Acta Otorrinolaringol Esp. 2009;**60(2):**99-103

Acta Otorrinolaringológica Española

www.elsevier.es/otorrino

ORIGINAL ARTICLE

Intratympanic dexamethasone as therapeutic option in sudden sensorineural hearing loss

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Received September 17, 2008; accepted November 18, 2008

KEYWORDS
Sudden sensorineural hearing loss;
Intratympanic dexamethasone;
Systemic corticosteroids

Abstract
Introduction and objectives: The administration of systemic corticosteroids has demonstrated effectiveness on the treatment of idiopathic sudden sensorineural hearing loss. However, its systemic toxicity and subsequent difficulty for its justification in some patients have led to it being applied intratympanically. The main aim of this study is to determine the effectiveness of intratympanic dexamethasone in these patients. In addition we evaluate the relationship between the prognosis of this condition and the magnitude of initial hearing loss, the presence of vertigo or delay in the beginning of therapy.
Methods: We performed a retrospective case study of 18 patients. All of them were treated with intratympanic dexamethasone (4 mg/mL), administered weekly for 3 weeks. The follow-up was 1 month at least. The therapeutic success was arbitrarily defined to be a mean improvement of 25 dB or greater.
Results: Sixty-two point two percent of the population recovered hearing successfully. The mean auditory threshold prior to treatment was 91 (25) dB versus 51 (35) dB after the end of it ($P<.0005$). In addition, we observed that the initial severity of the hearing loss, the presence of vertigo, and the delay in starting therapy cannot be considered as indicators of poor auditory prognosis.
Conclusions: Intratympanic dexamethasone appears to be an effective therapeutic option for patients with sudden onset sensorineural hearing loss who, for whatever reason, cannot be treated with systemic steroids. Nonetheless, randomized controlled trials should be instituted to improve levels of scientific evidence.

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0001-6519/$ - see front matter

PALABRAS CLAVE
Hipoacusia neurosensorial súbita;
Dexametasona intratimpánica;
Corticosteroides sistémicos

Dexametasona intratimpánica como opción terapéutica en hipoacusia neurosensorial súbita

Resumen
Introducción y objetivos: La administración de corticosteroides sistémicos tiene efectividad comprobada en el manejo de pacientes con hipoacusia neurosensorial súbita idiopática. Sin embargo, su toxicidad sistémica y, en consecuencia, la dificultad para utilizarlos en algunos pacientes, ha llevado a su aplicación por vía intratimpánica. El objetivo principal de este estudio es determinar la efectividad de la dexametasona intratimpánica en estos pacientes. Como objetivo secundario, intentamos establecer la relación entre la magnitud inicial de la hipoacusia, la presencia de vértigo y la demora en el inicio del tratamiento con el pronóstico de esta afección.
Métodos: Se estudió, de forma retrospectiva, a 18 pacientes tratados con dexametasona intratimpanica (4 mg/ml), en dosis de 1 ml semanal, durante 3 semanas consecutivas. Se realizó un seguimiento de, al menos, 1 mes. El suceso terapéutico fue definido en forma arbitraria, ante una recuperación auditiva promedio de, al menos, 25 dB.
Resultados: El 72,2% de los pacientes recuperó la audición exitosamente. El umbral auditivo promedio previo al inicio del tratamiento fue de 91 ± 25 dB, mientras que el posterior fue de 51 ± 35 dB ($p < 0,0005$). Además, observamos que la magnitud inicial de la hipoacusia, la presencia de vértigo y la demora en el inicio del tratamiento no pueden considerarse como indicadores de mal pronóstico auditivo.
Conclusiones: La dexametasona intratimpánica puede ser una un opción efectiva en pacientes con hipoacusia neurosensorial súbita que no pueden ser tratados con esteroides sistémicos, aunque se necesitarán ensayos clínicos controlados y aleatorizados para obtener mayor evidencia al respecto.

Table 1 Known causes of sudden-onset sensorineural hypoacusis

Cochlear causes
Infectious (viral and bacterial)
Traumatic (traumatism of petrous apex, otoneurosurgery, etc)
Vascular: Buerger disease, leukaemia, myeloma, cardiopulmonary bypass, etc
Systemic autoimmune diseases: nodal polyarteritis, systemic lupus erythematosus, Cogan's disease, etc
Endolymphatic hydrops (including Ménière's disease)
Metabolic disorders: renal insufficiency, diabetes mellitus, hypothyroidism
Ototoxic drugs: aminoglucosides, salicylates, non steroid anti-inflammatory drugs, vancomycin, etc
Retrocochlear and central nervous system causes
Meningitis
Sarcoidosis
Multiple sclerosis
Amyotrophic lateral sclerosis
Friedrich's ataxia
Guillain-Barré syndrome
Vogt-Koyanagi-Harada syndrome
Tumours: acoustic neurinoma, metastasis in the cerebellopontine angle
Central hypoacusis: cortical encephalitis, Wallemberg's syndrome, Alzheimer's disease

