Labio-palatine Cleft, Morphological Substrate

CRISTIAN ROMANEC[1], MARIANA PACURAR[2], MIOARA DECUSARA[3]*, MONICA MIHAELA SCUTARIU[4]*, DELIA HINGANU[5], MARIUS VALERIU HINGANU[5], CORINA CIUPILAN[5]

[1] Grigore T.Popa University of Medicine and Farmacy Iasi, Department of Orthodontics, 16 Universitatii Str., 700115, Iasi, Romania
[2] University of Tg. Mures, Faculty of Medicine and Pharmacy, Department of Orthodontics, 48 Gh. Marinescu Str., 540142, Tg. Mures, Romania
[3] University Dunarea de Jos of Galati, Faculty of Medicine and Pharmacy, Department of Dentistry, 47 Domneasca Str., 800008, Galati, Romania
[4] Grigore T. Popa University of Medicine and Pharmacy Iasi, Dental Medical Faculty, Department Implantology, Removable Restorations, Technology, Oro-Dental-Diagnosis and Gerontostomatology, 16 Universitatii Str., 700115, Iasi, Romania
[5] Grigore T.Popa University of Medicine and Farmacy Iasi, Department of Morphofunctional Sciences I, Discipline of Anatomy, 16 Universitatii Str., 700115, Iasi, Romania

Labio-palatin clefts are the most common type of craniofacial malformation encountered in practice and among the most common congenital abnormalities; it represent morphological and functional defects in newborns caused by genetically changes or environmental factors; those of the cervico-facial region have an increased incidence due to local embryological complexity and multifactorial etiology. The anomaly, with its variants, results from an inherent defect between the internal and external nasal buds, both from the frontal and upper maxillary bud. Labio-palatine clefts are characterized by a tissue deficiency as well as an abnormal disposition of the present tissues. It is believed that the labial clefts are consecutive to the lack of apoptosis of the ectoderm which envelops the internal maxillary and nasal buds, thus constituting a barrier to the fusion process of buds. Depending on the location and the extentension of the cleft, the labial cleft occurs, or the more frequent, the labial-alveolar cleft. The study group consisted of 22 patients with labio-palatine clefts, of which 16 boys (72.72%) and 6 girls (27.27%), who presented in the clinic for treatment. When the causative factor acts earlier, the clfet develops posteriorly, since mesodermization begins from the posterior to the anterior. The more disturbing factor acts, the greater the cleft. The increase in the incidence of labial-palatine cleft is believed to be mainly due to the increase in the number of women of older gestational age in women; women over 35 years of age have a double risk of having children with labio-palatine clefts, the risk being three times higher for mothers over the 39years.

Key words: labi-palatine clefts, medical recovery, complex treatment

It is well known that both genetics and the environment play an important role in the etiology of labio-palatine cleft. Embryogenesis of the cleft occurrence can occur through several mechanisms: the lack of contact between the maxillary buds which may occur as a result of the volume change of the buds and, also, the lack of contact can occur [1] by distortion of some cranial-faced portions, even if the buds has normal dimensions; lack of epithelial fusion, even under the contact of buds - is a poorly accepted mechanism; perforations of the epithelial fusion points by the occurrence of epithelial cysts and pearls along the fusion area, which may increase and cause failures of buds union [2]. It has been found that palatine clefts are more common in females [3]. This might be due to the fact that the ascendancy of the palatine processes would later occur in female gender during the organogenesis. However, overall, the male gender is more affected by labio-palatine clefts than the female gender. It is generally accepted that there is a genetic component in the cause of clefts, about 40% of cases presenting a family history of labio-palatine cleft; this genetic predisposition is exacerbated by environmental factors [4].

The failure of mesenchymal migration is considered to be the most important mechanism in the production of cleft. Mesenchymal migration may be defective due to initially low amounts, or under the influence of various environmental factors.

From an etiological point of view, most of the cases of clefts can have a complex etiology, with interactions between predisposing genetic factors and environmental factors [5].

Identifying environmental factors that increase or decrease predisposition to oro-facial clefts continues to be of major concern. Disclosing the mechanism underlying maternal smoking and oral clefts could reveal the possible pathways leading to the defect [6].

