Paediatr Croat. 2017;61:137-40
PREGLED / *REVIEW*
www.paedcro.com
http://dx.doi.org/10.13112/PC.2017.20

Dental management in osteogenesis imperfecta

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Osteogenesis imperfecta is a very rare heterogeneous genetic disorder associated with the development of connective tissue resulting in fragile bones and frequent fractures. More than 50% of patients affected with osteogenesis imperfecta have a hereditary developmental disorder known as dentinogenesis imperfecta. Dentinogenesis imperfecta is caused by irregularities in the formation, composition and organization of dentin matrix during tooth development. It is caused by mutations of the genes that encode basic proteins of the organic matrix, collagens and phosphoproteins. The purpose of this review is to describe the histopathologic and clinical features of teeth typical of dentinogenesis imperfecta type I, which occurs within osteogenesis imperfecta, with special emphasis on targeted dental treatment to achieve optimal rehabilitation of the masticatory system.

Key words: developmental bone disease; dentinogenesis imperfecta; rehabilitation

OSTEOGENESIS IMPERFECTA AND HEREDITARY DENTIN DYSPLASIA

A group of genetic disorders characterized by improper structure of dentin, the basic building hard dental tissue, is called hereditary dentin dysplasia (DD). Disorder in the dentin structure is a consequence of irregularities in the formation, composition and organization of dentin matrix during tooth development. It is caused by mutations of the genes that encode basic proteins of the organic matrix, collagens and phosphoproteins. Hereditary DD includes dentinogenesis imperfecta (DI) and dentin dysplasia. Type I dentinogenesis imperfecta, which occurs within osteogenesis imperfecta (OI), a heterogeneous genetic disorder associated with the development of connective tissue, is particularly important (1). In more than 50% of patients with OI, there is a hereditary developmental dentition disorder known as dentinogenesis imperfecta (DI) (2).

DENTINOGENESIS AND ETIOPATHOGENESIS OF DENTINOGENESIS IMPERFECTA

Dentin is a hard tooth tissue that builds the majority of the tooth. In the crown, it is covered with enamel and in the root, it is covered with cement. It is formed during tooth development with complex interaction between epithelium and ectomesenchyme. Differentiation of ectomesenchyme in the peripheral layer of dental papilla, in the bell stage, produces odontoblasts, cells that create dentin. Similar to osteoblasts in the bones, odontoblasts synthesize and excrete the organic component of dentin. The mature dentin contains about 70% of inorganic substances, 20% of organic substances, and 10% of water. Most of the organic component, about 86%, consists of collagen type I, and in the smaller part of collagen types III, V and VI. Of non-collagen proteins, there are dentin phosphoprotein (50%) and in the smaller part sialoprotein and glycoprotein (3).

Hereditary DD is a complex group of disorders in the tooth structure and the most commonly used classification is the Shields classification into five types. There are three types of dentinogenesis imperfecta (types I, II and III) and two types of dentin dysplasia (types I and II). Dentinogenesis imperfecta Shields type I occurs with OI and is characterized by disorder in collagen type I formation. Dentinogenesis imperfecta Shields type II (also known as hereditary opalescent dentin) is the most common type of DI and is not as-

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Primljeno/Received: 3. 9. 2017., Prihvaćeno/Accepted: 9. 10. 2017.

sociated with OI. Dentinogenesis imperfecta Shields type III is very rare and has been diagnosed in the population of Brandywine, Maryland, USA (4). Unlike DI Shields type I, which is like OI caused by mutation of the genes involved in collagen coding, DI Shields types II and III are caused by mutation of the dentin sialophosphoprotein gene (5, 6).

For the first time in history, this dentin disorder was described by *WC Barrett* in 1882 (7). It was initially considered a defect of the enamel, and in 1908, *Fargin-Foyelle* and *Malassez* recognized that it was primarily an irregularity in the structure and composition of dentin. The term "hereditary opalescent dentin" was used until 1939, when *Roberts* and *Schour* introduced the term dentinogenesis imperfecta (8).

Dentinogenesis imperfecta type I is inherited as an autosomal dominant trait and is manifested in the phase of tissue differentiation during tooth development. The basic characteristics are structural defects in the formation of dentin that may affect the primary and permanent dentition, in varying degrees. The incidence of DI is 1 *per* 8000 (9). DI that is present in OI inherited in autosomal dominant manner most often occurs in individuals with COL1A1 (17q21.31-q22.05) or COL1A2 (7q22.1) gene mutations. These genes encode pro-alpha-1 or pro-alpha-2 collagen type I strains. DI that occurs with OI inherited in autosomal recessive manner is a variable manifestation in individuals with mutations of *FKBP10*, *LEPRE1*, *CRTAP* and *PPIB* genes (6, 10).

CLINICAL FEATURES AND DENTAL TREATMENT

Osteogenesis imperfecta, known as "fragile bone disease", is a genetic disorder affecting connective tissue. People with OI tend to have recurrent, multiple bone fractures (11). They can also have hearing loss, bluish hue sclerae, joint hyperextensibility, DI, asthma, and kyphosis/scoliosis (12). The incidence of OI is 1 *per* 20,000-30,000 live births (13).

Since DI may be the most prominent clinical feature in individuals with OI, it is very important to take detailed medical history and examine for the previous occurrence of bone fractures, joint hyperextensibility, hearing loss, and shade of sclerae (14).

Detailed medical history and physical examination help determine whether the condition is not acquired but inherited. If the patient comes for the first time with existing permanent dentition, it is necessary to examine whether primary dentition was affected by similar changes. It is important to ask the patient targeted questions about the color of primary teeth, accelerated wear of dental structure, frequent abscesses, increased mobility, and early loss of primary teeth. Old photographs of the patient with their primary teeth can be helpful.

