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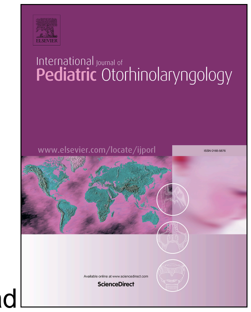

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Cochlear Implantation in Children with Auditory Neuropathy Spectrum Disorder: A Multicenter study on Auditory Performance and Speech Production Outcomes

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1 Introduction

Auditory neuropathy/dys-synchrony, first described by Starr et al. in 1996, is a condition in which otoacoustic emissions (OAEs) and/or cochlear microphonics (CMs) are preserved, and auditory brainstem response (ABR) waves are absent or severely distorted [1]. Pure tone thresholds evaluated by behavioral audiological assessments range from normal to profound levels [2,3]. The pathophysiology of the disorder includes: presynaptic (inner hair cell disorders), postsynaptic (disorders affecting the auditory ganglion, dendrites, and axons), and central (auditory brainstem) disorders [4]. This etiologic heterogeneity led to the adoption of the nomenclature 'auditory neuropathy spectrum disorder (ANSD)' [5]. The dys-synchrony of neural discharges in auditory pathways resulted in the disruption of temporal processing, impaired speech discrimination, and signal processing in noise [1,6–8]. Auditory neuropathy spectrum disorder is not an uncommon cause of hearing impairment, with a prevalence of 0.5% to 15% in infants with hearing loss [9–12].

Although the early reports of the cochlear implantation in children with ANSD suggested limited efficacy [13], later studies demonstrated more promising results: A systematic review, which in 2015 evaluated the performance of hearing skills in children with ANSD after cochlear implantation, reported similar improvements in the performance of hearing skills in children with ANSD compared to children with sensorineural hearing loss, using cochlear implantation [14]. Cochlear implantation was recommended for children with poor performance with conventional hearing aids [15] and subjects with profound hearing loss [16].

In the current study, the auditory performance and speech production outcomes of cochlear implantation in children with ANSD were evaluated in four tertiary referral centers and the effect of age at the time of implantation on these factors was reported.

2. Patients and Methods

2.1. Study Design

The current retrospective, multicenter study was carried out on children with auditory neuropathy spectrum disorder, receiving a cochlear implant at four tertiary referral centers between January 2003 and December 2015. The study was an anonymized chart review, conducted after obtaining the ethical approval of the research center.

2.2. Diagnostic Tests for Auditory Neuropathy Spectrum Disorder

The audiological test battery for the diagnosis of the ANSD including otoacoustic emission (OAE), auditory brainstem response (ABR) and cochlear microphonics (CMs), tympanometry, acoustic reflex, and age-appropriate behavioral audiometry (pure tone audiometry or visual reinforcement audiometry) were performed. The presence of OAEs or CMs and seriously abnormal ABR responses or the absence of responses with a maximum output level was used to establish the ANSD diagnosis.

2.3. Subjects

After the diagnosis of the ANSD, a thorough history and physical examination was performed on all the subjects. Magnetic resonance imaging (MRI) of the temporal bone and brain, and temporal bone high-resolution CT scan (HRCT) were performed on all the patients. The subjects with the following criteria were included in the study: 1) children with bilateral severe-to-profound sensorineural hearing loss at the time of surgery; 2) the patients who did not show hearing improvement with hearing aids; 3) the cochlear implantation surgery was performed at the pre-school age (before seven years old); 4) normal appearance tympanic membrane at otoscopy, and type A tympanogram. The subjects with a bilateral cochlear implantation (simultaneous or sequential), any component indicating an additional conductive hearing loss in the audiological test battery, an absence of the cochlear nerve in imaging, surgical complications as listed in [17], and failure to keep up with follow-up at least for one year post-operatively were excluded from the study.

2.4. Cochlear Implantation and Activation

All the subjects received auditory rehabilitation for at least three months with hearing aids and did not show hearing improvements. Afterwards, the patients underwent the unilateral cochlear implantation surgery with multichannel devices. The device selection was performed based on the expert cochlear implantation team of each center. The implantation devices consisted of the Cochlear Nucleus Contour Advance^{TM} (Cochlear Ltd., Centennial, USA), Hifocus^{TM} (Advanced Bionics LLC, Valencia, USA), and Sonata^{TM} (MED-EL Corporation, Innsbruck, Austria) electrodes. The cochlear implantation fitting was performed after four weeks postoperatively.

