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THE STRUCTURAL SYSTEM'S INFLUENCE ON THE ARCHITECTURAL FEATURES OF THE BUILDINGS

Marija Miloshevska Janakieska

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Abstract. *The function of structural systems in buildings is to resist loads acting on structures and provide a skeleton in the building which encloses and subdivides space to provide a protected environment for the users. Therefore, the structural system gives strength and stability to the building. Besides these strengthening characteristics, observed from a structural point of view, the structural systems also influence the architectural features of buildings, such as the room's organization and size, the pattern of movement, the arrangement of furniture and other interior elements, the functionality, the total interior, and exterior design, the choice of structural and non-structural materials for walls, floors, ceilings, envelopes, doors, windows, façade, etc. In this study, the structural system influence on architectural features of buildings will be analyzed through a detailed examination of a case study – project of a hotel building, located near the border between Kosovo and Macedonia.*

Keywords: *structural system, architectural features, case study, hotel building.*

1. STRUCTURAL SYSTEMS IN BUILDINGS

The structural system can be defined as a group of inter-related or inter-dependent elements which form a complex connected structure, designed and built to resist different loads. The elements of the structural system can be illustrated as the bones of the human body. If the bones are weak, not aligned properly, and integrated into the human body, then the human body would not be able to work or perform well. Similarly, if the structural system elements are not properly integrated, then the structure would not be able to receive and transfer loads [1].

Nowadays, the input of new and modern structural systems into the construction industry has created a competitive environment. Choosing the most suitable structural system has become increasingly difficult. Some structural systems have priority over others due to their unique features, as well as the special requirements of various construction projects. In this process, many project features should be taken into consideration and detailed analysis should be done. Contemporary constructions, sustainable development, biophilic design, improvement in the quality of life, better comfort, and housing enhancement indices, require a transition from traditional construction methods to new technologies [2].

Furthermore, a building structure's ecological impact due to the embodied carbon in the chosen materials has become an increasingly prominent factor in the selection of building structural systems [6]. From an architectural point of view, the elements of the structure play an important role, not just in the load-bearing capacity of the building, giving it the needed strength and stability, but also in the internal organization, patterns of movement, the shape of the building, the type of façade, the materials, the function, the aesthetics, etc.

Some of the structural systems that are commonly used in high-rise buildings are wood frame as a lightweight structural system, reinforced concrete frame or massive structural system, and steel frame structural systems. In addition, there are some newly engineered products that are slowly finding their way in the construction sector, due to their positive characteristics. There are proposed procedures and guidelines for the selection of optimum structural systems and materials in two stages. Stage one is based on a list of criteria, including architectural considerations. Stage two evaluates selected systems and materials for optimum performance of criteria considered critical for a given project. However, the selection of structural system and material is often done according to personal experience or perception without being evaluated as it should be for optimum performance [1].

1.1 The Importance of the Structural Systems in Architecture

Vitruvius believed that an architect should focus on three central themes when preparing a design for a building: firmitas (strength), utilitas (functionality), and venustas (beauty) [5]. All three of them are as equally important and inter-correlated.

Figure 1. The importance of the structural system in determining the shape and aesthetics of a building

The functionality is usually the most important and primary theme and it is based upon the needs of the users, the organization of spaces, and patterns of movement, while the shape of the building should be in accordance with it. On the other hand, the strength of the building is obtained by its structural system and should be aligned with the shape. In the end, all these aspects are giving the building aesthetics, whether it is exterior or interior. The architect must have a good knowledge of the structural systems because having only an idea for the shape is not enough (Figure 1).

2. CASE STUDY OF A HOTEL BUILDING IN MACEDONIA

The impact of the structural systems on certain architectural features in buildings will be examined through a case study – project of a hotel in Macedonia (Main Project for B5 - Hotel Complexes: Hotel and Business Hall - Casino, with the technical number 11/21-1, from April 2021, main designer Marija Miloshevska Janakieska, Graduated Engineer Architect). The location of the building is in the Municipality of Chucher Sandevo, near the Kosovo-Macedonia border – border crossing Blace (Figure 2).

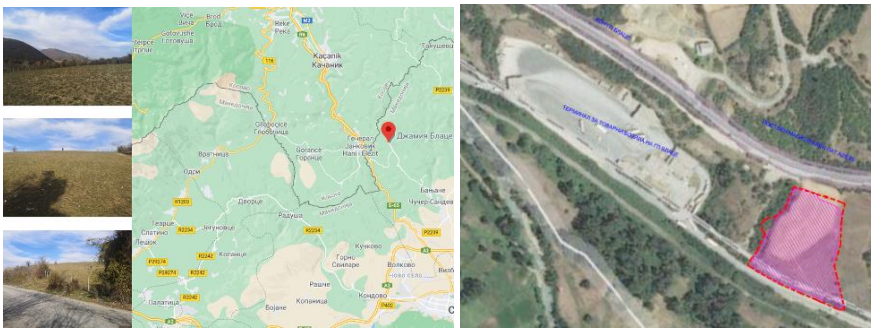

Figure 2. Location of the Building

Vehicles can enter the site from the access street on the south side of the location, and the movement is through an inner street, which starts with an 8% slope, in order to overcome the height of the terrain, which is quite steep. The design of the inner streets enables vehicles and buses to move through them smoothly and comfortably. The parking lot is within the location and all parking spaces can be reached via an inner street.

The building consists of four levels: underground, ground, first, and second floor. From a functional point of view, all technical and staff rooms, such as storage (including food storage, waste room, cold storage, deep and beverage storage), laundry and ironing facilities, administration rooms (info desk, offices with meeting room, wardrobes, showers and toilets for employees, kitchen and room for employees), hydro room, documentation room, machine room, server room, mechanical and electrical room, are located on the underground level. The ground floor is the biggest floor plan, and this is where all important areas, such as reception, wardrobe for guests, lobby, registration area, gaming area - casino, kitchen, restaurant, hotel facilities (bar, office, doctor's office, toilets, etc.) are placed. In addition, five hotel rooms are positioned on this floor (Figure 3). The first and second floors are reserved only for hotel areas, with five rooms on each of them.

The organization of the premises and the functionality is made in accordance with the architectural, urban, and climate conditions of the location, following the Urban Plan, the existing regulations and norms for this kind of buildings, as well as in agreement with the wishes, directions, proposals, and requirements of the investor.

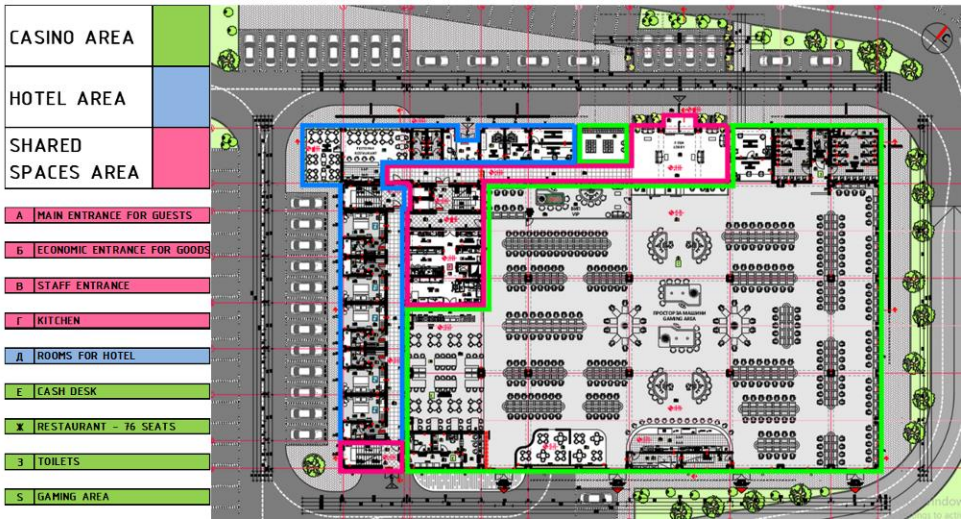

Figure 3. Ground Floor Plan (Main Project B5 - Hotel Complexes, with technical number 11/21-1, responsible designer Marija Miloshevska Janakieska)

The structural system of the building is mixed and it consists of different types of structural elements and different materials. The canopy structure at the main entrance for guests consists of steel columns connected with steel trusses, positioned in two directions. The hotel premises (marked with blue color in Figures 4 and 5) have reinforced concrete frame structures, with reinforced concrete columns, beams, and slabs. The main hall, which is intended for the casino (gaming area), has a structural system with two different materials: reinforced-concrete columns and primary beams, connected with steel trusses, placed in the opposite direction of the beams. The spans between the columns in this part are approximately 12 meters (Figure 4 and 5).

