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RISK FACTORS FOR CONGENITAL MALFORMATIONS OF THE MAXILLOFACIAL REGION

*Chuiкин Oleg Sergeyeovich
Viktorovna Viktorova Tatyana
Gilmanov Marsel Venerevich
Muratov Azamat Maratovich
Galiakberov Ildar Shafkatovich*

*Department of Pediatric Dentistry and Orthodontics,
Bashkir State Medical University, Ufa*

Annotation. The article provides a review of the literature on the study of the causes of congenital malformations and dentofacial anomalies, the identification of which is a prerequisite for substantiating and conducting an integrated system for the prevention of this pathology in children and adolescents.

Key words: congenital malformations; neural tube defects; crevices of the upper lip and palate, dentition.

Congenital malformations (CHD) occupy a leading position in the structure of childhood morbidity, disability and mortality and represent an important medical and social problem. [1-10]

The causes of congenital malformations can be varied: the effects of teratogens, maternal diseases, chromosomal aberrations, mutations of certain genes, and others. However, in a significant part of cases, the nature of VLD remains unknown. It seems most likely that the etiology of congenital malformations is multifactorial; in other words, both the genotype of the mother and the fetus, as well as the influence of environmental factors, affect the risk of congenital malformations. In the 60s of the last century, the first evidence appeared in the world literature that impaired folate metabolism and folic acid deficiency in pregnant women can affect the risk of spontaneous abortion and neural tube defects in the fetus. [5-15] This discovery aroused keen interest: in numerous studies of the 80-90s it was shown that the consumption of multivitamins with a high content of folic acid or folate-rich foods before conception and in early pregnancy reduces the

frequency of neural tube defects - as in mothers who already have a baby with such a pathology, and in women without a history of fetal neural tube defects. Many of these works were performed on small samples, and it remained unclear whether folate itself or other multivitamin components had a protective effect.

To date, several dozen studies have been carried out to study the association of polymorphic variants of folate metabolism genes with the risk of congenital malformations. Most of the work was performed on samples of 200-300 people in the experimental and control groups and focused on several of the most studied single nucleotide polymorphisms (SNPs), such as MTHFR C677T (rs1801133), RFC1 A80G (rs1051266), MTR A2756G (rs1805087), MTHFD1 G1958A (rs2236225).

In recent years, large works have begun to appear that analyze the associations of certain nucleotide substitutions with different types of CDF. However, associations with specific SNPs identified in some studies are not always reproduced in other studies. With confidence, only the association of the MTHFR 677TT

genotype with a neural tube defect can be stated, and only in populations of non-Latin European origin (Germans, Poles, English, etc.). This association was also confirmed in the Russian sample [5].

As a result of a number of studies, it was found that in pregnant women with a fetal neural tube defect, an increase in the blood level of homocysteine amino acid is observed, associated with impaired function of the enzyme 5,10-methylenetetrahydrofolate reductase (MTHFR). With a decrease in MTHFR function, delivery and metabolism of folic acid consumed by the body are disrupted. The lack of folic acid, the metabolites of which act as coenzymes in the biosynthesis of amino acids, DNA and RNA, leads to the development of hyperhomocysteinemia and disruption of the mitotic activity of cells in critical stages of embryogenesis, which possibly contributes to the development of various congenital malformations of the fetus. [16-19]

According to the literature, the MTHFR gene polymorphism caused by the replacement of C677T reduces the activity of the enzyme methylenetetrahydrofolate reductase, which leads to the accumulation of homocysteine and a decrease in the level of DNA methylation. This suggests that the accumulation of homocysteine or the violation of methylation plays a role in the etiology of a neural tube defect [9].

Among other genetic loci, associations of which were reproduced in at least two studies, RFC1 A80G (rs1051266), for which the association of the GG genotype with the risk of neural tube defect was shown, MTHFD1 G1958A (rs2236225), is the association of the A allele with the risk of neural defect tubes, MTRR A66G (rs1801394) - association of the GG genotype with the risk of neural tube defect, MTHFR C677T (rs1801133), - association of the T allele with the risk of cleft lip and palate, and congenital malformations of the circulatory system, BHMT G742A (rs3733890) - risk of neural labor defect ki. It should be noted that mainly such a type of congenital malformations as a neural tube defect was investigated, while the study of other types of congenital anomalies is very small [11].

The most common congenital malformations are congenital clefts of the upper lip and palate. The birth rate of children with this defect is up to 38% of all malformations in children [2, 3].