The age of the patient, previous dental procedures and experiences often affect the possibilities and types of treatment.

Although dentin changes may manifest on both dentitions, changes are generally more severe in primary teeth (15, 16). Tooth color varies from brown to bluish, often depicted as amber with opalescent surface. The enamel may be hypoplastic or hypocalcified locally in one-third of patients, and it is also prone to shearing from defective dentin. Exposed dentin is then subjected to extensive and expedited wear. Radiographic findings include bulbous crowns due to accentuated narrowing in the cervical area, followed by narrow and short roots, obliteration of pulp chamber, taurodontism and periapical radiolucency (17). The pulp chambers can be initially exceptionally voluminous, but are soon subjected to major obliteration (4). The dentinoenamel junction is not scalloped as in healthy teeth. In most cases, the mantle dentin has a normal structure, while the tubules in the circumpulpal dentin are broad and branched and their total number is smaller. The frequent findings are hypomineralized atubular dentin sites and decreased number of odontoblasts. Greater areas of interglobular dentin may also be present (18).

Severe types of OI are usually associated with malocclusions due to changes occurring in the area of viscerocranium bones (19). According to literature data, Angle Class III is present in 70%-80% of OI cases, with a high incidence of open bite. Tooth formation failure was observed in 21% of patients with OI type III, whereas rapid development was observed in 23% of patients with OI type IV (16).

Children with OI require multidisciplinary treatment, and it is especially important to include doctors of dental medicine. Early treatment of teeth with DI should be directed to ensuring good occlusion, i.e. function and aesthetics, favorable facial bone and temporomandibular joint growth, and necessary conditions for eruption and proper placement of permanent teeth. Treatment is primarily focused on the elimination of pain and prevention and treatment of caries. Since hypomineralization or enamel hypoplasia is present in one-third of DI cases, the teeth are susceptible to caries formation (20). Due to reduced mineral content, caries penetrates faster to dental pulp and periapical abscesses are common. Teeth with deep caries and periapical lesions should be subjected to endodontic treatment as soon as possible after diagnosis has been made, as delay of the procedure can lead to complications due to extensive obliteration of the endodontic space (21). Careful radiographic examination is necessary because pulp calcifications can be the first indicator of suspected OI diagnosis (22). Glass-ionomer cements that continuously release fluorides and have anti-caries effect are a good choice of filling material for primary dentition. Composite materials can be used in aes-

thetic treatment of frontal teeth if appropriate working conditions for their use can be achieved. Due to the rapid wear of the tooth structure very early in primary dentition, the vertical bite dimension can be lowered. This can be prevented by the production of full metal crowns on primary molars immediately after their eruption (23-25).

Children and adolescents with DI should be actively followed up and monitored, including frequent and detailed instructions for maintaining oral hygiene and regular check-ups.

Especially important, the time of development of permanent teeth and the measures to be taken to prevent caries should be emphasized to the parents. Occlusal overlay on the first permanent molars, and if necessary, on the premolars, ensures preservation of vertical dimension of the bite and reduces wear of the tooth tissue. If general extensive abrasion is present, overlay dentures are recommended. Due to increased mobility and short roots, early tooth loss is common. The use of dental implants is possible but only after finished growth and development, after 18 years of age. However, prior to dental implants, it is often necessary to perform alveolar ridge augmentation of upper and lower jaw that may be atrophic due to early loss of teeth and short rudimentary roots (26).

Pediatric dentistry, orthodontics, periodontology, dental prosthetics, and psychology departments have an important and unavoidable role in the treatment. Most DI cases are severe and require early intervention (27, 28). In clinical dentistry, such cases are very rare, but when one encounters a patient with DI symptoms, they should be paid due attention and referred to a children's dentistry specialist who is most competent for further course of treatment to prevent possible complications. In DI patients, the outcome of treatment greatly depends on the age of the patient when the disorder is diagnosed, as well as on the speed and quality of dental treatment being performed. If the diagnosis is set at an early age with co-operating parents who care about the child's oral health and follow dentist's instructions, it is possible to achieve satisfactory aesthetics and function. Good oral health has a beneficial effect on the overall health because good oral rehabilitation prevents nutritional deficit and psychosocial stress during growth and development of the child.

NOVČANA POTPORA/*FUNDING*

Nema/*None*

ETIČKO ODOBRENJE/*ETHICAL APPROVAL*

Nije potrebno/*None*

SUKOB INTERESA/*CONFLICT OF INTEREST*

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SAŽETAK

Stomatološko liječenje kod osteogenesis imperfecta

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Osteogenesis imperfecta je vrlo rijetka heterogena genetička bolest udružena s razvojem vezivnog tkiva, što rezultira krhkim kostima i čestim prijelomima. Više od 50% bolesnika s osteogenesis imperfecta ima nasljedni razvojni poremećaj poznat kao dentinogenesis imperfecta. Dentinogenesis imperfecta je uzrokovana nepravilnostima u stvaranju, sastavu i organizaciji zubnog matriksa tijekom razvoja zuba. Uzrokuju ju mutacije gena koji kodiraju osnovne bjelančevine organskog matriksa, kolagena i fosfoproteina. Namjera ovog pregleda je opisati histopatološka i klinička obilježja zubiju koja su tipična za dentinogenesis imperfecta tip I koji se javlja u sklopu osteogenesis imperfecta, s naglaskom na ciljano stomatološko liječenje kako bi se postigla optimalna rehabilitacija žvačnoga sustava.

Ključne riječi: razvojna bolest kostiju; dentinogenesis imperfecta; rehabilitacija