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LIP MALFORMATION: LITERATURE REVIEW

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Abstract: INTRODUCTION: Congenital malformations refer to failures during embryonic development, which are the biggest cause of infant mortality. Malformations are varied and can be structural, functional, metabolic, behavioral or hereditary, depending on the moment of onset of the lesion, etiology and pathogenesis. In the past, it was believed that the embryo was protected from environmental agents due to the presence of extra-embryonic membranes, but today it is known that congenital defects, in numerous cases, result from the use of drugs, for example. Lip malformation, characterized by an opening of the upper lip and even by communication between the oral cavity and the nasal cavity (configuring the clinical picture of cleft lip and palate), is very common in cases where the pregnant woman is a user of legal or illicit drugs.
OBJECTIVE: describe the biological changes that lead to this malformation.
METHODOLOGY: involved a literature review in electronic databases and books on embryology, histology, biochemistry and genetics, between March and May 2023.
RESULTS: cleft lip and palate affect the upper lip, gums and palate, being caused by anomalous tissue fusions during facial development. Oral cells vary in keratinization, influencing protection against friction during chewing. These malformations can occur alone or associated with genetic syndromes, but external factors increase the risk, interfering with facial tissue growth. Folic acid deficiency also contributes, as it is essential in the formation of the neural tube.
CONCLUSION: Cleft lip is a condition resulting from poor development of the epithelial tissue of the upper lip, forming a cleft lip. When the cleft reaches the gums, soft palate and/or hard palate, it is called a cleft palate. The exact cause involves genetic and environmental factors, such as folic acid deficiency, drug use, viral infections and exposure to alcohol and cigarettes during pregnancy.
Keywords: cleft lip, cleft lip and palate, congenital malformation.

INTRODUCTION

Congenital malformations are terms frequently used to describe developmental disorders present at birth, being the main cause of infant mortality (more than 20% of child deaths in North America are attributed to birth defects) and can be structural, functional, metabolic, behavioral or hereditary. However, no classification of congenital malformations is universally accepted, but nowadays a practical classification system is widely accepted among clinicians, which takes into consideration, the moment of onset of the lesion, the possible etiology and pathogenesis.

The branch of science that studies the causes, mechanisms and patterns of abnormal development is tetralogy. The basic principles of teratogenesis are the critical periods of development, the dosage of the drug/chemical compound and the genotype (genetic constitution) of the embryo. Until the 1940s, it was believed that embryos were protected from environmental agents (drugs, viruses...) by the extra-embryonic membranes (amnion and chorion) and by the mother's abdominal and uterus walls. However, it was discovered that about 7 to 10% of human birth defects result from the disruptive action of drugs, viruses, among others.

Thus, the causes of congenital anomalies are divided into genetic factors, such as chromosomal abnormalities, and environmental factors. However, most congenital anomalies are caused by genetic and environmental factors together (multifactorial inheritance). Furthermore, major developmental defects are much more common in early embryos (10 to 15%),

but most have spontaneous abortions and chromosomal abnormalities are present in 50 to 60% of those that are spontaneously aborted.

A very common malformation is the cleft lip, which is characterized by an opening that begins on the side of the upper lip and is divided into two parts, and the cleft palate, which is an opening in the lip or palate (roof of the mouth), which can be complete, lip and palate.

In this sense, the objective of this study is to describe the biological changes that result in labral malformation.

METHOD

Searches were carried out in electronic databases (PubMed and Google Scholar) and in textbooks on embryology, histology and genetics, between March and May 2023.

DEVELOPMENT

When it comes to cleft lip, malformations can be seen in the facial region of the upper lip, which divides it into two parts; In some cases, the structures of the gums, soft palate and hard palate are affected and are classified as cleft palate. In more serious cases, a crack in the jaw and teeth may occur. The soft palate and hard palate make up the entire roof of the oral cavity and the floor of the nasal cavity, they have the function of aiding speech and pronunciation of consonants, preventing the entry of food and liquids into the nasal cavity during swallowing and finally participating of the vomit reflex process. the soft palate is limited superiorly by the respiratory mucosa of the nasal cavity, inferiorly by the mucosa of the oral cavity, posteriorly it is not limited and is located suspended in an inferior angle directed to the larynx, holding the uvula in its midline, posterolaterally it forms part of the portion superior of the palatopharyngeal and palatoglossal folds and anteriorly is connected to the bony hard palate by an aponeurotic plate (thick tendinous aponeurosis of the tensor muscles of the soft palate on both sides at the level of the vibratory line). The soft palate, which is equivalent to 1/3 of the palate, does not have bone structures, only muscular fibers, and its muscles are composed of the uvular muscle, the tensor veli palatini, the levator veli palatini, the palatopharyngeus muscle and the palatoglossus muscle.[1] The hard palate is the bony subsection of the palate of the mouth and is equivalent to 2/3 of the palate. The anterior part of the hard palate is limited anteriorly and laterally by the maxillary teeth, superiorly it is covered by the breathing epithelium of the nasal cavity and inferiorly by the chewing epithelium of the oral cavity. Later, this palate is connected to the soft palate.[2]