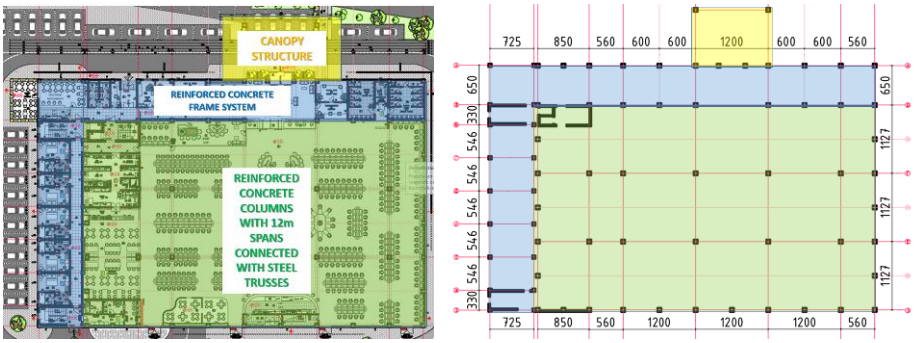

Figure 4. Structural system of the building and module spans represented in ground floor plan

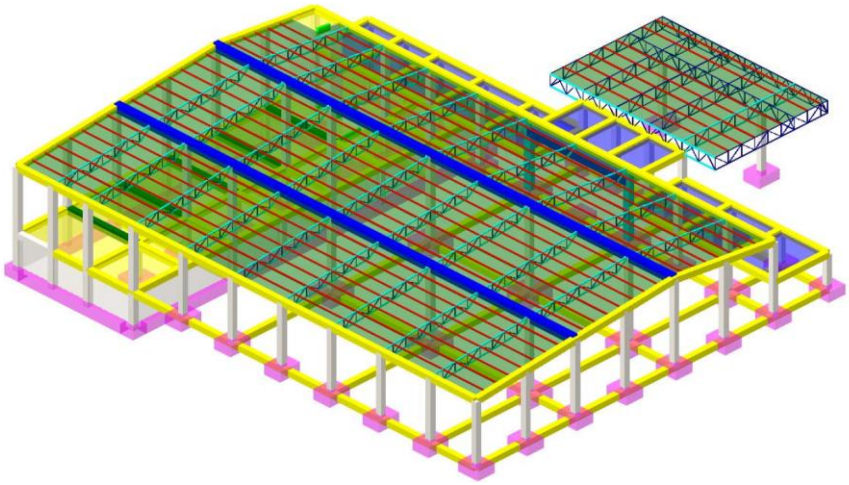

Figure 5. Structural system of the building represented in 3D

The foundations of the building are also mixed, differing only in typology. In choosing the type and material for the foundation, several factors, such as the type of the soil, the purpose of the building, the number of floors, the loads, and the availability of the materials, play a key role. Reinforced concrete is mostly chosen as a material for the foundations, due to its high load-bearing capacity and water and humidity resistance. As for the shape, the foundations can be designed as single foundations, linear foundations, foundational beams for strengthening the single foundations, and foundations slabs.

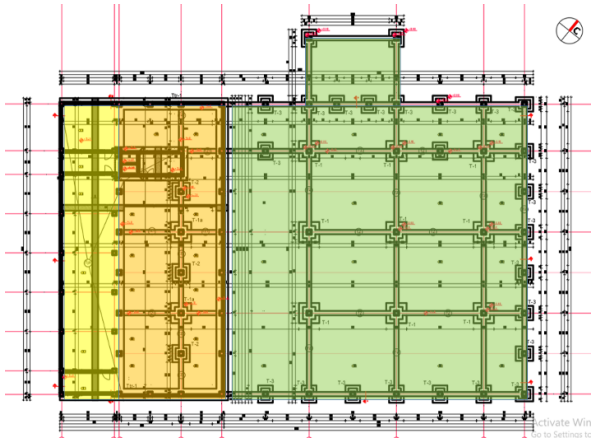

Figure 6. Different types of foundations represented on a Foundation Floor Plan

Due to the complex shape and the mixed structural system, in this building, there are several types of foundations on different parts. The highest part of the building, where the hotel rooms are located, has a slab foundation. The other part of the building, which is not so high, has single foundations, connected with foundational beams (Figure 6).

The building is under construction and the majority of the hotel portion has already been erected (Figure 7).

Figure 7. Photos of the construction site

A few months after the construction began, the investor requested a change in the structural system of the building, only in the casino - gaming area, so that the reinforced concrete columns will be replaced with steel columns, with bigger spans. The changes in the structure caused changes in all other phases and parts of the project and therefore a Project for changes during construction was prepared. This project included all changes in every phase: construction, architecture, electrical installations, mechanical engineering, water supply and sewerage, fire protection, and energy efficiency.

2.1. The Influence of the Changes of the Structural System on the Architectural Features of the Building

It is constantly debated which material to choose for the construction of a building. The debate intensifies, especially when it comes to steel or reinforced concrete. Each has its benefits. While concrete may make use of readily-available materials and aggregates, structural steel has an edge due to its high tensile strength, weld ability, and toughness [7]. Due to the lightness, high strength, and stiffness per weight, the steel allows bigger spans between the columns, compared to the reinforced concrete, which can be observed in the two projects (Figure 8). In addition, the dimensions of the steel columns are smaller. This resulted in a different organization of the floor plan, especially in the interior design and the internal layout of the slot machines in the casino area. The organization of the structural system has an important role in designing and positioning of the rooms and the furniture. The walls and other partitions are usually aligned with the structural elements, especially with the columns and the beams. In this case, a completely different arrangement of the furniture was designed, so it will adjust to the new position of the columns.

The number of steel columns and their dimensions are smaller compared to the concrete ones and therefore the net area of the casino is bigger with the steel structure. In the first project, with reinforced concrete columns, the net area

of the casino is 1461.70m^2 and in the second project (Project for changes during construction), the net area of the casino is 1466.70m^2. The difference is 5m^2 more free space, and here the coatings of the steel columns are already taken into consideration.

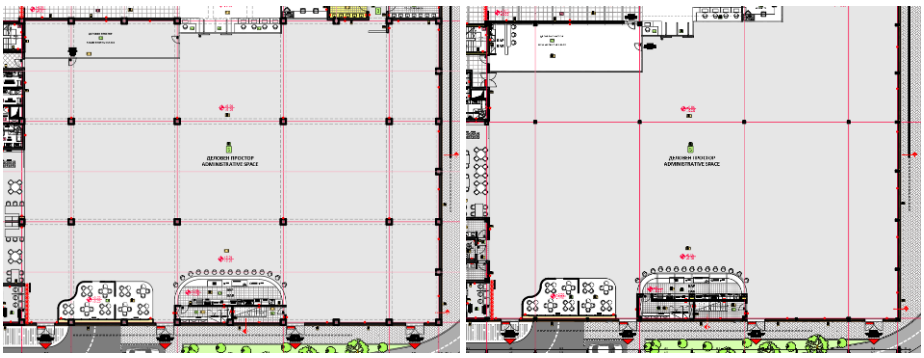

Figure 8. Comparison of both structural systems in floor plan: old structural system with reinforced concrete columns on the left and new structural system with steel columns on the right

The steel structures are very light in comparison to other structures such as concrete ones, which is a positive aspect, especially in seismic active regions such as Macedonia. Moreover, the steel elements are easy to be fabricated, so they are generally used for mass construction. The steel members can be easily replaced, changed, assembled, or disassembled, compared to concrete. Furthermore, the erection and installation are faster and easier, which was a crucial turning point in the investor's decision. Formwork, which is essential for the reinforced concrete, in this case, is unneeded. Due to the light weight, steel elements are very easy to transport.

Additionally, the changes in the structural systems caused changes in the choice of materials, especially in the facade and interior walls. In the first project with reinforced concrete columns, masonry walls with a "wet" procedure were taken into account. On the other hand, with the lighter steel structure, heavy masonry has been replaced by lightweight prefabricated sandwich walls as a more logical choice (Figure 10). The light construction in combination with the light walls will enable a better response of the building to seismic forces under the action of an earthquake, which is another positive feature.

The structural system is completely closed with a façade and roof envelope, and as a result, the changes did not influence the shape and exterior aesthetics of the building. Otherwise, if the construction was exposed, the impact on the building form would be striking. The roof structure which is composed of steel trusses is covered with a suspended gypsum board as a ceiling, so there are no visible changes in this part, as well. However, there is more space for mechanical installations in the second project above the suspended ceiling.

