Ear malformations, hearing loss and hearing rehabilitation in children with Treacher Collins syndrome

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KEYWORDS
Treacher Collins syndrome;
Mandibulofacial dysostosis;
Ear malformations;
Hearing loss, Bone-anchored hearing aids; Hearing rehabilitation

Abstract
Objective: The aim of this study was to assess the main ear malformations, hearing loss and auditory rehabilitation in children with Treacher Collins syndrome.
Methods: We performed a retrospective study of 9 children with Treacher Collins syndrome treated in a central hospital between January 2003 and January 2013.
Results: This study showed a high incidence of malformations of the outer and middle ear, such as microtia, atresia or stenosis of the external auditory canal, hypoplastic middle ear cavity, dysmorphic or missing ossicular chain. Most patients had bilateral hearing loss of moderate or high degree. In the individuals studied, there was functional improvement in patients with bone-anchored hearing aids in relation to conventional hearing aids by bone conduction.
Conclusions: Treacher Collins syndrome is characterized by bilateral malformations of the outer and middle ear. Hearing rehabilitation in these children is of utmost importance, and bone-anchored hearing aids is the method of choice.
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PALABRAS CLAVE
Síndrome de Treacher-Collins;
Disostosis mandibulofacial;
Hipoacusia;

Malformaciones del oído, hipoacusia y rehabilitación auditiva en los niños con el síndrome de Treacher-Collins

Resumen
Objetivo: Evaluar las principales malformaciones del oído, hipoacusia y la rehabilitación auditiva en los niños con síndrome de Treacher-Collins.

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Métodos: Estudio retrospectivo de 9 niños con síndrome de Treacher-Collins tratados en un hospital central, entre enero de 2003 y enero de 2013.

Resultados: Este estudio demostró una alta incidencia de malformaciones del oído externo y medio, como microtia, atresia o estenosis del conducto auditivo externo, la cavidad timpánica hipoplásica, la cadena de huesecillos dismórfica, o ausente. La mayoría de los pacientes tenían una hipoacusia de conducción grado moderado o alto. En los sujetos estudiados, se observó una mejoría funcional en los pacientes con audífono anclado en hueso en relación con los audífonos convencionales de conducción ósea.

Conclusiones: El síndrome de Treacher-Collins se caracteriza por malformaciones bilaterales del oído externo y medio. La rehabilitación auditiva en estos niños es muy importante, y el audífono anclado en hueso es el método de elección.

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Introduction

The Treacher-Collins syndrome (TCS), also known as mandibulofacial dysostosis is an inherited entity, with autosomal dominant transmission which affects 1 in 50,000 live births. In most cases, it is caused by a mutation in TCOF1 gene in loci 5q31.3, which encodes a nucleolar phosphoprotein – Treacle, essential for the development of the 1st and 2nd branchial arches. The penetrance of these mutations is complete, but its expressivity is variable. In cases of complete expression of TCS, the diagnosis can be based on clinical features. Common manifestations of the syndrome include hypoplasia of the facial bones, in particular the mandible and the zygomatic complex, downslanting palpebral fissures, lower eyelid coloboma and cleft palate. Conductive hearing loss is present in 50% of the cases, which is due to malformations of the outer and middle ear.

The approach to these patients is complex and requires integrated care of a large team of experts along their lives. During the evaluation protocol, determining the degree of hearing loss and hearing rehabilitation should be performed as early as possible, through close monitoring by an otolaryngologist, audiologist and speech therapist so as to allow normal development of the language in these children.

Since its first use in children in 1984, the bone-anchored hearing aids (BAHA) are an effective way to hearing rehabilitation in children with Treacher-Collins syndrome, with the advantage of being a relatively simple and fast surgical procedure, with a low rate of complications and possible to be performed at pre-school age.

This work has two main objectives:

1. To characterize the main ear malformations, hearing alterations, type of hearing rehabilitation and outcomes in children with Treacher-Collins syndrome, oriented in our centre.
2. To compare the results with the most recent studies on this topic.

Methods

The authors performed a retrospective analysis of all children with TCS examined at HCP, between January 2003 and January 2013. Patients with definite diagnosis of Treacher-Collins (patients with a mutation in gene TCOF-1 or those with typical phenotype) and below 18 years of age were included in the study. The exclusion criteria were: patients not assessed by computed tomography of the temporal bone (CT-TB), patients without audiometric assessment or totally incomplete clinical process.

Data from clinical processes relating to age, gender, medical history, audiometric evaluation, CT-TB, hearing aid use were collected. In cases of patients with osteo-anchored prosthesis, information about the surgery and its complications were analyzed.

