

Risk factors and the prevention of oral clefts

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Abstract: This article presents general aspects of risk factors and particularities of the management of individuals with oral clefts (OCs). A practical manual of prevention and management of this congenital defect was prepared based on a review of the literature and using data from Brazilian multicenter studies. Since OCs require efforts from all levels of healthcare, the data herein presented permits appropriate follow-up for affected individuals and their families. Also, the recognition of risk factors is crucial for planning and implementing preventive measures at the individual and population levels.

Keywords: Cleft Lip; Cleft Palate; Risk Factors; Primary Prevention; Tertiary Prevention.

Introduction

Recognition of etiology, risk factors and natural history is essential to define how prevention and treatment should be planned and implemented, as well as to measure the efficacy of such intervention. These issues, associated with the assessment of outcomes and patient satisfaction, form the knowledge base which is critical for developing sensible and equitable healthcare policies.

Oral clefts (OCs) are a heterogeneous and important group of congenital defects with prevalence of 1:600–1,000 among newborns.¹ It includes syndromic and non-syndromic cleft lip (CL), cleft palate (CP) and cleft lip and palate (CLP). OCs are an etiologically heterogeneous group. Approximately 70% of the cases are isolated (non-syndromic) with etiologic complexity, involving several genetic and environmental risk factors, following a multifactorial threshold model of inheritance. In this situation, familial recurrence is often present and family history should be carefully investigated.

Laboratory facilities have improved the rate of specific diagnosis, and more than 600 syndromes involving OCs have already been recognized.^{2,3,4,5,6} Mental retardation and association with other congenital defects are often seen in this group, in which chromosomal aberrations are the most frequent etiology. Among them, the 22q11.2 deletion syndrome deserves special attention, since the phenotype is heterogeneous and changes with age.⁷

Mendelian/heterogeneous abnormalities and teratogenic factors are the next most prevalent etiologies.^{8,9,10,11} Teratogenic agents are important and preventable factors for congenital defects in general.

Despite all the available technologies, around 50% of patients with syndromic OCs represent cases of multiple congenital anomalies without any identifiable etiological factor.^{6,8,9,10,11}

The World Health Organization (WHO)¹² acknowledges that OCs require investment in public policies, in view of their high prevalence, their association with other congenital defects and co-morbidities and their need for prolonged treatment that requires efforts from all levels of healthcare.

Considering the potential for prevention at the population and individual levels, this article describes general aspects of risk factors and particularities of the management of OCs.

Prevention

In OCs, the preventive approach can be related to two different strategies:

- education of the population about risk factors and
- genetic counseling for families (or individuals) at risk.

Most risk factors can be recognized during family planning and prenatal consultations. Families who receive diagnosis and guidance before or during the prenatal period have the opportunity to seek information and treatment earlier.¹³

The common risk factors are discussed below.

Lifestyle, maternal illness, nutrition and environmental factors

With regard to OCs, maternal exposure to tobacco and alcohol use, metabolic status (diabetes, obesity or low weight), viral infection, medicinal drugs (anticonvulsants) and teratogens (solvents, agricultural chemicals), as well as the preventive role of vitamin supplements, have been investigated. Maternal smoking during pregnancy is consistently linked with increased risk of OCs, and second-hand smoking has been investigated as well. Findings on the other risk factors and gene-environment interactions have been inconclusive due to methodological issues.^{3,4,5}

In order to educate the population and health professionals, recommendations for healthy pregnancies have been made.^{14,15}

Parental age

A meta-analysis approach of parental age showed that fathers 40 years or older have a 58% higher probability of having a child with cleft palate (CP); for mothers over 40 years of age, the probability is 28% higher for CP and 56% higher for CLP.¹⁶

Consanguinity and recurrence

It has been suggested that there is a greater genetic component in the etiology of CL based on the observation of an excess of individuals with CL over CLP in the offspring of consanguineous parents.¹⁷

A population-based study conducted in Denmark showed that anatomical severity does have an effect on recurrence in first-degree relatives, and the type of cleft is predictive of the recurrence type. Third-degree relatives also have an increased recurrence risk compared to the background population.²

Genetic evaluation and counseling is needed for virtually all patients with OCs because of its heterogeneous etiology and significant association with minor and major defects.^{5,18} Furthermore, the importance of accurate and detailed phenotype descriptions of OCs to produce good etiological and epidemiological studies has recently been emphasized. In this regard, attention should be given to subphenotypic features of the lip (completeness of the cleft, presence of pits/prints, dental and orbicularis oris muscle anomalies) and palate (completeness of the cleft, submucous defects, bifid uvula and ankyloglossia).³

Also, identification of the etiology of a syndromic OC would help management of the patient and prevention for the entire family.