2.5. Auditory Performance Assessment

The categories of auditory performance (CAP) scaling system was used to evaluate the auditory perception of the subjects, preoperatively and postoperatively. The CAP was developed in 1995 to evaluate the auditory perception of children with hearing loss in daily life [18]. Based on this scoring system, the auditory performances were divided into eight hierarchical categories, which are described in Table 1. The inter-user reliability of this scaling system has been proven before [19]. The CAP scores of the subjects were evaluated before surgery, one and two years after cochlear implantation by expert rehabilitation professionals.

2.6. Speech Production Assessment

The speech intelligibility rating (SIR) scale was used to evaluate the speech production ability of the subjects after implantation. This scale was developed in 1998 to quantify the intelligibility of the speech in deaf children with cochlear implants [20]. Based on the SIR scaling system, the speech production ability of the subjects is categorized into five ordinal scores, which are mentioned in detail in Table 2. The reliability of this scaling system has been confirmed before [21]. The SIR scores of the subjects were evaluated one and two years after the cochlear implantation, by expert speech and language therapists.

2.7. Data Collection and Statistical Analysis

By a retrospective review of the patients' charts, the age at the diagnosis and surgery, and the surgical outcomes in the field of auditory performance and speech production (CAP and SIR scores, respectively) were determined. The subjects were divided into two groups based on the age at the time of the cochlear implantation; Group I: subjects who received cochlear implantation at the age of ≤24 months, and II: patients who underwent cochlear implantation surgery after the age of 24 months.

SPSS (version 16, SPSS Inc., Chicago, USA) was used for data analysis. The continuous variables were summarized using mean and standard deviations. The CAP and SIR scores were reported in medians and interquartile ranges (IQRs). The CAP score improvement at each follow-up was defined as the CAP score at the time of follow-up minus the former CAP score of the same subjects. The SIR score improvement was assessed in the same way. To evaluate the improvement of outcomes, the Wilcoxon signed-rank test was conducted. The Mann-Whitney U test was used to compare the surgical outcomes in different age groups. A p value < 0.05 was considered as statistically significant.

3. Results

3.1. Patients' Characteristics

A total of 136 patients (63 girls and 73 boys) met the inclusion criteria and thus, were included in the study. The mean age of the subjects at the time of the ANSD diagnosis was 10.9 ± 8.9 months (range: 1–42 months). The mean age at the time of implantation was 31.9 ± 14.7 months (range: 9–79 months). Forty-eight subjects (35.3%) were fitted in Group I (aged ≤24 months old) and 88 patients (64.7%) were in Group II (>24 months). The implanted electrodes were: Contour Advance^{TM} in 114 patients (83.8%), Hifocus^{TM} in 14 subjects (10.3%), and Sonata^{TM} in eight patients (5.9%). The position of the electrode was confirmed by postoperative imaging, and no complication was reported after surgery. The final programming strategies were achieved in six months after device activation in all the subjects. All the patients were referred for first-year evaluations. A total of 79 out of 136 patients (39 patients of Group I and 40 subjects of Group II) completed the evaluations of auditory performance and speech production at the second-year follow-up.

3.2. Auditory Performance Assessment

The median pre-operative CAP score was one with an interquartile range (IQR) of 0–1. In Group I (children ≤24 months) only 17 out of 48 patients were aware of environmental sounds (score 1) preoperatively (median CAP score: zero, IQR: 0–1). The median CAP score in Group II (>24 months) was one (IQR: 0–1). (Table 3)

The evaluation of the CAP scores one year postoperatively represented a significant increase in all the patients (median CAP score one year after surgery: four; IQR: 3–4; p value <0.001). The median CAP score improvements were two (2–3) and three (2–3), in Group I and II, respectively. The median score improvement was significantly higher in children >24 months (p value: 0.007).

The median CAP score, two years after surgery, was five (IQR: 5–6). The median score improvement during the second year after surgery was significantly higher in children ≤24 months (median score improvements were three (2–3) and two (1–2), in Group I and II, respectively, p value <0.001).

3.3. Speech Production Assessment

The median pre-operative SIR score was one with interquartile range (IQR) of 1–1. In Group I (children ≤24 months) the median SIR score was one (1 – 1). The median SIR score in Group II (>24 months) was one (IQR: 1–1). (Table 3)

The evaluation of the SIR scores one year postoperatively, represented a significant increase in all the patients (median SIR score three (2–3), p value<0.001). There was no significant difference between Group I and II (median: three (2–3), and three (2–3), respectively, p value: 0.409). The SIR improvement after the first-year follow-up was two (1–2). Regarding the SIR score improvement, there was no significant difference after the first year between Groups I and II (median: two (1–2) and two (1–2), respectively, p value: 0.589).