The legal representatives of the children involved have authorized their inclusion in the described study.

In CT-TB the external auditory canal, middle ear, ossicular chain, mastoid cavity, cochlea, vestibule, semicircular canals and internal auditory canal were evaluated.

Hearing evaluation was performed by using pure tone audiometry, free field audiometry with and without use of hearing aids. Hearing loss is presented in pure tone average (PTA), determined by the average of pure tone thresholds of frequencies 500, 1000, 2000 and 4000 Hz; and classified according to the International Bureau of Audiology (BIAP) in mild (21–40 dB), moderate grade I (41–55 dB), moderate grade II (56–70 dB), severe grade I (71–80 dB) severe grade II (81–90 dB) and profound (>90 dB). The results are presented as PTA in free field unaided (UA-PTA) with conventional prosthesis (CP-PTA), with Softband (Softband-PTA) or BAHA (BAHA-PTA); audiometric gain with conventional bone prosthesis (Gain-CP = UA-PTA–CP-PTA) with BAHA (Gain-BAHA = UA-PTA–BAHA-PTA) and audiometric gain of the BAHA over conventional prostheses (Gain-BAHAasCP = CP-PTA–BAHA-PTA). Only the audiometric results obtained after 3 months of use of hearing aids were analyzed.
In the statistical analysis of data the SPSS® Statistics 20.0 software was used.

Results

In the present study 9 children with TCS were evaluated: 7 female and 2 male, a total of 18 ears were assessed by using CT-TB and audiology. They were between 1 month and 14 years old, with an average age of 1 year and 7 months in the first observation in this service. The follow-up of the children ranged from 6 to 21 years, and there was no abandonment. Only two of the studied children had kinship with each other (monozygotic twins).

The epidemiological characteristics and key clinical information are summarized in Table 1.

Ear malformations

The main ear malformations are described in Graphic 1.

The majority of patients had symmetrical malformations of the pinna (8/9, 89%) being the most common abnormality microtia (95% of cases) that, according to the classification of Marx, can be divided into type I (n = 5; 28%) and type II (n = 12, 67%). One patient had cup-ear and all of them had the pinna with morphological changes. All the patients had symmetrical changes in the external auditory canal (EAC) of 2 types: atresia (14/18, 78%) and stenosis (4/18, 22%).

The middle ear cavity was hypoplastic and dysmorphic approximately symmetrically in all subjects (Fig. 1). In the assessed patients the ossicular chain showed changes mainly symmetrical (7/9, 78%) as dysplasia (8/18, 44%) or absence of the ossicular chain (10/18, 56%).

No change was observed at the level of the structures of the inner ear (cochlea, vestibule, semi-circular canals and internal auditory canal).

To note that two individuals had bilateral changes in the path of the facial nerve (4/18, 22%) and all the patients had hypoplastic and poorly pneumatized mastoid cavities.

Audiometric results

All the patients had bilateral conductive hearing loss, which according to the classification of BIAP, ranged from moderate grade I to severe grade II, with an average hearing loss (± standard deviation) of 64.3 ± 8.5 dB. Of all the assessed ears, 3 had moderate hearing loss grade I (52.3 ± 2.5 dB), 12 had moderate hearing loss grade II (63.8 ± 4.1 dB), 2 had severe hearing loss grade I (75.5 ± 2.1 dB) and 1 had severe hearing loss grade II (83 dB). In 3 individuals, the degree of bilateral hearing loss did not fall into the same category; however, the difference was only of one category (moderate grade I/moderate grade II, grade II moderate/severe grade I, grade I severe/severe grade II) and averaging 7.3 ± 4.2 dB. The right hearing loss values were in average 65.3 ± 9.4 dB and left 63.2 ± 7.9 dB, with an average difference between the two ears of 5 ± 3.8 dB. The free field audiology (without hearing aid) showed an average hearing loss of 60 ± 5.3 dB.

The relationship between the ear malformations (external and middle ear) and the degree of hearing loss was...
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Ear malformations

![Graph 1: The main ear malformations]

