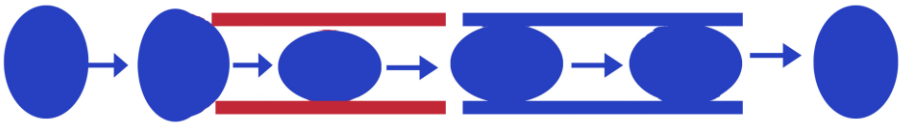


Fig. 16

The following diagram (Fig. 17) shows the imaginary flow of normal red blood cells in the capillary bed during a state of micro-capillary dilatation.

Fig. 17

The following figure (Fig. 18) demonstrates the imaginary flow of the old spherical red blood cells during micro-capillary dilatation where these cells recoil in the dilated arterio-venous junction and gain a blunt end therefore get stuck at the venous side.

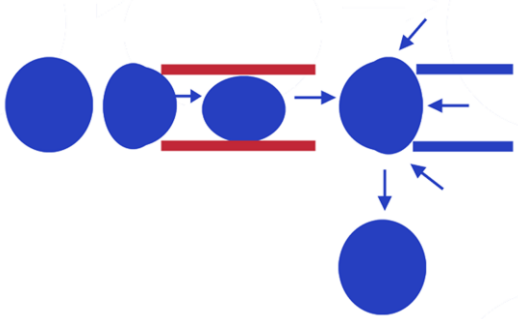


Fig. 18

Figure 19 demonstrates how the old spherical red blood cells could fall out of the circulation during micro-capillary dilatation shortly after the cupping procedure constituting the blood that accumulates and would be withdrawn out in the future cupping procedure.

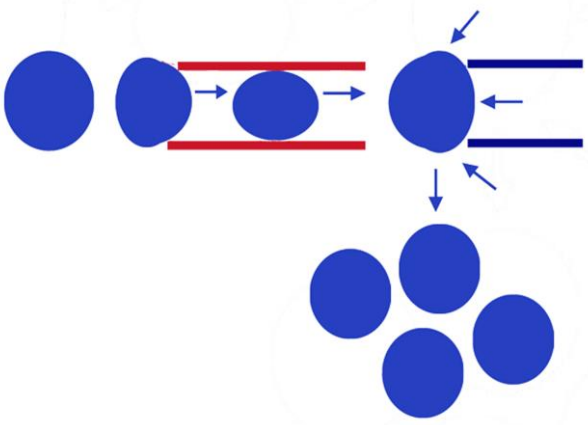


Fig. 19

Aim

This study aims at demonstration of the integral healthy biological benefits of cupping therapy that could not be achieved via several clinical measures; these benefits are worthy enough to be employed by the modern medicine in order to assist the results of medical therapy.

Review

The latest reports in literature illustrate some adequate research activities demonstrating the high biological value of cupping therapy in many medical challenges. The role of BLO cupping therapy has been frankly demonstrated in female pelvic congeston syndrome which is a medical challenge as most symptoms improved such as lower abdominal pain, dysmenorrhea, menstrual irregularities, dysparunea and even the delay of gestation where many females got pregnant within three months after three successive cupping sessions (Nasrat et al., 2015f). Good therapeutic results were also achieved in male pelvic congestion syndrome as concerns fertility and the erectile function (Nasrat et al., 2016). The value of cupping therapy among patients with hepatitis where the cupping therapeutic talent of sero-clearance helps elimination of most of the viral load even to low undetectable levels in the morning following an evening session of cupping. Sero-clearance also improves the individual immunity, therefor; the aim and target of cupping in hepatitis is repeated seo-clearance with repeated lowering of the viral load thus avoiding complications and repeated augmentation of the individual immunity that could counteract the virus until reaching rdical cure thus taming of the wild hepatitis B virus and eradication of hepatitis C virus were just possible and promising (Nasrat et al., 2015c; Nasrat et al., 2015g). Cupping therapy has shown dramatic immediate and comlete relief of symptoms in angina and angina risk management after a single cupping session even in patients with recurrence of symptoms within three months from a successful cardiac catheter and stents, those patients were followed up for sufficient years without showing any recurrence of symptoms (Nasrat et al., 2015a). Dramatic immediate relief effects have been also shown with a single session of cupping therapy in cervical disc pathologies (Nasrat et al., 2015d). Cupping is the treatment of sclerosis due to elimination of the inflammatory tissue acidic mediators which are the reason of micro-capillary spasm, hence cupping therapy is an integral savior in diabetic leg critical ischemia (Nasrat et al., 2015e). Marked therapeutic effects were achieved in various skin pathologies like eczema, psoriasis and idiopathic dermatitis (Nasrat et al., 2015h). A significant cupping therapeutic answer has been given for the controversy of insulin cardio-protection among dysglycemic patients and that was due to the effect of elimination of the acidic metabolites via blood-letting out (Nasrat et al., 2015b). The effect of combined colon clear and cupping therapy in cease of disease progress among middle-aged female patients with endometriosis and ovarin cystic disease has been also interestingly emphasized (Nasrat, 2016).

Discussion

A good deal of scientific research activities dealing with the dramatic benefit of BLO cupping therapy has been reviewed in various medical conditions where all of them were true medical challenges and most of these research activities demonstrated almost complete medical cure (Nasrat et al., 2015f; Nasrat et al., 2015c; Nasrat et al., 2016; Nasrat et al., 2015g; Nasrat et al., 2015a; Nasrat et al., 2015d; Nasrat et al., 2015e; Nasrat et al., 2015h; Nasrat et al., 2015b; Nasrat, 2016). The biological benefit of BLO cupping therapy is being illustrated via the scientific theory of cupping therapy which is "The highly selective pooling of the whole circulation within a localized sector of the capillary bed over a limited interval" where the localized sector of the capillary bed constitutes the area of the cupping procedure and the limited interval represents the life time of the liberated nitric oxide during the cupping procedure which is the one to two hours following the cupping session (Nasrat et al., 2015f). Therefore comes the question; why the modern medicine does not employ the biological talents of BLO cupping therapy to assist improving the outcomes of medical therapy!!

The biological benefits of cupping therapy that concerns the modern medicine should include: 1. Activation of the local, general circulation and micro-capillary circulation due to histamine release because of skin scratcting and the endothelial-derived nitric oxide liberation due to a shear stress effect caused by the act of repeated suction; 2. Sero-clearance or clearance of the circulation from its undesired old blood elements via a selective pooling of the circulation due to histamine release together with the localized micro-capillary dilatation caused by nitric oxide liberation; 3. Guarding against vascular accidents due to elimination of the old red blood elements preventing un-necessary hemoconcentration via the biology of sero-clearance; 4. Withdrawal of the inflammatory toxic tissue mediators with the blood which is let out as being obliged to it; 5. Correction of any existing micro-capillary compromise due to elimination of any accumulating inflammatory tissue mediators which are the reason of the micro-capillary spasm; 6. Protection towards complications of diabetes in the heart and leg or foot due to elimination the toxic metabolic mediators; 7. Guarding against chronic illness and cancer due to elimination of the acidic inflammatory mediators and cure of any existing micro-capillary compromise which are the main hidden reason behind chronic, major illness and cancer; 8. Augmentation of the individual immunity due to sero-clearance and improving the quality of oxygen and nutrients carrying capacity of red blood cells; and 9. Activation of the un-differentiated stem cells which is still a subject of continued research and under accurate re-dtermination (Nasrat 2017; Morishita, 1972).

The mechanism of function in cupping therapy to achieve its biological benefits is therefore dependant mainly and simply upon histamine release and nitric oxide liberation. For example, the mechanism of sero-clearance in cupping therapy is based on pooling of the circulation in a limited sector of a dilated micro-capillary bed due to

histamine release and nitric oxide liberation. The mechanism of cure of micro-capillary compromise and protection towards chronic illness and cancer is through elimination of the toxic tisuue inflammatory mediators with the blood which is let out as being obliged to it. According to continued reseach studies on chronic illness and cancer between 1962 and 1966, it has been reported in 1968 that the main hidden reason behind chronic illness and cancer is the micro-capillary compromise because of accumulation of the toxic inflammatory mediators in tissues and circulation (Morishita, 1972). In cupping therapy, the toxic tissue mediators are eliminated during the cupping session being obliged to the blood which is let out while the toxic mediators in the circulation are expelled into the tissues with the undesired old red blood cells sacrificed from the circulation during the brief duration following the cupping session whereas both of them, the old blood and the mediators, are expected to be let out during the future cupping procedure. These mediators have been isolated during the cupping procedure, tested, and documented to be almost cytokines and chemokines (Nasrat, 2017). The following figure (Fig. 20) demonastrates a step near end of the cupping procedure where a few bright blood appears together with the toxic mediators that look as clear reddish spots (left) while in a next step also near end of the cupping procedure (right picture) the toxic mediators appear as clear fluid drops.

Figure 20

The natural instincts of the physiological behavior of blood during BLO cupping therapy are quite interesting. 1. As the blood has been trapped within the tissues in layers so that the oldest is deepest and therefore it is darker and faster in clotting when it is let out. It is worthy to mention that it has been observed that the blood respects its cue during letting out and does not mix with blood of other layers otherwise the blood which is let out would be rather similar in color and speed of clotting during the whole cupping procedure which is not the case at all; 2. The blood which is let out during the cupping procedures responds to suction and its response to suction is a propery of the blood itself not a property of suction meaning that the blood goes towards the suction not the suction which is pulling it towards the cup as proved by the observational finding that performing cupping with scratching around an abscess where there is accumulation of pus, exudate and blood among the abscess; it was found that what is let out is only blood. Incision of the abscess shows drainage of pus, exudate and blood confirming existence of the three materials, placing the cup

over the abscess incision and doing repeated suction reveals only blood indicating that the blood goes to the suction by its own natural instinct towards the suction not the suction which is pulling it otherwise all three materials should come to the suction cup; 3. Blood-letting out from the body is a natural or physiological instinct of the blood trapped within the tissues as demonstrated by the observational finding upon doing the cupping therapy some distance from a limb hematoma and while the blood is starting to be letting out in the cup, a tourniquet is applied between the cup and the hematoma, this elicited severe pain either at the site of the cup or the hematoma, pain disappears with release of the tourniquet and returns with re-applying it; and 4. BLO cupping therapy is entitled for a biological function as concerns tissue health support as observed in a cupping therapy procedure for a patient with critical leg ischemia with impending gangrene and amputation was considered where blood-letting out was starting to go slower then stopped, when the cup is removed blood started to slope passively without suction, the slop of blood got fixed in place once the cup and suction were re-applied and so on, that is the blood slopes passively without suction and stops instantly with re-suction, no explanation was concluded for this strange behavior of the blood except after incision of the skin with appearance of the muscles dark and unviable, therefore; cupping could function for health of the tissues but if the the tissues are not viable hence cupping has got no reason (Nasrat, 2017; Nasrat et al., 2015e).

