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ORIGINAL ARTICLE

Hearing preservation using topical dexamethasone alone and associated with hyaluronic acid in cochlear implantation

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Abstract

Conclusion: Topical dexamethasone associated with hyaluronic acid in cochlear implant surgery demonstrated a statistically significant difference in the preservation of low-frequency thresholds when compared with topical dexamethasone alone and a control group. Topical dexamethasone alone was not superior in hearing preservation when compared to the control group. *Objective:* To compare the effects of topical dexamethasone alone and associated with hyaluronic acid intraoperatively in hearing preservation in cochlear implantation. *Methods:* Eighteen severely to profoundly hearing-impaired adult patients with measurable hearing were divided into three groups preoperatively: cochlear implantation as a control group (group 1), cochlear implantation using topical dexamethasone intraoperatively (group 2), and cochlear implantation using topical dexamethasone associated with hyaluronic acid intraoperatively (group 3). Preimplant and postimplant low-frequency pure-tone averages (PTAs) were calculated from unaided audiograms at 125, 250, and 500 Hz. *Results:* The mean changes in the low-frequency PTA comparing postoperative against preoperative thresholds were 28.03 ± 6.77 dB in group 1, 30 ± 14.53 dB in group 2, and 7.23 ± 6.12 dB in group 3. There was statistical difference when comparing group 3 with groups 1 and 2 using one-way ANOVA ($p = 0.002$) followed by Scheffé *post hoc* test.

Keywords: *Hearing loss, cochlear implant, pharmacotherapy*

Introduction

Hearing preservation was not an issue with the early cochlear implant models, as the available electrode designs resulted in extensive intracochlear injury, causing an irreversible loss of residual acoustic hearing [1]. In-depth knowledge of the anatomy and function of the inner ear as well as the inflammatory repercussions caused by the insertion trauma led to the development of soft surgery principles, new electrode designs, and pharmacotherapy.

Glucocorticosteroids are used in various application forms to reduce the acute insertion trauma as well as the foreign body reaction of the implanted electrode [2]. A previous study has shown that topical use of steroids provides higher drug concentration in the perilymph with minimal side effects [3]. In recent years, hyaluronic acid has been used in cochlear implantation as a lubricant to facilitate nontraumatic electrode insertion [4] and as an inner ear sealant, avoiding perilymph contamination [5,6].

Previous studies evaluating hearing preservation with different types of electrodes associated or not with pharmacotherapy have focused on the incidence of postoperative preserved thresholds. Most of them are retrospective studies with no control group. Therefore, the role of topical dexamethasone and hyaluronic acid for hearing preservation in cochlear implantation remains unclear. The purpose of this study was to compare the effects of topical dexamethasone alone and associated with hyaluronic acid intraoperatively in hearing preservation in cochlear implantation.

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Material and methods

Subjects

This was a prospective randomized study perfomed at a tertiary university hospital with institutional review board approval (Protocol no. 0297/11). Eighteen adults undergoing cochlear implantation by the same surgeon with Cochlear Corporation® (Lane Cove, Australia) Hybrid L24 between August 2011 and December 2012 were evaluated. Inclusion criteria for this study were age older than 18 years, pure-tone audiometric thresholds better than 80 dB hearing level (dB HL) at 125 Hz, 90 dB at 250 Hz, and 100 dB at 500 Hz. Patients were included in this study only after indication for cochlear implantation. Subjects were randomly allocated following the sequence of surgery indication (six in each group) into three groups: group 1 (control), group 2 (dexamethasone), and group 3 (dexamethasone associated with hyaluronic acid). All subjects participated voluntarily and provided signed informed consent in accordance with the Declaration of Helsinki.

Audiometric evaluation

All audiometric testing was performed using a calibrated Interacoustics (Assens, Denmark) AC33 audiometer with maximum output of 90 dB HL at 125 Hz, 110 dB HL at 250 Hz, and 120 at 500 Hz. Testing was performed in a double-walled sound booth using headphones for unaided testing. Preoperative audiograms were obtained at the time of the patients' initial preimplant evaluation. Responses to pure-tones spanning from 125 to 500 Hz were measured for the implanted ear in unaided condition. Postoperative audiograms were also obtained and repeated at 1, 3, and 6 months after implantation. Low-frequency pure-tone averages (PTAs) were calculated for the frequencies 125, 250, and 500 Hz preoperatively and postoperatively at 6 months after implantion. Audiologists who were in charge of audiometric testing were blinded to the group in which the patient was included.