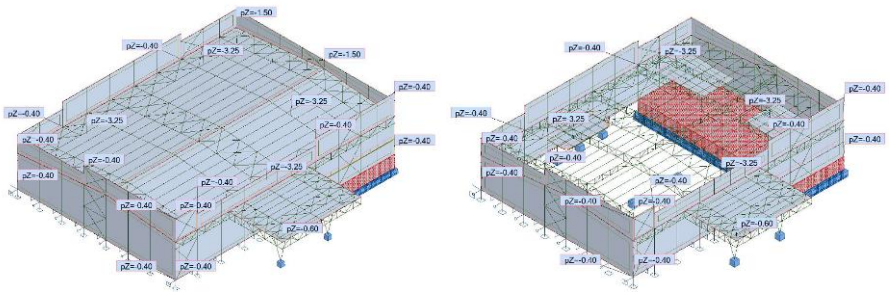

Figure 9. New steel structural system represented in 3D

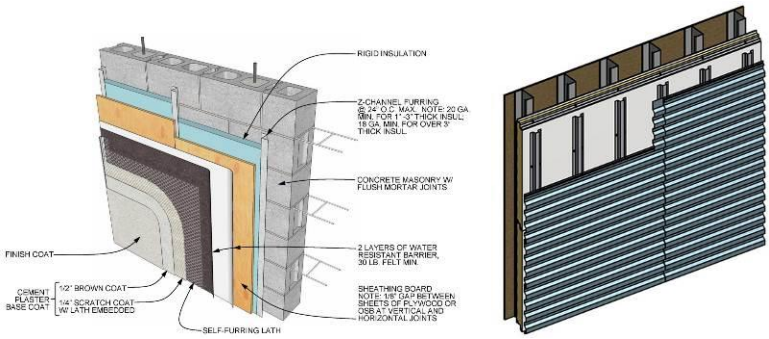

Figure 10. Comparison of different types of wall details: old structural system with masonry block walls on the left and new structural system with sandwich walls on the right

3. CONCLUSION

The structural system is a very important and irreplaceable part of the building and therefore should be designed with special care, taking into consideration all aspects, such as the strength, stability, functionality, organization, finances, needs, ideas, ecological impact, building shape, and materials. In this study, the influence of the structural systems on certain architectural features was examined through a case study – project of a hotel in Macedonia.

For this building, two separate projects with differences in the structure were prepared, which made it suitable for analysis. The results of this study showed that the type of structural system, together with the structural elements and materials have a very big impact on the architectural features of the building. The replacement of reinforced concrete columns with steel caused changes in the organization of the interior space, different arrangement of the furniture, changed patterns of movement, and increased in the net area of the inside space for 0.34%. The interior space became visually larger, with fewer visual interruptions and a clear perspective view, which improved the space quality and comfort.

In addition, the steel structures are very light compared to concrete ones and the steel members can be easily replaced, changed, assembled, or disassembled. The erection and installation are faster and easier and the formwork, which is crucial for the reinforced concrete, in this case, is unneeded. Due to the light weight, steel elements are very easy to transport.

The changes of the structural systems are changing the choice of materials for different architectural elements, especially in the facade and interior walls. This resulted in a light construction in combination with light walls which will enable a better response of the whole building to seismic forces under the action of an earthquake.

In cases where the structure is exposed, whether in the exterior or interior, its impact on the building shape will be noticeable. There are architectural examples where the impressionability of the external appearance arises from the structural system of the building.

Finally, the results of this study emphasize the importance of the structural system in buildings from an architectural point of view, and therefore engineers should pay attention in the process of selecting and designing the structure. Additionally, the knowledge of the engineers who are involved in the designing part must be expanded through demonstration projects, workshops, lectures, and collaboration among representatives of different sectors, in order to achieve a better understanding of the potential of the structure.

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FORENSIC DENTAL MEDICINE AND ITS SIGNIFICANCE IN JUDICIAL MEDICAL EXPERTISE

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Abstract. *Moral perceptions are a reflection of time and social circumstances, and they are ethical principles of humanity and justice for human beings. As in other professions, where there is the liability for knowingly, or unknowingly making a mistake in the course of work, the same liability exists for physicians for damage directly caused by the physician's negligence, omissions, misdiagnosis, and incorrect treatment. However, the medical profession also carries certain risks, so the doctor cannot be held responsible for every failure in his work, published in the Official Gazette, he cannot be held responsible for the failure of his work. The material-legal responsibility of the doctor is a consequence of the damage caused to the patient by the doctor in:*

- *Non-compliance with the established scientific and professional methodological and technical principles (vitium artis)*
- *Violation of the principles of humanity, specific to the medical profession and title*
- *Non-compliance with medical protocols*
- *Negligence during the diagnosis and implementation of treatment.*

Because the main goal of the medical profession is to alleviate and later eliminate the pain and discomfort that the patient feels, to improve and maintain the patient's health, and to extend the patient's life, it is necessary for the doctor and other health professionals to do their job. Perform it as conscientiously as possible, respecting the rules of the medical profession. However, due to certain circumstances, which are often associated with insufficient practical health expertise and skill of the doctor, increased number of patients, and insufficient commitment, due to the general approach of the doctor, may have side effects on the patient's health, which entails a certain responsibility by the doctor, namely: disciplinary responsibility, civil liability, and misdemeanor liability - criminal (criminal) liability. It is considered that the most common reasons for the unethical actions of doctors are the desire to earn money, recklessness, sexual interest, false certificates, and false testimony).

1. INTRODUCTION

The entire knowledge of the doctor in dental medicine is based on professional knowledge, knowledge, as well as a humane attitude towards the patient. The well-known and often cited maxims "primum non nocere" (above all do not harm the patient) and "primum utilise esse "(above all be useful), contain all the medical codes, and their roots go back and have them in the time of Hippocrates and are given in the Hippocratic Oath *. They represent the basic principles of medical ethics and deontology. Namely, the concept of utility for patients represents the essence of medicine as a science and medical activity, which is of special social interest.

Medical ethics is the most important link between doctor and patient. Neglecting and disrespecting this relationship can seriously undermine that concept, undermining the integrity of the medical profession and practice. On the other hand, it is self-evident that the practice of non-medical medicine should be beneficial to the patient, which is much more important than taking care only so as not to harm the patient, not to take certain Professional activities that are in the interest of the patient's health Doctors of dental medicine and patients are not perceived as enemies, but on the contrary as friends, whom the patient completely trusts.

The patient sees the dentist as a lifeline for him based on that. It can be said, that the doctor's work depends mostly on the patient because the doctors are here for what the patients need. However, first, it is the patient to gain the dentist's

trust and cooperate with him. However, with the process of commercialization of health care, the doctor-patient relationship has largely lost its “light”, which has always been of great importance to the medical profession and has become a business. Profession, i.e. the basic principles of the medical profession have been lost, namely ethics and morality, all in the interest of profit, characteristic especially in transition countries. Doctors are obliged to treat each patient and provide him with the necessary medical care. , and all this results either in the healing of the patient or not even in unprofessional and unscrupulous work of the doctor leads to injury or damage to the health of the patient. In law, medical or dental intervention means the use of means and procedures, with Corpus Hipocraticum, originated in ancient Greece between the 5th century BC and to this day is a source point of the medical oath and codex. Which are about the ethical aspects of the medical activity, which achieves the social goal, which is to protect the life and health of the patient. By undertaking these procedures and interventions, the patient gets a much better chance of recovery than if taken nothing, no procedures, and procedures, thus losing any opportunity to solve the patient's health problem, i.e. to protect the health of the citizen (patient) and the doctor remains false adherence to the moral and ethical principles of his profession. [1]

From here, it can be freely said that there is no illegal error because all undertaken procedures and procedures lead to the preservation of the health of the citizen (patient).

However, every work performed, including the work of health workers, is subject to certain errors, which can be made on different grounds. It is quite justified that medical error is given much more attention than errors made in any other activity, i.e. from any area.

In the Republic of Macedonia, there are no official statistics on the number of medical errors. Health organizations generally do not keep records of possible errors during the treatment of patients, and the competent ministries do not have such information. However, lately, we are aware that there are more lawsuits for compensation for psychological and professional damage due to alleged errors in the medical treatment of the patient.

Unlike medical ethics, which speaks of the ethical and moral responsibility of the doctor, medical deontology prescribes and elaborates the obligations and duties of doctors in the performance of their professional work.

The word deontology was first mentioned in the 19th century. The term medical deontology is often equated with the term medical ethics. But today it is quite clear that deontology as a science, in addition to ethical norms and principles, also includes legal regulations, which are related to the medical title and the medical profession. On the one hand, medical deontology, it borders and to some extent coincides with medical-legal postulates (jurisprudence), and on the other hand, it coincides with the medical ethical norms, Grmek. [1]

The word "deontology" comes from the Greek word "deon" which means "duty" or "obligation", ie it means respecting certain norms and obligations, which are necessary for the realization of any profession, including the medical profession.