Is BLO cupping therapy empirical! BLO cupping therapy could never be empirical but it is integral and fundamental as documented by the physiological instints of the natural behavior of blood during cupping therapy procedures. As emphasized, the trapped blood within the tissues responds the to suction and the response of blood to suction is a property of the blood itself not a property of the suction, therefore; the tiny skin scratching in cupping procedures are better effective in suction than skin cuts or weldone scratches exactly similar to the impossibility of trying to swallow a drink from top of a bottle while it is easy via a narrow straw. In addition to the physiological insticts of the behavior of blood during cupping procedures, the fundamenta facts in cupping therapy particularly the source of blood which is derived during cupping that it is from within the tissues in the interstitial space not from the circulation; whoever decides to desconstruct the biological building of cupping therapy should first devalidate this integral fact namely the source of blood which is let out during cupping therapy or from where the blood in cupping therapy is derived out!! (Nasrat, 2017).

It is necessary to confirm that the process of sero-clearance is a biological event which is part of the normal human physiology where the old red cells are destroyed in the blood sinusoids of spleen and liver for the purpose of re-circulation to build up new proteins and hemoglobin while the old undesired useless red cells are eliminated in the upper back, that is the blood which would be withdrawn out if cupping therapy is ever done. This normal physiological process of sero-clearance taking place inside the human body is slow and occurs over long periods while sero-clearance in cupping

therapy is a huge biological process that completes clearance of the whole circulation from all of its undesired red blood cell elements in just two hours or at most over a night. Hence, the upper back is the area of the body which is capable and entitled to accommodate the unhealthy blood elements expelled from the circulation via a slow incomplete biological process over long periods and therefore; the upper back is the essential area of the body for cupping therapy and prophylaxis while the the interstitial space is the intelligent yard where BLO cupping therapy exerts its biological talents (Nasrat et al., 2015c; Nasrat, 2017).

Summary

This study introduced cupping therapy in brief details strating with the definition of cupping therapy, the cupping procedure in delicate scientific steps, the fundamental facts in cupping therapy and the scientific theory in cupping therapy or mechanism of function of cupping therapy. Reviw of the scientific research activities by the author of this study in BLO cupping therapy with successful results among several medical challenges was emphasized aiming to attract the interest of modern medicine to employ these beneficial results in medical practice. Discussion of the biological benefits of cupping therapy was also illustrated with the purpose of getting the attention of modern medicine towards these benefits. The hypothetical events that encounter the red blood cells within a localized sector of the capillary bed of the cupping area as concerns the scientific theory of cupping included in this study is further emphasized and powered by a moving slide show illustration.

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Conflict of interest

No conflict of interest is existing.

Conclusion

BLO cupping therapy is a clinical procedure with huge biological benefits that could assist the outcomes of medical therapy.

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Autism is not a Disease of Definitive Cure but it is a Typical Disease of Definite Prevention

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Abstract

Aim: Demonstration of a possible role of ***Helicobacter pylori*** in the etio-pathology of autism that makes prevention of the disease possible. **Background:** ***H. pylori*** was suggested as a reason related to many medical challenges. ***H. pylori*** when forced to migrate to the colon due to the antibiotic violence; the accumulated ***H. pylori***-produced colonic ammonia in profuse amounts conforms with the elevated serum ammonia among autistic children and its toxic effect with the hypothesis of the entire brain compromise suggested in autism. Interestingly, kids develop ***H. pylori*** trans-familial during the time of weaning which is the typical timing of developing autistic features. Ammonia is the producer of nitric oxide in the gut via a shear stress effect while nitric oxide is a cure and a poison at the mean time; that is in normal residual levels it is healthy while in excess amounts it is toxic. This could explain the early brilliant behaviors in some autistic kids which are followed by loss of skills later. A striking observation has been emphasized by some study where all parents of the autistic kids of that study were having frank ***H. pylori*** dyspepsia, the kids were also positive for ***H. pylori*** fecal antigen and some kids were recovered from prodromal symptoms via early colon clear from the colonic ***H. pylori*** strains. **Conclusion:** Autism then, when established, is not a disease of definitive cure but it could be a typical disease of definite prevention via protection from transmission of parents ***H. pylori*** strains to kids.

Keywords: ammonia, autism, colon clear, Helicobacter pylori, nitric oxide.

Introduction

Autism constitutes a challenging puzzle affecting disadvantaged children at early age where they grow normal until age of 18-24 months then they begin failure to develop some skills or loose already developed skills. The exact etiology of the condition remains unclear while all promises of complete cure are unsuccessful. Autism is a brain disorder that limits a person's ability to communicate, correlate and relate to

other people. It is a series of neuro-developmental disorders that are characterized by deficits in both social and cognitive functions (Li& zhou, 2016). Autism spectrum disorders (ASD) affect about one child in 68, striking nearly five times as many boys as girls (Woolfenden et al., 2016; Baio, 2009). It was concluded that genetic and environmental factors are both responsible for the etiology of ASD. Although epidemiological studies have been conducted to clarify these factors but this conclusion remains unclear (Galichi et al., 2016; Kiely et al., 2016). Careful observers could early discover development of signs of autism in a child. Some children develop normally until 18-24 months of age and then they just stop or loose previously acquired skills. Signs of development of ASD could include repeated motions (rocking or spinning), avoiding eye contact or physical touch, delay in learning to talk, repeating words or phrases and getting upset by minor changes (Kiely et al., 2016; Allen, 1988). Young infants are very social even in the first year of age, therefore; it is possible to detect early signs of autism as early as how babies interact with their world. At this age, a child with ASD may not turn to a mother's voice, respond to his own name, look people in the eye, have no babbling or pointing and no smiling or responding to social cues from others (Emberti Gialloreti, et al., 2016; Spjut Jansson, et al., 2016; Locke, 2016). Children with autism may sometimes have physical symptoms including digestive troubles such as constipation and sleep problems. It was long believed that autism affects only those regions of the brain that control social interaction, communication and reasoning but instead it is suggested that the disorder in autism affects the entire brain (Galichi et al., 2016; Dinan& Cryan, 2016; Richter et al., 2015).

Most investigators were successful to come in agreement that various gastro-intestinal (GI) factors may contribute to behavioral disorders in children with autism (Li& zhou, 2016; Galichi et al., 2016) but they mostly missed to successfully achieve the real pathology behind these GI factors in contribution to autistic behavior. The last three decades have demonstrated prevalence of abnormal-behavior ***Helicobacter pylori*** strains and the flare up of a lot of medical challenges related to these ***H. pylori*** strains via inflammatory, toxic, immune or different unknown reasons to the extent that the medical world has believed that ***H. pylori*** eradication should be a necessary attempt (Farinha& Gascoyne, 2005; Nasrat et al., 2015a).

Aim

Demonstration of a possible role of the bacterium ***H. pylori*** in the etio-pathology of autism that makes prevention of the disease possible.

Review

Although various reports in literature refer with great concern to the role played by ***H. pylori*** in disease pathology (Farinha& Gascoyne, 2005; Nasrat et al., 2015a), research studies seldom indicated directly to the possibility that ***H. pylori*** could be hidden behind the pathogenesis of autism. Recent clinical studies have apparently revealed a high prevalence of the GI symptoms such as inflammation and dysfunction

in children with autism. Mild to moderate degrees of inflammation were almost found in both the upper and the lower intestinal tracts with an obvious decreased digestive enzyme activity in many autistic children. Treatment of these digestive problems appeared to constitute positive effects on autistic behaviors; these new observations represent only just a piece of this unsolved puzzle which is "autism" and should stimulate more researches towards the brain-gut connection (Horvath& Peman, 2002).

As ASD is often associated with different GI disturbances which may also impact behavior, therefore; alterations in autonomic nervous system functions should be also expected frequently in ASD. The relationship between these findings in autism is not clearly known. It was suggested that autonomic functions and GI problems are intertwined in children with ASD (Ferguson et al., 2017). Although the exact etiology and pathology of ASD remain unclear, a disorder of the microbiota-gut-brain axis is emerging as a prominent factor in the generation of autistic behavioral disorders. Clinical studies have shown clearly that GI symptoms and compositional changes in the gut microbiota frequently accompany cerebral disorders in patients with ASD. A disturbance in the gut microbiota which is usually induced by a bacterial infection or chronic antibiotic exposure has been implicated as a potential contributor to ASD. The bi-directional microbiota-gut-brain axis was often suggested to be acting mainly through neuro-endocrine, neuro-immune and autonomic nervous mechanisms. It was reported that application of modulators of the microbiota-gut-brain axis such as probiotics and certain special diets might be a promising strategy for the treatment of ASD. Different observations about disruption of the microbiota-gut-brain axis as concerns the pathogenesis of ASD have therefore suggested its potential therapeutic role in autistic deficits (Li& zhou, 2016).

A gut to brain interaction in ASD and the role of probiotics on clinical, biochemical and neuro-physiological parameters in autistic individuals have been emphasized and confirmed in further reports. It was furthermore adequately reported that the high prevalence of the frequent GI disturbances in patients with autism might be linked to gut dysbiosis representing a phenotype of a "gut-brain axis" disruption. Employment of strategies that could restore the normal gut microbiota and reduce the gut production and absorption of toxins such as probiotic supplements in diet might represent a non-pharmacological option in the treatment of GI disturbances in ASD. The effect of probiotic supplements in autistic children is not only specific on GI symptoms but also to improve the core deficits of the brain disorder, cognitive and language development, brain function and connectivity (Santocchi, et al., 2016). It was further reported that specific assessment of gut functions including the microbiome would be necessary to evaluate the contribution of gut physiology to functional constipation observed in autistic children (Marler, et al., 2016). As much as GI symptoms were frequently reported among autistic children, an impact of GI co-morbidity on ASD behavioral problems has been hypothesized. 'Constipated' and 'Not-Eat' were described as the most frequent GI symptoms in autistic individuals

(Fulceri, et al., 2016). Alteration in intestinal function which was often referred to as a "leaky gut" due to mucosal inflammation has been attributed to children who are on the autism spectrum; this particular symptom was even put into consideration to identify children with autism who have atypical symptoms (Kushak, et al., 2016).

The concept of gut-brain axis, its regulation by the microbiota and its role in the biological and physiological basis of neuro-developmental and neuro-degenerative disorders could thus constitute a considerable role in the pathogenesis of autism. The importance of early life gut microbiota in shaping future health outcomes should be also considered. Disturbances of this composition by way of antibiotic exposure could result in long-term effects on physiology and behavior (Dinan& Cryan, 2016; Kushak, et al., 2016). ***H. pylori*** in the stomach is leading the behavior of natural bacteria as it does not exist in the gastric lumen during presence of food and it remains settling just juxta-mucosal under the mucus layer of gastric mucosa with the ammonia at its immediate vicinity functioning to protect the gastric wall from its acid if it goes in excess (Farinha& Gascoyne, 2005; Nasrat et al., 2015a). Therefore; the antibiotic violence towards ***H. pylori*** forcing it to migrate towards the colon could definitely disturb its natural microbiotic function with its sequels on human body physiopathology.

