

Association of the moment of administration of intratympanic dexamethasone with the auditory results in patients with sudden idiopathic hearing loss: 101 cases

Asociación del momento de administración de dexametasona intratimpánica con los resultados auditivos en pacientes con hipoacusia súbita idiopática: 101 casos

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Abstract

Objective: To evaluate the association of the moment of administration of intratympanic dexamethasone with the auditory results in patients with sudden idiopathic hearing loss. **Method:** An observational, longitudinal, analytical, retrospective study on patients treated for sudden idiopathic hearing loss with dexamethasone sodium phosphate as initial management. Auditory threshold, auditory gain (dB) and percentage of patients who improved from those who started treatment in the first week (group 1S) versus those started management from the second week (group 2S) are compared. A $p < 0.05$ was considered significant. **Results:** 101 cases (37 males and 64 female) were included. Before disease, patients had similar auditory function, after treatment patients in group 1S had significantly better phonetic discrimination than those in group 2S (33.9 ± 18.3 vs. 43.6 ± 26.1 dB; $p = 0.036$) hearing gain in group 1S was 32.0 ± 11.9 dB and in group 2S was 18.2 ± 9.5 dB ($p < 0.001$). 93.5% of those who started treatment the first week had auditory improvement while only 61.8% in second week ($p < 0.001$). **Conclusions:** Intratympanic dexamethasone sodium phosphate administered in the first week was more effective in inducing better phonetic discrimination in most cases and is safe than in the second week.

Key words: Dexamethasone. Sudden idiopathic hearing loss. Results.

Resumen

Objetivo: Evaluar la asociación del momento de administración de dexametasona intratimpánica con los resultados auditivos en pacientes con hipoacusia súbita idiopática. **Método:** Estudio observacional, longitudinal, analítico y retrospectivo de pacientes tratados por hipoacusia súbita idiopática con fosfato sódico de dexametasona como manejo inicial. Se compararon el umbral auditivo, la ganancia auditiva (dB) y el porcentaje de pacientes que mejoraron de los que iniciaron tratamiento en la primera semana (grupo 1S) y aquellos que lo iniciaron a partir de la segunda semana (grupo 2S). Se consideró significativo un valor de $p < 0.05$. **Resultados:** Se incluyeron 101 pacientes (37 hombres y 64 mujeres). Antes de la enfermedad, los pacientes tenían una función auditiva similar. Tras el tratamiento, los pacientes del grupo 1S tuvieron significativamente mejor discriminación fonética que los del grupo 2S (33.9 ± 18.3 vs. 43.6 ± 26.1 dB; $p = 0.036$). La ganancia auditiva en el grupo 1S fue de 32.0 ± 11.9 dB y en el grupo 2S fue de 18.2 ± 9.5 dB ($p < 0.001$). El 93.5% de los que iniciaron tratamiento la primera

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semana tuvieron mejora auditiva y el 61.8% en la segunda semana ($p < 0.001$). **Conclusiones:** El fosfato sódico de dexametasona intratimpánico administrado en la primera semana, en comparación con la segunda semana, fue más eficaz e indujo mejor discriminación fonética en la mayoría de los casos.

Palabras clave: Dexametasona. Hipoacusia súbita idiopática. Resultados.

Introduction

Idiopathic sudden hearing loss is characterized by a sensorineural loss of more than 30 dB in three or more consecutive pure frequencies, established in less than 3 days, with all sudden hearing loss etiologies having been ruled out^{1,2}. This condition is considered a rare ear, nose and throat (ENT) emergency, with an incidence of 5-20 cases per 100,000 persons/year³. It has been estimated that 71% of cases of acute hearing loss are idiopathic⁴.