Medical deontology has a special significance in everyday life, due to the specific conditions of the title. This profession can not be compared with any other profession, because the subject of observation and treatment is the man-patient who treats him. The profession that is, an occupation, in the deepest sense of the word, is neither a skill nor a profession, but a devotion to the man and his health as an individual, Pejakovic2. Hence, starting from the complexity of medical behavior and action, it can be concluded globally that his responsibility may be:

- Ethical
- Professional
- Legal

Deontology is a science that covers the entire legislation, with all the accompanying regulations that regulate medical work. The purpose of the legislator is to protect the company or the patient from unscrupulous, irresponsible, and unprofessional doctors with certain legal regulations. Era, laws, and regulations were created, which regulated the work of doctors, and the penalties for unsuccessful work or intervention were quite severe. Namely, for the first time,

the civil and criminal responsibility of the doctor is mentioned in the special law passed in Babylon, during the reign of Hammurabi from 1791-1759 AD. In that famous Hammurabi law, the monetary amount for each intervention. For example, if a patient dies due to a medical error or loses one eye, both hands should be amputated [3].

The first code of conduct for the doctor is presented in the famous Hipokrat oath, the text of which is preserved in the collection of works written by Hippocrates (460-377 BC), which originate from the Pythagorean school.

The Geneva formulation of the Hippocratic Oath (1948), which is based on the morals of the Hebrew physician and philosopher Moisa Maimonoides of the twentieth century my soul with love for my profession and for all your creations. Do not let the desire for fame and earnings influence me in the realization of my profession, because the enemies of truth and humanity can use it, and divert it from the path of my noble duty, profession, to do good for my children"

However, the rapid technical-technological development of the medical profession and science brought with it opposite expectations, that is, it brought erosion of morality from every point of view, loss of ethics, as well as weakening of the initial responsibilities of the health staff. With the emergence of teamwork, with the emergence of "my term" and the time limitation of the patient's examination, the doctor's obligation for numerous imposed administrative responsibilities, all distances the doctor from the patient, i.e. the patient as a person and subject of treatment, more easily lost. On the other hand, the personal responsibility of the doctor is reduced.

From here it is inevitable to distinguish the legal from the moral obligations of the doctor of medicine or dentistry, and this is what forensic or forensic medicine deals with, which is a scientific-professional foundation of the platform for providing legal aid, which refers to medical or health issues. In civil or criminal proceedings.

Legal obligations are regulated by legal regulations, while moral duty is based on ethical principles, which are shaped and formed in the social community, during the historical development of social relations and the development of medical theory and practice. [5]

Moral perceptions are a reflection of time and social circumstances, and they are ethical principles of humanity and justice.

As in other professions, where there is a liability for knowingly or unknowingly making a mistake in the course of work, the same liability exists for physicians for damage directly caused by the physician's negligence, omissions, misdiagnosis, and incorrect therapeutic treatment.

However, the medical profession also carries certain risks, so the doctor can not be held responsible for every failure in his work. , published in the Official Gazette, he can not be held responsible for the failure of his work. [4, 6, 7, 8]

The material-legal responsibility of the doctor is a consequence of the damage caused to the patient by the doctor in:

- Non-compliance with the established scientific and professional methodological and technical principles (vitium artis)
- Violation of the principles of humanity, specific to the medical profession and title
- Non-compliance with medical protocols
- Negligence during the diagnosis and implementation of the therapeutic

Because the main goal of the medical profession is to alleviate and later eliminate the pain and discomfort that the patient feels, to improve and maintain the patient's health, and to extend the patient's life, it is necessary for the doctor and other health professionals to do their job. Perform it as conscientiously as possible, respecting the rules of the

medical profession. However, due to certain circumstances, which are often associated with insufficient practical health expertise and skill of the doctor, then, increased number of patients and insufficient commitment, due to the general approach of the doctor, may have side effects on patient's health, which entails a certain responsibility on the part of the doctor, as follows:

Disciplinary liability - decided by professional associations and disciplinary measures are imposed as a reprimand, a fine until the temporary or permanent revocation of the license.

Civil liability - refers to the form of compensation for individual wrongdoing, which leads to injury to the patient (compensation is determined by civil law).

Misdemeanor liability - occurs in case of omissions, insufficient and untidy medical documentation, or non-compliance with medical confidentiality, usually, a fine is imposed.

Criminal liability - refers to negligent treatment, unauthorized transplantation of tissues and organs of the human body, disturbance of the patient's health, failure to apply appropriate treatment measures, use of inappropriate drugs for treatment, and causing death.

- not providing first aid
- issuing fake medical certificates
- giving false statements

It is considered that the most common reasons for the unethical actions of doctors are the desire to earn money, recklessness, and sexual interest. False certificates, false testimony).

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GLUCOCORTICOIDS IN ORAL MEDICINE

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Abstract. *Through, widely known as the body's stress hormone, cortisol has a variety of effects on the different functions of the body; it is mainly been released from the zona fasciculata, a layer of the adrenal cortex. Glucocorticosteroid receptors are present in almost all tissue in the body. Therefore, cortisol is able to affect nearly every organ and system: nervous, immune, cardiovascular, respiratory, reproductive, musculoskeletal, and oral disorders. Cortisol has many functions in the human body, such as mediating the stress response, regulating metabolism, inflammatory responses, and immune function. Steroids are been used as anti-inflammatory, antiallergic, and immunosuppressive drugs in many general and oral diseases. Steroids can be manufactured synthetically as drugs, available in the form of fluid for injections, tablets, ointment, solution, and gels. Steroids are of the most broadly used drugs in dentistry and readily act as an immunosuppressive agent. Corticosteroids have modernized the treatment protocol for several disease conditions inclusive of many oral diseases. These are strong and effective anti-inflammatory drugs resembling cortisol. Their function is to decrease inflammation, particularly when the body inaccurately activates the inflammatory system. Many oral and maxillofacial clinicians apply the usage of corticosteroids established on their effectiveness to control the consequences of any dental procedure or surgery. The present review focused on the pharmacology, use of corticosteroids in oral medicine, and side effects of corticosteroids.*

1. INTRODUCTION

The adrenal cortex consists of the cortex and medulla. The cortex produced steroid hormones including glucocorticoids. Mineralocorticoids and adrenal androgens, and the medulla produce catecholamine, epinephrine, and norepinephrine. (Fig. 1)

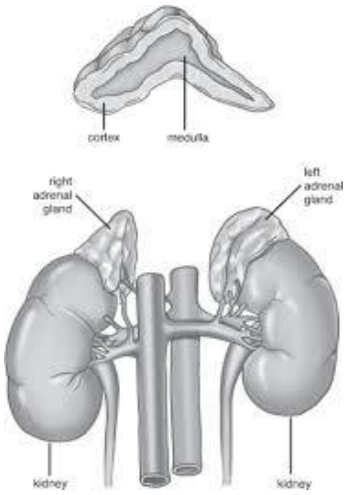

Figure 1. Adrenal Cortex

The adrenal cortex takes part in steroidogenesis, producing glucocorticoids, mineralocorticoids, and androgen precursors. It has three distinct functional and histological zones: the zone glomerulosa, zona fasciculata and zona reticularis. Each layer produces steroid hormones from the precursor cholesterol. The zona glomelurosa produces mineralocorticoids, the zona fasciculata produces glucocorticoids and zona reticularis produces androgen precursors

Endogenous cortisol by the adrenal gland is been controlled by the hypothalamic-pituitary-adrenal axis and occurs in a diurnal and circadian pattern every 24 hours. The hypothalamic-pituitary-adrenal (HPA) axis is involved in the production of glucocorticoids and adrenal androgens from zona fasciculata and zona reticularis. In response to circadian rhythms or stressors, paraventricular neurons (PVN) in the hypothalamus make and secrete a corticotropin-realizing hormone (CRH). CRH binds receptors on the anterior pituitary gland, which leads to the synthesis of ACTH (corticotropin) from pre-pro- opomelanocortin (pre- (POMC). ACTH from the anterior pituitary is been released into the circulation and engages the melanocortin type 2 receptors (MC-2 R) in the zona fasciculata of the adrenal cortex predominantly to induce the synthesis of glucocorticoids. [1, 2]

Circulating glucocorticoids negatively feedback on the hypothalamus and the anterior pituitary, suppressing the release of CRH and ACTH respectively. This is the prevention of the continued rise of glucocorticoid levels. Sl.2

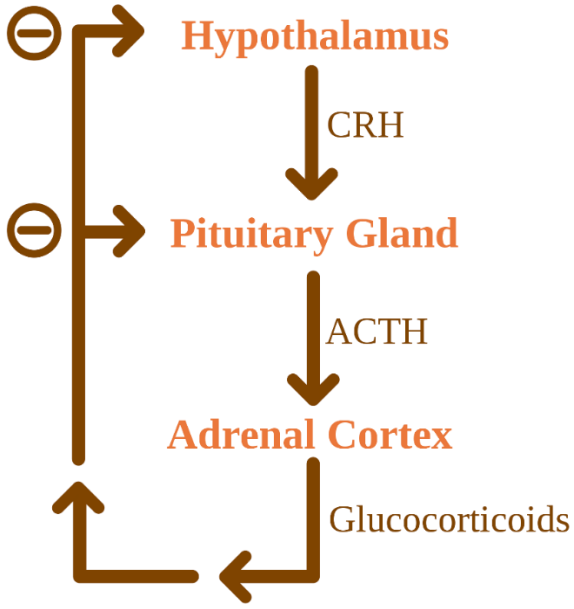

Figure 2.

