PREGLED LITERATURE – REVIEW ARTICLE

The Importance of Preventive Dental Health Care in Children with Rare Diseases

Značaj preventivne stomatološke zdravstvene zaštite dece sa retkim bolestioma

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Summary Rare diseases are chronic, life-threatening conditions that affect fewer than 5 people out of every 10,000. They involve an extremely heterogeneous group of progressive and degenerative diseases. Each of them has a distinct clinical manifestation which may include anatomical, physiological and/or neurological disorders and it can also be accompanied by changes in different parts of the body. Over 7000 rare diseases have been identified with orofacial anomalies accounting for about 15% of them. The first symptoms usually appear during the earliest childhood. In most cases, accurate diagnosis of rare diseases requires a long period of time. Consequently, therapy is complex and requires a multidisciplinary approach.

Caries and gingival-periodontal diseases are very common in the vast majority of children with rare diseases and require timely treatment. Unfortunately, the help of a pediatric dentist is most often sought in the advanced stage of disease and present complications, when complex, invasive, mostly high-risk dental treatment is indicated. It requires a strict individual plan of therapy with a multidisciplinary approach and represents a great challenge for pediatric dentists. Its effectiveness requires a good knowledge of the clinical manifestation of a rare disease by a pediatric dentist, which is frequently not an easy task. Therefore, children with rare diseases are a highly vulnerable population that must be adequately considered in the field of preventive dental health care. By doing this, many difficulties and their detrimental effects on the quality of life for these kids and their families could be avoided.

Key words: rare disease, children, oral health, preventive dental care

Sažetak Retke bolesti su hronična, po život opasna stanja koja pogađaju ne više od 5 na 10 000 osoba. Uključuju izuzetno heterogenu grupu progresivnih i degenerativnih bolesti. Svaka od njih ima jedinstvenu kliničku manifestaciju koja može uključivati anatomske, fiziološke i/ili neurološke poremećaje imože biti praćena i promenama na različitim delovima tela. Identifikovano je preko 7000 retkih bolesti od kojih je oko 15% njih povezano sa orofacijalnim anomalijama. Prvi simptomi se obično javljaju tokom najranijeg detinjstva. Precizna dijagnoza retkih bolesti uglavnom zahteva dug vremenski period. Shodno tome, terapija je složena i zahteva multidisciplinarni pristup.

Karijes i gingivo-parodontalna oboljenja su veoma česta oralna oboljenja kod velike većine dece sa retkim bolestima i zahtevaju blagovremenu terapiju. Nažalost, pomoć dečjeg stomatologa se uglavnom traži u stadijumu uznapredovale bolesti i prisutnih komplikacija, kada je potreban složen, invazivan, uglavnom visoko rizičan dentalni tretman. On zahteva strogo individualni plan terapije sa multidisciplinarnim pristupom i predstavlja veliki izazov za dečije stomatologe. Za njegovu efikasnost potrebno je da dečji stomatolog dobro poznaje kliničku manifestacije retke bolesti, što često nije jednostavno. Stoga, deca sa retkim bolestima predstavljaju visoko vulnerabilnu populaciju koja nužno zahteva da bude adekvatno sagledana u oblasti preventivne stomatološke zdravstvene zaštite. Time bi se mogle izbeći brojne komplikacije i njihov negativan uticaj na kvalitet života ove dece ali i njihovih porodica.

Ključne reči: retke bolesti, deca, oralna higijena, preventivna stomatologija

Introduction

Rare diseases are chronic, life-threatening conditions that affect fewer than 5 people out of 10,000 (1). Due to their rarity, in certain parts of the world, these diseases are also called "orphan diseases" (2).They involve an extremely heterogeneous group of progressive diseases and generally require lifelong therapy, unless there is a proven effective treatment for them. Often, they are associated with a short lifespan (3). Although majority of rare diseases have a genetic basis (72%), literature has also mentioned infectious agents and autoimmune processes as potential etiological factors (4). Quite often, patients with rare diseases remain without an etiological diagnosis (5). The first symptoms usually appear during the earliest childhood. They are generally non-specific, which is why their diagnosis requires additional, extensive laboratory and genetic analyses. Correct diagnosis often requires a long period of time, on average 5 to 7 years (6). Consequently, therapy and the provision of health care within the health care system are

complex, financially exhausting, and require a multidisciplinary approach. As a result, rare diseases pose a significant medical, social, and economic challenge for individuals as well as the entire healthcare system in both developed and developing countries (7).