Although its pathophysiology is not clear, various infectious, vascular and immune causes have been proposed^{5,6}. The inner ear is particularly sensitive to transient ischemia because of its high metabolic requirements and lack of a collateral blood supply⁷. Histopathological studies have found a loss of hair cells and support cells of the organ of Corti, loss of tectorial membrane, support cells and stria vascularis, loss of cochlear neurons and vascular alterations, among others, which might result from a pathological activation of cellular stress and inflammation pathways that involve nuclear factor kappa B within the cochlea, without histopathological data suggesting membrane ruptures, perilymphatic fistulae or vascular occlusion, leukocyte invasion, hypervascularity or hemorrhage within the labyrinth, as might be expected in viral cochleitis⁸.

A variety of known factors affect the recovery from sensorineural hearing loss, including disease duration, hearing loss severity, age, and presence of other symptoms⁹.

During the diagnostic approach, careful clinical and paraclinical assessment is necessary in order to exclude causes that may be fatal or treatable, such as vascular events and malignant diseases; in addition, patients should be urgently referred for additional evaluations that include imaging and serological tests¹⁰.

The therapeutic strategies that have been used so far include antivirals, oxygen-based vasoactive agents and corticosteroids^{11,12}. However, corticosteroids are the only useful compounds for the management of sudden chronic hearing loss, and the proposed mechanism of action is their inflammatory and anti-cellular stress activity, which has been shown to

decrease inner ear inflammation and edema¹³. Previous studies have shown that intratympanic administration of corticosteroids is as effective as oral prednisone and is therefore associated with fewer adverse effects than high-dose oral corticosteroids¹⁴⁻¹⁶. However, according to previous reports, the use of oral corticosteroids is ten times more common, and only 8% of otolaryngologists in the United States of America use intratympanic corticosteroids, which makes for reports on intratympanic use to be scarce and mostly involving small sample sizes¹³.

The present study evaluates the association of the timing of intratympanic dexamethasone administration with auditory outcomes in patients with idiopathic sudden sensorineural hearing loss who had previously not received treatment.

Method

An observational, longitudinal, analytical, retrospective study of cases of patients who were cared for at *General Ignacio Zaragoza* Regional Hospital, in Mexico City, for idiopathic sudden hearing loss in the 2009-2019 period was carried out. Previously untreated patients with a sensorineural hearing loss of 30 dB in three consecutive frequencies in less than 72 hours, with contralateral ear normal hearing and normal otoscopy were included. Diagnostic workup revealed normal complete blood count, metabolic profile, serum electrolytes and erythrocyte sedimentation rate; rheumatologic diagnostic tests included antinuclear antibodies, which were indicated when patient history was suggestive of autoimmune etiology; Venereal Disease Research Laboratory (VDRL) and fluorescent treponemal antibodies tests were resorted to if neurosyphilis suspicion was high; and findings on skull and inner auditory canals thin-section contrast-enhanced computed tomography (CT) were normal. In case of suspected inner ear neoplasm based on CT results, gadolinium magnetic resonance imaging (MRI) of the brain and inner auditory canals was also performed; the only patient who had a neoplasm was discarded for this study. Patients who were allergic to dexamethasone or who had a history of chronic otitis media, skull or acoustic trauma, Ménière's

disease, meningitis, otologic surgery, radiation, exposure to ototoxic drugs or ipsilateral tympanic perforation were not included. Patients who did not complete treatment with intratympanic dexamethasone, as well as those who had dexamethasone allergy or acute otitis externa or media, were eliminated.

Pure tone audiometry was carried out prior to the treatment and one month after its completion, by the same professional audiologist and with a calibrated equipment under the standard for headphones and bone transducers. Hearing thresholds with air- and bone-conductive pathways stimuli in both ears were established at 250, 500, 1000, 2000, 4000, 6000 and 8000 Hz frequencies, with 3000 Hz being added if a difference of 20 dB was found between the 2000 and 4000 Hz thresholds. Hearing impairment was determined with pure tones average at the 500, 1000, 2000 and 4000 Hz hearing thresholds. A hearing threshold of up to 24 dB was defined as normal, a threshold of 25-39 dB as superficial hearing loss, a threshold of 40-59 dB as moderate hearing loss, a threshold of 60-79 dB as severe hearing loss, a threshold of 80-99 dB as profound hearing loss, and a loss > 100 dB was defined as anacusis¹⁷.