Cortisol is a major glucocorticoid and increases in response to stress, which activates the HPA axis. Therefore, all of its functions can be thought of as allowing the body to function with increased stress. Upon engaging glucocorticoid receptors, cortisol increases the expression of genes that will regular metabolism, the immune system, cardiovascular function, growth, maintaining blood pressure, the sensitivity of vascular smooth muscle, and suppresses the release of vasodilatation like nitrous oxide.!)Regarding metabolism, cortisol increased gluconeogenesis and decreases peripheral glucose uptake and the next effect is an increase in serum glucose. Generally, growth is inhibited, leading to muscle atrophy, increased bone resorption, and thinking of the skin. [3]

1.1 Pharmacology of Corticosteroids

Corticosteroids are classified into three groups: corticosteroids with short acting; intermediate-acting and long-acting (hydrocortisone, triamcinolone, dexamethasone, clobetasol, and mometasone. (table 1)

Table 1.

Drug	Route of administration	Duration of action (hours)	Equivalent glucocorticoid dose (mg)	Relative potency — anti-inflammatory	Relative potency — mineralcorticoid
Short-acting					
Hydrocortisone	Oral, parenteral	8–12	20	0	++
Cortisone	Oral, parenteral	8–12	25	0	++
Intermediate-acting					
Methylprednisolone	Oral, parenteral	12–36	4	+	0
Prednisone	Oral	12–36	5	+	+
Triamcinolone	Oral, parenteral	12–36	4	+	0
Long-acting					
Dexamethasone	Oral, parenteral	24–72	0.75	++	0
Betamethasone	Oral, parenteral	24–72	0.60	++	0

The corticosteroids may be used systematically administrated (orally intravenously and topical (creams, ointments, nasal oral inhalation, intraarticular injection) the pharmacology efficacy chiefly depends on the anti-inflammatory immune-suppressive and antiproliferative, effect. [4, 5]

The physiologic and metabolic effect of corticosteroids is numerous. Glucocorticosteroids bring inhibition of white blood cells function, and lysozyme membrane stabilization inhibits plasminogen activation and decreases the synthesis of inflammatory mediators like prostaglandins and leukotrienes. These drugs might be directed systematically or topically, are metabolized in the liver after conjugation, and are excreted through urine [9]. Corticosteroids help to decrease inflammation by inhibiting phospholipase A2, consequently blocking the production of prostaglandins, leukotrienes, and other substances associated with thromboxane A2. The production of these end products is a mixture of effective inflammatory mediators and has the capacity to alleviate lysozyme membranes, diminish the discharge of inflammation-causing lysozymes, and reduce the permeability of capillary thus preventing diapedesis. Bradykinin production, which is a powerful vasodilator, is also reduced. [6, 7]

1.2 Immunosuppressive action

Steroids inhibit several in vitro and in vivo T-cells function normally: Reduced lymphokine synthesis.

T-cell's reaction against autologous tissue is mostly eliminated even in physiological concentration. Inhibition of the undefined cytolytic activity of lymphocytes against allogenic cells. Corticosteroids drugs are used in various oral diseases: (topically, sub focal application, or systematically). Topical corticosteroids are frequently used in the management of many oral mucosal. Their use should be based on detailed medical history event intake of any medication and accurate diagnosis of the oral lesion. One of the factors that play a major role in determining the success of the treatment with topical corticosteroids is the amount of time the drug comes indirectly connected with the lesion, which depends on the means used for applying topical corticosteroids. The mode of application most often used in oral pathology is adhesive ointments and aqueous solutions. Among adhesive ointments, the orobase ointment is one of the most commonly used agents. [8]

Figure 3. Ulcerative vesicular -bullous disease (aphthous ulcers; Behchte-s disease, erythema multiform, pemphigus)

2. TREATMENT OF RECURRENT APHTHOUS LESION WITH CORTICOSTEROIDS

Recurrent aphthous ulcers top the list of the commonest oral mucosal lesions encountered by any dental practitioners. Generally, this condition is self-limiting and resolves within 2-2 weeks with the exception of major recurrent aphthous ulcers. Despite it being self-limiting the pain and the frequency of recurrence treatment options for recurrent aphthous ulcers are no longer effective in relieving the discomfort caused by these ulcers. (Figure 3)

Corticosteroids are one available treatment option for recurrent aphthous ulcers.

The most commonly used steroids for local application topically are:

- Triamcinolone on acetonide (adhesive paste containing 0.1% of the steroid)
- Hydrocortisone hemisuccinate (pellets 2.2 mg)

Ulcerative that are located in the areas which are inaccessible can be controlled by:

- Topical Dexametason elixir 0.5 mg/5 ml held over the area of applied with a saturated gange pad to the ulcers, 4 times/day for 15 minutes

Betamethasone sodium phosphate rinse by dissolving 0.5 mg in 5 ml water and asking the patients to rine for 2-3 min.

Steroids aerosol Bethamethason disproportionate

A high potency topical corticosteroids such a clobetasol 0.05% in orobase or fluocinonide 0.05% in orobas.Pedersen (5)

Systemic application of corticosteroids in the aphthous lesson:

Major aphthous ulcers commonly require systemic treatment (intralesional application).[9, 10]

Prednisolon therapy 40 mg/day for one weak

- Bechet's syndrome, 40-60 mg prednisolone /day

3. TREATMENT OF ORAL LICHEN PLANUS WITH CORTICOSTEROIDS

Oral lichen planus may exist as a reticular, papillary, atrophic, erosive,bulous, or plaque-like form amongst which the erosive-atrophic forms are symptomatic.

Steroids have been shown to play an imperative role in symptomatic treatment (Kiran) Some options include topical application of corticosteroids and it is reasonably effective in the treatment of oral lichen planus. The use of the most potent corticosteroids is associated with more improvement following therapy. However, the incidence of oral candidiasis also increased in proportion to the potency of corticosteroid used. Carbone et all in 2003 reported that the use of topical corticosteroids can be as effective or even more effective than systemic corticosteroids in the treatment of oral lichen

Topical corticosteroids are reasonably effective in the treatment of the classic form of oral lichen. [11,12,13]

Topical application

- Triamcinolone acetonide 0.1%
- Gel 0.05% Behamethason valerate
- Gell clobetasol propionate 0.05%
- Gell Betamethasone valerate 0.05%
- Gell Fluconanide 0.05%Creame clobestrol 0.1%

Extensive lesions erosive lesion

- Subcutaneous injection of 0.2-0/4 ml a 10 mg/ml solution of triamcinolone acetate
- Intralesion triamcinolone acetonide in dose 0.5-1 ml a 1mg/ml suspension in the form—of weekly injection injections

Systematic steroid therapy

The commonly used systemic corticosteroid is prednisolone which is usually prescribed within the range of 40-80vmg/day to achieve a clinically response to avoid adverse effects of this drug, it is best to prescribe the lowest dose for the shortest duration possible.To achieve this, prednisolone can either be given for a brief period of 5-7 days and stop abruptly or the dose can be tapered down by 5-10 mg/day gradually over a period of 2-4 weak (Al=Hashimi,

- Prednisolon 40-80 mg.day

4. TREATMENT ERYTHEMA EXUDATIVE MULTIFORM WITH CORTICOSTEROIDS

It is an acute,self-limiting inflammatory mucocutaneous disease, that manifests on the skin and mucosal surface namely oral mucosa and genitalia. Erythema multiforme is considered a hypersensitivity reaction, the most common factors being HSV infection or drug reaction to NSAIDS or anticonvulsants (12).

Topical steroid therapy

- Clobetasol propionate (mouthwashes in aqueous solution is commonly used 15)

Systemic steroid therapy

- Prednisolon 20-40 mg/day,4-6 days for erythema exudative multipphorme (minor form)
- Prednisolon 60 mg/day over 6 weak (Erithema exudative multiform (major form)

It is a chronic autoimmune disease to a group of autoimmune, chronic mucocutaneous diseases that cause blisters and erosions of the skin and mucous membrane by intraepidermal acantholytic structure.

