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MAIN ARTICLE

Efficacy of low-dose intratympanic dexamethasone as a salvage treatment for idiopathic sudden sensorineural hearing loss: the Modbury Hospital experience

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Abstract

Objective: To evaluate the efficacy of low-dose intratympanic dexamethasone therapy in patients with idiopathic sudden sensorineural hearing loss whose hearing in the affected ear had failed to improve following a course of oral steroid therapy.

Methods: A prospective pilot study was undertaken of eight patients with idiopathic sudden sensorineural hearing loss whose hearing had failed to improve after a course of prednisolone. These patients subsequently received 8 mg intratympanic dexamethasone therapy, delivered via a ventilation tube on a weekly basis for 1 month. Clinical outcome was assessed weekly with pure tone audiography.

Results: At the end of the 1-month treatment period, no significant hearing improvement was observed on pure tone audiography in any of the patients (i.e. improvements were all less than 10 dB).

Conclusion: The response to 8 mg of intratympanic dexamethasone used as a salvage therapy for idiopathic sudden sensorineural hearing loss was inadequate. A higher dosage of intratympanic dexamethasone might be required to achieve better outcomes.

Key words: Hearing Loss, Sensorineural; Dexamethasone; Treatment

Introduction

Sudden sensorineural hearing loss (SNHL) is defined as hearing loss which is sensorineural in nature, of more than 30 dB, affecting 3 consecutive frequencies, and occurring within 72 hours. It is thought to affect 5 to 20 people per 100 000 population.[1] Of affected cases, 85–90 per cent are thought to be idiopathic at initial presentation, i.e. the underlying cause is not identified despite performing a thorough medical history, physical examination, and laboratory and radiological studies.[2,3] Spontaneous recovery is reported in 32–65 per cent of cases,[1,4] with maximal improvement seen during the first 2 weeks.[1] Patients with sudden SNHL often report associated symptoms of tinnitus, aural fullness or blockage, and dizziness.[5]

Various treatment protocols for idiopathic sudden SNHL have been suggested in the literature; however, the most commonly used and accepted treatment is corticosteroid therapy. Currently, the mechanism of corticosteroid action in the inner ear is incompletely understood. Systemic corticosteroid therapy via the oral route is commonly used. However, in recent years the intratympanic route has gained in popularity as it produces far fewer unwanted side effects compared with systemic therapy.[3,6] Pharmacokinetic studies show that intratympanic administration allows direct penetration of steroid through the round window membrane, producing higher perilymph concentrations without significant systemic steroid absorption and strong toxicity, even at low doses,[7,8] thus producing far fewer unwanted side effects than systemic therapy.

The three principal suggested uses of intratympanic steroids are: (1) as initial therapy for idiopathic sudden SNHL, without systemic therapy; (2) as initial therapy for idiopathic sudden SNHL, with concomitant use of systemic steroid therapy; and (3) as a salvage therapy for idiopathic sudden SNHL patients whose hearing has failed to improve after initial systemic therapy.[3,6] No precise dose, frequency or duration of

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treatment has been defined as achieving optimal results;[3,6,8] however, therapy using higher concentrations has been shown to have better outcomes.[6] Several different techniques for intratympanic steroid administration have been used, including direct injection into the middle-ear space via myringotomy, administration through ventilation tubes, and use of a round window transport facilitator such as a micro-wick.[6]

In their March 2012 *Clinical Practice Guideline*, the American Academy of Otolaryngology Head and Neck Surgery suggested that intratympanic steroid therapy, used either as initial or salvage treatment, should comprise myringotomy with injection of 0.4 to 0.8 ml of 24 mg/ml intratympanic dexamethasone (i.e. 9.6–19.2 mg) into the middle-ear space every 3 to 7 days for a total of 3 to 4 sessions. Effectiveness of the treatment should be monitored with audiometric evaluation before each subsequent injection, on completion of the treatment course, and at delayed intervals thereafter. Pure tone audiography (PTA) and testing of pure tone threshold, word recognition and/or speech recognition threshold have also been suggested as appropriate audiometric evaluations.[6]

The Department of Otolaryngology Head and Neck Surgery of Modbury Hospital, Adelaide, South Australia, conducted a prospective pilot study of the efficacy of low-dose intratympanic dexamethasone, using 2 ml of a 4 mg/ml solution (the only readily available dexamethasone concentration in Australia), equivalent to a dexamethasone dose of 8 mg. Dexamethasone was used to treat patients with idiopathic sudden SNHL who had failed systemic therapy, and was given weekly for four weeks.

Materials and methods

Subjects

We conducted a prospective pilot study of eight patients referred to Modbury Hospital, Adelaide, South Australia, with idiopathic sudden SHNL, who were administered salvage intratympanic steroid injection between 1 January 2012 and 31 October 2012. All the patients included in this study suffered a SNHL of 30 dB or more over 3 contiguous audiometric frequencies, which occurred within 72 hours and failed to show more than 10 dB improvement (on PTA) following a 3-week course of tapering oral prednisolone starting at 1 mg/kg (using a maximum of 50 mg per day). In addition, no underlying cause of SNHL was identified on initial history or examination, and all patients had a negative magnetic resonance imaging scan.