Introduction

Idiopathic sudden-onset sensorineural hypoacusis (ISSNH) is an otological emergency defined as a sensorineural hearing loss greater than 30 dB in at least 3 contiguous audiometric frequencies, occurring over a period of not more than 72 h. The estimated annual incidence of this disease in the world is 5-20 cases/100 000 inhabitants.[1]

By definition, ISSNH is diagnosed only by exclusion, after ruling out known causes that may cause the hearing loss (Table 1), a situation which occurs in only 10%-15% of cases. There are various theories for the aetiopathogenic basis for ISSNH, including viral and vascular causes, rupture of membranes, and autoimmune response.[1-4]

As for the prognosis of this disease, it depends on several factors including the severity and pattern of the initial hearing loss, age, delay in starting treatment, and presence or absence of concomitant vertigo.[5,6]

Although many therapeutic regimens have been employed in the management of this disease, only the administration of systemic corticosteroids at high doses has demonstrated efficacy for a significant recovery of hearing in these patients.[2,7,8]

Stemming from the many adverse effects posed by the systemic administration of these drugs at high doses, their application is introduced directly into the inner ear through the round window membrane, thus obtaining a higher perilymphatic concentration of the drug, virtually no systemic toxicity and a very good tolerance by the patient. It is assumed that the mechanism of action of corticosteroids in the inner ear lies in increasing the flow of

the cochlear microvasculature and reduction of the action of the components of the local inflammatory response triggered by the insult posed by the disease.[9,10]

Moreover, there are some technical variations for the application of drugs directly into the inner ear, such as prior placement of catheters or transtympanic tubes in contact with the round membrane.[11-13]

Thus arises the main objective of this study, which is to determine the effectiveness of intratympanic dexamethasone (Dex-IT) as first treatment option in patients with ISSNH.

A secondary objective is to evaluate the impact of the initial magnitude of hypoacusis, the presence of vertigo as an associated symptom and the delay in starting treatment for the recovery of hearing in these patients.

Methods

This work was approved by the Ethics Committee at our institution.

We performed a retrospective study of 18 consecutive patients who attended the department of otolaryngology at our institution between April 2004 and June 2007.

Patients were selected according to the following inclusion criteria:

- Unilateral idiopathic sudden-onset sensorineural hypoacusis
- Absence of prior neuro-otological disease in the affected ear
- Course of the condition no longer than 6 weeks
- No previous medical treatment

Application technique

With patients in the supine position, we administered pre-anaesthesia with lidocaine spray at 10%. The intratympanic application of the drug was carried out under oto-microscopy, with a needle of 25 µm and tuberculin syringe, at the union of the anteroinferior and posteroinferior quadrants of the tympanic membrane; undiluted dexamethasone was administered (4 mg/mL), in doses of 1 mL weekly, for 3 consecutive weeks. To optimize the access of the drug to the round window, we instructed patients to maintain the head tilted 45° towards the healthy side for a period of 30 min.

Audiological evaluation

Before each application and 1 month after the last, the same graduate in phonoaudiology carried out a pure tone audiometry. The hearing thresholds obtained from each patient were expressed in dB, taking an average value between the 3 centre frequencies of the audiogram (500, 1000, and 2000 Hz), usually related to the perception of voice. All patients had an average monitoring of at least 1 month after the last application.

We arbitrarily stratified the study population into 2 groups, according to the magnitude of the initial hypoacusis:

- Group A: sensorineural hypoacusis ≥90 dB of mean threshold
- Group B: sensorineural hypoacusis less than 90 dB below mean threshold

Successful treatment with Dex-IT was arbitrarily defined as a mean hearing recovery of at least 25 dB.

Statistical analysis

We used the INSTAT program. All variables were independent and had a normal distribution. For comparison of mean values, Student *t* test, the Welch test, and the Tukey post-test were used.

For comparison of categorical variables we used the ^{2} test.

An alpha value <.05 was accepted as statistically significant.

Results

The group studied (n=18) consisted of 50% males (n=9) and 50% of women (n=9). The mean age was 55 (11) years.

The demographic and clinical characteristics of the patients are summarized in Table 2.

We noted that according to the magnitude of the initial hearing loss, the sample was distributed into: group A, 55.6% of patients (n=10) and group B, 44.4% of patients (n=8).

The most frequent concomitant symptom was tinnitus, present in 100% of patients. Twenty-seven point eight percent (n=5) of the population presented vertigo symptoms.