Etiopathogenesis of the clefts has been studied in detail but is still poorly elucidated; it is considered to be the result of intercourse between different genetic factors and the environment (exogenous).Teratogenic action depends on the so-called embryological schedule. After the end of the critical period specific to organ development, the teratogenic agents no longer have any malformative action [7]. The same teratogenic agent may cause various malformations, depending on when they act [8].

Of the chemical agents an important role is played by drugs. The intent of drug action on the embryo increased after the impact caused by the use of thalidomide. Aminopterin and other folic acid antagonists (such as Dilanthin) also have a teratogenic action. A series of antibiotics (Hadacidin) or antimitotic (cytostatic) are capable of producing malformations. Although no malformations have been observed in humans, Trasler recommends avoiding aspirin that caused clefts in mice.

* email: *mioaradecu@yahoo.com, monascutaru@yahoo.com*

The influence of physical factors and radiation on cell division is due to the discoverer of uranium radioactivity, H.Becqerel. The effect of radiation depends on: the penetration capacity; energy absorbed by irradiated tissue; relative ionization density; cell radiosensitivity that is directly proportional to proliferation capacity and inversely proportional to the degree of differentiation and varies with species. With regard to sources of contamination of the human body, they can be grouped into two categories: natural radiation and artificial radiation.

Basic nutritional deficiencies (nutritional factors): proteins, lipids, carbohydrates do not seem to play a role in the genesis of malformations in humans. The same can be said about mineral deficiencies. Probably some congenital dysplasia seen in some nutritional deficiencies are due to vitamin deficiencies [9].

Infectious factors may have teratogenic effects, causing under certain conditions structural changes, chromosomal and nuclear mutations, disruption of the cell division. The most well-known are the malformative consequences after viral infections of the pregnant mother. The cytomegalovirus inclusions were also teratogenic, herpes virus, urliane virus, influenza virus.

The uterine environment can influence the development of the embryo: anatomical and physiological variations in the uterus, such as altered blood supply (hypoxia) or changes in uterine pressure or uterine fluid quantities may more frequently cause malformations at the level of the palate; metabolic alterations have significant teratogenic potential. A series of hormones and metabolic degradation products can cross the placenta. Diabetes is a high-risk disease for the embryo. Thyroxine deficiency is another factor that is experimentally proven to be a producer of facial cleft.

The family study of children with facial malformations can bring forward a series of features that indicate a genetic predisposition [10]. Thus it is suggested that the parents of the children with a cleft have a lower development of the middle floor of the face, but unfortunately it is not possible to have a relevant control of the adult population. It also appears that the parents of the children with cleft can have a recurved upper lip, a larger transverse diameter of the face and a tendency of hypertelorism [11]. This suggests a deficiency of the skeletal component that derives mainly from embryonic mezenchim, in families with a history of positive facial malformations.

From the study of malformations transmission, we noticed the large incidence of multiple cases in the same generation in families without a teratological history, which advocates the possibility of mutations under the influence of environmental factors in germ cells of the past generation [12].

In cases where malformations of the face, tramsmitted to 2-3 generations, it could be observed, a great variability of the transmission directions of these. Probably the intervention of the numerous endo- and exogenous factors determines the irregular nature of the transmissibility of these defects, the persistence or, on the contrary, their extension. It can be deduced that the transmissibility of such congenital defects has a dynamic character [13].

The same impression is left behind by the comparative study of clinical-anatomical types. Two major trends can be observed: to maintain the type of malformation and polymorphism, with a marked predilection to aggravation [14]. This latter trend suggests the alteration of the hereditary substrate, which can be expressed variably under the influence of environmental factors.

The finding that sometimes the labio-maxilo-palatine clefts are accompanied by malformations of other segments of the body, may prove the damage of genetic "nodules" with somatic consequences at different levels. Thus, the clefts can be included in some chromosomal anomalies that cause general syndromes such as Treacher-Collins, Pierre-Robin and Klippel-Fiel.

Treacher-Collins Syndrome, or mandibulo-facial disostosis has an autosomal dominant substrate. It is characterized by hypoplasia of the zigomatic bone and the mandible, which has a retrognative position, along with palpebral fisures, malformations of the ear structure and auditory deficiencies; 30% of cases have labio-palatine clefts [15].