Over 7000 rare diseases (about 10% of all human diseases) have been identified (8). On Orpha.net, an online portal for rare diseases, they are organized according to three hierarchical levels: *Group of disorders*, *Disorder* and *Subtype of a disorder* that determine the level of precision of each diagnosis included in the nomenclature (9). Each rare disease has distinct clinical manifestations which may include anatomical, physiological and/or neurological disorders (10, 11). Clinical presentations of these diseases often involve the nervous system and symptoms such as intellectual disability, neuropsychiatric disorders, epilepsy and motor dysfunction, and developmental and behavioural problems (12). They can also be accompanied by changes in different parts of the body, including the orofacial region (2, 13, 14). Orofacial anomalies that occur within some rare diseases include clefts, hemifacial microsomia, dental dysplasia, soft tissue anomalies, etc. Rare diseases related to orofacial anomalies account for 15% of all rare diseases (15).
However, there is no widely accepted classification for them. Salerno et al. have recently classified rare diseases associated with orofacial anomalies into those that include dental anomalies, anomalies of bone tissues, anomalies of soft oral tissues and mixed anomalies (13). A similar classification was given by Luo et al. (2). Although not officially adopted, they can be considered convenient because they make it easier for a clinician to facilitate accurate diagnosis as well as the development of a dental therapy plan, as the authors themselves suggested (13).

The state of oral health of children with rare diseases

Caries and gingival-periodontal diseases are extremely common oral diseases in the vast majority of children with rare diseases, both in deciduous and permanent dentition, as evidenced by a few studies that examined the state of oral health of these children (16-19). Only few studies are based on the fundamental characteristics of the disease. A better insight into the state of oral health of children with rare diseases is provided by case reports that offer a more detailed clinical manifestation of certain rare diseases, including possible concomitant oral diseases (2, 13, 20-24).

Both caries and gingival-periodontal diseases are infectious diseases of complex multicausal ethology. In the case of rare children's diseases, the predisposing factors are often related to the underlying disease. Poor oral hygiene and feeding issues significantly contribute to the high prevalence of these diseases in children with rare diseases, in addition to a number of other predisposing factors (18, 19).
Basically, they arise from the limitations of the underlying disease, such as physical or motor limitations, oromotor dysfunctions. Difficulties in performing oral hygiene also arise from parents' preoccupation with the underlying disease and the lack of information about the importance of oral hygiene for the child's overall health, which leads to improper or no oral hygiene. In addition, a few uncommon haematological conditions and illnesses associated with haemorrhagic syndromes, such as quantitative platelet deficiency or coagulation factor deficiency, as well as some rare neurological diseases accompanied by a series of consecutive epileptic seizures such as alternating hemiplegia of childhood (ACH) syndrome, pose a risk themselves, which is why parents refuse to brush their children's teeth or rarely do so.

Untreated oral diseases inevitably lead to numerous complications such as acute and chronic pain, odontogenic infections and eventual tooth loss (25, 26). This has an additional negative impact on the quality of life of those children and their families, it disrupts their sleep, nutrition, speech and daily activities and further complicates the clinical picture of the underlying disease (16, 27, 28). Unfortunately, the help of a pediatric dentist is most often sought in the advanced stage of oral diseases and complications.

Children with rare diseases in dental practice

Dental treatment of children with rare diseases is complex and often extremelly risky, especially in the case of invasive dental treatments. In addition, it requires a strictly individual treatment plan with a multidisciplinary approach and represents a great challenge for pediatric dentists.

Some of rare diseases are well known in pedontological practice, such as congenital ectodermal dysplasia, epidermolysis bullosa hereditaria, congenital erythropoietic porphyria, Fanconi anemia, syndromes such as Guillain-Barre, Kawasaki, Prader-Willy, Pierre-Robin, Lesch-Nyhan syndrome, or rare metabolic diseases, etc. However, a larger number of rare diseases continue to be poorly understood by pediatric dentists and require them to be informed about the disease and its clinical manifestations in order to perform dental interventions safely. This is supported by a recent study that revealed that, despite dentists' awareness of the value of understanding the clinical picture of rare diseases, their knowledge of these conditions is insufficient in terms of the clinical picture as well as in terms of screening and treatment for these conditions (29).

For paediatric dentists, the most common sources of information on rare diseases are case reports described in scientific and professional literature, which mainly analysed a small number of patients due to the low frequency of the disease. However, dentists can find important data related to rare diseases on the aforementioned website Orpha.net (9), an online portal for rare diseases that provides clinicians with reliable information about the symptoms, as well as on

other web portals such as Genetic and rare diseases information centre (30).