In the study of CDF, it is worth paying attention to subgroups within the same group. For example, when examining the congenital malformations of the maxillofacial region, cleft palate and cleft upper lip, as well as various types of adentia, should be examined separately. The variety of samples according to the degree of representation of defects of various etiologies in them can lead to a significant difference in the results.

The causes and risks of dentition are varied. All risk factors are divided into three groups of manageability: "managed", "hard to manage", "unmanaged". Most risk factors are manageable, i.e. timely elimination or weakening of their action prevents the formation of dentofacial anomalies. The "controlled" risk factors for the formation of

dentoalveolar anomalies include: low fluorine content in drinking water; a decrease in the immunological reactivity of the body (frequent colds, rickets, etc.); early artificial feeding; improper posture during sleep and wakefulness; the prevalence of soft foods in the diet; impaired breathing, swallowing, chewing; irrational use of nipples (dummies); bad habits (sucking fingers, objects, tongue, lips, etc.). "Hard-to-manage" risk factors include chronic and acute illness of the mother during pregnancy; toxicosis of pregnant women, the threat of termination of pregnancy, anemia, premature and postponed birth; birth complications; asphyxia, malnutrition, hemolytic disease, allergic and infectious diseases of the child, etc. Uncontrollable factors include factors that we cannot influence, such as heredity.

In areas of the Republic of Bashkortostan with developed petrochemicals, the prevalence of dentoalveolar anomalies was found in 36.0% of preschool children [Mukhametova E.Sh., 1991] and in 46.6% of schoolchildren [Averyanov SV, 1999]. In Beloretsk, the Republic of Bashkortostan, the prevalence of school-age children was 66.3% [S. Averyanov. et al., 2003]. In the city of Ufa, which is the center of the petrochemical industry of the Republic of Bashkortostan, a high level of prevalence of dentoalveolar anomalies in children is revealed (71.20%). In the structure of dentoalveolar anomalies among all examined children, combined anomalies prevail - 47.72%, anomalies of individual teeth make up 19.63%, anomalies of the dentition - 16.68%, anomalies of occlusion - 15.97% [5].

S.A. Gunaeva (2006) when examining 2375 children living in a city with a petrochemical industry, risk factors were identified at different periods of the formation of the dentofacial system. Thus, in children during a temporary bite, the prevalence of risk factors and impaired functions of the dentofacial system is $47.37 \pm 3.18\%$, and in the early shift bite, along with an increase in the number of dentofacial anomalies, the frequency of risk factors also increases to $54.24 \pm 1.93\%$. In a late shift and permanent bite, the frequency of risk factors decreases to 27.10% and 25.93%, respectively [5].

Congenital cleft of the upper lip and palate belongs to the category of the most severe malformations of the maxillofacial region. The frequency of this pathology according to different authors varies in the range from 12 to 36% of all human malformations [S.V. Dyakova et al., 2002; V.V. Roginsky et al., 2002].

In the Republic of Bashkortostan, the birth rate of children with congenital cleft of the upper lip and palate is higher than the national average [1, 3, 9].

It has been revealed that over the years in the Republic of Bashkortostan, congenital cleft of the upper lip and palate has occupied the first place in frequency among all malformations in children, with an increase in the dynamics over the past 4 years from 14.2% to 16.4% [2].

Shaikhutdinova D.I. (2005) analyzed the incidence of congenital malformations in the Republic of Bashkortostan. According to the data obtained in

2005, according to the monitoring results, congenital cleft lip and palate came out on top among other malformations of strict accounting and amounted to 17.7% [10].

The clinical characteristics of children with congenital cleft upper lip and palate showed a high incidence of severe forms. These include congenital cleft palate (38.68%) and combined cleft palate, alveolar ridge, hard and soft palate (35.31%). Their total frequency was 73.99%. More often, congenital cleft of the upper lip and palate occurred in boys - 55.40% [7].

Chuykin S.V. and Averyanov S.V. conducted an epidemiological dental examination of 1170 children aged 6 to 16 years living in the city of Sterlitamak. Examination of children revealed dentoalveolar anomalies in 677 children (57.86%). Of these, anomalies of individual teeth were observed in 140 children (11.97%), anomalies of the dentition in 114 (9.74%), anomalies of occlusion in 101 (8.63%), combined anomalies in 322 children (27.52%)) The prevalence of dentoalveolar anomalies among the children of Sterlitamak in the temporary bite was 38.46%. During the period of an early intermittent bite in children, the prevalence of dentoalveolar anomalies was 56.26%. In the period of a late intermittent bite, the frequency of dentoalveolar anomalies was 60.78%, and in a permanent bite it increased to 61.85% [1, 8].