Relevant clinical information was obtained from medical records, including age, gender, affected ear, time from symptom onset to treatment and comorbidities, such as overweight, diabetes mellitus, dyslipidemia, and hypothyroidism.

A gain > 20 dB in pure tones or speech discrimination > 20% one month after intratympanic therapy completion was regarded as hearing improvement.

Treatment was administered in all cases at the office, with the patient in decubitus contralateral to the affected ear and with the head turned 45 degrees, and consisted of application of five doses (2 mg/0.5 mL) of dexamethasone sodium phosphate, 2 mg, separated by 24 hours. First, 10 mg of 2% lidocaine are infiltrated to the external auditory canal, at its middle third, under microscopic vision (S100/OPMI pico, Carl Zeiss, Oberkochen, Germany), and with a 24-G needle, a puncture is made on the tympanic membrane posteroinferior quadrant for dexamethasone to be administered. The patient is maintained in position for 30 minutes, optimal time for diffusion towards the inner ear through the round membrane. Prior to administration of the drug, the patient is asked to avoid swallowing, speaking, or performing Valsalva maneuvers to prevent elimination of the drug through the Eustachian tube, and, at discharge from the office, he/she is instructed to perform dry ear care of the ear that is being treated, placing a cotton ball and covering

Table 1. General characteristics of included patients (n = 101)

Age (years)	50.0 ± 15.3
Gender, % (n)	
Males	36.6 (37)
Females	63.4 (64)
Comorbidity, % (n)	
Diabetes mellitus	17.8 (18)
Hypertension	25.7 (26)
Dyslipidemia	33.7 (34)
Overweight/obesity	15.8 (16)
Chronic kidney disease	4.0 (4)
Hypothyroidism	2.0 (2)
Affected ear, % (n)	
Left	55.4 (56)
Right	44.6 (45)

the outer surface with solid petroleum jelly until the tympanic membrane heals, which occurs within the first month. When the drug was administered, 22.7% of patients had vertigo that subsided within the first 10 minutes, and 6.9% noticed mild burning otalgia.

The study was approved by the Local Bioethics and Research Committee and took into account the ethical considerations for research on human subjects of the Declaration of Helsinki, the Nuremberg Code and the General Statute of Health of the Mexican United States.

Statistical analysis was carried out with the SPSS v.25 program, whereby descriptive statistical tests were performed, which consisted of mean and standard deviation for quantitative variables, and frequencies and percentages for qualitative variables. The chi-square test and Fisher's exact test were used to determine significant differences in qualitative variables, and Student's t-test or related samples t-tests for quantitative variables. A p-value < 0.05 was considered significant.

Results

One-hundred and one patients who met the criteria for idiopathic sudden sensorineural hearing loss and who were treated with intratympanic dexamethasone sodium phosphate, with an average age of 50.0 ± 15.3 years, were included. Two-thirds were females and one-third were males. Comorbidities were reported in 63.3%. Main concomitant diseases were dyslipidemia (33.7%), hypertension (25.7%) and diabetes mellitus (17.8%). Affected ear was the left in 55.4% of cases and the right in 44.6% (Table 1). One

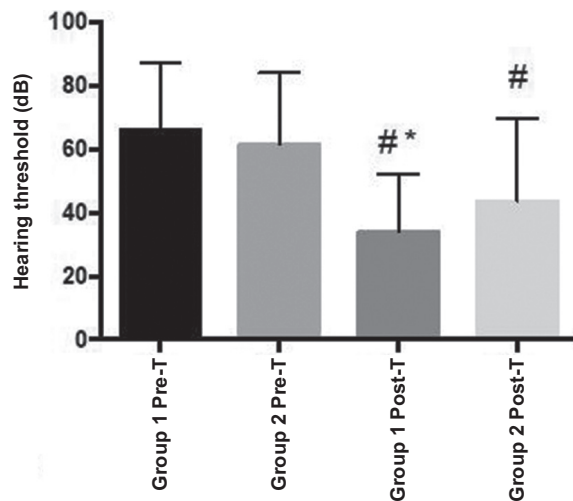


Figure 1. Speech discrimination comparison between groups before and after treatment and decibel gain. $p < 0.001$. *Student's t-test of independent samples vs. group W2. #Paired t-test vs. before treatment.