The routes of communication between the microbiota and brain are being unraveled and could include the microbial metabolites such as ammonia (Dinan& Cryan, 2016; Farinha& Gascoyne, 2005). As ***H. pylori*** could migrate or get forced to migrate to the colon under the influence of antibiotics, it will continue producing ammonia for a reason or no reason, unopposed or buffered by any acidity, leading to accumulation of profuse toxic amounts of ammonia. Colonic ***H. pylori*** strains in their abnormal colonic habitat could lead to adverse toxic effects in the body; certainly the delicate physical structure of a child during early growth could be also severely affected by these aggressive drastic strains and the delicate integrity of the child's growing brain could further in susceptible children be a fragile target to the toxic influence of colonic ammonia (Farinha& Gascoyne, 2005; Nasrat et al., 2015a; Nasrat et al., 2015b).

The hypothesis of the entire brain involvement in autism was designed on the basis of impairment of the histology of whole areas of the brain in order to explain inability of autistic children to perform complex tasks (Donovan& Basson, 2017; Grecucci et al., 2016; Richter et al., 2015; Jou et al., 2011; Dinan& Cryan, 2016; Peeva, 2013; Casanova, 2013). In spite of the finding that many investigators have demonstrated rise of serum ammonia level among autistic children, they missed to indicate the possibility that elevated levels of serum ammonia could influence the entire functions of the whole brain of those kids (Burrus, 2012; Abu Shmais et al., 2012; Wang et al., 2012; Cohen, 2006; Corker& Tuzun, 2005; Fallon, 2005).

Discussion

H. pylori colonized the stomach since an immemorial time as if both the stomach and the bacterium used to live together in peace harmless to each other and hence ***H.***

pylori has been considered by some investigators a natural bacterium (Farinha& Gascoyne, 2005; Nasrat et al., 2015a). ***H. pylori*** when forced to migrate to the colon mainly under the influence of the antibiotic violence would lead to different dyspeptic symptoms and accumulation of profuse toxic amounts of ammonia in the colon with consequent elevated levels of serum ammonia (Farinha& Gascoyne, 2005; Nasrat et al., 2015a; Nasrat et al., 2015c; Nasrat et al., 2015d). It is common that ladies develop dyspepsia during pregnancy; abnormal ***H. pylori*** strains are responsible for most cases of functional dyspepsia but it is rarely recognized that this dyspepsia among pregnant ladies is ***H. pylori***-related (Nasrat, 2015). Accordingly; serum ammonia would be elevated in both maternal blood of those dyspeptic pregnant ladies and in the fetal blood in turn with the possibility of a toxic influence of ammonia on the delicate structure of the developing fetal brain leading also to sensitization of the fetal brain during early embryonic life to the adverse effect of ammonia. It has been reported that the neuropathology of autism starts early during embryonic life due to heterogeneity (Donovan, 2016; Chang et al., 2015; Blatt, 2012). The sustained elevated ammonia level in fetal blood caused by the colonic ***H. pylori*** strains of dyspeptic pregnant mothers could constitute a trigger of a causative pathology for neuro-development of autistic disorders confirming accordingly with the suggestion that both environmental and genetic factors are responsible for the etiology of autism (Galichi et al., 2016; Kiely et al., 2016).

The suggestion that the elevated residual serum ammonia level in fetal blood plays an early causative pathogenic factor in leading to autistic neuro-developmental disorders since embryonic life is supported by an observational finding expressed by mothers of 7 autistic children during their delivery. The mothers confirmed a frank history of ***H. pylori***-related dyspepsia during their pregnancy which had been confirmed by specific laboratory tests, they were just able to follow gastric sedatives. They were astonished that their babies did not cry immediately after delivery and suction of their secretions in spite of their good general condition (Nasrat et al., 2017). Those mothers continued having ***H. pylori*** dyspepsia symptoms after delivery because of a contraindication for eradication therapy or failure of therapies as antibiotics are seldom effective against extra-gastric ***H. pylori*** strains (Farinha& Gascoyne, 2005; Nasrat et al., 2015a; Grünberger; 2006). Later, their kids developed autism between the age of 2-3 years.

Existence of ***H. pylori*** in children occurs trans-familial via food at an early age; this matter is confirmed by the fact that ***H. pylori*** strains of children are often identical with that of their parents. Interestingly, children maintain the same strain genotype life-long even after moving to a different environment unless eradicated. ***H. pylori*** travels between parents via oral to oral route while transmission to kids occurs via meals (Nasrat et al., 2015b). The kids develop the abnormal-behavior colonic ***H. pylori*** strains at the time of their weaning when they start to share the dining table with their parents; that is typically the critical timing where children begin to develop

autistic features or loose already developed skills (Kiely et al., 2016; Allen, 1988; Farinha& Gascoyne, 2005; Nasrat et al., 2015a).

Migration of ***H. pylori*** to the colon occurs mainly under the influence of antibiotic exposure. Existence of ***H. pylori*** in the colon is typically life-long unless eradicated as antibiotics are seldom effective against extra-gastric ***H. pylori*** strains and no available measure has been proved to effectively eradicate ***H. pylori*** from the colon except the senna purge (Farinha& Gascoyne, 2005; Nasrat et al., 2015a; Grünberger; 2006; Nasrat et al., 2015e; Nasrat et al., 2015f). Accordingly; pregnant ladies who develop abnormal colonic ***H. pylori*** strains via an outside-home query meal would mostly remain dyspeptic and would become in most instances the mothers of autistic children due to persistence of a causative pathology which has triggered its early effect during pregnancy and made the fetal brain already sensitive to the toxicity of ammonia earlier throughout the embryonic life.

In addition to the toxic influence of ammonia, excess amounts of ammonia in the colon is smooth muscle spastic leading to multiple colonic spasms and a high rectal spasm which were demonstrated in ***H. pylori***-dyspeptic adults by colononoscopy. These spasms interfere with the integral colonic function of forming the motion contents, instead it squeezes the colonic contents leading to constipation and formation of small pieces of dried stool (Nasrat et al. 2015c). Existence of ***H. pylori*** in the colon was confirmed by a specific test (***H. pylori*** fecal antigen) which was found positive in all children and parents of many studies in literature. Constipation and passage of small pieces of dried stool are cardinal signs of colonic ***H. pylori***-related dyspepsia (Nasrat et al., 2015c; Nasrat et al., 2015d); these cardinal findings were found constant features in all autistic children in some studies.

The constant association of GI symptoms with autism to the extent that a gluten-free diet and probiotics were employed to improve these symptoms could further support the possibility of the role of ***H. pylori*** behind the pathogenesis of the disease. It has been further suggested that strategies of probiotic supplements that could help to restore normal gut microbiota and reduce the gut production and absorption of toxins have been advised and employed not only to improve GI symptoms in autism but also to improve the core deficits of the brain disorder (Santocchi, et al., 2016). Small bowel enteropathy has been reported in literature among patients with autism that could be attributed to embedding of ***H. pylori*** colonization towards small intestinal mucosa which is a further unrecognised unusual behavior of ***H. pylori*** (Farinha& Gascoyne, 2005; Nasrat et al., 2015a; Torrente et al., 2004; Nasrat, 2023). GI symptoms were frank and constant among patients of many studies; minute-size continuous intestinal sounds were diffusely audible over the center of abdomen that had been related to small intestinal irritation. Small intestinal enteropathy could account for the observations of “No Appetite”, “No Hunger” and “No Eat” symptoms among autistic children of these studies as kids would feel continuous abdominal discomfort that interferes with the natural desire to food. It was suggested that autonomic functions

and GI problems in autistic children are linked together (Nasrat, 2023; Ferguson et al., 2017); therefore, the quite passive peaceful attitude of some autistic children; "Non-Smiling", "Non-Reactive" was attributed in some studies to a degree of parasympathetic activation caused by the minor dull painless somatic intestinal insult. The improvement of intestinal symptoms among children of these studies upon intake of a warm mint drink, a soft caffeine drink or chocolate was explained to the improvement of this autonomic compromise. Constipation, weak appetite, passage of small pieces of dried stool or leaking small amount of soft retained/overflowing stool were encountered as constant features among those children (Nasrat et al., 2017).

Major colonization of abnormal-behavior ***H. pylori*** strains is necessary to induce symptoms and toxic complications. Spontaneous reduction below the pathologic level (50%) or even spontaneous elimination of ***H. pylori*** from the colon could occur due to variable reasons such as diarrhea or intake of foods containing bio-organic acids like lactic, formic, citric or acetic (Farinha& Gascoyne, 2005; Nasrat et al., 2015a; Zentilin et al., 2003). This could explain the wide variation in autistic features and the observation that some children develop some autistic symptoms then they skip the disease as they grow up.

A unique study has included two children newly diagnosed for autism, one was two years of age who started pronouncing some words and then he lost this skill. Immediate colon clear was employed for him and his parents within few days the clinical diagnosis was made up, that was followed by complete recovery of the child's skills. The other was three years old when diagnosed but he had lost the developed verbal skills one year earlier; he improved a little bit but did not recover completely after colon clear. That study also included a girl 11 months old; it was surprising to find a baby of that age who does not cry or even smile in response to her mother's plea, she was looking constantly to one direction and was never responsive or attentive towards her mother's voice. She was typically constipated and was crying only during passing the motion in the form of small pieces of dried hard stool. The father was having frank constipation and severe colonic dyspeptic symptoms due to frequent outside-home meals during business lunch and dinner meetings. ***H. pylori*** fecal antigen test was strongly positive for the girl and the parents; definitely the bacteria travelled from husband to his wife who gave it to her kid possibly while preparing and tasting the enfant's feeds or kissing her baby on the lips. Unfortunately, that girl was seen few months after she developed these features; immediate colon clear with a calculated dose (45 CCs) of the senna leaves extract purge was employed for her followed by vinegar-mixed fruit yoghurt twice daily. The girl improved within few days but did not recover completely because of late discovery and management of her condition; her bowel motion became easy without tragedy, the girl started to smile, look towards her mother, respond to her mother's voice and most importantly she learned to cry like any baby of her age when neglected for short time. ***H. pylori*** DNA extraction in the stool and ***H. pylori*** strain genotyping were done for the girl and parents; they were found having the same strain genotype with existence of

cytotoxin-associated gene A (cagA) positive ***H. pylori*** strains (Nasrat et al., 2017). It was emphasized that cagA of ***H. pylori*** encodes a highly immunogenic and virulence-associated protein; the presence of this virulent gene in the body could affect the clinical out-come in many children (Bulut, 2006 Jul).