Surgical techniques

Each patient was given a perioperative, weight appropriate dose of intravenous hydrocortisone of 4 mg/kg and a single dose of cefazolin (1 g) before intubation as part of the routine anesthesic protocol. A standardized soft surgical technique was used. A classic transmastoid procedure followed by a wide posterior tympanotomy via facial recess was perfomed. The tectulum was removed using a 1.2 mm diamond burr to allow a wide exposure of the round window membrane. Bony debris and blood were flushed away with saline solution irrigation of the cavity and middle ear. The anterior border of the round window membrane was entered with a delicate probe. No suctioning of perilymph was performed. The electrode array was then slowly inserted into the scala tympani. The round window was sealed with a small collar of temporalis fascia positioned around the electrode array.

Group 1 was the control group without any application of drugs. In group 2 the middle ear cavity was filled with dexamethasone (4 mg/ml) for a period of 15 min. During this time the receiver bed was drilled out. The steroid solution was then suctioned, followed by the opening of the round window membrane and insertion of the electrode array. After sealing the electrode insertion site with temporalis fascia, the middle ear was filled with a final load of dexamethasone via the posterior tympanotomy. In group 3 dexamethasone administration was perfomed as described for group 2. In addition, hyaluronic acid (Provisc®, Alcon Laboratories Inc., Puurs, Belgium) was placed over the membrane after suction of the steroid solution and opening of the round window membrane. Furthermore, the electrode array was coated with Provisc®. After the electrode insertion, Provisc® was placed in the middle ear cavity and over the round window membrane before positioning of the temporalis fascia. After sealing the electrode insertion site with temporalis fascia, the middle ear was filled with a final load of dexamethasone via the posterior tympanotomy.

Statistical analysis

The data were reported as mean ± standard deviation (SD). All statistical analyses were performed using STATA software (version 11). Differences between the three groups were compared using a one-way ANOVA followed by Scheffé *post hoc* test. Statistical test results with a probability value of ≤ 0.05 were considered statistically significant.

The data were analyzed for changes in the low-frequency PTA at 6 months postoperatively against preoperative thresholds, comparing results between groups. For the purpose of calculation, we used 10 dB above the maximal audiometer output for each frequency for which no responses were present.

PTA difference was classified as complete hearing preservation (0–10 dB), moderate preservation (11–20 dB), marginal preservation (21–40 dB), and no preservation (>40 dB or no measurable responses) [5].

Results

Table I shows the deafness etiology, gender, age at surgery, ear implanted, mean preoperative and postoperative low-frequency PTA, and changes in low-frequency PTA for each group.

The mean age was 47 ± 17.75 years in group 1; 40.83 ± 22.07 years in group 2, and 44.17 ± 18.72 years in group 3. There was no difference between groups ($p = 0.86$).

Hearing was preserved in 16 patients (88%). No audiometric responses were present in two patients; these patients belonged to group 2.

The mean preoperative low-frequency PTA was 70.57 ± 12 dB (mean ± SD) in group 1; 76.4 ± 9.86 dB in group 2, and 72.22 ± 22.15 dB in group 3. There was no difference between groups ($p = 0.8$).

The mean changes in the low-frequency PTA of postoperative thresholds at 6 months after implantation against preoperative thresholds were 28.03 ± 6.77 dB in group 1; 30 ± 14.53 dB in group 2, and 7.23 ± 6.12 dB in group 3. There was statistical difference when comparing group 3 with groups 1 and 2 using a one-way ANOVA ($p = 0.002$) followed by Scheffé *post hoc* test (Tables II and III).

The mean changes in hearing thresholds for 125, 250, and 500 Hz were, respectively, 20.83, 28.33, and 35 in group 1; 20.83, 32.5, and 36.67 in group 2; and 3.33, 6.67, and 12.5 in group 3.