The median SIR score at the second-year follow-up was four (3–4), and the difference between two groups was not significant (Group I: median four (4–4), group II: four (3–4.75), p value: 0.401) (Table 3). The median SIR improvement during the second-year follow-up was one (1–2). The comparison of the second-year SIR improvement between Group I and II represented a significant difference (median: two (1–2) and one (1–2), respectively, p value: 0.003).

4. Discussion

The results of the current study suggested that all the children with ANSD benefited from the cochlear implantation. In a systematic review performed by Roush and colleagues, the outcomes of cochlear implantation in children with ANSD were evaluated. A total of 15 studies with 88 participants were analyzed in this systematic review. The pure tone thresholds improved significantly after implantation, in all the studies. Considering that the speech perception measures reported in the different studies were not identical, comparison of the results across studies was difficult. Overall, it was mentioned that cochlear implantation is beneficial in children with severe-to-profound hearing loss [13]. The performance of hearing skills in children with ANSD after cochlear implantation was evaluated in a systematic review, performed by Fernandes and colleagues. A total of 18 articles and two dissertations were analyzed in this study. A significant improvement in speech perception skills was reported, which was similar to the cochlear implantation outcome in children with sensorineural hearing loss, in the majority of the subjects [14]. The objective assessment of the speech recognition ability after the cochlear implantation in children with ANSD was evaluated in a systematic review performed by Humphriss and colleagues. The post-operative results represented that the children achieved useful open-set speech recognition, but due to the small sample size and methodological bias of the studies analyzed in this systematic review, the generalizability of the results, and evaluation of the effectiveness of cochlear implantation in improving speech recognition is not possible [22]. In the current multicenter study, the outcome of the cochlear implantation in 136 children with ANSD was evaluated. To the best of our knowledge, this is the highest number of participants evaluated for the cochlear implantation outcome in children with ANSD.

The categories of auditory performance is a global measure to evaluate the outcome of hearing developments in the daily life of children with hearing loss, who are as young as six months, or earlier. This observational scale is useful in the assessment of short and long-term outcomes following cochlear implantation [23], with high repeatability and inter-user reliability [19]. Kontorinis and colleagues evaluated the outcome of the cochlear implantation in children with ANSD in a retrospective study. Twenty seven children with a mean age of 35.4 months were implanted, and their auditory performances were evaluated postoperatively (mean follow-up duration: 63.1 months). The mean pre-operative CAP, measured with hearing aids, was 2.5. The mean CAP scores improved to 5.8, postoperatively. The difference between the pre and postoperative CAP score was significant (p value <0.001) [24]. Jeong et al. performed a retrospective review with nine children with ANSD to evaluate the auditory performance after the cochlear implantation. The median CAP score was zero (0–2) preoperatively, and improved to five (4–5), after implantation. All the subjects benefited from the cochlear implantation, and comparison of the auditory performance of six of the nine patients mentioned above, with 12 matched children without ANSD after cochlear implantation, showed no significant difference [25]. In the current study, the mean age at the time of implantation was 31.9 ± 14.7 months. The median CAP score of the patients before the implantation was one (0–1). The median CAP score improved to four (3–4) and five (5–6), one year and two years after the cochlear implantation. There was a significant improvement in the auditory perception ability after the cochlear implantation (p value <0.001). These values are consistent with the results of the studies mentioned previously.

Several studies demonstrated that cochlear implantation in children with a sensorineural hearing loss at younger ages (especially before two years old), led to improved speech and language developments [26–30]. The effect of age at the time of cochlear implantation in children with ANSD was evaluated by Liu and colleagues. Ten children with a mean age of 35.5 ± 26.2 months were Implanted and followed up for mean 45.6 ± 23.9 months. Finally, six of ten subjects achieved a maximal CAP score. Comparison of the CAP scores in children implanted before 24 months and older subjects showed that cochlear implantation before 24 months tended to achieve greater CAP scores [31]. In the current study, the patients ≤24 months tended to show improved CAP scores during the second year of follow-up compared to the older subjects (p value <0.001), which is consistent with the study mentioned above. Nikolopoulos et al. evaluated the importance of age at implantation in pediatric cochlear implantation, with 126 children with prelingual deafness. Based on their results, age is a strong negative predictor of auditory performance in long-term follow-ups (at least after two years). However, there was a positive predictor effect of age in follow-ups less than two years [32]. In the current study, the same outcomes are shown for auditory performance in ANSD children. The CAP improvement was significantly higher in older children at the first-year follow-up (p value: 0.007), but younger children achieved significantly better CAP score improvements than subjects >24 months, during the second-year follow-up (p value <0.001).