Technique

All the included patients had a ventilation tube inserted into the posteroinferior quadrant of the tympanic membrane in the affected ear, under general anaesthesia. This was performed within four weeks of completion of systemic oral prednisolone treatment. A 2 ml solution of 4 mg/ml dexamethasone was directly injected into the middle ear via the ventilation tube, with excess solution allowed to rest in the external ear canal. The patient was then placed in a lateral position with the affected ear facing upward for 30 minutes. This position was maintained in an attempt to maximise the exposure of the dexamethasone solution in the middle-ear space to the round window membrane.

Subsequent intratympanic dexamethasone therapy was given at the out-patient clinic on a weekly basis for a minimum of four weeks. Audiography was performed before each subsequent treatment and on completion of the treatment course.

Outcome measures

Pure tone audiometry and speech audiometry were performed at initial presentation of hearing loss, after completion of oral prednisolone treatment, during salvage intratympanic dexamethasone treatment, and on completion of this latter treatment. In each patient, the average of results for three consecutive, most affected frequencies was used for analysis. Both subjective and objective measures of hearing were assessed. In this study, we defined complete recovery as PTA improvement to within 10 dB of the unaffected ear, no recovery as PTA improvement of less than 10 dB (compared with pre-treatment values in the affected ear), and partial recovery as a PTA improvement between these two extremes.

Statistical analysis

The results of this study were analysed using GraphPad Prism 5.0 software (GraphPad Software Inc, San Diego, California, USA). Comparisons between groups were performed using Wilcoxon matched-pairs sign ranked tests for paired data. Means, medians, standard deviations and interquartile ranges are reported where relevant.

Results and analysis

Demographic data

Eight patients, six men and two women, were involved in this study (Table I). The mean patient age was 58.1 years. The mean delay between onset of symptoms and initial systemic steroid therapy was 6.87 weeks, with a range of 1 to 26 weeks, whilst the mean time period between onset of symptoms and initiation of salvage intratympanic dexamethasone therapy was 12.62 weeks. All patients received intratympanic dexamethasone within one month of completing oral steroid therapy.

Pre-treatment hearing loss

Prior to intratympanic dexamethasone therapy, 1 patient (12.5 per cent) had low-frequency hearing loss, 2 (25 per cent) had mid-frequency loss, 3 (37.5 per cent) had high-frequency loss and 2 (25 per cent)

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TABLE I
PATIENT CLINICAL PROFILES

Pt no	Age (years)	Sex	Time elapsed from HL (weeks)		Associated symptoms?	
			To systemic Rx	To ITD	Tinnitus	Vertigo
1	52	M	2	7	Yes	No
2	71	F	3	10	No	No
3	54	F	8	15	Yes	No
4	38	M	26	32	Yes	Yes
5	49	M	8	15	No	No
6	82	M	4	9	No	Yes
7	74	M	1	6	Yes	No
8	45	M	3	7	Yes	Yes
Summary statistic	58.1 (15.6)*	6:2†	6.9 (8.1)*	12.625 (8.6)*	62.5%‡	37.5%‡

*Mean (standard deviation); †male:female ratio; ‡prevalence of symptom. Pt no = patient number; HL = hearing loss; Rx = treatment; ITD = intratympanic dexamethasone; M = male; F = female

showed global hearing reduction across all tested frequencies. The severity of hearing loss ranged from mild to profound. Following oral prednisolone therapy, 3 patients (37.5 per cent) showed non-significant improvement, 3 (37.5 per cent) showed no change and 2 (25 per cent) showed deterioration (Table II).

Associated symptoms

In addition to hearing loss, at the time of initial presentation 5 patients (62.5 per cent) reported tinnitus in the affected ear and 3 (37.5 per cent) reported vertigo (Table I). Regarding these associated symptoms, subjective improvement in tinnitus was reported by 1 out of 5 patients (20 per cent), and improvement in vertigo by 1 out of 3 patients (33.3 per cent), during or at completion of intratympanic dexamethasone therapy. No patient experienced any side effects during the intratympanic dexamethasone treatment course (Table I).

Hearing loss following steroid therapy

Overall, there was no statistically significant improvement in hearing following intratympanic dexamethasone, either compared with baseline or with post-oral prednisolone audiometric results ($p = 0.8$ for both comparisons, Wilcoxon matched-pairs sign ranked tests); see Figure 1. In patients whose improvements were less than 10 dB, 3 out of 8 patients (37.5 per cent) showed improved hearing following systemic steroid therapy, and 4 out of 8 patients (50.0 per cent) showed improvement in hearing following salvage intratympanic dexamethasone treatment. Subjective hearing improvement was reported by 2 out of 8 patients (25 per cent).