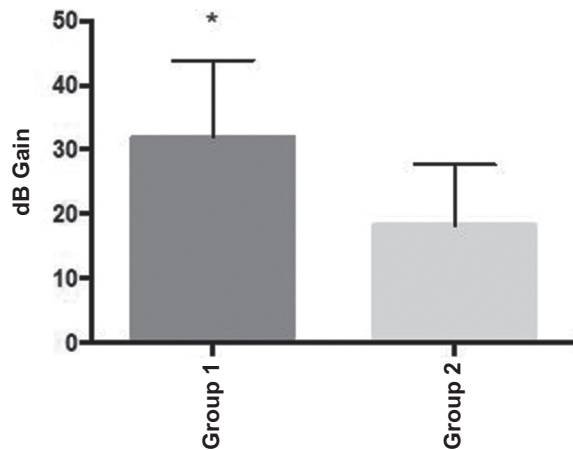


Figure 2. Decibel gain comparison between groups. $p < 0.001$. *Student's t-test

patient was diagnosed with neurosyphilis and was excluded from the study.

A total of 46 patients started treatment during the first week after the onset of clinical symptoms (group W1) and 55 patients started it at 2 weeks (group W2). Prior to treatment, there were no significant differences hearing threshold between groups. However, after treatment, patients from group W1 had significantly better speech discrimination than those in group W2 (Fig. 1). Consequently, after treatment, patients in group W1 had significantly superior hearing gain in comparison with those in group W2 ($32.0 \pm$

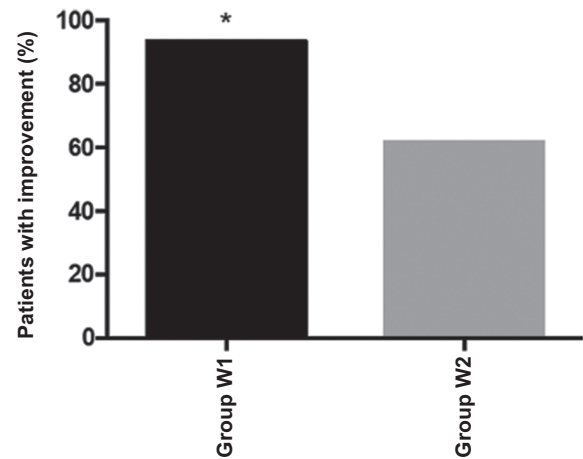


Figure 3. Percentage of patients with improvement. *Chi-square test vs. group W2.

Table 2. Comparison of treatment-emergent adverse events between groups

Adverse events	Group W1 (n = 46) % (n)	Group W2 (n = 55) % (n)	p
Otalgia	2.1 (1)	10.9 (6)	0.142
Vertigo	19.6 (9)	25.5 (14)	
None	78.3 (36)	63.6 (35)	

11.9 vs. 18.2 ± 9.5 dB; $p < 0.001$) (Fig. 2). When the percentage of patients who had hearing improvement after treatment was compared, 93.5% of those who started treatment at first week improved, as well as 61.8% of those who started at second week ($p < 0.001$) (Fig. 3). No significant differences were found between groups in the frequency of adverse events during treatment administration (Table 2).

In those patients with initial superficial, moderate and severe hearing loss, the rate of improvement was 81.8-88.9%, in comparison with 53.3-57.1% in those who initially had profound hearing loss or anacusis ($p = 0.033$) (Table 3).

Comorbidities were documented in 63.3% of the patients. The difference between patients with and without comorbidity who improved (75% [48] vs. 78.3% [29]) was not statistically significant ($p = 0.700$) (Table 4).

