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Treacher collins syndrome: An update from a stomatological point of view

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Abstract
Introduction: Treacher Collins syndrome (TCS) is congenital craniofacial disorder, in which mainly the malar, a maxillary hypoplasia and peri orbital anomalies are affected.
Objective: To analyze the literature on TCS from a dental perspective, to investigate information on the etiology, diagnosis, clinical and oral manifestations, and its treatment.
Methodology: Using the keywords "Treacher Collins", "etiology", "prevalence", "oral manifestations" and "clinical management", the MEDLINE/PubMed and ScienceDirect databases were searched, with emphasis on the last 5 years. It was evaluated with the PRISMA and AMSTAR-2 guidelines.
Results: Its incidence was found to be 1:50000. It is mainly due to 3 genes, POLR1D, POLR1C and TCOF1; these genes manifest individually. Diagnosis can be clinical and by some genetic tests. The most common features range from mandibular hypoplasia, involvement of the external auditory canals, downward palpebral fissures, among others. Most of the anomalies can have an impact on tooth eruption, malocclusion and temporomandibular joint. The maxillary and mandibular cranial region is the most affected in this syndrome. The most common treatments in dentistry are orthodontics, palate correction and cleft lip.
Conclusions: It is important to know the affectations that these patients present to be able to provide a better diagnosis and have in mind which are the possible treatments that we can apply to these patients. The work is multidisciplinary and begins at an early age to increase the quality of life and lifestyle.

Keywords: Treacher collins, syndrome, etiology, treatment, oral, TMJ, maxillary hypoplasia

1. Introduction
Treacher Collins syndrome (TCS) is a congenital craniofacial disorder, in which mainly the malar, maxillary hypoplasia and periorbital anomalies are affected [1-3]. Its name was credited to the British ophthalmologist Edward Treacher Collins, where he described the problem in 1949, it was described as a zygotemporomandibular dysplasia [3].
Unfortunately, there is a paucity of treatment strategies for patients affected with TCS. Bone manipulation usually occurs, along with soft tissue reconstruction. Treatment in children is usually a multidisciplinary approach, in order to address the wide range of anomalies that present; we see specialists ranging from plastic surgeons to ophthalmologists, dentists, pathologists and pediatricians, etc. [2-5].
TCS is usually very rare, it is an autosomal dominant disorder of craniofacial development in which one in 50000 births usually present this failure; the failure is mainly due to mutations in TCOF1, POLR1D and POLR1C; it should be noted that the mutations are individualized, and no studies have been found where the 3 mutations are found in a single organism [1, 6-8]. Sixty percent of cases are usually spontaneous and 40% familial [6]. As the biosynthesis of ribosomes of neural crest and neuroepithelial cells is blocked, it has been reported that there is a reduction in the number of these cells, resulting in hypoplasia of the first and second branchial arches [7].
Nowadays there is a great lack of attention to differently abled patients, some of them are born with these alterations and have a negative impact on the development of life; there comes a time for the dentist that becomes a great challenge in the care of these patients, such is the case

of patients with TCS. TCS will have several craniofacial alterations of great magnitude, so it is important to know how it manifests itself and the treatment plan to be done. Thus, the objective of this work is to analyze the literature on Treacher Collins syndrome and its impact in the area of care for the dentist, here we present information about the etiology, prevalence, diagnosis, general manifestations, impact on the stomatognathic system and its treatment.

2. Methodology

Articles on the subject published through the Pubmed, SCOPUS and Google Scholar databases were analyzed, with emphasis on the last 5 years. The quality of the articles was evaluated using PRISMA guidelines, i.e., identification review, choice, and inclusion. The quality of the reviews was assessed using the measurement tool for evaluating systematic reviews [9].

The search was performed using Boolean logical operators AND, OR, and NOT. It was realized with the words ¨Treacher Collins¨, diagnostics¨, ¨oral manifestations¨, ¨treatment¨ and ¨clinical manifestations¨.

3. Results

3.1 Etiology and prevalence

TCS was described in 1900, consisting of a set of anomalies of the facial bones, palate, eyes and ears, referred to as mandibulofacial dysostosis. Its prevalence is one in 50000 births [10-12]. Other authors mention that its incidence may also be 1 in 25,000 births [13, 14].

It arises from the abnormal development of skeletal and soft tissues derived from the first and second branchial arch, it is usually an autosomal dominant disorder with variable phenotypic expression [15-18].

As for its etiology, it is mainly due to mutations in the TCOF1, POLR1C and POLR1D genes. The TCOF1 gene plays an important role in ribosomal RNA synthesis [13, 18, 19]. Sixty percent of the cases are usually due to the POLR1D and POLR1C genes, which increase neuroepithelial apoptosis during embryogenesis, resulting in a lack of neural crest cells, these cells are involved in the formation of cartilage and facial bones. POLR1C is due to a fault on chromosome 6p21 and POLR1D on chromosome 13q12, while TCOF1 on chromosome 5q32 [15, 20].

It has been found that its incidence may be somewhat common, about 1:50000. It may be mainly due to 3 genes, POLR1D, POLR1C and TCOF1; where these genes manifest their mutations individually, i.e. only one mutated gene has been found for each individual and not all 3 together.

3.2 Diagnosis

Regarding its diagnosis, it has been found that there are phenotypic overlaps in this syndrome and in other diseases, so it can be difficult to diagnose it. Similarities have been found in syndromes such as Nager, Miller and Goldenhar. The development of technologies in terms of genetic and radiological tests makes the diagnosis more accurate [21].