Discussion

Corticosteroids are currently the treatment of choice for idiopathic sudden SNHL. Although the precise mechanisms of action are unknown, steroids are effective in cases of hearing loss due to viral, vascular and autoimmune causes, endolymphatic hydrops, and other aetiologies. Theories on mechanism of action include a decrease in inflammation, an improvement in cochlear blood flow, protection against cochlear ischaemia, protection against noise-induced hearing loss, and regulation of inner-ear protein synthesis.[3] Studies have showed that the effectiveness of initial corticosteroid treatment is equal via either the oral or intratympanic route, at equivalent doses.[6] Thus, intratympanic steroid administration is a valuable alternative for patients for whom oral steroid therapy is contraindicated. However, the efficacy of corticosteroid therapy for hearing improvement is greatest when steroids are administered within two weeks of disease onset; less benefit is apparent if treatment is delayed until four to six weeks post-onset.[6]

TABLE II
PATIENT PURE TONE AUDIOGRAPHY RESULTS

Pt no	Pre-treatment (dB)	Post-oral Rx* (dB)	Post-ITD (dB)
1	61.7	60.0	65.0
2	86.7	86.7	81.7
3	73.3	73.3	90.0
4	51.7	55.0	50.0
5	46.7	46.3	38.3
6	110.0	113.3	113.3
7	75.0	65.0	61.7
8	66.7	66.7	66.7
Med (IQR)	70.0 (54.2–83.8)	65.9 (56.3–83.4)	65.9 (52.9–88.0)

*Prednisolone. Pt no = patient number; Rx = treatment; ITD = intratympanic dexamethasone; Med = median; IQR = interquartile range

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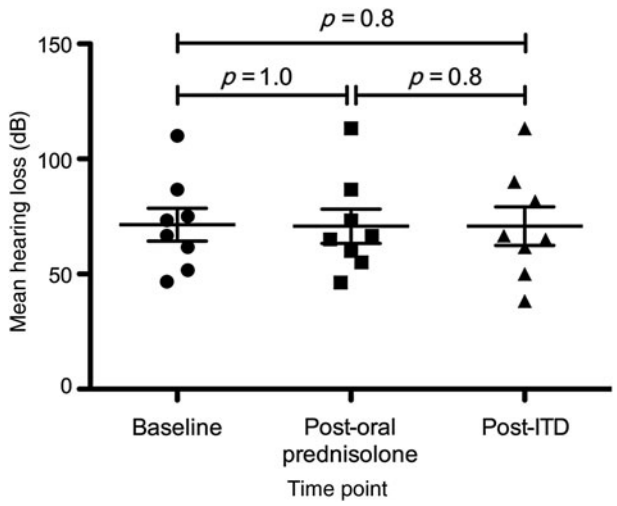

FIG. 1

Change in hearing loss following steroid therapy. Midline rule = median; lower whisker = first quartile; upper whisker = third quartile

Many studies have assessed the efficacy of intratympanic dexamethasone as a salvage therapy to improve hearing. Various steroid types, concentrations, routes of intratympanic delivery, times to treatment, and frequencies of treatment have been assessed, and a wide range of hearing improvements reported.[6] In 3 of the 4 randomised, controlled trials evaluating salvage intratympanic steroid therapy, hearing improvement was seen in 53–90 per cent of patients.[6,9,10]

- **Steroids are the treatment of choice for idiopathic sudden sensorineural hearing loss (SNHL)**
- **Intratympanic steroid therapy is gaining popularity as it avoids the systemic side effects of oral steroids**
- **It can be used initially in idiopathic sudden SNHL, or as salvage therapy if oral therapy fails**
- **The best dose, frequency and duration of intratympanic treatment are unknown**
- **In this study, patients receiving 8 mg salvage intratympanic dexamethasone showed no improvement**

The results of the current study indicate that intratympanic dexamethasone therapy with 4 mg/ml dexamethasone solution does not significantly improve hearing. Several factors may have contributed to this outcome, including: (1) the low concentration of dexamethasone used; (2) possible loss of dexamethasone via the eustachian tube and nasopharynx, or via middle-ear reflux through the ventilation tube into the external auditory canal; (3) delayed commencement of therapy due to delayed referral by general practitioners; and (4) patient factors (e.g. middle-ear adhesions impeding round window absorption into the inner ear).

To further evaluate the efficacy of intratympanic dexamethasone for salvage treatment of idiopathic sudden SNHL, we intend to conduct a second pilot study using a higher dexamethasone dosage (i.e. 24 mg/ml dexamethasone solution).

Conclusion

Despite previous, consistent evidence for hearing improvement following intratympanic corticosteroid treatment for idiopathic sudden SNHL, this study did not demonstrate hearing improvement following intratympanic treatment with 8 mg dexamethasone. Injection of a more concentrated steroid solution into the middle ear may be required in order to maximise hearing recovery, together with education of primary clinicians regarding early initiation of steroid therapy.

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