Pemphigus is characterized by the rapid appearance of vesicles and bullae, vying in diameter from a few millimeters to several centimeters. These lesions contain a thin, watery fluid shortly after development, but this may soon may purulent or sanguineous. When the bulla rupture, they have a raw eroded surface.

Pemphigus is a serious disease. Prior to the advent of corticosteroids, the mortality rate was approximately 95%, particularly for pemphigus Vulgaris. Today steroids and antibiotics therapy for secondary infection has reduced the mortality so that only 30 to 40 % of patients will die either of the diseases still run an acute course despite treatment and terminate in early death.

Oral mucosal lesions in pemphigus are common and predominantly appear as buccal erosions in the occlusal line, which is most exposed to trauma and also on the palate, gingival, and tongue.

It is important to realize that, while systemic therapy is important to the overall treatment of the disease, topical therapy of both skin and oral lesions is especially necessary because of the pain and discomfort suffered by these patients.

Corticosteroids can be prescribed in the form of the paste, an ointment or a mouthwash administrated as monotherapy or as adjunctive therapy with systemic therapy

Severe cases are advised high doses of pemphigus behind the topical application of corticosteroids: 100-200 mg/per day, un clinical signs decline, and then the dose can be slowly decreased to a maintenance level of 40-50 mg/daily. [14, 15] In the therapy, topical corticosteroids are used in cases where the pemphigus is not extensive and lesions are limited to the oral cavity. [17, 18]

Topical corticosteroid is used in skin and oral mucosa:

- Triamcinolon acetate 0.1% in or base 3 times/day
- Flucononide o.5% ointment,2-3 time/per day
- clobestrol propionate 0.05%%
- halobetasol 0.05%

Intralesional injection:

- Triamcinolonbacetonide (20 micrograms per liter) or
- Paramethason every 7-15 days [15,16]

Chronic treatment with systemic corticosteroids is associated with numerous and significant risks for adverse reactions and toxicities. These agents affect every organ and system and metabolic process in humans. The risk for adverse effects from corticosteroid therapy is related to the dose and the duration of therapy as well the specifics agent used. Historically, short courses of systemic corticosteroids were not thought the cause significant long-lasting toxicities. [14]

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TOOTH AGENESIS: THE MOST COMMON DEVELOPMENTAL ANOMALY

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Abstract. Tooth agenesis is a condition at which the patient is missing one or more teeth, due to their failure to develop. Missing teeth are one of the most common developmental anomalies.This condition is an aesthetic as well as functional deficiency. The prevalence of missing teeth depends on the ethiological factors, gender, race, geographic and demographic distribution. Most common congenital tooth absence is affecting the teeth that are last developed in each group (lateral incisors, second premolars, third molars).The aim of this study is to make a review of the literature about the prevalence, the conditions associated with tooth agenesis and possible factors that can cause this anomaly.

1. INTRODUCTION

The development and growth of the human being is strictly determinant process of organogenesis, morphogenesis and differentiation. Deviation from the normal process can lead to anomalies in the structure or function. These deviations, if present during the childbirth, as a result of an abnormal prenatal structural development are called congenital anomalies [1, 2].

These changes can present just an aesthetic defect and then they are considered as mild forms of anomalies. However in addition to the aesthetic defect, the anomaly can be more severe and might cause a functional problem, too. The mild forms of anomalies are more common with 15% prevalence among newborns, while the severe ones are rare with prevalence of 1-2% [3, 4].

The main goal of orthodontics is to ensure harmony between the jaws and the teeth. Any violation in this relationship leads to aesthetic and functional issues.

One of the reasons that lead to aesthetic and functional imbalance is tooth agenesis. Tooth agenesis is a condition where the patient misses one or more teeth due to the developmental absence of its germ [5].

Dentogenesis present a complex process in which a tooth formation occurs. This process is a result of the interaction between the embryonic cells during the intrauterine period. The tooth germ is composed of three parts: enamel organ, the dental papilla and the dental follicle. This process is regulated by different types of genes like: Msx2, Lef2, Shh, Bmp2, Fgf8, Fgf20, Wnt10a, Wnt10b и Edar [6].

There are four phases of the process of dentogenesis: initiation, morphogenesis, differentiation and eruption. During these stages a lot of epithelial-mesenchymal interactions occur among the cells and tissues that determinate the tooth formation. Improper interaction between these processes can lead to number of developmental anomalies and malformations of the tooth structures and even tooth agenesis.

Depending of the number of teeth that are missing, tooth agenesis can be divided in three groups. Hypodontia describes situation when up to 6 teeth are missing, not including the third molars. Oligodontia is when more than 6 teeth are missing and anodontia present a situation when there is no single tooth in the patients mouth as a result of developmental issue (Figure 1 and 2).

Figure 1. a), b) hypodontia on 12, 22, 35, 45
c), d) hypodontia on 15, 14, 24, 25, 35 45
e), f) oligodontia on 15, 14, 12, 22, 25, 31, 35, 44, 45
(http://www.nature.com/bdj/journal/v203/n4/images/bdj.2007.732-f1.jpg)

Figure 2. Anodontia (https://classconnection.s3.amazonaws.com/836/flashcards/489836/png/untitled1.png)

Some authors report different classification for hypodontia according to their severity. Most common one includes: mild with 1-2 congenitally missing teeth, moderate with 3-5 congenitally missing teeth and severe with 6 or more missing teeth [7, 8, 9].

Congenital absence of the teeth can be seen as an isolated phenomenon (non-syndromic) or as an associated symptom of a sindromic disease (syndromic hypodontia). Non-syndromic hypodontia can be familial or sporadic. Sporadic hypodontia is when the tooth agenesis is present as an isolated case of hypodontia in one family member, while familial hypodontia is when tooth agenesis is present among several members of the same family [10]. The presence of tooth agenesis among several members of the same family indicates the hereditary factor in this anomaly.

On the other hand the syndromic hypodontia points out that the formation of the teeth and formation of other organs is under control of the same molecular mechanisms. The agenesis of the teeth can be present in more than 60 syndromes like ectodermal dysplasia, Pierre-Robin syndrome, Van Der Woude syndrome, Crouzon syndrome, Schöpf-Schulz-Passarge syndrome, tricho-odonto-onycho-dermal dysplasia, orofacial digital syndrome and Downsyndrome [11, 12, 13]

2. LITERATURE REVIEW

Tooth agenesis is the most common congenital dento-facial anomaly [14, 15]. Hypodontia presents functional as well as aesthetic problem [16, 17]. Patients with tooth agenesis could have: difficulty in mastication, incorrect pronunciation, lower anterior face height and insufficient development of alveolar bone. Additionally it can be accompanied with: abnormalities in the size and shape of the teeth (microdontia or peg-shaped teeth), anomalies in roots of the teeth (dilaceration), late teeth eruption, ectopic canines or enamel hypoplasia [18, 19, 20].

According to Krezci et al. tooth agenesis on permanent teeth has negative impact on the sagittal growth of the jaw and is followed by an increased over-jet [21]. The agenesis of the permanent teeth leads to a decrease in anterior facial height and maxillary retrognathism [22, 23].

Very often microdontia can be found in patients with tooth agenesis. The review of the literature shows positive correlation between the number of missing teeth and the prevalence of microdontia [24, 25]. Microdontia has been reported in healthy patients without missing any permanent teeth, but with relatives who are already missing more permanent teeth [26]. Teeth that are most commonly affected are those located in the anterior segment [27, 28] (Figure 3).

Figure 3. Tooth agenesis of the lateral incisor with microdontia of the contralateral incisor (http://egloos.zum.com/q8imcs/v/10726756)

The tooth agenesis can be associated with the changes in the shape of other teeth. Most commonly there is a change in the shape of the maxillary lateral incisor, when the contralateral is missing [29, 30]. Changes can be found in reduction of the number of cusps in premolars and molars or conical shape of the canines [31, 32].

An ectopic position of the permanent teeth can be also associated with the tooth agenesis. Some articles report that the risk for palatal positioned maxillary canine is six times higher in patients with an existence of another anomaly of the adjacent lateral incisor (tooth agenesis, microdontia, changes in the shape of the tooth) [33, 34]. The existence of a connection between these anomalies has also been noted among family members [35]. According to these reports, the palatal position of the maxillary canine is a consequence of local etiological factors influencing the lateral incisor, whose root has the role to guide the canine through its eruption.

Connection between these malformations and tooth agenesis indicates a common defect at the primary level.

Hypodontia in permanent dentition is one of the most common dentofacial anomalies with prevalence of 2,6-11,3% among different populations with third molars excluded from the study [36]. Teeth that are most commonly missing are those that develop last in their group like lateral incisors, second premolars and third molars [37]. The prevalence of the missing third molars is so common present in more than 25% of the population [38, 39]. That is why this condition is sometimes considered as normal.