Permanent compromise of some areas of the brain among autistic children such as impairments of grey or white matter, decreased cortical thickness or cortical thinning leading to dysfunction of complex interactions in disadvantaged children was confirmed in literature (Richter et al., 2015; Peeva et al., 2013; Casanova et al., 2013; Misaki et al., 2012); possibly for this reason, most researchers were just able to achieve improvement through employing different measures but never complete cure of their autistic patients. The results of various studies conform with the literature results in achieving incomplete cure of autistic features which could indicate that autism might not be a disease of definitive cure but it could be a typical disease of definite prevention via restriction of antibiotic use unless seriously indicated, extreme carefulness towards outside-home meals, natural colon care and natural colon clear on developing dyspeptic symptoms. If there is a chance for fundamental cure in autism, it might be via colon care and colon clear for both kids and parents. Early diagnosis and management are precious in this situation; recovery of the developed verbal skills for the two-years old child mentioned above with the lucky advantage of early discovery of the onset of the disease upon losing the developed verbal words is an ideal example (Nasrat et al., 2017).

Prevention is always far better than treatment; scientific research efforts could not reach until to date an adequate cure of autism while it could be greatly preventable by protecting children's brain from the bad sequels of the abnormal ***H. pylori*** strains of their dyspeptic mothers (Nasrat et al., 2015c; Debevere et al., 2001; Nasrat et al., 2017).

The reason that there are some conditions that have developed autism before the last three decades which is the particular period of the abnormal-behavior ***H. pylori*** strains prevalence, is most probably due to chronic antibiotic exposure or the frequent antibiotic abuse that would force ***H. pylori*** to migrate to the colon; the suggestion of chronic antibiotic exposure in leading to autistic disorder has been suggested by some investigators (Li& zhou, 2016). The last three decades demonstrated flare up of abnormal-behavior ***H. pylori*** strains after the the development of the strategic triple therapeutic violence against the stomach bacterium by two Australian physicians with consequent flare up of medical challenges related to these drastic abnormal-behavior ***H. pylori*** strains. It might seem that the antibiotic violence has rendered a domestic bacterium to become wild in attitude and sequels instead of getting rid of it. The challenge of autism first appeared before the lastest three decades but it has mostly dominated during these last three decades (Li& zhou, 2016; Farinha& Gascoyne, 2005; Nasrat et al., 2015a; Aksoy& Sebin, 2015; Nasrat et al., 2015g; Nasrat et al., 2017).

The literature reports indicate increased risk and rising prevalence of identified ASD among U.S. children. An investigator with his 45 collaborators reported in 2009 that the increased prevalence of identified autism among U.S. children need to be regarded as an urgent public health concern (Galichi et al., 2016). The reason that autism prevails among U.S. children could be most probably related to the fact that U.S. is a typical country of fast food dependency and the food handlers are mostly poor people migrating from poor developing countries with inadequate health care standards carrying with them abnormal-behavior ***H. pylori*** strains (Farinha& Gascoyne, 2005; Nasrat et al., 2015a). According to some personal communications; some mothers of autistic children indicated frankly that they love fast food to the extent that some particular fast food meals run in their blood while some mothers admitted that they are lazy to cook when they are pregnant and they depend on outside-home meals. Others mentioned that when they get pregnant while the previous baby is still between 2-3 years old, they depend mainly upon fast food delivery for themselves and their kids (Nasrat et al., 2017).

Summary

In Summary, realization of the real clue of a challenging illness constitutes the main success in its management; the hypothesis of the toxic influence of elevated serum ammonia in leading to the onset of an autistic behavioral disorder might remain just hypothetical until approved or disapproved but the unsolved puzzle of ASD has been considered as a "sequence" rather than a syndrome (Casanova et al, 2013). Apparently, the current available literature knowledge might seem articulating together without any little dislocation to support a concept that the spread of the abnormal-behavior/existence colonic ***H. pylori*** strains could just lie hidden behind the pathogenesis of a complex sequence of spectral events leading to the prevailing challenge known as the disorder of autistic spectrum. Therefore; research investigators should feel quite very enthusiastic towards this concept in order to support and approve or disapprove it for the sake of the possibility to alleviate misery of many kids and families of autistic children. Prevalence of the abnormal-behavior ***H. pylori*** strains followed the antibiotic violence towards this bacterium during the last three decades while flare up of medical challenges related to these ***H. pylori*** strains started also during the latest three decades; autism could be simply one member among these disease challenges. Autistic behavioral syndrome appeared earlier than the last three decades possibly also because of antibiotic abuse but it has dominated and flared up during the late decades. Antibiotic exposure was suggested as a factor leading to autism, the association of GI troubles and autism is frank and constant, development of autistic features or loss of developed skills occurs at the typical age where children could gain abnormal ***H. pylori*** strains trans-familial from their parents, ***H. pylori*** in the stomach was suggested to lead a behavior of natural bacteria while the role of microbiota and probiotics in autism is strongly suggested in literature, the elevated serum level of ammonia among autistic children is constant in most scientific reports and the toxic effect of ***H. pylori***-produced ammonia on the

whole brain conforms with the hypothesis of entire brain compromise suggested to explain inability of autistic children to perform complex interactions; all these findings seem quite articulated together to refer to the pathogenic influence of the abnormal ***H. pylori*** strains in the development of autism.

Accordingly, it seems that autism might not be a disease of definitive cure due to a permanent compromise of areas of the brain responsible for development of skills caused by a sustained toxic influence of ammonia throughout a critical period of brain growth during a child's early life. For this reason, scientific research efforts were just able to get improvement of autistic behavioral symptoms but did not achieve a real or definitive cure of autism. On the other hand, autism could be a typical disease of definite prevention via extreme carefulness towards outside-home meals, restriction of antibiotic use unless seriously indicated and natural colon care/colon clear for mothers who develop ***H. pylori***-related dyspeptic symptoms before or during pregnancy also while nursing their kid's during the early critical ages of child's growth. Early diagnosis and management of autistic features in a child could greatly improve the out-coming results of the attempts to correct the condition through colon clear for the kids themselves. Accordingly; the next kids after an autistic one could be simply at least saved from the disease as the matter of ***H. pylori*** is an environmental sanitary conflict before it is an actual medical challenge and prevention remains always far better than treatment.

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Conflict of interest

No conflict of interest is existing.

Conclusion

Autism, when established, might not be a disease of definitive cure due to permanent compromise of some areas of the brain responsible for development of skills during a critical period of a child's brain growth but it could be a typical disease of definite prevention. The value of this review study is the promising opportunity it gives for a child when discovered at the early prodromal symptoms to recover and skip the disease or at least next kids of an autistic one could be saved from developing autism via colon clear for parents.

The anti-***H. pylori*** antibiotic strategies might need to be subjected to extreme scientific revision and severe accurate re-determination owing to the possibility of having rendered an innocent biologic bacterium to become wild in attitude and sequels instead of getting rid of it.

Potent natural measures should be employed in order to control the challenge of ***H. pylori*** and functional dyspepsia instead of antibiotics.

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HELLP Syndrome, the Importance of Doppler Intervention

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Abstract

WHO has classified Preeclampsia a cause of maternal mortality and morbidity worldwide as Preeclampsia is remaining one of 5 pregnancy diseases cause morbidity and mortality as well in Albania [2]. The neurological complications of preeclampsia and eclampsia are responsible for a major proportion of the morbidity and mortality for women and their infants alike. HELLP syndrome are a group of disorders related to endothelial damage triggered by pregnancy. Hormonal changes during pregnancy and the puerperium carry an increased risk of venous thromboembolism including cerebral venous sinus thrombosis (CVST). I have reported a patient with CVST at 37th week of pregnancy and was diagnosed as HELLP syndrome at 34th week of pregnancy and the case trough intensive care at Obstetrics and Gynecology University Hospital "Mbretëresha Geraldinë" in Tirana through a very well control protocol of treatment with a successfully determination.

Keywords: Syndrome, HELLP, Importance, Doppler, Intervention

Introduction

WHO has classified preeclampsia a cause of maternal mortality and morbidity worldwide [1]. Preeclampsia is remaining one of 5 pregnancy diseases cause morbidity and mortality as well in Albania [2]. The neurological complications of preeclampsia and eclampsia are responsible for a major proportion of the morbidity and mortality for women and their infants alike. Hormonal changes during pregnancy and the puerperium carry an increased risk of venous thromboembolism including Cerebral Venous Sinus Thrombosis (CVST). The pregnancy-related syndromes of

preeclampsia, eclampsia, and HELLP syndrome are a group of disorders related to endothelial damage triggered by pregnancy. Preeclampsia is defined as gestational hypertension (blood pressure ±140/90 mmHg) with proteinuria >0.3 g/24 hours. It is seen in about 3–8% of all pregnancies [3]. Cerebral venous sinus thrombosis is a frequently unrecognized cause of stroke affecting predominantly young women. Its typical clinical signs include headache, visual problems, and seizures. I have report a patient with CVST at 36th week of pregnancy and was diagnosed as HELLP syndrome at 36th week of pregnancy.

Case Presentation

A 29-year-old woman, gravida 2 was admitted to Obstetrics and Gynecology University Hospital "Mbretësha Geraldinë" at 36th week of gestation with headache and blurred vision. On ophthalmological examination was done and there was bilateral papilledema and visual field loss was detected. At 34th week of gestation, she was hospitalized for high blood pressure, headache, nausea, and vomiting. The blood pressure was 220/140 mmHg and laboratory findings were as follows: aspartate transaminase (AST): 227 U/L, alanine transaminase (ALT): 221 U/L, INR: 1.7, white blood cell (WBC): 13.100 U/L, hemoglobin (Hb): 14.7 gr/dL, thrombocyte count (PLT): 164000 U/L, and 3+ proteinuria in the urine analysis. Hematological and urinary parameters were consistent with severe preeclampsia. It was recommended a magnetic resonance imaging of the brain revealed CVST was diagnosed as HELLP syndrome at 36th week of pregnancy. An anticoagulant treatment with enoxaparin sodium 0.6 mL has started immediately. Hematological investigations showed thrombophilia She underwent cesarean section at 37th week of gestation due to severe preeclampsia. By cesarean section, a baby weighing 1280 g with 1 minute APGAR 9 and 5 minute 10 APGAR scores was delivered. The patient had no significant bleeding during and after cesarean section, but atony-related postpartum hemorrhage developed at 12th postoperative hour. Laboratory investigations showed WBC: 21000 U/L, Hb: 7 gr/dL, PLT: 59000 U/L, AST: 1347 U/L, and ALT: 681 U/L. Due to postpartum hemorrhage, uterine massage was performed and uterotonic drugs were administered. The patient received 8 units of whole blood. At 10th postoperative day, she was discharged from the intensive care unit and monitoring continued in the clinic. Laboratory tests and blood pressure returned to normal at 10th postoperative day. Headache and blurred vision did not improve and bilateral papilledema still existed. The patient was started paracetamol and enoxaparin sodium. A CT venogram showed canalized sinus thrombosis. She was discharged and followed up for one month.