Complete residual hearing preservation (change in low-frequency PTA <10 dB) was accomplished in four patients (66.67%) in group 3 and one patient (16.67%) in group 2. Moderate preservation (change in low-frequency PTA between 11 and 20 dB) was seen in one patient (16.67%) in group 1, one patient (16.67%) in group 2, and two patients (33.33%) in group 3. Marginal preservation (change in low-frequency PTA between 21 and 40 dB) was observed in five patients (83.33%) in group 1 and two patients (33.33%) in group 2. No preservation was seen in two patients (33.33%) in group 2.

Discussion

When the soft surgery technique was first proposed, many of the principles were based on reports,

Table I. Subjects' characteristics, preimplant and postimplant pure-tone average, change in pure-tone average, and hearing conservation category.

Patient no.	Sex	Age at CI (years)	Etiology	Side	Group	Preoperative PTA* (dB HL)	Postoperative PTA* (dB HL)	ΔPTA (dB HL)	Hearing conservation category†
1	F	23	Unknown	R	3	68.3	76.7	8.4	Complete
2	F	72	Unknown	L	2	75	116.7	41.7	None
3	M	44	Unknown	L	1	80	113.3	33.3	Marginal
4	M	67	Ototoxicity	L	3	75	90	15	Moderate
5	F	25	Congenital	L	3	83.3	83.3	0	Complete
6	F	41	Meningitis	L	1	81.7	106.7	25	Marginal
7	F	33	Unknown	L	2	90	105	15	Moderate
8	F	64	Unknown	R	2	65	103.3	38.3	Marginal
9	F	38	Meningitis	L	3	90	90	0	Complete
10	M	64	Unknown	R	1	65	88.3	23.3	Marginal
11	M	22	Rubella	R	2	86.7	96.7	10	Complete
12	M	35	Unknown	L	2	71.7	116.7	45	None
13	F	49	Meningitis	R	3	86.7	95	8.3	Complete
14	M	18	Unknown	R	1	80	100	20	Moderate
15	F	63	Unknown	R	3	30	41.7	11.7	Moderate
16	F	48	Unknown	R	1	51.7	90	38.3	Marginal
17	M	19	Unknown	R	2	70	100	30	Marginal
18	M	67	Unknown	R	1	65	93.3	28.3	Marginal

CI, cochlear implantation; F, female; HL, hearing level; L, left; M, male; PTA, pure-tone average; R, right.
*PTA was calculated as an average of thresholds at 125, 250, and 500 Hz (maximum audiometer output + 10 dB used at frequencies with no response).
†Complete, changes in pure-tone average of 0–10 dB; Moderate, changes in pure-tone average of 11–20 dB; Marginal, changes in pure-tone average of 21–40 dB; None, no residual hearing or changes in pure-tone average > 40 dB.

Table II. Comparison of preimplant and postimplant pure-tone average (PTA) between groups.

PTA	Group 1	Group 2	Group 3	*p* value
Preoperative* (± SD)	70.57 dB (± 12 dB)	76.4 dB (± 9.86 dB)	72.22 dB (± 22.15 dB)	0.8
Postoperative* (± SD)	98.6 dB (± 9.92 dB)	106.4 dB (± 8.47 dB)	79.45 dB (± 19.55 dB)	0.01
Changes in PTA (± SD)	28.03 dB (± 6.77 dB)	30 dB (± 14.53 dB)	7.23 dB (± 6.12 dB)	0.002

Differences between the three groups were compared using a one-way ANOVA followed by Scheffé *post hoc* test. The *post hoc* test results are presented in Table III. SD, standard deviation.
*PTA was calculated as an average of thresholds at 125, 250, and 500 Hz (maximum audiometer output +10 dB used at frequencies with no response).

Table III. Scheffé *post hoc* test results comparing preimplant and postimplant pure-tone average between groups.

	Group 1	Group 2
Group 2	0.94	
Group 3	0.009	0.004

The results presented are the *p* values for each of the *post hoc* tests perfomed between the groups.

common sense, and experience with middle ear surgery such as stapedectomy. However, there are still many issues related to hearing preservation that need to be studied in cochlear implantation, including the use of medications and the routes of administration.