The lip tissue is cornified stratified squamous epithelium. Furthermore, we have tissue from the ventral part of the tongue, which does not have taste buds (which are structures distributed on the back and upper part of the tongue, concentrating, above all, on the sides and tip of this important organ of the human body), which is also of the stratified pavement type. The tissue of the oral cavity has a large number of mucus-producing glands and few serous glands. Depending on the region of the mouth, the stratified squamous epithelium can be keratinized or not and the soft palate, lips, cheeks and floor of the mouth are covered by non-keratinized squamous epithelium. Found in the gums and hard palate, keratin serves to protect the oral mucosa from friction caused during chewing. The lamina propria of this tissue has several papillae and is in direct contact with the periosteum. The main structures affected in the cleft lip have their specific histology, which is: the lip tissue is of the non-keratinized corneized stratified squamous epithelium type (but also has a transition zone from the non-keratinized oral

epithelial tissue to the keratinized epithelium of the skin), the tissue of the mouth, cheek, floor of the mouth and soft palate are all of the non-keratinized squamous epithelium type, the gums and hard palate are of the keratinized stratified squamous epithelium type, and the vestibule of the nose, another structure affected by cleft lip, is made up of a mucosa that is the continuation of the skin of the nose that is initially formed by the stratified squamous epithelium of the skin that loses its keratin layer to the connective tissue of the dermis that will generate the lamina propria of the nasal mucosa.[3]

The congenital malformation of the cleft lip, also called cleft lip, is characterized by an opening that in all cases begins on the side of the upper lip, which divides it into two segments. This non-closure of the structures may be restricted only to the lip, but it may also progress to the groove between the lateral incisor and canine teeth, to the upper jaw, to the gums and finally it may progress to the nose. The cleft palate is characterized by an opening across the roof of the mouth and the base of the nose, meaning there is no separation between these structures, thus forming direct communication between them. This malformation can also cause bifid uvula (a condition in which the uvula is divided into two parts). From the fourteenth week of pregnancy onwards, it is possible to diagnose cleft lip using ultrasound examinations.[4] Cleft lip and palate is a consequence of the failure of the first upper brachial arch to complete fusion with the arch in the frontonasal process during pregnancy. The predisposition for the formation of cleft lip arises through failure of penetration of the mesoderm and extinction of the ectodermal grooves, responsible for the formation of facial processes. In medial nasal and frontonasal development, the formation of the medial portion of the nose and the anterior portions of the maxilla and palate are affected.[5] Within this process, the formation of the upper lip occurs through maxillary and medial nasal processes, which develop towards the midline, which must be fused, however, when there is not, it derives divisions that vary between cleft palate, labial unilateral, bilateral, bilateral and palatal.[6]

These facial clefts can occur as isolated malformations or associated with genetic syndromes with Mendelian inheritance, syndromes with multiple malformations or syndromes that result from chromosomal aberrations. Furthermore, only 20% of pregnant women do not ingest any chemical drug during pregnancy and some of these compounds have been considered teratogenic, potentially causing facial cracks[7], and there may be some genetic influence in a third of cases, but it is usually external factors that cause the malformation without knowing the cause. There has been talk about the influence of taking some medications, viral infections, radiation, among others.[8]

According to a study carried out at the Biosciences Institute of ``Universidade de São Paulo`` (USP), hypotheses were raised that the deficiency in the metabolization of folic acid, which is a water-soluble vitamin belonging to the B complex for the formation of structural proteins and hemoglobin during Pregnancy is one of the factors that can increase the risk of developing cleft lip. In addition to cleft lip, folic acid also influences another malformation that involves the mouth, the cleft palate. This occurs because folic acid is important for the proper development of the neural tube, which is an embryonic structure that will give rise to the fetal brain and spinal cord, as well as the development of the upper lip. According to the coordinator of the scientific work, Maria Rita Passos Bueno, explains that it is not correct to say that metabolic insufficiency is a maternal disease, as the mother would only function as an environmental factor for the appearance

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of cleft lip, whereas other studies suggest that changes in the expression of genes involved in signaling growth factors, such as connective tissue growth factor (CTGF) and epithelial growth factor (EGF), may be involved in the development of cleft lip. Furthermore, exposure to toxic substances during pregnancy, such as alcohol and smoking, can increase the risk of developing lip malformations, as these substances can interfere with growth factors and the proper formation of facial tissues. It is also important to highlight that the development of these lip malformations is multifactorial and may involve many other factors in addition to biochemistry. Treatment usually involves a multidisciplinary approach, which may include plastic surgery, speech therapy and dental care.[9].

CONCLUSION

Cleft lip and palate represent significant challenges in healthcare, affecting not only facial aesthetics, but also speech and eating functionality. This study highlighted the complexity of embryonic development and the multifactorial factors that contribute to these conditions, including genetic and environmental influences.

Histological analysis revealed specific features in the affected structures, providing insights into the formation processes and the anatomical regions involved. Furthermore, the search for evidence in electronic databases and academic sources contributed to the understanding of risk factors, highlighting the importance of folic acid and exposure to toxic substances during pregnancy.

A multidisciplinary approach to treatment was highlighted as crucial, involving plastic surgery, speech therapy and dental care. A deeper understanding of these malformations allows not only more effective therapeutic interventions, but also preventive strategies, such as promoting adequate folic acid consumption during pregnancy.

Ultimately, research into the biological modifications that result in these malformations not only expands scientific knowledge, but also contributes to the development of more comprehensive and personalized approaches to caring for these conditions, providing a better quality of life for those affected.

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