Orofacial anomalies related to rare diseases have negative impact on the quality of life of children and their families. Unfortunately, it is not possible to influence these anomalies in terms of their primary prevention, however, the functional and aesthetic problems they cause can be corrected or at least lessened with prompt and appropriate dental care. If it is medically justified, dental treatment usually lasts several years and requires the involvement of a pediatric dentist, orthodontist, oral and maxillofacial surgeon with paediatricians of various subspecialties who treat the child's underlying disease must also be consulted and give their consent.

From the pedontological point of view, rare diseases that require extremely risky dental treatment due to the underlying disease are of particular importance. Such diseases are often accompanied by serial epileptic seizures, as well as sensory, mental and behavioural disorders characterized by inabilty to cooperate with a child.

Therefore, routine dental treatments in ambulatory care conditions are difficult or almost impossible, and treatment under sedation and general anaesthesia is the method of choice for such patients. However, in case ofsome rare diseases, there is a risk of dental treatment under general anaesthesia, most often due to the weakness of respiratory muscles or repeated serial epileptic seizures. This is the case with Marfan syndrome, CHARGE syndrome, alternating hemiplegia of childhood (AHC) syndrome and other rare diseases (31-33).

In terms of dental treatment, extremely high risk is present in children with rare haematological and cardiovascular diseases, diseases from the haemorrhagic syndrome group, rare connective tissue diseases, and diseases accompanied by respiratory muscle issue. In these patients, routine dental procedures in ambulatory care conditions also pose a high risk. Depending on the specifics of the underlying rare disease, each of these situations calls for coordination and agreement with paediatricians of various subspecialties for the eventual dental treatment.

Possibilities of primary prevention of oral diseases in children with rare diseases

Preventive dental health care is the basic step of primary dental health care. Its aim is to prevent or stop oral disease in order to avoid classic dental treatment. Preventive dental health care is necessary for all age and population groups. However, its key importance is the most obvious in extremely vulnerable groups such as children with rare diseases.

It is obvious that in children with rare diseases, the essential need for preventive dental health care stems from the high prevalence of caries and gingiva-periodontal diseases as well as numerous complications and nature of their underlying disease and finally the complex, often high-risk dental treatment. Unfortunately, this population of children is not considered enough regarding the prevention of oral diseases. It is well understood that, in addition to factors at the individual level, factors at the family and immediate surrounding level, as well as macro or state level, are responsible for the occurrence of oral diseases (34).

However, for now, there are no adequate global oral health programs aimed at the primary prevention of oral diseases in children with rare diseases, as suggested by some authors (13, 18, 19). Such programs would undoubtedly aim to reduce the frequency of oral diseases and their complications, thereby avoiding risky and expensive dental treatments.

With certain exceptions, preventive-prophylactic work with children with rare diseases does not differ significantly from that indicated in the general pediatric population. Along with working with the parents of these children on health education, it includes a hygiene diet regime and the use of fluoride according to the current protocol. When a rare disease is discovered, which is frequently in early childhood, primary prevention strategies and measures should be implemented immediately. Therefore, apart from neonatologists, paediatricians, pediatric neurologists, and nutritionists, part of the team engaged in the treatment of rare diseases of children should necessarily include pediatric dentists as well.

The full efficacy of primary prevention measures and procedures requires a completely individual approach, which is especially evident in children with rare syndromes. Therefore, it is crucial to harmonize preventive-prophylactic measures with the nature of the disease itself. Furthermore, regardless of age, the focus is on parental preventive practices, which are considered essential for the primary prevention of oral diseases in these children. Therefore, health education of parents should start as early as possible and should not be limited on providing information only.

Moreover, it requires regular examinations with constant motivation and re-motivation of parents to adopt and practice good oral hygiene habits every day. This represents the basis of oral health promotion, whose essential importance becomes evident in these most vulnerable population groups. Additionally, by doing so, many complications and their detrimental effects on the quality of life for these kids and their families could be avoided.

Conclusion

The essential need for preventive dental healthcare in children with rare diseases stems from the high prevalence of caries and gingiva-periodontal diseases in this group of children as well as numerous complications they carry, the

nature of the underlying disease and, finally complex, often high-risk dental treatment. Many complications and their negative impact on the quality of life of these children and their families could be avoided if adequate preventive-prophylactic measures were implemented on time.

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