**Table 2** Relationship between ear malformations and hearing loss.

<table>
<thead>
<tr>
<th>Malformation</th>
<th>Total</th>
<th>Ossicular chain</th>
<th>Absent</th>
</tr>
</thead>
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<tr>
<td><strong>External auditory canal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stenosis</td>
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<td>n=0</td>
<td>n=4</td>
</tr>
<tr>
<td>Atresia</td>
<td>n=4</td>
<td>n=10</td>
<td>n=14</td>
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<tr>
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<td>n=10</td>
<td>n=18</td>
</tr>
<tr>
<td><strong>Middle ear cavity</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Dysplasia</td>
<td>N=18</td>
<td>N=14</td>
<td>N=10</td>
</tr>
<tr>
<td>Absence</td>
<td>N=0</td>
<td>N=4</td>
<td>N=8</td>
</tr>
<tr>
<td>Malformations</td>
<td>N=4</td>
<td>N=4</td>
<td>N=0</td>
</tr>
<tr>
<td><strong>Inner ear</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ossicular chain</td>
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<td>N=12</td>
<td>N=14</td>
</tr>
<tr>
<td>Aberrant path</td>
<td>N=10</td>
<td>N=10</td>
<td>N=0</td>
</tr>
</tbody>
</table>

**Figure 1** (A) 3D Reconstruction from the axial skull-brain CT – showing malar and mandibular hypoplasia, absence of the zygomatic complex and atresia of the left EAC; (B) Axial CT of the temporal bone and (C) coronal reconstruction from axial CT – showing hypoplastic tympanic cavity, absence of the ossicular chain, and atresia EAC.

analyzed as described in Table 2. For this purpose, at the external ear level only changes of EAC (atresia or stenosis) were analyzed, since the authors believe that the alterations found at the pinna, besides being similar, slightly contribute to the overall degree of hearing impairment. At the middle ear level, since all individuals had similarly hypoplastic tympanic cavities and only the ossicular chain showed significant variability, just changes at the level of the ossicular chain (dysplasia or absence) were considered.

**Conventional hearing aids**

All individuals were subjected to hearing rehabilitation by conventional bone conduction hearing aid applied in stem glasses, headband or in using Softband, having two children first used the prosthesis in headband and then the Softband, one due to headband maladaptive and the other as a form of adaptation and preparation for BAHA. The use of hearing aids began in average at 5 months of age.

The average PTA in free field with conventional prostheses by bone conduction was $26.8 \pm 4.1 \text{dB}$, with an estimated $32.8 \pm 8.3 \text{dB}$ gain. When analyzed separately,
the prosthesis by bone conduction in the stem of the glasses/headband obtained an average PTA of 30.1 ± 2.3 dB, with a gain of 29.3 ± 5.5 dB; the Softband got an average PTA of 23.2 ± 2.7, with a gain of 39.5 ± 6.2 dB.

Bone-anchored hearing aid – BAHA

Four of 9 of the children involved in this study placed BAHA, having this procedure been performed by the same surgical team, using the same surgical technique under general anaesthesia and not integrated with other procedures. The average age of children at the time of the surgery was 9 ± 5.5 years, with ages between 5 and 17. No child received bilateral BAHA and all of them were implanted on the right side. The site of implantation was decided according to the thickness of the temporal bone, the laterality of the patient and degree of hearing loss in each ear. All surgeries took place in two stages, with an average interval between procedures of 6 ± 2.9 months and all had no intraoperative complications. As postoperative complications, there is a case of extrusion of the implant 6 months after 2nd surgery time, which was promptly surgically solved by placing the abutment 5mm away from the initial site. To note that one of the children, 3 years after the placement of BAHA, suffered a concussion during a football game with destruction of the BAHA processor without any other complications, so it was only necessary to adapt to a new processor. The average PTA in a free field audiology with BAHA was 18.3 ± 1.3 dB, with an average gain of 38 ± 5.5 dB relatively to the background values and of 11 ± 1.4 dB to the conventional hearing aids.

Multidisciplinary approach

Apart from the follow-up in Otorhinolaryngology, the children were observed by other areas, such as: Plastic and Reconstructive Surgery (n = 9); Stomatology (n = 7), Ophthalmology (n = 5), Speech Therapy (n = 7), Psychology (n = 6), Pulmonology (n = 1), Paediatrics (n = 9), Dermatology (n = 2), Cardiology (n = 2) and Genetic Medicine (n = 6). Including the placing of BAHA, in average, the analyzed children were subjected to 3 surgeries, a minimum of 2 and a maximum of six procedures. The most commonly performed surgical procedures were: correction colobomas/external canthopexy (n = 8); otoplasty (n = 6); BAHA (n = 4); Mandibular distraction (n = 3); cleft palate repair (n = 3); malar and zygomatic reconstruction (n = 3); tooth extraction (n = 2) and tracheostomy (n = 1).

Discussion

The TCS, for its clinical importance and impact on the child development, has been approached under various aspects, having the authors of the present work focused on an otologic and audiologic manifestations approach, as well as on hearing rehabilitation, stressing the importance of a multidisciplinary team and an early intervention of the otorhinolaryngologist in these cases.