In the present study, the use of topical dexamethasone associated with hyaluronic acid intraoperatively in cochlear implant surgery demonstrated a statistically significant difference ($p = 0.002$) in the preservation of low-frequency thresholds when compared with the use of topical dexamethasone alone and a control group. The use of topical dexamethasone alone was not superior in hearing preservation when compared with the control group.

The results of the present study suggest that hyaluronic acid perfoms an important role in hearing preservation. The possibility of an atraumatic scala tympani insertion and better sealing of the inner ear facilitated by the use of hyaluronic acid has been shown by several authors [4,6]. Previous studies have shown that hyaluronic acid may not only reduce insertion-induced trauma but also post-insertion inflammation [7]. Nevertheless, histological analysis would be necessary to investigate new bone formation, fibrous tissue growth, and other inflammatory parameters.

In the present study, it was not possible to evaluate the individual effect of hyaluronic acid, since there was no group using this lubricant alone. Meanwhile, hyaluronic acid associated with topical dexamethasone showed a positive effect related to hearing preservation in cochlear implantation. Our hypothesis is that hyaluronic acid has the potential of prolonging the duration of round window membrane exposure to dexamethasone with higher perilymph steroid levels, as proposed by some authors [8,9]. This hypothesis corroborates with the good results of topical dexamethasone associated with hyaluronic acid in the treatment of low-frequency hearing loss in Meniere's disease, as demonstrated previously [10]. In contrast with other authors [6], we used hyaluronic acid after the electrode insertion to seal the inner ear and to prolong the duration of round window membrane exposure to dexamethasone that filled the middle ear at the end of the procedure.

Despite the anti-inflammatory effects and hearing protection shown in the literature [11,12], the distribution and penetration of topical steroid administration in all cochlear turns are still unclear. The 15 min exposure period assigned in the present study probably was not enough to reach the maximum drug effect. According to previous research, this time would be at least 1 or 2 h [13]. One of the objectives of this study was to evaluate dexamethasone effects with an exposure period that would not affect the duration of the surgery, becoming a practical and useful tool. An alternative could be a transtympanic injection of methylprednisolone in depot form immediately after intubation, as shown in a recent study [14].

Our 88% preservation rate is lower than that in other studies that used short, straight, and atraumatic electrodes. Gantz et al. [15] showed hearing preservation in 46 (96%) of 48 patients and Lenarz et al. [16] achieved success in 31 (97%) of 32 patients, both using the Hybrid-L electrode. However, we demonstrated similar results when comparing our group 3 patients, in that we achieved hearing preservation within 15 dB in 100% of patients. Kiefer et al. [12] and Di Nardo et al. [17] analyzed threshold changes in each frequency separately using longer electrodes. Kiefer et al. [12] reported median increases of 10, 15, and 17.5 dB, while Di Nardo et al. [17] reported mean increases of 11, 12, and 13 dB at 125, 250, and 500 Hz, respectively. We showed better results in group 3 patients, since mean increases in thresholds

observed were 3.33, 6.67, and 12.5 dB at 125, 250, and 500 Hz, respectively, comparable to results with the Hybrid-L array with a median loss of 10 dB across all frequencies [16].

As we only evaluated the PTA in this study, we believe that gender, deafness etiology, and duration of hearing loss do not influence the hearing outcomes. These could be key factors for the results of speech perception outcomes in the long term [18].

Although our patients were not candidates for electric acoustic stimulation, D'Elia et al. [19] showed that preservation of residual hearing should be attempted in all cases. Larger electric dynamic range can be achieved, despite results for speech perception that did not show improvement in patients with hearing preservation [19,20].

Based on the present study, the use of topical dexamethasone associated with hyaluronic acid intraoperatively in cochlear implant surgery demonstrated a statistically significant difference in the preservation of low-frequency thresholds when compared with the use of topical dexamethasone alone and a control group. The use of topical dexamethasone alone was not superior in hearing preservation when compared to the control group. However, further studies are needed with a higher number of patients to enable evaluation in the long term as well as speech perception outcomes.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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