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Intratympanic steroid delivery by an indwelling catheter in refractory severe sudden sensorineural hearing loss

Diego Zanetti [b], Federica Di Berardino [b,*], Nader Nassif [a], Luca Oscar Redaelli De Zinis [a]

[a] *Otorhinolaryngology Department—University of Brescia, Italy*
[b] *Audiology Unit, Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico Milano, Department of Clinical Sciences and Community Health, University of Milano, Italy*

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ABSTRACT

Objective: Many studies over the last decade showed favorable outcomes with intratympanic (IT) steroid treatment, alone as salvage treatment or in combination with conventional systemic therapy (ST). However, in severe to profound sensorineural hearing loss resistant to ST, the optimal infusion mode, the type and concentration of the solution, the preferable drug, its total amount, and the duration and fractionation of the treatment are still debated. Aim of the study was to investigate the feasibility and the outcomes of a direct and constant IT delivery of dexamethasone (DEX) by means of a new indwelling catheter.

Methods: A prospective case-control study in a tertiary referral university hospital. Ninety-nine subjects treated with ST only and 28 with additional IT DEX have been included in the study. A 4 Fr catheter inserted in a sub-annular fashion with a minimal postero-inferior tympanotomy through and endocanalar approach under local anesthesia. DEX 4 mg/ml delivered daily, up to 7 days. Daily bone and air-conducted pure tone and speech audiometry were performed with a follow-up at 1, 3, 6 months after treatment.

Results: Twenty-one out of 28 patients (75%) refractory to ST gained on average 24.0 dB ± 20.5 dB HL after IT-DEX, compared to 35.4% (average 6.7 dB ± 16.6 dB HL) of those receiving only medical ST ($p < 0.001$). No significant side effects were noted.

Conclusion: In severe to profound sudden deafness refractory to conventional ST, the daily perfusion of 4 mg/ml DEX through an intratympanic catheter is an easy, well accepted procedure that enables patients to receive a drug in the middle ear in a repeatable or sustained form, with minimal discomfort and a partial rescue (67.86%) and a speech recognition gain of 39%.

1. Introduction

Severe to profound sudden sensorineural hearing loss (SSHL) is commonly treated with systemic administration of steroids associated with other drugs or physical therapies such as hyperbaric oxygen, carbogen inhalation, hemodilution and plasma apheresis [1,2]. Most series report improvement of the spontaneous recovery rate of SSHL, that ranges between 30 and 60% of untreated cases, by means of parenteral infusion of glucocorticoids [2].

Many studies over the last decade suggest favorable outcomes also with intratympanic (IT) steroid treatment, alone as salvage treatment or in combination with standard treatment (ST) [3–5]. Local administration of dexamethasone, methylprednisolone,

* Corresponding author at: Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico Milano, Department of Clinical Sciences and Community Health, Audiology Unit—University of Milano, Via Pace 9, 20122 Milano, Italy, Fax: +39 02 503 20756.
E-mail address: federica.diberardino@unimi.it (F. Di Berardino).

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Table 1
Clinical characteristics of the 2 groups in the analysis.

Group (no. of patients)	Females	Males	Age	Time interval between the onset and treatment (days)	Initial hearing level (PTA)	Presence of vertigo at the onset
Standard treatment [ST] (99)	35.4% (35)	64.6% (64)	55.5 ± 15.3	9.3	84.4 ± 18.1	10.1% (10)
Intratympanic treatment [IT] (28)	50.0% (14)	50.0% (14)	58.4 ± 13.1	5.5	102.5 ± 15.1	64.3% (18)
	p = 0.2		p = 0.5	p = 0.3	p < 0.001	p < 0.001

triamcinolone and hydrocortisone seems to warrant at least the same chance of recovery, without the side effects of systemic delivery [4]. However, some administration parameters are not yet well established: the optimal infusion mode, the type and concentration of the solution, the preferable drug, its total amount, and the duration and fractionation of the treatment, are still to be identified.