Oligodontia and anodontia are rare conditions which usually occur as a symptom within a syndrome and rarely as an isolated case. The prevalence of oligodontia is between 0.08-0.16 with predomination in females [40]. Anodontia on

the other side is extremely rare condition, usually found as part of hypohidrotic ectodermal dysplasia. Its prevalence varies depending on gender, race, geographical and demographical distribution as well as ethnicity [41, 42].

Tooth agenesis can be found in the permanent as well as in the primary dentition. The prevalence of hypodontita in primary dentition is significantly lower with prevalence 0.08-1.55% [43]. There is a correlation between the tooth agenesis of the primary teeth with the permanent teeth. In most of the cases the tooth agenesis of the primary tooth is followed with a tooth agenesis of its permanent successor [43, 44]. The tooth agenesis in primary dentition is equally distributed between genders, with primary maxillary lateral incisors missing the most [45].

There is no significant difference between the affected sides, left or right, in permanent and in primary dentition. Also there is no significant difference between jaw distribution of the missing teeth in permanent dentition [46]. On the other hand there is significant difference between distribution of the missing teeth in both jaws in the primary dentition mostly due to the missing maxillary lateral incisor [47].

The cause for congenitally missing teeth remains fully unclear, although it is believed that this condition is correlated with the genetic factors as well as with the environmental factors that have impact during the developmental period, like the mothers age, the presence of systematic diseases, low weight of the newborn, virus infection during the fetal period, trauma and some drug exposition [48, 49, 50, 51, 52]. Smoking of mother can also be a possible risk factor for tooth agenesis [53].

According to some studies the most common missing teeth are those which get innervation last [54, 55].

Tooth agenesis often can be hereditary and also can be associated with certain genetic disorders, like ectodermal dysplasia and Down syndrome or to be a result of a hormonal imbalance (hypoparathyroidism).

Hypodontia is very common anomaly in patients with cleft lip and palate. Tooth that is most commonly affected is maxillary lateral incisor, followed by maxillary second premolar [56, 57]. The prevalence of tooth agenesis in these patients increases proportionally with the severity of the cleft [29]. Therefore the tooth agenesis is can be mostly seen in patients with bilateral cleft of the lip and palate and at least in patients with only cleft of the lip.

Hereditary factor is predominant factor for tooth agenesis compared to environmental factors. A lot of mutations have been detected in patients with tooth agenesis. These mutation can be inherited like autosomal dominant forms, autosomal recessive, X-linked or as a polygenic pattern. More genes have their impact in the process of inheritance. Mutations in these genes cause phenotypic changes, among others tooth agenesis. With these mutations there is an incorrect transcription of proteins that play role in dentofacial development.

A lot of studies have been made in order to find the exact genes that are responsible for this anomaly. Genes that are most commonly correlated with tooth agenesis are MSX1, PAX9, AXIN2, IRF6 and WNT10A [58, 59, 60, 61].

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THE EFFECT OF HYALURONIC ACID ON GINGIVAL INFLAMMATION AND GINGIVAL BLEADING DURING GBR

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Abstract. *The management of periodontal defects has been an ongoing challenge in clinical periodontics. This is mainly a result of the fact that tissues which comprise the periodontium, the periodontal ligament, and the cementum and alveolar bone, represent three unique tissues in their own right. Thus, reconstruction of the periodontium is not just a simple matter of regenerating one tissue but involves at least three quite diverse and unique tissues. Resective surgical therapy, with or without osseous recontouring, was considered the norm during the 1950s and the 1960s, in the belief that attainment of shallow pocket depths was a worthwhile goal. More recently, attention has been focused more on regenerative and reconstructive therapies, rather than on respective therapies. Among the many mediators used in periodontal regeneration is hyaluronic acid. In the field of dentistry, hyaluronic acid has shown anti-inflammatory and anti-bacterial effects in the treatment of periodontal diseases. The article reviews recent evidence of the effects of hyaluronic acid on periodontal deffects.*

Keywords: *hyaluronic acid, bone regeneration, periodontal regeneration and reconstructive therapies, gingival inflammation and bleading.*

1. INTRODUCTION

Hyaluronic acid has been identified in all periodontal tissues in varying amounts and is more pronounced in non-mineralized tissues, such as the gingival and periodontal ligaments, compared with mineralized tissues such as cement and alveolar bone. In addition, due to the high levels of hyaluronic acid in the circulating blood serum, it is constantly present in the gingival blood flow fluid (GCF) which is a factor in serum overload[1] . Natural hyaluronic acid is an extremely hydrophilic polymer that exists, as viscous does not in itself have the structural features needed for use as a surgical product. Hyaluronic acid ester synthesized by esterification of a carboxyl group with benzyl alcohol is less soluble in water and is therefore more stable. Due to its unique molecular structure, hyaluronic acid can accumulate at different molecular weights such as lyophilized or esterified in different structural configurations such as membranes. The rate of biodegradation of these materials can be manipulated by changing their degree of lyophilization or esterification. Thus, hyaluronic acid may be useful as a reproductive material in regenerative surgical procedures[2] . Hyaluronic acid is an anionic, glycosaminoglycanic acid widely distributed throughout connective, epithelial, and nerve tissues. It is unique among glycosaminoglycans in that it is non-sulfated and forms in the plasma membrane instead of in the Golgi apparatus. The human synovial hyaluronic acid averages about 7 million daltons per molecule, or about twenty thousand disaccharide monomers, while other sources mention 3-4 million daltons. One of the major components of the extracellular matrix, hyaluronic acid, contributes significantly to cell proliferation and migration, and may also be involved in the progression of some malignancies. The average 70 kg person has approximately 15 grams of hyaluronic acid in the body, of which one third is degraded and synthesized every day[3] . Hyaluronic acid is also a component of group A streptococcal extracellular capsule, and is believed to play an important role in virulence.Hyaluronic acid is one of the most well-known hygroscopic molecules known in nature.

When HA is incorporated in aqueous solution, hydrogen bonding occurs between adjacent carboxyl and N-acetyl groups; this feature allows hyaluronic acid to maintain conformational stiffness and retain water. One gram of hyaluronic acid can bind up to 6 L of water. As a physical material, it has functions in spatial filling, lubrication, shock absorption, and protein exclusion[4]. The viscoelastic properties of the material can slow down the penetration of viruses and bacteria, a feature of particular interest in the treatment of periodontal disease. Hyaluronic acid as a viscoelastic substance helps in periodontal regenerative procedures by maintaining spaces and protecting surfaces[4] . By recognizing its hygroscopic and viscoelastic nature, hyaluronic acid can affect cell function by modifying surrounding cellular and extracellular micro and macro media. The hyaluronic acid has many structural and physiological functions within tissues, including extracellular and cellular interactions, the interaction between the growth factor and the regulation of osmotic pressure, and tissue lubrication, which helps maintain the structural and homeostatic integrity of tissues[5] .

Considering the various beneficial effects of hyaluronic acid, we focused our interest on the review of the effects of hyaluronic acid on gingival bleading and gingival inflammation in guided tissue regeneration.

2. Materials and Methods

30 patients were followed in the study. Patients were selected according to the following criteria:

- aged between 20 - 45 years
- without anamnestic data for general disease
- non-smokers
- -finding of both contralateral similar type of periodontal destruction both in volume and type
- All will have a clinical examination before the intervention and then will be measured:
- depth of the periodontal pocket,
- loss of attachment,
- recession,
- gingival bleeding and gingival inflammation (measurements will be made on a Silnes Loë gradient)

Prior to the intervention, all patients were given advice on proper oral hygiene and it will be checked whether they implemented. The modified Widmann method was made for all patients, with BioOss beef bone (control group) applied to each patient on one side and BioOss with 16% BDDE hyaluronic acid from Stylage, Vivacy, applied on the other side. Paris in a ratio of 2: 1, enough until a thick, sticky bone ratio is obtained - (examined group). In all patients, the results were monitored by CBCT-conbim (computed tomography in which X-rays are divergent to form a cone beam) and measurements will be made before and after 12 (twelve) months.