Discussion

Pregnancy is a hypercoagulable state. The tendency to thrombosis, has been developed rapidly and has been linked to many aspects of pregnancy. The combination of combined oral contraceptive and thrombophilia greatly increases the risk of CVST. [4]. In our case, there was a history of oral contraceptive used. Recurrent miscarriage has been associated with thrombophilia and pregnancy complications such as severe preeclampsia, intrauterine growth retardation, abruptio placentae, and stillbirth may be associated with thrombophilia [5,6]. My patient had a history of contraceptive uses, no preeclampsia and sinus thrombosis. Thrombophilia are inherited or acquired conditions which predispose an individual to thromboembolism. Deficiencies of protein S, protein C, and antithrombin are rare and each of them is found in about 3% of patients with thrombosis. Heterozygosity for the FVL mutation is found in about 5% of the population and the mutation is responsible for 20–30% of venous thromboembolic events [7,8]. Due to the rapid evaluation the heterozygous factor V H1299R mutation was not identified.

The main clinical manifestations of CVST include papilledema (62%), headache (62%), hemiparesis (48%), seizures (31%), and cranial nerve palsy (7%). Patients are managed with heparin (Enoxaparin 0,6) followed by warfarin for 6 months. Death due to CVST has shown remarkable reduction because of early diagnosis and appropriate anticoagulation [9].

Patients with CVST may develop—as well as sometimes present with—chronic intracranial hypertension with headache and papilledema. The priority is prevention of visual function loss; intracranial hypertension should be controlled with acetazolamide and occasionally with repeated lumbar punctures if vision is still threatened. Refractory cases may need a cerebrospinal fluid shunting procedure . My patient is improving with medical treatment but this measure should be in consider for the future. Thrombophilia and CVST are rarely encountered conditions during pregnancy and augment the risk of life-threatening maternal complications and adverse perinatal outcomes in preeclamptic patients [10]. Therefore, the etiology of thrombophilia should be investigated in a timely manner. Further signs of increased intracranial pressure should be monitored closely.

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Use of Concentrated Growth Factor (Cgf) in Reconstruction on Two-Wall Bone Defect After Cystectomy, An Alternative to Traditional Regeneration- Case Report

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Abstract

Aim: The purpose of this clinical case report was to describe an alternative technique performed to ensure bone regeneration after removing a cystic lesion in the upper jaw. Bone defect after cystectomy was filled with autologous fibrin rich clots containing CGF. **Materials and methods:** A 45 years old female patient was suspected to have a cystic lesion with massive bone destruction on the vestibular and palatal walls between teeth

2.2 and 2.3. Concentrated growth factor (CGF) was used to cover the defect in order to favourite the bone grow. **Results:** After 12 months, the clinical and radiological follow-up examination showed that the tooth was asymptomatic and that the healing was in progress. **Conclusions:** this article describes a different way to treat a two-wall defect involving both the palatal and buccal bone, after removing a cystic lesion, with the use of CGF as an alternative to traditional use of autologous or heterologous bone. CGF fibrin could promote new bone formation in jaw defects, with benefit to the healing of bone tissue and, thus, is a promising bone repair material.

Keywords: jaw cysts; platelet-derived growth factor; cgf;

Introduction

Bone regeneration processes are highly dependent on the range and extent of the defect, provided that coagulum formation process is not impaired. The average healing time of small cystic defects is usually up to one year, while healing time extends with the size of a defect, ranging from two to five years for medium-size and large cysts [1]. After removal of cystic sac and closing the wound primarily, the bone defect is filled entirely. The initial blood clot formation is followed by clot retraction and serum extrusion, this producing peripheral serum-filled spaces between bony wall and coagulum surface. This significantly interferes with protrusion of vascular epithelium and the healing process. On the other hand, the space formed by the removal of dental cysts usually provides favourable conditions for microbial growth and a risk of infection. Therefore, stabilization of blood coagulum and preservation of primary healing has been accomplished by several methods, such as autotransplantation, allotransplantation, xenotransplantation, or application of autologous platelet concentrate (APC) and concentrated growth factor (CGF) procedures [2]. Growth factors are proteins, which regulate complex processes during wound healing. Growth factors are mainly located in blood plasma and platelets, and perform an important role in cell migration, cell proliferation and angiogenesis during bone regeneration[3]. Most important and representative growth factors are: platelet derived growth factor (PDGF), transforming growth factor (TGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF) and insulin like growth factor 1 (IGF 1) [4,5].

The first generation of platelet concentrates are Platelet Rich Plasma (PRP) and Plasma Rich in Growth Factors (PRGF). PRP and PRGF require chemical additives, such as anticoagulants and thrombin or calcium chloride, to induce fibrin polymerization before applying to the surgical site. Platelet rich fibrin (PRF) and concentrated growth factors (CGF), as second generation of platelet concentrate, utilize patient's venous blood alone to trigger platelet activation and fibrin polymerization.

Concentrated GF (CGF) was developed by Sacco in the year 2006[6].

CGF is a therapeutic protocol that shows higher tensile strength, more growth factors, higher viscosity and higher adhesive strength than PRF. The use of autologous fibrin does not cause any side effect and it is a safe and simple procedure for a specialist, and inexpensive and efficacious for the patients[1].

Concentrated growth factor is mainly used in bone regeneration[7].

CGF fibrin could promote new bone formation in jaw defects, with benefit to the healing of bone tissue and, thus, is a promising bone repair material. A variable-speed centrifugation strategy with physical acceleration and deceleration, at constant temperature, was used to fully activate alpha-granules in platelets and produce autologous blood products enriched with greater concentrations of growth factors compared with PRF and hematopoietic stem cells (CD34+ cells)[8].

CGF acts by degranulation of the alpha granules in platelets which play a vital role in early wound healing[9]. It has been found that CGF contains more GFs than other platelet-based preparations such as platelet rich fibrin (PRF) and platelet-rich plasma (PRP), and unlike PRP, CGF does not dissolve rapidly following application[10].Qin et al. proved that CGF could release GFs for at least 13 days[11].

MATERIAL AND METHODS: CASE REPORT

A female 45 years old, was presented with pain and swelling in the anterior upper jaw region. Clinical examination revealed swelling in the lower vestibule, painful and fluctuant to palpation. The mucosa above the swelling was regular in colour and moisture.

Subsequent to the clinical examination, orthopantomography (OPT) and Cone Beam Computed Tomography (CBCT) scans were taken, showing a clearly demarcated oval radiolucency, localized in the anterior region of the upper jaw (Fig. 1), and indicating massive bone destruction on the vestibular and palatal walls between teeth 2.2 and 2.3.

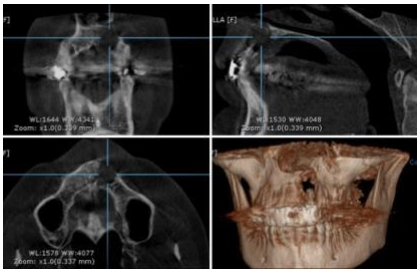

Fig. 1 pre-operative CT scan

Preoperatively, the patient was fully informed about the surgical protocol and personally signed and dated the consent form before treatment. A prophylactic oral antibiotic (Augmentin 1 g.) was used, beginning one day prior to the procedure and continuing for five days postoperatively. Before the surgery, the patient rinsed her mouth with an antiseptic mouthwash containing 0.2% chlorhexidine digluconate to reduce the risk of contamination of the surgical field. Under local anesthesia a vestibular triangular flap access was made, with one horizontal incision and one vertical incision, the latter located distally to tooth 1.1 Endodontics on 2.2 was done 1 week earlier (Fig. 2).

Fig 2 periapical rx on #22 taken after root canal therapy

A full thickness flap was elevated and it was irrigated continuously to prevent dehydration of the periosteum. Following flap elevation, evidence of buccal bone fenestration was clearly detected. Following cystectomy, root resection of the affected tooth 2.2 was done (Fig. 3). The resulting bone defect was restored by placing *two fibrin-rich blocks* with CGF, which completely filled the bone cavity.

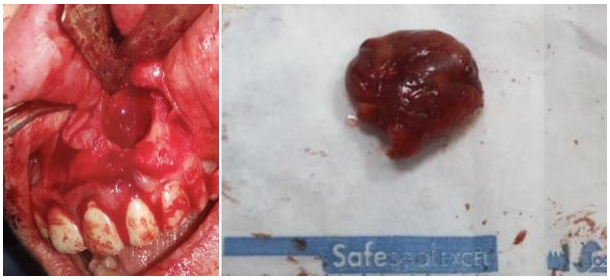

Fig. 3 Resulting bone defect after cystectomy

20 CC of patient's peripheral venous blood was taken from patient's vein, and was used to fill 2 tubes (without anticoagulant) each of 10 mL. The CGF was prepared following the instructions provided by the manufacturer (Silfradent, Medifuge MF200, Italy).

The resulting bone defect was restored by placing *two fibrin-rich blocks* with CGF, which completely filled the bone cavity. 20 CC of patient's peripheral venous blood was taken from patient's vein, and was used to fill 2 tubes (without anticoagulant) each of 10 mL. The CGF was prepared following the instructions provided by the manufacturer (Silfradent, Medifuge MF200, Italy).

The tubes were placed at the two opposite sides of the centrifuge and immediately centrifuged in the following manner: 30'' acceleration, 2' 2700 rpm, 4' 2400 rpm, 4' 2700 rpm, 3' 3000 rpm, 36'' deceleration until end. At the end of the procedure, four layers are obtained from bottom to top: RBC layer, GF and stem cell layer (CGF), Buffy coat layer, serum layer (PPP). The CGF layer is separated using sterile surgical scissors (Fig. 4). The CGF clot is then squeezed in a special box at a thickness of 1 mm. The CGF is then placed over the target site.

Fig. 4 Preparing CGF

In order to mobilize the flap and facilitate its repositioning, periosteal incisions were performed, releasing muscle tension. The reflected tissues were then replaced into their original position (Fig.5) and sutured with a resorbable 5-0 suture (Ethicon Inc., Piscataway, NJ, USA). After surgery, the patient was advised to avoid mouth rinsing, hard and hot food, hot drinks, heavy physical work, and tooth brushing on the day of

surgery. The patient was instructed to rinse his mouth twice daily with 0.2% chlorhexidine digluconate for plaque control up to 10 days after surgery.

Non-steroidal analgesics (ketoprofen) were prescribed for pain relief if needed and steroidal ones (Bentelan 1mg cp), with decreasing dosage were prescribed after the surgical procedure, for swelling control if needed. Sutures were removed seven days after surgery. After 12 months of follow-up, the tooth was asymptomatic on clinical examination and a radiographic evaluation showed that healing was in progress.