Of the total sample, 72.2% (n=13) recovered hearing satisfactorily (Figure 1). The comparison between mean hearing thresholds of patients who regained their hearing and those who did not showed statistically significant differences in audiometries II, III, and IV (Student *t* test) (Table 3).

Table 2 General characteristics of the study population

Patient	Gender	Age	Latency, d	Tinnitus	Vertigo
1	Female	72	4	Yes	No
2	Male	53	19	Yes	No
3	Female	69	20	Yes	No
4	Male	42	15	Yes	No
5	Male	30	30	Yes	No
6	Male	52	11	Yes	No
7	Male	62	5	Yes	No
8	Female	58	5	Yes	Yes
9	Male	66	7	Yes	Yes
10	Female	50	11	Yes	Yes
11	Male	66	8	Yes	No
12	Female	34	5	Yes	Yes
13	Female	59	7	Yes	Yes
14	Male	61	30	Yes	No
15	Female	53	12	Yes	No
16	Female	60	4	Yes	No
17	Male	54	20	Yes	No
18	Female	52	12	Yes	No

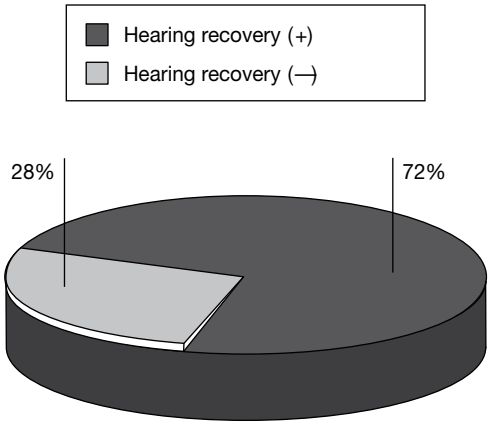

Figure 1 Effectiveness of dexamethasone IT in the study population.

Table 3 Mean hearing thresholds between patients with and without response to treatment with dexamethasone IT

	Hearing recovery (+) patients (n=13)	Hearing recovery (—) patients (n=5	*P*
Audiometry I	88 (24)	100 (27)	.352
Audiometry II	50 (30)	96 (27)	.009
Audiometry III	40 (26)	95 (27)	.002
Audiometry IV	37 (27)	88 (25)	.003

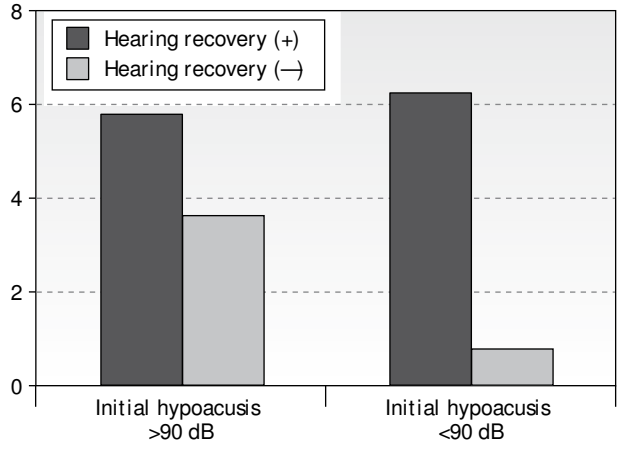

Figure 2 Comparison of hearing recovery rates between group A (initial hypoacusis >90dB) and group B (initial hypoacusis <90dB). ^{2} test, *P*=.32.

Comparing the values obtained in group A and group B, we noted that the improvement in the first was 60%(n=6) and 87.5%(n=7) in the second (Figure 2) (^{2}, *P*=.32).

With regard to vertigo and recovery of hearing, we observed that, among patients with this symptom (n=5), 80% (n=4) recovered hearing, while in the group without vertigo (n=13), 69.2% (n=9) regained hearing (^{2}, *P*=.15) (Figure 3).

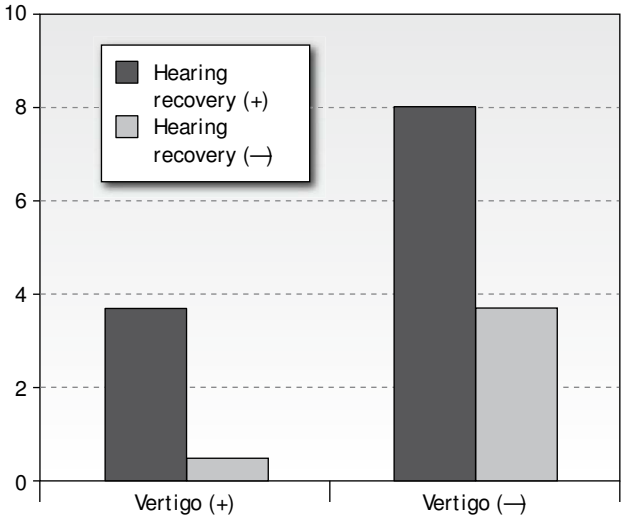

Figure 3 Comparison of hearing recovery rates between the group of patients with vertigo (+) and the group of patients without vertigo (—). ^{2} test, *P*=.15.