In the present study, we found more cases in individuals of female gender. However, it is not described in the bibliography any predominance of gender. This can be explained by the limited number of analyzed cases.

All the studied individuals had bilateral and mostly symmetrical malformations of the outer and middle ear. The most common abnormalities of the outer ear were microtia (95%), the atresia (78%) and stenosis of the EAC (22%); and of middle ear were hypoplastic and dysmorphic tympanic cavity (100%), dysplastic ossicular chain (56%) or absent (44%). These results are consistent with those found in most studies. Symmetry of ear malformations is one of the features that allows the differential diagnosis of TCS with other syndromes of different aetiologies but of similar characteristics, such as facial microsomia.

No children showed changes in the inner ear. This finding is consistent with the bibliography consulted, because the inner ear malformations are rarely described in association with TCS, since this has distinct embryological origin and development of the middle and outer ear.

About 50% of individuals with TCS have unilateral or bilateral conduction hearing loss, usually of moderate or high degree, mainly motivated by otologic malformations of the middle ear. In our study, all subjects had moderate or high conduction hearing loss, roughly symmetrical in most cases, which is in line with most of the anatomical changes in the external and middle ear, yet they are also symmetric. By analysing the relationship between malformations of the outer and the middle ear and the degree of hearing loss, we found that most ears had atresia of the EAC and, simultaneously, the absence of the ossicular chain, being these changes associated in average with a higher degree of hearing loss than the others (70 ± 6.1 dB). As well as in the consulted bibliography, this study showed that, in average, atresia of the EAC (67.4 ± 6.7 dB) and the absence of the ossicular chain (70 ± 6.1 dB) are associated with a higher degree of hearing loss than stenosis of the EAC (53.3 ± 2.8 dB) and the ossicular dysplasia (57.1 ± 4.8 dB).

Early detection of conduction hearing loss improves the possibility for rehabilitation of hearing and speech, and in this context, brainstem auditory evoked response plays a very important role. The hearing rehabilitation of such patients should be conducted as early as possible, usually using conventional prostheses by bone conduction, or more recently using the Softband. Our study, as well as others, found that in average, the results of Softband are slightly higher than those of conventional prostheses.

In patients with STC, the BAHA is a very effective method of hearing rehabilitation, enabling better audiometric results compared with conventional prostheses and the Softband. The results of this study with an average PTA in free field with BAHA 18.3 ± 1.3 dB, with an average audiometric gain of 38 ± 5.5 dB relatively to background values, and of 11 ± 1.4 dB over conventional hearing aids are similar to those found in other studies with children. The functional gains analyzed were very close to normal hearing, being the degree of satisfaction of patients and their caregivers very high. The main advantages of using BAHA over conventional prosthesis are: the best amplification and sound quality, better bone conduction, comfort and aesthetic appearance, a relatively simple and fast surgical procedure with few complications. In the analyzed patients, and in accordance with international guidelines for paediatric BAHA, this surgery was performed only after 3 years of age. The option of performing surgery in a single
operation or in two surgical times is a target matter of great debate, especially in patients where general anaesthesia and intubation can be complicated.22 The choice of two surgical times, spaced over a recommended period of 3–6 months allows a better bone integration of the titanium implant.22 One of the inherent risks to the use of the BAHA is the possibility of the prosthesis destruction with or without extrusion of the implant, associated for example, to trauma, as it was the case of one of our children. These risks can be significantly reduced through a psychological evaluation of the patient, teaching of postoperative care to children and their caregivers. The fact that the bone integration of the implant has failed in a child is in accordance with recent studies indicating that the failure rate is about 20%.24

The malformation peculiarities of children with TCS require a multidisciplinary team approach, with the aim of functional and aesthetic correction, and normal psychosocial development, as it can be proved by the high number of medical consultations in different specialties and surgical procedures performed. Despite not having occurred in this study, we noted that the placement of BAHA should, wherever possible, be combined with other surgical procedure, given the anaesthetic risk and the high number of surgeries that these children are subject to.13

Conclusions

The Treacher–Collins syndrome (or mandibulofacial dysostosis) is a hereditary entity with autosomal dominant transmission characterized by abnormalities of the structures that are developed from the 1st and 2nd branchial arches, affecting 1 in every 50,000 live births. Most children have bilateral and symmetrical morphological alterations of the outer and middle ear, conditioning different degrees of conduction hearing loss. Hearing rehabilitation in these children is extremely important, and the BAHA is the chosen method, since these children usually have difficulty in adapting to conventional hearing aids due to malformations of the external ear.

Conflict of interest

The authors declare no conflict of interest.

References