Fig. 5 after surgery

Results

CGF contains high concentrations of platelets, large amounts of fibrinogen, various growth factors, and CD34+ cells. New bone tissue, of satisfactory quality (density) and quantity, is formed within 12 months, and it's associated with minimum postoperative complications (Fig.6).

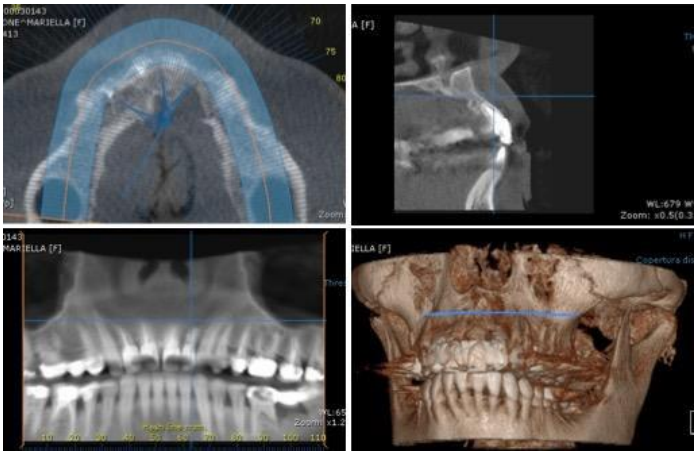

Fig. 6 post-operative CT scan

Conclusion

Moreover, the procedure is economically acceptable to the patient. CGF was applied to the bone defect area of the jaw, and 2 biochemical indicators, (osteocalcin and BAP) were used to clarify the concentration of the growth factor fibrin. BAP is an osteoblast marker active in the process of bone tissue repair.18,19 Osteocalcin is a bone matrix protein synthesized by osteoblasts. BAP and osteocalcin both reflect the osteogenesis status of osteoblasts.20 Increased levels of osteocalcin promoted bone healing in the patients with jaw fracture and bone defects. CGF might have both osteoconductive and osteoinductive capabilities and constitute a complementary functional repair material that is highly biocompatible and allows cells to secrete a variety of specific proteins that promote bone formation. Thus, CGF would have the dual abilities of bone guidance and osteoinduction. Histologic observations showed that more preosteoblasts and osteoblasts were seen in the CGF group 4 weeks after surgery. Also, more new bone tissue was present in the CGF group than in the control group, which could have been related to the high concentration of growth factors released by CGF.

The CGF membrane was placed in the defect in the jaw bone, and the released growth factors guided the body's undifferentiated mesenchymal cells to chemotaxis, adherence, and differentiation to the surface of the bone defect, relying on fibrinogen and other biologic materials as scaffolds to gradually proliferate, mineralize, and fuse the bones to achieve the goal of new bone formation. At 8 weeks postoperatively, a large number of flaky new bone formation was observed in the CGF group. In contrast, the new bone area in the control group was small.

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Diet, Physical Activity and Body Condition of Young People

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Abstract

The promotion of a healthy lifestyle and nutrition education programs that aim the correction of the improper nutritional habits, present one of the prior principles in the WHO educational strategies for human health.The goal of this study is the development of a database with regard to the nutritional teenagers attitude in its quantitative aspect (food consume) and qualitative (nutrition style) as a necessary demand for the planning of the nutritional and sanitary education interventions. In this study are enrolled 721 children aged 14-19 years old from the secondary schools district of Tirane (selected according to four categories :sex, age ,economic level and residence zone) This study made possible for the first time the calculation of the average values of the daily energy intake for this age group and evaluation of the diet in qualitative aspects. The values of the daily energy intake are lower that the recommended norms of the WHO, mainly in the males/ rural zones and with a tendency for a non equilibrated nutrition in the population with scarce economic level. The diet is a typical Mediterranean one with some light deviations with regard to the frequent consumes of the bread, milk and fish according to the recommended values.

Key words: educational, prevalence, healthy food, qualitative life, nutrition.

Introduction

Promoting a healthy lifestyle and nutrition programs on education in order to correct the wrong food habits, the principles represent a priority in health education strategies. C. Price, D. Cohen, P. Pribis, and J. Cerami (2017)

From recent studies on the mode of nutrition in adolescents show that their diet is characterized by nutrition mistakes that are recognized as responsible for the development of chronic diseases, especially cardiovascular. These data and the fact that the prevalence of obesity is essential in pediatric age is steadily growing, indicate the need for appropriate interventions undertaken in the field of nutrition. M. Racey, C. O'Brien, S. Douglas, O. Marquez, G. Hendrie, and G. Newton (2016)

An important factor determining the health is physical activity. Impact of inactivity izik is increased risk for developing chronic diseases. M.C. De Menezes, L.B. Bedeschi, L.C. Dos Santos, and A.C.S. Lopes (2016)

The emphasis is on new population that is prone to change their behavior and where future interventions are likely to give maximum effect in terms of health.

Methodology

This is a transversal study in which were included 721 students aged 14-19 years. Participants in the study follow the education system in Tirana. Specific weight of the number of secondary school students in Tirana, the report defines urban / rural: 73% / 27%. This geographic distribution is conditional on drawings in order extrapolation of information for youth hanger subpopulation high school in Tirana, T. Forneris, at all. (2010) young age varies from 14 years old 19, but most (81%) belong 15-18 years age group. Pupils completed a detailed questionnaire on food consumption frequency. Consumption frequency questionnaires that consist in recording the frequency of food enterprises and their quantitative analysis, based on memory, aided by visual presentation of food portions with sides atlases. R. Amani, and M. Soflaei (2006) The basic principle of this method is that the average diet for a long period, eg. making weekly, monthly or yearly exhibition is conceived as an important in relation to the making of a few days. D. Wang, D. Stewart, Y. Yuan, and C. Chang (2015) The questionnaire is divided into three parts. The first part contains general data of the respondents. The second part includes questions about nutrition, foods and their frequency of consumption and the third part includes questions on physical activity of young people. All data analysis was performed using the statistical package SPSS (Statistical Package for Social Sciences, version 20.0) and M. Office Excel 2010. Pearson correlation coefficients were used to estimate the linear relationships of numerical variables, where they were considered statistically significant values $p \leq 0.05$.

Results and discussion

It is noted that 69.2% of respondents to the question **If last year you eat out of the ordinary, give reason why?** *Responded that they did not significantly change in the way of eating versus 30.8% who responded that they had changed the way of nutrition.* This change in diet because women (51%) is more evident in comparison with males (33%) explained that even with the higher tendency of women to guard against obesity.

Graphic no1 Differences diet in total

Graphic no2 Differences in diet between genders

Graphic no3 Physical activity in young people

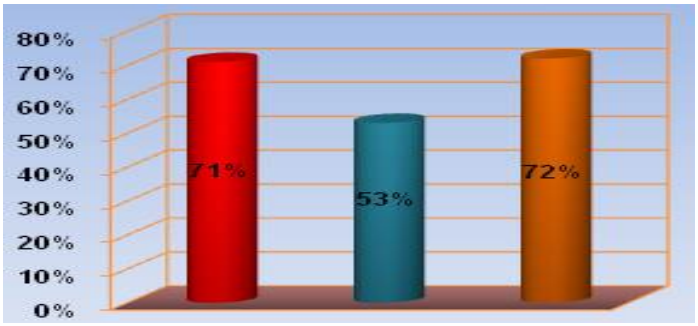
For the first time this study provides data on the daily average ranging kalorazhin: boys-2647 kcal / day, girls - 2545kkal/day, values according to town / village: 2619 / 2548 kcal / day, because this difference that the economic level that area exists between urban / rural areas in Albania. There is also a difference according to level of kalorazhit economic level of well-2666 kcal / day Average -2572 kcal / day Slender-2884 kcal / day, the trend values the highest level of young people that refer to weak economic security as a result of the biggest part of energy from cereals (mainly bread, diet food base that Albanian former -70% of the total calorific).

2657 KCAL/ DAY BOYS

2545 KCAL/ DAY GIRLS

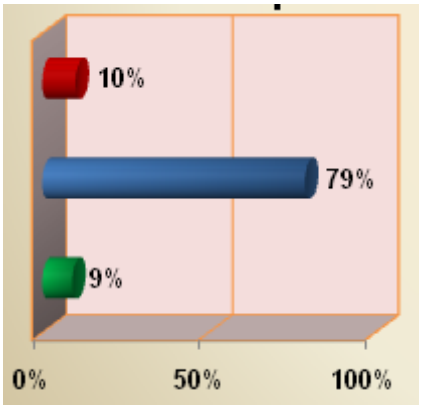
The study also points to an active life of our young people, 71% of them make rapid walking in step with> 2 hours in week, 53% regularly use bicycle, and 72% of them participate in organized sports activitie; 2 hours in week. H.S. Yuksel, F.N. Şahin, N. Maksimovic, and P. Drid Bianco, (2020)

Graphic no 4 Reported values on body weight perception



71% rapid walking 53% bicycle 72% sports activitie

Logical and realistic reflection of enterprises caloric and physical activity level values are also reported body weight perception, where only 9% of young people feel at risk for overweight, 79% feel normal and 10% do not know.



9% risk for overweight 79% feel normal 10% do not know

Regarding the food that we often found with the youth daily menu, they are: bread and other cereals (95.55%), fruits and vegetables (84%), cheese (64%, but with a very low daily intake of 17% milk), meat (mostly white meat and red 48%), but with a lower consumption of fish (15%) due to higher prices in the spot trading market. There is a tendency to use for cooking fats of plant origin mainly sunflower oil and olive oil, low consumption of alcohol (about 38.7% claim not to have ever consumed beer or wine and 23% <1 time / month).

Conclusions

-The study of the mode of nutrition of young people in our country allowed, for the first time, the calculation of average values for this age group calories day and in the assessment of diet quality plan.

- It is noted that caloric intake are lower than rates, (8) expressed in these particular male sex / rural areas and with a tendency towards unilateral feeding in layers with weak economic level.

Be the corresponding diet typical Mediterranean (Albania is also a Mediterranean country) with some minor deviations in terms of frequency of consumption of bread, milk and fish in relation to the recommended values.

- Albanian youths continue to make an active life in terms of level of physical activity and a low intake of alcohol.

- The data obtained will serve as an important basis in the planning and implementation of future programs in nutrition education, promoting a healthy lifestyle and prevention of illnesses from malnutrition.