3. Results

Gingival inflammation in the studied group in different control periods

	x	**sd**	**t**	**p**
begining	**2,11**	**0,55**		
After 3 months	**0,78**	**0,18**	**12,41**	**≤0,05**
After 6 months	**0,44**	**0,25**	**14,76**	**≤0,05**

After 8 months	**0,33**	**0,45**	**14,09**	**≤0,05**

Gingival inflammation in the control group in different control periods

	x	**sd**	**t**	**p**
begining	**2,33**	**0,68**		
After 3 months	**1,56**	**0,48**	**5,75**	**≤0,05**
After 6 months	**1**	**0,23**	**11,135**	**≤0,05**
After 8 months	**0,78**	**0,63**	**10,81**	**≤0,05**

Difference in gingival inflammation index values between baseline and control periods for study and control groups

	Study group	**Control group**	**p**
After 3months	**0,77**	**1,33**	**≤0,0001**
After 6 months	**1,33**	**1,67**	**0,027**
After 8 months	**1,55**	**1,78**	**1.337**

The differences between the initial values and the different time periods for the index of gingival inflammation were; for the control period of 3 months o.77 for the examined and 1.33 for the control, for the period of 6 months 1.33 for the examined and 1.67 for the control while for the period of 8 months 1.55 for the examined and 1.78 for the control. The difference is significant for the third month p ≤0.05.

Gingival bleeding in the studied group in different control periods

	x	**sd**	**t**	**p**
begining	**2,67**	**0,23**		
After 3 months	**1,67**	**0,23**	**11,81**	**≤0,05**
After 6 months	**0,56**	**0,25**	**24,26**	**≤0,05**

After 8 months	**0,67**	**0,45**	**19,29**	**≤0,0001**

Gingival bleeding in the control group at different control periods

	x	**sd**	**t**	**p**
begining	**2,56**	**0,25**		
After 3 months	**1,89**	**0,11**	**8,928**	**≤0,05**
After 6 months	**1,44**	**0,25**	**12,449**	**≤0,05**
After 8 months	**1,11**	**0,33**	**15,092**	**≤0,05**

Difference in gingival bleeding index values between baseline and control periods for study and control groups

	Study group	**Control group**	**p**
After 3 months	**1**	**0,67**	**≤0,026**
After 6 months	**2,11**	**1,12**	**≤0,0001**
After 8 months	**2**	**1,45**	**≤0,00001**

The differences between the initial values and the different time periods for the index of gingival bleeding is for the control period of 3 months 1 for the subject and 0.67 for the control, for the period of 6 months 2.11 for the subject and 1.12 for the control while for the period of 8 months 2 for the tested one and 1.45 for the control one. The difference is significant for the sixth and eighth months $p \leq 0.05$.

4. DISCUSSION

Today HA is widely used in many branches of medicine with interesting potential applications in dentistry for the treatment of acute and chronic inflammatory disease. Data obtained from the present review of 20 clinical studies demonstrates that, due to its positive action on tissue repair and wound healing, topical administration of HA could play a role not only in postoperative dental surgery, but also in the treatment of patients affected by gingivitis and periodontitis, with a significant improvement in their quality of life. Further, laboratory-based research and large-scale randomized controlled clinical trials on a larger scale are advisable to confirm these promising results. From the perspective of current research, hyaluronic acidbased bone regenerative scaffolds are more biocompatible and

bioactive with biomimetic strategies. As a matrix component, hyaluronic acid, especially sulfated HA, may trigger cell behavior modulation via several signaling pathways, leading to faster and more desirable bone formation. Scaffolds and carriers based on HA are shaped into either rigid forms or colloids. As a rigid scaffold material, when incorporated with other materials, HA may alter the scaffold morphology and improve mineralization, making it more desirable and more functional for bone regeneration. Moreover, hyaluronic acid is chemically versatile, with its properties changed via simple chemical modification and crosslinking. The viscidity, rheological properties, pH, and charge properties of hyaluronic acid can be modulated into states suitable for gelation or delivery. This leads us to the carrier hyaluronic acid. Either by mixing, or by chemically or electrostatically encapsulating a diverse range of growth factors, drugs, mineralized components, or cells in HA-based carriers, bone formation can be markedly enhanced and accelerated. New bone formation could more closely resemble that of the original tissue. Some strategies can also perform superbly in Osseo integration for implantation. HA-based hydrogels and micro particles can covalently bind to metal implant surfaces and release bioactive components, resulting in better osteogenesis and Osseo integration. However, the specific mechanisms behind the effects of HA on osteogenesis still require proper investigation controlled delivery as well as biomimetic scaffold and carrier designs, not just HA-based forms. Bone regeneration in periodontal bony defects.More recently, cross-linked HA products were used as gel barriers to cover the osseous defects around the implants and implant recipient sites and thereby promoting GBR [6] . Claar performed a lateral coverage of the augmentation followed by use of cross-linked HA in gel form, which was developed especially for GBR[7]. The principles of GBR applications[8, 9] are as follows: - Cell exclusion: Creating a barrier to prevent forming fibrous connective tissue by epithelial cells. - Tenting: New wound space beneath the membrane must be regenerated solely around soft tissues so that high quality of new tissue can be gained. - Scaffolding: At first, a fibrin clot is seen in this space which is a scaffold for progenitor cells. Adjacent hard tissues serve as storage for stem cells. - Stabilization: To gain successful healing, the defective area must be protected from environmental effects such as flap movement, bacterial invasion, exposure of region, etc. by fixing the membrane into position.

The findings of our investigation clinical study indicate that the use of HA + GTR as a regenerative material was found to be effective in improving the clinical parameters compared to GTR alone, also we prove that first 3 months we have more control on gingival bleading and gingival inflamation , who representiv key of succesful periodontal regeneration. Engström *et al*. investigated the anti-inflammatory effect and the effect on bone regeneration of Hyaluronan in surgical and non-surgical groups. No statistical difference was found on radiographs in the non-surgical group, whereas the decrease in bone height was found for both groups after scaling. Probing depth (PD) reduced after the surgical treatment as well as after scaling and root planning (SRP). Hyaluronan in contact with bone and soft tissues had no influence on the immune system.[10]

In our present study, the differences between the initial values and the different time periods for the index of gingival inflammation were; for the control period of 3 months o.77 for the examined and 1.33 for the control, for the period of 6 months 1.33 for the examined and 1.67 for the control while for the period of 8 months 1.55 for the examined and 1.78 for the control. The difference is significant for the third month $p \leq 0.05$. Hyaluronan gel is effective in controlling inflammation and gingival bleeding. Studies have documented reduction in the depth of gingival pockets along with a significant reduction in epithelial and lymphocyte cell proliferation with the use of HA gel.[11]

0.2% Hyaluronan containing gel has a beneficial effect in the treatment of plaque induced gingivitis. All studied sites had a significant decrease in peroxidase and lysozyme activities after 7, 14, and 21 days.[12] Hyaluronan gel is also effective in controlling inflammation and gingival bleeding. Pilloni *et al*., in their randomized controlled clinical pilot study, evaluated the efficacy of an esterified form of HA gel on periodontal clinical parameters. The periodontal clinical parameters were plaque index (PI), BOP, PPD, gingival index (GI), and probing attachment level. In the end of the study, they concluded that an esterified gel form of HA has shown an effect in reducing the gingival inflammation when used as an adjunct to mechanical home plaque control and that it could be successfully used to improve the periodontal clinical indexes.[13]

Also in our study, we presentiv the differences between the initial values and the different time periods for the index of gingival bleeding is for the control period of 3 months 1 for the subject and 0.67 for the control, for the period of 6 months 2.11 for the subject and 1.12 for the control while for the period of 8 months 2 for the tested one and 1.45 for the control one. The difference is significant for the sixth and eighth months $p \leq 0.05$. Therefore in our present study, radiographic monitoring of alveolar bone changes was carried out as end point variable. The most reliable outcome variable for assessing periodontal regeneration is human histology. Due to ethical considerations and patient management limitations, no histological evidence was obtained to establish the proof of periodontal regeneration. The importance of wound stability for bone and periodontal regeneration has been reported, thanks on stability of gingival inflamation and bleading controlled by hyaluronic acid. Based on the histological evidence from human material, it may be assumed that the clinical improvements following esterified HA treatment may represent at least to some extent, a real periodontal regeneration characterized by the increase of osteoblastic activity by stimulating differentiation and migration of mesenchymal cells.[14] Moreover, the physiochemical properties of HA help keep the growth factors responsible for tissue repair in situ.[15]

5. CONCLUSION

The results of this research are expected to contribute to the knowledge of the impact of hyaluronic acid on periodontal regeneration and its application in the daily life of periodontology.

The obtained research results together with the data from the literature give us relevant knowledge for optimal scientifically supported planning and realization for successful periodontal treatment. The scientific contribution of this research is the optimism that the scientific findings from this research will arouse interest and need for new research on this issue. From the analysis of the results and within the limitations of the present study, it can be concluded that regenerative approach using hyaloss in combination with GTR for the treatment of human infrabony defects resulted in a significant added benefit of anti inflamatory proces who prese nt no gingival bleading and inflamation in first 3 months , they build the succes of periodontal regeneration , in terms of CAL gains, PPD reductions and radiographic defect fill, as well as LBG, compared to the GTR alone.

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