Diffusion of the drug from the middle to the inner ear occurs through the membrane of the round window (RW), that can be reached by trans-tympanic injections, by instillations through ventilation tubes with or without oto-wicks, by direct application on sustained delivery vehicles positioned in the RW niche with a tympanotomy; or by intra-tympanic catheters. Experimental and clinical studies suggest an advantage of a sustained release of steroids to the perilymph, compared to repeated single shot deliveries. For this purpose, a continuous perfusion of the labyrinth, with controlled dosage, delivered through a micro-infusion pump have been proposed [6–10].

In this prospective pilot study, we meant to investigate the feasibility and the outcomes of an intratympanic delivery of dexamethasone by means of an indwelling catheter, in order to rescue severe to profound sudden deafness not responding to conventional intravenous treatment.

2. Materials and methods

A prospective study was conducted on 28 consecutive new cases admitted at the Department of Otolaryngology of the University of Brescia for SSHL. The study spanned over a 2 years period. A retrospective analysis of selected patients from the database of the department provided a matched control group.

The main audiological inclusion criterion was a hearing threshold that exceeded a pure tone average (PTA) of 65 dB HL at 0.5, 1, 2 and 4 kHz, and the maximum speech discrimination score (SDS) in the affected ear had to be lower than 50%. According to the generally accepted definition of SSHL, its onset and progression had occurred within a frame of 72 h [9]. SSHL had to fit the definition of "idiopathic"; thus, exclusion criteria involved patients in whom a clear etiology could be established, such as other ear diseases (e.g. chronic otitis media, otosclerosis), previous ear surgery, ear or head trauma, previous meningitis or other neurological disorders involving the auditory pathways, use of ototoxic drugs, noise trauma, exposure to industrial solvents, inherited hearing loss, and labyrinthine fistula. Patients referred to the hospital more than 30 days from the onset of their hearing loss were excluded as well.

A total of 127 patients were eligible for the study. There were 78 males and 49 females; the mean age was 56.0 years ± 13.8 (range 18–83 years). There were 54 right-sided and 73 left-sided affected ears. The ST group (n = 99) included 64 males and 35 females, 39 right and 60 left ears. The IT group (n = 28) included 14 males and 14 females, 15 right and 13 left ears. The mean age was 55 ± 15 years for the ST group and 58 ± 13 years for the IT group (p = 0.5). Mean PTA before treatment was 84 ± 18 dB in the ST group and 102 ± 15 in the IT group. Clinical features of the two groups of patients are reported in Table 1.

Air (AC) and bone conduction (BC) thresholds were obtained with a 5 dB step and appropriate masking with narrow band noise of the opposite ear with the plateau method. A clinical audiometer model AC 40 (Interacoustics, Denmark) was employed. SDS were measured with the phonetically balanced disyllabic word recognition task, delivered through TDH-49 earphones from a recorded CD. All tests were conducted in a sound isolated booth. Pure tone and speech audiometry were performed daily up to the end of treatment.

Initial systemic treatment consisted in dexamethasone aqueous solution, 4 mg/ml, 8 mg twice a day, associated with i.v. low molecular weight dextrane infusion (500 ml once a day) and subcutaneous low-molecular weight heparin (seleparin 100 units/kg body weight twice a day). Treatment was continued over a 5–8 days period and pure-tone audiometry was checked daily. If no improvements were seen on day 4, heparin was stopped and the next day the patient underwent the surgical positioning of an intratympanic catheter under local anesthesia. (Fig. 1) Care was used to clear any fibrous adherences obstructing the RW niche in all patients; a complete fibrous obliteration was found in one patient.

After the catheter insertion, all patients continued to receive dexamethasone by means of a "shotgun" intratympanic route only, with a single [daily] slow infusion of an average amount of 0.5 ml of the 4 mg/ml solution. The soluted drug was delivered through the catheter under direct control by the physician, over a 2 min infusion time. The patient was instructed to lie in a supine position with the head tilted 45° toward the untreated side for half an hour.

The daily infusions were repeated up to day 5 if no positive effect was noted; conversely, they were discontinued two days after a relevant improvement was observed (equal or better than 10 dB HL at PTA).

At the end of treatment, the catheter was removed under otomicroscopic control, the tympanomeatal flap repositioned. An oto-wick was left in place for 6 days and removed at the subsequent office control. Pure tone and speech audiometry

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