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The World's Burden of Diabetes During the Latest Three Decades

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Abstract

The World's Burden of Diabetes During the Latest Three Decades Might Not Be on the Account of Type II Diabetes but on Potential Stress Diabetes; Type II Diabetes is Not Curable While Stress Diabetes Could Be Corrected. **Aim:** Demonstration of an observational association between the flaring challenge of ***Helicobacter pylori*** and the spreading world's diabetic phenomena during late three decades so that control of diabetes spread could be possible. **Background:** The spread of DM is rising all over the world in a dramatic way same as the fire spreading in hey especially in developing countries giving the term "diabetic epidemic" an actual credibility. The late three decades demonstrated rediscovery and antibiotic aggression towards ***H. pylori***, development of migrating ***H. pylori*** strains and flare up of diabetes mellitus. Any study which does not correlate between these findings of the last three decades is definitely not employing any clinical sense. ***H. pylori*** could be forced to migrate to the colon under the influence of the antibiotic violence with consequent accumulation of profuse toxic amounts of colonic ammonia unopposed or buffered by any acidity leading to a biological toxic stress to the body that could predispose to stress diabetes among disadvantaged susceptible population. Administration of oral hypoglycemic pills to a stressed pancreas constitutes an insistence to flog a tired horse turning a potential condition into an established chronic illness with consequent flare up of the diabetic phenomena all over the world. **Conclusion:** The world's spread of diabetes during latest three decades might not be on the account of type II dibetes but stress diabetes due to a potential toxic stress signifying that the diabetic condition could be corrected and the world's diabetes spread could be readily and adequately controlled.

Keywords: ammonia, diabetes, Helicobacter pylori, stress diabetes, type II diabetes.

Introduction

The widespread prevalence and the challenges constituted by ***Helicobacter pylori***; namely its close relation to acid peptic disease, gastric carcinoma and lymphoma have led to the widely-established improper unjustified medical concept that ***H. pylori*** eradication should be a necessary attempt. Although eradication regimens apparently eradicate ***H. pylori*** from the stomach; the emergence of antibiotic-resistant ***H. pylori*** strains, the severe side effects and the high costs are major drawbacks of these treatments particularly if it is proved that these

medications do not readily eradicate the bacterium but actually force it to migrate from the stomach elsewhere where adverse sequels could begin. The exact prevalence of the abnormal-behavior/existence migrating ***H. pylori*** strains constitutes lately more than 80-90% among population of developing countries (Volk et al, 1996; Farinha& Gascoyne, 2005; Nasrat et al., 2015a). More efficient, economic and friendly drugs need to be developed.

The latest reports in literature demonstrate a definite flare up of many medical challenges strictly related to ***H. pylori*** existence through immune or different unknown reasons. Autoimmune thyroiditis, autoimmune pancreatitis and idiopathic thrombocytopenic purpura are examples of these challenges (Farinha& Gascoyne, 2005). The flare up of these ***H. pylori***-related medical challenges is sufficient to denote that the current combined antibiotic eradication strategies are inadequate to control all the problems associated with the stomach bacterium.

H. pylori colonized the stomach since an immemorial time (Farinha& Gascoyne, 2005; Nasrat et al., 2015a); as if both the stomach and the bacterium used to live together in peace harmless to each other; what does this could mean!! Could ***H. pylori*** be a ntural innocent bacterium and falsely committed with pathologic crimes which are not induced by its own or it has been forced against its nature to the pathologic sequels related to it!! Could ***H. pylori*** have a real biologic function that could issue its innocence certificate!!

Aim

Demonstration of an observational association between the flaring up challenge of ***H. pylori*** and the spreading world's diabetic phenomena during late three decades so that control of diabetes spread could be possible.

Review

DM in developing countries has been lately described as the fire when spreads in hay giving the title "diabetic epidemic" an actual credibility (Al-Nozha et al., 2004 Nov). Traditional risk factors do not appear fully sufficient to explain this dramatic spread of diabetes in these countries; in a way that further indicates that the traditional measures employed to control the spread of the disease would never be adequate or decisive (Nasrat et al, 2015b).

The ill-decisiveness and the obvious length of the current ***H. pylori*** eradication treatment courses allowed the chance to the stomach bacterium to mutate or develop drastic or resistant strains. In addition, the aggression made by antibiotics could have forced this bacterium to hide or migrate where it could influence or compromise the immune system. (Farinha& Gascoyne, 2005; Nasrat et al., 2015a). Frankly and in scientific words, if ***H. pylori*** is a natural bacterium entitled for a biological function in the gut, then no power could overcome it except forcing it to migrate from its normal habitat of natural function where its biological value is sacrificed while complications and undesired pathologic dilemmas could rise up somewhere else (Nasrat, 2017).

DM, a disease of rich, which was once considered a disease of the developed world has become a worldwide pandemic resembling an ocean tusnami wave flooding the whole world with two thirds of the poor diabetic population living over the developing side of the globe. (Katulanda, 2006; Wissow, 2006). As much as the precise statistical revision strongly correlates between the prevalence of ***H. pylori*** and the flare up of DM in developing countries, it also reveals that the diabetic challenge was not as such in these countries before the antibiotic violence towards

H. pylori (Hossain et al, 2007; Einecke, 2006; Yach, 2006). The literature reports indicate that most of the diabetic patients in the world are inadequately controlled in spite of regular follow up of medications and extreme carefulness about style of life that could mean existence of a missed underlying environmental error influencing the challenge of diabetes (Nasrat et al, 2015b).

Discussion

A lot of controversy has been encountered as concerns the current strategies for ***H. pylori*** eradication. The efficacy of ***H. pylori*** eradication strategies, the appropriate length of treatment and the cost effectiveness, all appear controversial (Ikeda, 2001; Mason, 2002). Further reports in literature have devaluated the triple therapy and suggested a quadruple one (Songür, 2009).

H. pylori recurrence; whether it is gastric recurrence from dental plaques, fecal-oral recurrence or recurrence via meals is hardly avoidable (Nasrat et al, 2015a). The current antibiotic therapies appear to be successful only in forcing ***H. pylori*** outside the stomach to recur later or migrate and hide elsewhere mostly in the colon. The migrated ***H. pylori*** strains in the colon would continue producing ammonia for a reason or no reason leading to accumulation of profuse toxic amounts of ammonia, un-opposed or buffered by any acidity; this matter could constitute a biological toxic stress to the body that could lead to stress diabetes. Administration of traditional oral hypoglycemic pills to a stressed pancreas means an insistence to flog a tired horse leading to turn a potential condition into an established chronic illness with consequent dramatic flare up of the diabetic phenomena all over the world (Nasrat et al, 2015b).

A comparative study done in 2015 has demonstrated superiority of natural measures in the form of the potent naural senna purge extract and vinegar therapy over the anti-***H. pylori*** antibiotic eradication strategies (Nasrat et al., 2015c). The effectiveness and safety of natural measures in the management of the challenge of ***H. pylori*** have been also emphasized in further studies (Nasrat et al., 2015d; Nasrat et al, 2015e).

In a further study in 2015, the newly discovered diabetic condition has been successfully and permanently corrected in most patients of the study, 16 patients out of a total of 18 patients (88.9%), via mere colon care and colon clear employing natural measures namely the potent senna purge and vinegar therapy (Nasrat et al., 2015b).

In the light of the accurate determination of recent findings and statistics, a revision of the current guidelines for the management of ***H. pylori*** and newly discovered DM might be needed. It might be incorrect that the current world's burden of DM is on the account of type II diabetes. It seems that the antibiotic violence has obliged a domestic bacterium to become wild in attitude and sequels instead of getting rid of it. The stress element caused by the accumulated toxic amounts of colonic ammonia in leading to an onset of diabetes is not just hypothetical as upon the basis of this concept the diabetic condition has been readily and adequately corrected in good number of newly-discovered diabetic patients. (Nasrat et al., 2015a; Nasrat et al., 2015b).

Summary

H. pylori colonized the stomach since an immemorial time and it is leading in the stomach the natural behavior of biological bacteria in the gut. It seems clear that it is true whenever man

interferes severely in the nature dilemmas are brought up. ***H. pylori*** escapes from the stomach sacrificing its biological function in the stomach to do the good biological job in an improper site (Farinha& Gascoyne, 2005; Nasrat et al., 2015a). The onset and flare up of stress diabetes all over the world during the latest three decades due to accumulation of colonic ammonia of the migrating colonic ***H. pylori*** strains in profuse toxic amounts consequent to a third world antibiotic medical war against an innocent bacterium is not just a scientific fantasy as upon this concept the diabetic condition has been readily and permanently recovered among many newly-discovered diabetic patients via mere natural colon care and colon clear (Nasrat et al., 2015b; Nasrat et al., 2015f).

Acknowledgement

This study appreciates the clinical support of Zaitona Medical Cupping Center in Medina.

Conflict of interest

No conflict of interest is existing.

Conclusion

The world's spread of diabetes during the latest three decades might not be on the account of type II diabetes but on stress diabetes due to a potential toxic stress caused by accumulation of potential toxins in the colon signifying that the diabetic condition could be corrected and the world's diabetes spreading challenge could be readily and adequately controlled as type II diabetes is not curable while stress diabetes could be recovered.

It is worthy if this hypothetical concept of stress diabetes all over the world during the latest three decades and its direct etiologic association with the migrating ***H. pylori*** strains could find the attention of research investigators for its further assessment, revivision and accurate re-determination as rendering this concept valid would be quite promising for the welfare of the global healthcare.

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Consumption of Insulins in Primary Health Care in Albania during 2010-2020

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Abstract

Aim: evaluation of trends in out-of-hospital utilization and to prescribe of Insulin in Albania using the Anatomic Therapeutic Chemical Classification/ Defined Daily Dose -(ATC/DDD methodology). Methods: The study was retrospective, and we analyzed the data collected from Health Insurance Institute (HII) of these drugs classes in the primary health care in Albania during 2010-2020. The data about the consumption of drugs were expressed as a number of Defined Daily Dose (DDDs) /1000 inhabitants/day. For all the period under study 2010-2020, there were collected and analyzed data of import and domestic production of drugs, which represent the real consumption of drugs in the country. These data were subsequently included in a comparative analysis with the utilization data according to the Health Insurance Institute. Results: The consumption of all insulin were 3.49-10.66 DDD/1000 inhabitants/day (respectively 2010-2020). The consumption of insulin fast-acting were 1.58-4.93 DDD/1000 inhabitants/day (respectively 2010-2020). The consumption of insulin intermediate-acting were 0.56-1.06 DDD/1000 inhabitants/day (respectively 2010-2020). The consumption of insulin intermediate-acting combined with insulin fast-acting was 1.00-1.46 DDD/1000 inhabitants/day. The consumption of insulin long-acting was 0.34-3.21 DDD/1000 inhabitants/day. Conclusions: There is an increase in Insulin use from HII covering but still low values in comparison with other countries.

Keywords: Drug utilization DDD, Insulin

Introduction

Diabetes mellitus (diabetes) is a chronic and potentially life-threatening condition where the body loses its ability to produce insulin, or begins to produce or use insulin less efficiently, resulting in blood glucose levels that are too high. Over time, blood glucose levels above the normal range can damage your eyes, kidneys and nerves, and can also cause heart disease and stroke.