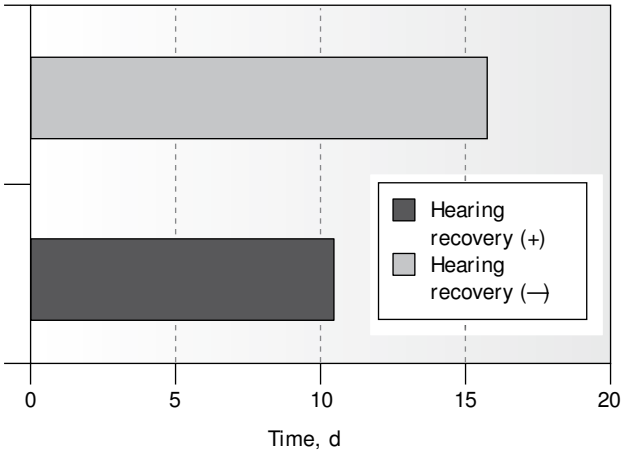

Figure 4 Comparison of mean time delays between patients with and without response to treatment with dexamethasone IT (Welch test, *P*=.296).

As for the mean delay in starting treatment, in the group of patients who recovered hearing successfully, it was of 11 (6) days, whereas in the group that had no positive response to treatment, it was of 17 (12) days (Welch test, *P*=.296) (Figure 4).

The incidence of adverse reactions, secondary to the administration of Dex-IT was 5.5% (n=1), represented by a mild episode of vertigo occurring immediately after application, which remitted spontaneously within minutes.

Discussion

There is no consensus on the exact patho-physiogenic mechanisms facilitating the onset of ISSNH; the theories most commonly advanced are vascular, autoimmune, and

viral.[24] This concept has, in addition, generated many therapeutic regimens including different drugs such as diuretics, vasodilators, volume expanders, corticosteroids, and immunomodulators. We should not underestimate the theory, promoted by Mattox et al,[1] of spontaneous resolution of ISSNH as part of the natural course of the condition; in a non-randomized and non-controlled study, there was a 65% hearing improvement without any treatment.

Despite this, systemic administration of high doses of corticosteroid is a widely used treatment with proven effectiveness in patients suffering from ISSNH.

Wilson et al,[2] in a controlled clinical study (n=119) revealed a significant hearing improvement in 61% of patients receiving oral steroids and only 32%in those in the control group ($P<.05$).

Although the systemic administration of these drugs at high doses is effective, it has also been shown that it is associated with numerous adverse reactions (digestive ulcer, hyperglycaemia, hypertension, etc), which resulted in the incorporation of an alternative treatment, which achieved an effective endolymphatic concentration of the drug with virtually no toxicity: the trans-intratympanic administration of steroids.

Chandrasekhar et al,[9] in a retrospective study of 10 patients receiving Dex-IT (0.5 mg), obtained an overall effectiveness of 73%; while Parnes et al[10] in a retrospective study of 26 patients treated with intratympanic methylprednisone and/or dexamethasone, obtained an improvement of 27.2 (5.7) dB.[11,14]

Moreover, in a retrospective study of 21 patients treated with 62.5 mg/mL of IT methylprednisone (3 applications), Fitzgerald et al[15] observed an improvement of 67% (it is worth stressing that a 10 dB improvement in mean thresholds was considered), similar values to those found in our study (n=18; 72% effectiveness).

One of the points of convergence in the study of this disease is the fact that vertigo and profound initial hearing loss are valuable indicators of poor prognosis for hearing recovery in these patients, a fact that was amply demonstrated by Byl,[5] in 1984, in a series of 225 patients recruited over 8 years.

In our study, we found that the severity of initial hypoacusis, the presence of vertigo and the delay in starting treatment had no significant influence on the recovery of hearing in patients.

Conclusions

We can conclude, then, that although the notable effectiveness of Dex-IT in the treatment of ISSNH obtained in our study (72%) was statistically demonstrated and represents a viable option for patients who, for whatever reason, cannot be treated with systemic steroids, further randomized and controlled studies will be required to obtain more scientific evidence on the subject.

Acknowledgments

To the biochemistry graduate Silvia Barzón, for her essential contribution to the statistical analysis.

Conflict of interests

The authors have indicated there is no conflict of interest.

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