Also, alongside the cleft, a number of other congenital defects associated with certain systemic complications may occur to a greater extent than in the case of labial clefts [16]. These include cardiac, central nervous system, kidney and skeletal defects, which are associated with 20-25% of palatine clefts and often complicate treatment management.

Pierre-Robin's syndrome is characterized by a retrognate mandible, hypoplasia, glossoptosis and palatine clefts, leading to a respiratory distress, a hallmark of this syndrome [17].

Klippel-Fiel syndrome is manifested by an irregularity of cervical vertebrae, along with clefts. It should be noted that these syndromes are encountered with a fairly low frequency. Labio-palatine cleavage syndromes are associated with genomic polymorphisms of genes (TGFA) encoding growth and transformation factor-alpha (TGF-V), a ligand-containing epidermal growth factor receptor (EGFR) comprised of the majority of the epithelium [18].

Labio-palatine clefts are embryogenesis disorders of the stomatognathic system that occur due to the action of genetic or non-genetic factors in weeks 5-6 of intrauterine life. The clefts fall into the group of congenital malformations of the face. They appear from birth as a slit in the upper lip, hard palate and/or soft palate [19].

If the maxillo-facial development is almost normal in unoperated labio-palatine clefts, there is a developmental deficit in all three directions of the space, due to postoperative scars and bone hypoplasia, with consequences on dento-maxillary functions [20]. The monstrous face from the moment of birth, as well as the feeding difficulties of the infant, the defect of speech and hearing of the child with labia-palatine cleft causes psychic trauma over the families from which it originates.

Treatment of labio-palatine clefts is complex and interdisciplinary and lasts for a long time, from birth to late, after puberty.

Early treatment steps are: preoperative orthopedic treatment, especially between 1 and 4 weeks of age, this phase being used in a small number of patients where the alveolar segments are very large and may complicate an appropriate surgical treatment [21].

The lip plasty is also known as cheiloplasty. It is practiced within 10-12 weeks of life. Surgery is performed when the immune system is more developed. A rule that has successfully passed the time trial and applies for the first surgery is: the child must have over 10 weeks, over 10mg% hemoglobin and about 5kg [22].

Restoring the continuity of the orbicular muscle by cheiloplasty allows the alveolar segments to fit the anterior region into a functional matrix; eliminates abnormal lateral traction by the orbicular, especially the premaxilar fragment. These two effects allow the alveolar segments to occupy a position as close to normal as possible by re-positioning the protruding fragments.

Plasty of palate is the most controversial stage in terms of timing, staging and surgical technique; it can be practiced around the age of 18-24 months.

The controversies arise from the fact that it was clinically established that a satisfactory phonation requires a morphological and functional integrity of the secondary palate (the bony palate and soft palate) as early as the child begins to speak. For this reason, operators prefer to make the interventions around the age of 12 -18 months [23].

Another controversial element is the area of surgical intervention: palatine plastic surgery is initially limited to the restoration of the soft palate (the palatine veil and the lueta), and then to make the bone palate plasty (the two-stage restoration), or to practice palatin raffia in one time. The techniques most commonly used are the von Langenbeck technique (bipedicular palatine muco-periostic flaps) and the V-Y-push-back technique.

Early orthodontic treatment refers to the alignment of teeth and the correction of crossed occlusions or inverse angles in deciduous dentition or mixed teeth. The aim of orthodontic treatment is to correct any frontal inverse angles, reverse posterior lateral occlusion. As a rule, the disturbances that occur during this period, especially the posterior crossed occlusion, are an indicator of the severity of late dental-alveolar involvement [24].

Logopedic (phoniatric) treatment is more intense in the 6-11 years, but can begin earlier than this age. The most disturbing disorder that occurs and causes defective phonation is the air discharge on the nose during speech (rinolalia aperta). The appearance occurs when the palatinal vein can not come into contact with the posterior wall of the pharynx, or when it presents mobility disorders or the presence of oro-nasal fistulas. Misalignment of the incisors and tight labial and alveolar scarrs may cause phonation disorders. The primary objective of speech therapy is to correct articulation errors.