With type 1 diabetes, the body does not make any insulin and therefore insulin has to be injected regularly every day to stay alive. With type 2 diabetes, the body does not make enough insulin, or the insulin that is made does not work well. Insulin injections are sometimes needed to manage blood glucose levels. Insulin is grouped according to how long it works in the body. Rapid- or short-acting insulin helps reduce blood glucose levels at mealtimes and intermediate or long-acting insulin helps with managing the body's general needs.

Insulin therapy is an essential part of diabetes management; all type 1 and most type 2 diabetes patients require insulin at some stage. Drug utilization studies using administrative pharmacy claims data can provide useful insights into the prescribing patterns and patient medication-taking behavior in typical usual-care settings [Okano GJ 1997, Venturini F 1999]. Thus, pharmacotherapy has the potential for significant clinical, economic, and humanistic impact. For these reasons takes a great importance the evaluation of drug utilization parameters associated with pharmacological management of type 1 and two diabetes among members of a large drug-insured population.[Kakariqi et al. 2016]

Materials and Methods

The data were obtained from the Health Insurance Institute (HII) [http://www.fsdksh.com.al, *last accessed July, 2022*]. All data were collected and analyzed reflecting the ambulatory and outpatient use for the period 2010-2020. The analysis included the total number of prescriptions, and quantities of drugs. The data about the population were obtained from the Institute of Statistics (INSTAT) [http://www.instat.gov.al/en *Last accessed July, 2022*]. The data about the consumption of drugs were expressed as a number of Defined Daily Dose (DDDs)/1000inhabitants/day. All drugs were classified by groups of Anatomic Therapeutic Chemical Classification (ATC).

Data on real consumption (import and domestic production)

For all the period under study 2010-2020 there were collected and analyzed data from the import and domestic production of the drugs, [http://www.dogana.gov.al/english/ *Last accessed July, 2022]*] which represent the real consumption of drugs in the country. It was noted that the increase in consumption from one year to another were small, e.g. the consumption from 2018 to 2020 (i.e. 3 years) was increased by only 1.96%. Consequently, in order to obtain an updated study, there were chosen the data of import and domestic consumption only for the last three years, 2018, 2019,2020, and those were involved in a comparative analysis with the equivalent consumption data according to HII. In order to minimize the effect of variations consumption-inventory balances from one year to another, it was calculated and put to analysis the annual average value of the three chosen years (on one hand that of the import and domestic consumption, and on the other hand that of HII).

II. RESULTS

The insulin included in the reimbursement list for this period were insulin fast-acting, insulin intermediate-acting, insulin intermediate-acting combined with insulin fast-acting and insulin long-acting. The last one was involved in the scheme since 2008.

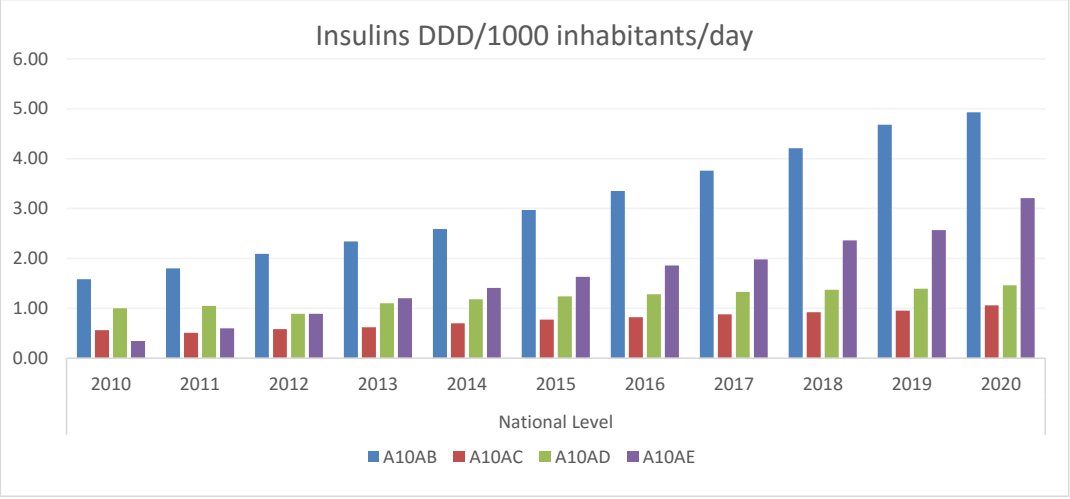

Figure 1 Annual average value of consumption of Insulin in national level in Albania

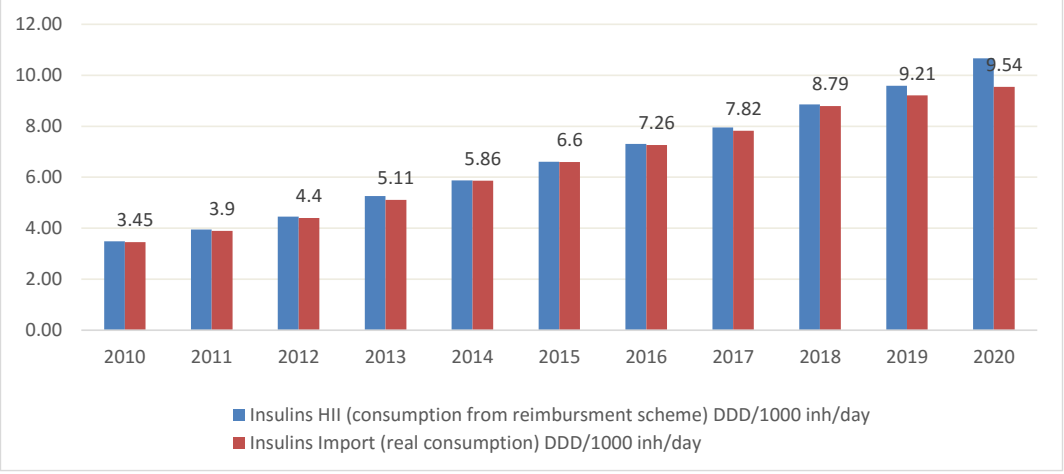

Figure 2 Annual average value of consumption of Insulin: consumption based on import (real consumption) [*] versus consumption based on HII.

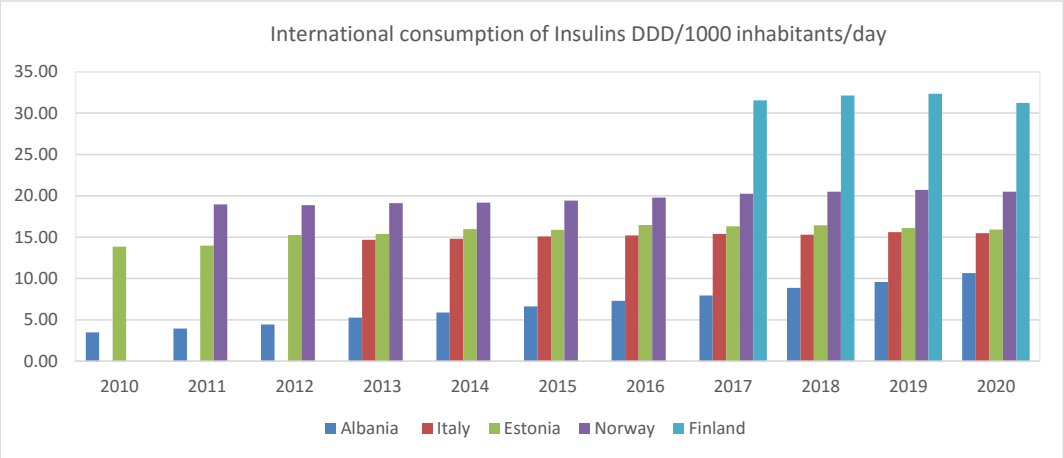

Figure 3 International comparison in the consumption of Insulin (DDD/1000 inhabitants/day): Albania, Italy [7], Estonia [8], Norway [9-12], Finland [13-16]

III. DISCUSSION

Diabetes mellitus consists in a metabolic pathology with multiorgans damages, which is accompanied by high expenses of the health insurance system. The primary objective of the treatment is to keep good control over glycemic values. The lack of control over glycemia exposes the diabetes patient to a high risk of acceleration, worsening of the disease and appearance of micro- and macrovascular complications [Boccuzzi Associates, 2001].

In 2030, this number is expected to be double the current worldwide value [Wild S, et al 2004].

In Figure 1 can be noted an increase in consumption values that includes all insulin classes. The class with higher values of prescription are fast-acting insulin, meanwhile the class with the highest increase are long-acting insulin.

Aiming to understand better the real situation, we have included in the analysis the import data (representing the actual consumption) of antidiabetic drugs in the three latter years 2018, 2019, 2020.

In total, the use of insulin seems well-equilibrated, a fact evidencing that insulin are taken almost entirely under the reimbursement scheme. . The figures indicate that for rapid-acting insulin, the most used group of insulin, the consumption based on the HII is higher than the real consumption based on import data – a fact which cannot be true considering that import data include all drugs that are distributed in the primary health care service in our country. This finding can be explained with the fictive prescriptions by doctors for the most used group of insulin.

Therapeutic guides increasingly suggest AE insulin (with prolonged action) to reach a better control over diabetes type 2. In Albania, the family doctor has the right to

prescribe AE insulin for diabetes type 2 patients, combined with oral antidiabetic, only for those patients that have gone through an acute myocardial infarction, cerebral insult and diabetic gangrene of the foot. The increase in consumption, especially of insulins, may reflect the better level of adherence of the doctors to the excellent guides that recommend intensification of the control to the glycemia levels [The American Association of Clinical Endocrinologists 2002 update; International Diabetes Federation 1999]. The increase in consumption of insulins may also be explained by the fact that the provision of insulin is necessary for a better control of diabetes type 2, in the cases where the diet and the oral hypoglycemic drugs do not result sufficiently.

International comparison of consumption

As shown in Figure 3, the consumption of Insulin in Albania, as compared to other countries, is very low (consumption values presented for all countries, including Albania, are the official values as referred by the respective reimbursement systems).

In Portugal, studies suggest that Insulin and their analogs, have a consumption of 5.3 DDD/TID in 2005 and 15.4 DDD/TID in 2017 exhibited an annual average growth rate that was greater than the increase in the consumption of antidiabetic drugs. Ultimately, insulin and their analogs represented 17.4 % of the total consumption of antidiabetic drugs [Moura, A.M., et al 2021].

Conclusions

There is an increase in Insulin drugs use from HII covering during 2010-2020. The consumption of insulins seems well-equilibrated, a fact evidencing that insulins are taken almost entirely under the reimbursement scheme. Further studies need to be performed in the future to get more details about this topic.

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