The diagnosis of SCT is established in almost 97% of cases by detection of autosomal dominant variant, TCOF1, POLR1D and POLR1B in autosomal recessive variants and POLR1C or POLR1D by molecular genetic testing, where the latter belongs to 3% [11, 22-25].

It is usually clinical and can be performed during the prenatal period, either by ultrasound or chorionic villus biopsy [12, 22, 23, 25-28].

Diagnosis can be made in two ways, clinically, either by ultrasound and chorionic villus biopsy; and by genetic testing, where mutations in the aforementioned genes are evaluated.

3.3 Clinical Manifestations

The malformations that occur within TCS are usually slightly different from other craniofacial diseases, except for soft tissue and bone anomalies that occur bilaterally and are symmetrical. The most affected parts are the peri orbital areas, ears, zygomatic bones, zygomatic arches with 81%, upper and lower jaws with 78%. Ocular anomalies are found in 89% of cases blepharoplasty, 69% defects of the lower eyelid and defects of the inner part of the eyelid, 33% loss of vision, 37% strabismus, cataracts and small eye globules, also obstructive sleep apnea, due to retraction of the jaw [8, 10, 15, 21, 29].

It has been classified the features in 5 categories, the first is complete type are all known features; the second of incomplete type, mild deformities of ear, eyes, cheekbones and jaw are presented; the third of stunning type, where the lower eyelid is affected and a malar hypoplasia; the fourth is unilateral, where it is limited to anomalies of one side of the face; and the 5 irregular, where it is combined with other anomalies that do not belong to this syndrome [30].

Radiographically, a reduction in the volume of the cheekbone, shortening of the zygomatic arch and lack of width and length of the face can be observed [8, 21, 29], so there may be some incidence of temporomandibular joint disorders and its stiffness is usually greater in these patients, along with the involvement of the outer and inner ear [8, 21, 29, 30].

In the following, the characteristics will be named in terms of their frequency. The most frequent are downward slanting palpebral fissures, malar and zygomatic hypoplasia, conductive hearing loss, hypoplasia and mandibular micrognathia. Then we have atresia of the external auditory canal, microtia, coloboma of the lower eyelid, speech delay, asymmetry, preauricular hair displacement. Rarely, nasogastric tube or gastrostomy in newborns, cleft palate, intubation or tracheotomy, stenosis, cardiac malformation, Rachis malformation, renal malformation, microcephaly, intellectual disability or delayed motor development and limb anomalies [7, 31, 32].

We found a wide range of manifestations that can occur in this syndrome, where mainly, only facial structures are affected. The most frequent characteristics range from mandibular hypoplasia, involvement of the external auditory canals, downward palpebral fissures, among others.

3.4 Influence on the Stomatognathic Apparatus

Most patients with TCS have been found to have some occlusal disorder, abnormal dentition number, increased interdental spacing, a high palatal arch or cleft palate [8, 21, 29].

Some patients have also been observed to develop temporomandibular joint (TMJ) ankylosis, parotid-cutaneous fistulization [33].

As mentioned above, both symmetric and bilateral hypoplasia of the malar bones of the mandible are alterations that can lead to malocclusion such as open bite, limited mouth opening due to temporomandibular joint involvement and ogival palate [12, 28, 34, 35].

Other characteristic facies are a receding chin, large mouth with determined hypoplasia of certain facial bones (Feregrino 2019). An obstruction of the airway due to widening of the base of the tongue and narrowing of the pharynx [36, 37].

Most of the anomalies can percuate the way teeth erupt and bring about malocclusion problems and TMJ alterations. The

maxillary and mandibular cranial region is the most affected in this syndrome.

3.5 Treatment

It has been found that reduced ribosomal biogenesis induced p53 expression, which resulted in cell death; therefore, it is thought conceivable that experimental rescue of the facial phenotype could be achieved by inhibition of p53, which, in turn, will block neuroepithelial apoptosis [6].

In vitro models have also been seen where haploinsufficiency of the TCOF1 gene is studied, resulting in neuroepithelial cell death by oxidative stress [38]. These high levels of stress were found in neuroepithelium with an adequate cellular level in normal development. However, apoptotic death and facial malformation have been found in animal studies [6, 39].

Treatment is usually multidisciplinary, involving ophthalmologists, otolaryngologists, maxillofacial specialists, surgeons, etc., who are evaluated every 3 months during infancy. Then every 6 months until the age of 3 years and reconstructive surgery is performed [35, 40, 41]. It will be tailored according to the specific needs of each individual, ranging from bone conduction amplification, tracheotomy, speech therapy, craniofacial reconstruction, cleft palate repair, etc. [11].

Some studies suggest that orthodontic, palate, cleft lip and eyelid treatments should be started at the age of 3 to 12 years. At 13 to 18 years of age, planning orthognathic surgery is recommended. And finally, include psychological support for the patient and family members. Most children achieve normal development and intelligence [3, 28, 36, 42-45].

It is important to plan in a multidisciplinary view, in order to obtain better results and improve the quality of life of patients, the most used treatments in dentistry are orthodontics, palate correction and cleft lip.

4. Conclusion

It is of utmost importance to know the affectations that these patients present in order to be able to provide a better diagnosis and have possible treatments that we can apply to these patients in mind. The work is usually multidisciplinary and, in most cases, treatment from an early age is obtained great results and increases the quality and lifestyle of the patient.

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