The plumage of the alveolar defect is indicated in the clefts that affect the primary palate, where the continuity of the alveolar arcade in the lateral incisors and canines areas is interrupted [25]; bone resorption at this level can occur with root denudation and tooth loss (lateral incisor, canine).

The necessity of realizing the dento-alveolar arcade continuity, of its symmetry and of preventing the periodontal damage of the teeth limiting the defect is evident. It uses autogenous or homogenous bone materials, or even materials that induce neoosteogenesis.

Surgical technique does not only create a union of muco-periostic flaps over the defect, but also initially places the bone graft, covering later with the mucous membrane. This intervention is not practiced early, with the primary or secondary palate plasty, since the removal of the muco-periostic flaps may affect the maxillary growth.

Experimental part

Materials and methods

The study aims to perform a statistical analysis on a group of patients with labio-palatine clefts, admitted to the BMF Surgery Clinic, during the period 2012-2016, with a view to establishing plastic surgical treatment or for plastic surgery at the level of postoperative sequelae.

The study group consisted of 22 patients with labio-palatine clefts, of which 16 boys (72.72%) and 6 girls (27.27%), who presented themselves in the clinic for the purpose of establishing specialized treatment.

The anamnesis of the mothers showed they suffered at least one viral infection during pregnancy. All of them denied having taken a medication with a possible teratogenic effect or smoking.

Results and discussions

In the studied group, the frequency distribution of the anatomical-clinical forms of the labio-palatine clefts, the highest percentage being recorded by the total bilateral clefts - 0%; unilateral anterior cleft 0%; anterior bilateral cleft 0%; total unilateral cleft - 27.27%; total bilateral cleft - 54.54%; incomplete posterior cleft-9.09%; complete posterior cleft-9.09%.

In terms of urban or rural origin, their percentage is urban - 82%; rural area -18%.

A correlation can be made between the presence of anterior and total clefts in rural children and anterior and total clefts in urban children. When the causal factor acts earlier, decay occurs later, since mesodermization starts from the posterior to the anterior. The more the disturbing factor acts longer, the greater the cleavage.

The cleft cases with normal birth weight have a frequency of 72.72%, 18.18% for dystrophic cases, and 9.09% for overweight patients.

It is found that in approximately 73% of cases, birth weight is unaffected, the affection being secondary to an embryopathy that occurs in the 4-12 weeks of intrauterine life. In some studies, it was found a correlation between weight at birth and the shape of the clefts, the more the gap is later, the lower the birth weight, and the higher the decay is, the higher the birth weight.

Treatment of labio-palata clefts is a complex treatment involving a team of specialists. Each of them intervenes at some point in order to ensure that the next therapeutic steps are carried out [26, 27].

Regarding the surgical management of the applied treatment, the following surgical interventions were carried out: the plasty of oro-nasal oriffice in two planes -18.18%, chyloplasty-27.27%, veloplasty -0.09%, plasty with palatal flap -18.18%; plasty with vestibular flap 27.27%.

Orthodontic active treatment begins around the age of 7 years [28]. The stage of alveolar grafting (8 to 10 years) is followed; to the age of 12-14 years, complex and individualized orthodontic procedures are performed for the final dentition. For some patients, orthodontic treatment may take up to 18-20 years.

Approximately 65% of cases occurred with postoperative sequelae of the labio-maxilo-palatine clefts. The causes are multiple, the most important being the intrinsic changes caused by splitting, as well as the fact that the surgery is naturally followed by the organization of a fibrous scar tissue. Therefore, it is necessary for the primary intervention to achieve an approximation of the ends of the lip muscles and, in the case of large bilateral clefts, to allow a smooth passage of the muscle fibers into the prolabium [29].

Also, muscle suture should reorient muscle fibers in a physiological manner to allow for a good lip function. Vestibuloplasty is most often required after bilateral clefts when the vestibular denture is tight or scarred [30]. A dense, normally conformed vestibular ditch favors the normal functionality of the orbicular. Thus, as secondary changes in the lip were observed either the shortening and the prominence of the lateral lip area, or the lip was too short or too long on the affected side, or where the restored lip is too strained [31].

In the bilateral cleft, there was a crash of the nasal dome, the nostrils were horizontal and the columela was shortened.