Clinical management

Specialized treatment

Multidisciplinary specialized care has been considered *state of the art* for treatment of OCs.¹ It is long-lasting and dependent on surgical correction. When postponed, it increases morbidity and impairs the child's development.^{13,19} In addition, orthodontics and speech therapy are usually indicated, depending on the severity of the cleft.

The affected child should be closely followed and monitored to detect feeding difficulties, the presence

of other congenital defects, co-morbidities and nutritional failure.

Feeding difficulties

Insufficient suction, regurgitation of milk into the nasal cavity, ingestion of insufficient amounts of food and, in special situations, aspirations are described for babies with OC.^{20,21} These disorders need to be addressed quickly to ensure that nutritional needs are met and to avoid or minimize the related complications.^{1,22}

Feeding should promote efficient caloric support for growth and development and for appropriate weight gain for surgical correction at the expected time.^{23,24} Recommendations and reviews have been published regarding methods and resources for different types of cleft.^{22,25,26,27} Notwithstanding, inadequate feeding is still a common problem.^{13,24,28,29,30,31}

A high rate of adherence to appropriate feeding and adequate growth is related to systematic monitoring of patients.³¹ The lack of follow-up after maternity discharge is particularly relevant and is reflected in nutritional problems.^{26,28,29,30,32} The data indicates the need for public policies for longitudinal follow-up for babies with OC in primary care.²⁶

Nutrition

Several reports emphasize the importance of the nutritional aspects related to postponement of OC surgical repair.^{13,28,29,32,33} Mainly, low weight gain and anemia, which should be preventable.³⁴

Although there are reports in the literature on the possibility of breastfeeding with any type of cleft, studies with adequate levels of evidence show that, unlike isolated CL, many patients with CP or CLP can only get breast milk through pumping methods.^{35,36}

The nutritional approach is essential for planning treatment. Orientation regarding feeding methods at birth and longitudinal follow-up are important. The encouragement of breastfeeding and, when that is not possible, the use of breast milk and the prevention and treatment of anemia should be priorities.³⁴

Co-morbidities

Secondarily to facial abnormalities, children with OC are subject to several complications, such as oti-

tis, pneumonia, oral communication disorders and otologic and/or hearing disorders. Emotional and social disturbances are significant and deserve attention from both families and health professionals.³⁷

Associated defects

Prevalence of structural defects in association with OC ranges from 8% to 75%, and the majority of reports show that CP has the highest and CL the lowest rates. The orofacial region and cardiovascular, central nervous, and musculoskeletal (including limbs, hands and feet) systems are most commonly involved. Although there are true population differences, methodological factors such as sample source and size, method of ascertainment, inclusion criteria, coding system and case classification account for much of this wide variation.^{4,9,11,18,38,39,40,41,42,43,44}

Management by unspecialized health professionals

Understanding of the needs and particularities of individuals with OC by health professionals is very important, especially considering the high prevalence of this congenital defect. Nevertheless, health professionals' knowledge of OC is relatively low.^{13,28,29,30,32,33}

Primary care is an excellent opportunity to reinforce, encourage and monitor dietary guidelines, as well as to prevent co-morbidities. However, it has been observed that healthcare professionals are unaware of how to manage individuals with OC.³³

A study involving Brazilian students during their last academic year for different health professions detected that their knowledge of OC was not systematized. In addition, in self-evaluations, 96.4% affirmed that they were not able to perform routine follow-up of an individual with OC in their own area of expertise. This data has not yet been published, but the authors are working on suggestions of topics to be used for training.

Discussion

OCs require efforts from all levels of healthcare in view of their high prevalence, their association with other congenital defects and co-morbidities and their need for prolonged treatment. In view of

the complexity of this congenital defect, it has been a challenge to deal with the special needs of individuals with OC during routine healthcare assistance. This is a global problem recognized by the WHO.¹²

This article is intended to help all health professionals understand this complex scenario and provide directions from different perspectives, which could be useful during clinical management.

Recognition of the risk factors and particular health needs of individuals with OC allows the provision of appropriate healthcare. This includes identification of risk factors, preconceptional and prenatal orientation, neonatal assistance for feeding, investigation of associated congenital defects, and follow-up at the primary care level for monitoring of nutrition and prevention of co-morbidities. This approach facilitates specialized treatment at the right time and may decrease the burden of this prevalent congenital defect.

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Conclusion

All the risk factors herein described can be identified and orientation can be offered during routine consultations. In addition, clinical management from birth can be improved with knowledge of all related aspects. To this end, training of health professionals should be emphasized.

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