An analysis of the literature indicates that researchers are paying close attention to various antenatal and postnatal causative factors of dentofacial anomalies. Despite the wide coverage of the issue of the influence of general and local factors on the development of dentofacial anomaly, studies of their relationship are not sufficiently informative and very controversial. Thus, the identification of the causes of pathology of the maxillofacial region, including genetic, is a prerequisite for the justification and implementation of their effective prevention.

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DENTAL MORBIDITY AND BIOCHEMICAL INDICATORS OF ORAL FLUID IN CHILDREN SUFFERING WITH CEREBRAL PARALYSIS

*Morozova Natalia Sergeevna
Kashtanova Maria Sergeevna*

Moscow State Medical University named after I.M. Sechenov

Annotation. Parents and medical specialists face the fact that for every 1000 children born, there are from 1 to 2–3 cases of giving birth to a child with cerebral palsy syndrome. Congenital malformations of the central nervous system are characterized by the multiplicity and combination of functional disorders. The maxillofacial region does not remain isolated from secondary changes in the morphological structure of bones, and damage to organs and tissues of the oral cavity becomes an integral part of cerebral palsy syndromes. As a result of damage to the musculoskeletal system, speech, and mental sphere, children cannot independently carry out rational oral care, therefore, they need constant care, and they certainly need help in taking measures to improve their oral cavity [1-4].

Key words: cerebral palsy, dental morbidity, biochemical parameters.

Relevance. Cerebral palsy is one of the most common diseases worldwide, leading to childhood disabilities due to impaired motor development. It occurs due to brain damage during the period of intrauterine development, childbirth and newborn, manifested by motor disorders (paresis, paralysis, hyperkinesia, impaired coordination). Given the development of not only the motor, but also the intellectual, psycho-speech and emotional spheres, the following forms of this disease are distinguished: double hemiplegia, spastic diplegia, hemiparetic form, hyperkinetic form, atonic-astatic form [5-13]. The Ural zone, which includes the Republic of Bashkortostan, is considered the most unfavorable in terms of child disability. The reason for the high prevalence of childhood disability is the high concentration of industrial enterprises in this territory. In cerebral palsy, cerebral structures responsible for voluntary movements are particularly affected. A motor defect is disabling not only because of the insufficiency or absence of certain skills, but also because it is a constant traumatic factor [14-17]. In addition, most children with cerebral palsy suffer from mental and speech changes. Thus, with cerebral pathology, the most important functions for a person suffer: movement, speech, psyche. Congenital malformations of the central nervous system are characterized by the multiplicity and combination of functional disorders. The maxillofacial region does not remain isolated from secondary changes in the morphological structure of the bones, and damage to organs and tissues of the oral cavity becomes an integral part of cerebral palsy syndromes. As a result of damage to the musculoskeletal system, speech, and mental sphere, children cannot independently carry out rational oral care and need constant care. Since children are easily

vulnerable to a disease such as cerebral palsy [18-19], dental measures should be carried out taking into account the specifics of neuromuscular pathology [1]. Prevention and treatment of dental diseases of such children should be of high quality and effective [3].

The aim of our study is to assess the state of the oral cavity in children with cerebral palsy, studying the kinematic viscosity and biochemical parameters of the saliva of children.

Materials and research methods. We conducted a clinical examination of children aged 12-15 years with a diagnosis of cerebral palsy of various forms (1 group - 40 people) and healthy children without neurological pathology (2 control group - 20 people). Children with cerebral pathology were examined on the basis of the State Educational Institution "Ufa Special Boarding School No. 13". External examination, examination of the oral cavity, assessment of oral hygiene was carried out visually and using a standard dental tool kit. To study the hygienic status, we applied the methods of Fedorov - Volodkina, Schiller - Pisarev tests, PMA and Green - Vermilion index. The quality of oral hygiene in patients was evaluated before conducting hygiene lessons, at the end and after a month of controlled brushing. The oral fluid was collected in the morning on an empty stomach, and the oral fluid was collected in 4.0 ml glass tubes. To determine the kinematic viscosity of saliva, a VPZh-4 capillary viscometer was used. Colorimetric determination of protein in saliva was carried out using the BELOK-PGK-NOVO reagent kit. When the protein interacts with pyrogallol red and sodium molybdate, a colored complex forms, the color intensity of which is proportional to the protein concentration in the sample. The photometric determination of calcium in saliva was determined using a set of reagents CALCIUM-NOVO. In an acidic