Conclusions

Congenital malformations are a major and complex public health problem to be addressed systematically and interdisciplinary, according to modern principles. The goal of these steps is, of course, to achieve the best possible individual results, ensuring that the development is as close to normal as possible.

The morphological aspects in the case of labio-palatine clefts are mainly characterized by the same elements, the individual changes being variations of a classic developmental pattern.

Viral infections during pregnancy is one of the most common cause for labio-palatine cleft.

References

1.BAYERLEIN, T., et. al. J Cranio-Maxillofacial Surg, 34, 2006, p. 57.
2.BING, Z., et. al., J Cranio-Maxillo-Facial Surgery, 39, 2011, p. 313.
3.CARSTENS, M.,H., Clinics in Pl. Surg, 2004.
4.CASH, A.C., Front Oral Biol. Basel, 16, 2012, p. 111.
5.DAW, J.L., PATEL, P.K., Clinics in Pl.Surg., 2004.
6.ENEMARK H., et.al., Cleft Palate Craniofac J, 38, no. 2, 2001, p:155.
7.EVANS, C.A., Clinics in Pl. Surg, 2004.
8.GKANTIDIS, N. et al., J Craniomaxillofac Surg. 2012.
9.HOUT, V. et.al., Clin Oral Invest, 15, 2011, p. 297.
10.IIZUKA, T., HALLERMANN, W., SETO, I., SMOLKA, W., SMOLKA, T., BOSSHARDT, D.D.,. Clin. Oral Impl., 16, 2005, p. 700.
11.LOSEE, J.E., KIRSCHNER, R.E., Comprehensive Cleft Care. McGraw-Hill Medical 2008.
12.JOSIP, B., PETER, P. et. al., J Cranio-Maxillofacial Surg, 34, 2006, p. 17.
13.KAPP-SIMON, K.A. Psychological Issues in Cleft Lip and Palate, Clinics in Pl. Surg. - Saunders, apr. 2004.
14.KARSTEN, K.H., GUNDLACH, C.M., J Cranio-Maxillofacial Surgery, 34, 2006, p. 1.
15.LALETIN, A.I., IASTREMSKI, A.R., Stomatologiia (Mosk), 91, no.2, 2012, p. 51.
16.LEONARD, B., KABAN, MARIA, J., Pediatric Oral and Maxillofacial Surgery. Saundres 2004.
17.LORE AND MEDINA. An Atlas of Head and Neck Surgery – Fourth Edition. Saundres 2005.
18.LUPAN I.: Recuperarea Medicala a Copiilor cu Malformatii Congenitale ale Fetei, Chisinau Medicina, 2004, p. 23-24, 27-30.
19.MARAZITA M.L., MOONEY M., Clinics in Pl. Surg., Saunders, 2004.
20.MARSH J.L., Clinics in Pl. Surg. - Saunders, 2004.
21.MCALLISTER, B.S., HAGHIGHAT, K., J Periodontol., 78, no.3, 2007, p. 377. .
22.MULLIKEN, J.B., Clinics in Pl. Surg., Saunders, 2004.
23.NOLLET, P.J., KUIJPERS-JAGTMAN, A.M., CHATZIGIANNI, A., SEMB, G., SHAW, W.C., BRONKHORST, E.M., KATSAROS, C. J., Craniomaxillofac Surg., 35, no. 6-7, 2007, p. 278.
24.PALARIE V., Medicina Stomatologica, 4, no. 21, 2011, p.19.
25.RANKO MLADINA et.al., J. Cranio-Maxillofacial Surg, 36, 2008, p. 335.
26.RENE MALEK. Cleft Lip and Palate. Martin Dunitz 2005.
27.SALYER, K.E., GENECOV, E.R., GENECOV, D.G., Clinics in Pl. Surg., 2004.
28.SANDOVE, A.M., CULP, J.A. Cleft Palate Repair, Art and Issue- Clinics in Pl. Surg., apr. 2004.
29.SEMB, G., Front Oral Biol., 16, 2012, p. 124.
30.SHETYE, P.R. Clinics in Pl. Surg., 2004.
31.VIEIRA, A. R.: Front Oral Biol. Basel, 16, 2012, p. 19

Manuscript received: 21.11.2017