Discussion

This study presents the results of idiopathic sudden sensorineural hearing loss management over a period

Table 3. Percentage of patients who improved according to hearing loss initial category

Initial hearing loss	Improvement (n = 77) % n	No improvement (n = 24) % (n)	p
Superficial	88.9 (16)	11.1 (2)	0.033
Moderate	81.8 (27)	18.2 (6)	
Severe	85.7 (18)	14.3 (3)	
Profound	53.3 (8)	46.7 (7)	
Anacusis	57.1 (8)	42.9 (6)	

Table 4. Treatment response in patients with and without comorbidity

Results	No comorbidity (n = 37) % (n)	Comorbidity (n = 64) % (n)	p
Improvement	78.3 (29)	75 (48)	0.700
No improvement	21.6 (8)	25 (16)	

of 11 years, with the attained results being compared according to the time elapsed from the onset of clinical manifestations to treatment. We found that treatment with dexamethasone sodium phosphate improved speech discrimination in both groups, but this gain was superior in those who started treatment in the first week of symptom onset than in those who started treatment on second week. Hearing outcomes were not different between patients with and without comorbidity. These findings highlight the importance of identifying sudden hearing loss and timely starting treatment, since the results are better when treatment is started in the first week, according to our findings.

In a study carried out by Narozny et al.¹⁸ to identify prognostic factors in patients with idiopathic sudden sensorineural hearing loss, treatment delay was found to be an important prognostic factor, with better results being obtained when treatment was started within 10 days of symptom onset, which is similar to the findings in our study.

In another study, no significant differences in the recovery rate were found in patients who started treatment early or late, although those who started treatment early (within the first 5 days) had hearing improvement more often¹⁹. In another study, which included 40 patients, those who responded to corticosteroids were found to have a significantly shorter time between the onset of symptoms and intratympanic

dexamethasone administration²⁰. However, average time from symptom onset to treatment was much longer (40 days on average) than in our case series. Perhaps this is due, at least in part, to the fact that patient recovery rate was only 40% in the case series by Haynes et al.²⁰, while in our patients it was higher than 90% when they started treatment within the first week from symptom onset and 61.8% in those who started treatment in the second week.

In turn, Battista²¹, in a series of 25 patients with idiopathic sudden sensorineural hearing loss to whom intratympanic dexamethasone was administered as initial treatment at 28 days from symptom onset, reported total improvement rates of 8% and partial improvement of 12%, which are figures lower than those attained in our study. The main differences with regard to our case series are that his series only included patients with profound hearing loss and with an average of 28 days from symptom onset, and we included patients with varying degrees of hearing loss severity and a good number of patients who started therapy during the first week after symptom onset, which highlights the importance of treatment early start and that the degree of improvement is also related to hearing loss severity. In fact, in our series, patients with initial profound hearing loss or anacusis had a lower improvement rate than those with lower initial hearing loss.

On the other hand, intratympanic corticosteroids were safe and were associated with a low frequency of adverse effects, which included otalgia and vertigo, and which did not require additional care; no severer adverse events occurred. In fact, in comparison with systemic corticosteroids, the use of intratympanic corticosteroids has been shown to be associated with fewer adverse effects, and since both have the same effectiveness, intratympanic corticosteroids are preferred in order to avoid the adverse effects of systemic administration²².

Although this study is observational in nature and has the weaknesses inherent to this type of studies, its strength lies in the fact that the sample size exceeds 100 cases and that it is one of the few studies reported on idiopathic sudden sensorineural hearing loss initial management with intratympanic corticosteroids, since most reports found in the literature involve the use of corticosteroids as rescue therapy in patients who had no initial response to another treatment modality²⁰. The proportion of hearing improvement was higher than in other studies.

Conclusions

Dexamethasone sodium phosphate intratympanic administration within the first week after symptom onset is effective, induces hearing improvement in most cases, and is safe. Therefore, administering it as early as possible is recommended in order to maximize the possibilities of success in patients with idiopathic sudden sensorineural hearing loss.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained informed consent from the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

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