Speech intelligibility rating is a global measure of a child’s spontaneous speech production in daily life after cochlear implantation, with a high reliability between observers [21]. In the study, which was conducted by Liu and colleagues, to evaluate the effect of age at the time of implantation on speech production, the SIR scores of the 10 subjects were measured for a mean follow-up duration of 45.6 ± 26.2 months. The scores of the SIR in children implanted before the age of 24 months were compared with the older subjects. There was no significant difference in the SIR score improvement between the two groups [31]. In the current study, the difference between the SIR scores in children ≤24 months and older subjects did not reach a significant level (p values of 0.409 and 0.401 at the first-year and second-year follow-ups, respectively), which is in agreement with the study performed by Liu et al. Regarding the SIR score improvement, there was no significant difference between groups during the first-year follow-up (p value; 0.589), but SIR scores improvement during the second-year follow-up was higher significantly in subjects younger than 24 months old, compare to older patients (p value: 0.003).

The systematic reviews evaluated the surgical outcome of cochlear implantation in children with ANSD and reported that the low number of participants and different measures used for reporting the results are two limiting factors in conducting statistical analyses of the available literature [13, 22]. In the current multicenter study, a high number of participants were evaluated by global measures for auditory performance and speech production. In the study performed by Teagle et al., the outcome of the cochlear implantation in a heterogeneous group of children with ANSD was evaluated. All the subjects benefited from the cochlear implantation except for the children with an auditory nerve deficiency, which was observed in pre-operative imaging [33]. In the current study, the patients with auditory nerve deficiency were excluded to decrease the heterogeneity of the participants.

The present study had some limitations: the long-term outcomes of the implantation were not available in all the patients, due to the retrospective nature of the study. The presence of comorbidities (such as cognitive disorders) may worsen the outcome of the cochlear implantation in the children [24]. The developmental and cognitive comorbidities were not documented in the current study. The clinical significance of the genetic mutations in patients with auditory neuropathy was presented before [34,35]. The genetic analysis was not performed for all the patients included in this study. Although the CAP and SIR are global measures to evaluate the outcomes of cochlear implantation in children, these scores are not sensitive enough to show subtle changes in the auditory performance and speech production [36].

5. Conclusion

The current study suggested that the children with ANSD benefited from the cochlear implantation. The improvement in auditory performance and speech production skills depend on age at the time of implantation and the duration of post-operative follow-up.

Conflict of Interest: None

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Keywords: Auditory Neuropathy Spectrum Disorder; Auditory Neuropathy; Auditory Dys-synchrony; Children; Cochlear Implantation

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Table.1: Categories of auditory performances (CAP) criteria (adapted from Archbold et al., 1995)[1]

Category	Criteria
7	Use of telephone with known listener
6	Understanding of conversation without lip-reading
5	Understanding of common phrases without lip-reading
4	Discrimination of some speech sounds without lip-reading
3	Identification of environmental sounds
2	Response to speech sounds
1	Awareness of environmental sounds
0	No awareness of environmental sounds

Table.2: Speech intelligibility rating (SIR) categories (adapted from Allen et al. 1998)

Category	Criteria
5	Connected speech is intelligible to all listeners. Child is understood easily in everyday contexts
4	Connected speech is intelligible to a listener who has a little experience of a deaf person's speech
3	Connected speech is intelligible to a listener who concentrates and lip-reads
2	Connected speech is unintelligible. Intelligible speech is developing in single words when context and lip-reading cues are available
1	Connected speech is unintelligible. Pre-recognizable words in spoken language. Primary mode of communication may be manual

Table.3: Auditory performance and speech production outcomes of cochlear implantation in children with ANSD (the values are reported in medians and IQRs)

	Categories of auditory performances (CAP)				**Speech intelligibility rating (SIR)**			
	Pre-op	1 year post-op	2 years post-op	P value	Pre-op	1 year post-op	2 years post-op	P value
Group I	0 (0-1)	3 (2-3)	7 (6-7)	<0.001	1 (1-1)	3 (2-3)	5 (5-5)	<0.001
Group II	1 (0-1)	4 (3-4)	6.5 (5.25-6.5)	<0.001	1(1-1)	3 (2-3)	5 (3.25-5)	<0.001
Total	1 (0-1)	4 (3-4)	7 (6-7)	<0.001	1 (1-1)	3 (2-3)	5 (4-5)	<0.001