

# Treatment of idiopathic sudden sensorineural hearing loss: systemic versus intratympanic methylprednisolone acetate

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## Background

The etiology of sudden sensorineural hearing loss is diverse; viral, vascular, immunologic, and abnormal cell stress responses have been proposed, the presentation of the disorder is abrupt, and hearing loss is progressive over a very short period. Steroids remain the treatment of choice irrespective of the etiology of hearing loss. Intratympanic corticosteroid injections have been widely used to deliver corticosteroids directly into the inner ear for those whom systemic steroids have not been successful. Complications such as perforations of the tympanic membrane, myringitis, and otitis media have been reported rarely.

## Objective

To compare the hearing recovery results in patients with sudden sensorineural hearing loss receiving systemic versus intratympanic methylprednisolone acetate.

## Methods

A randomized clinical trial was carried out over 4 years that included 46 patients randomly assigned to two groups of 23 patients each. Pretreatment hearing levels were compared with post-treatment audiograms up to 5 weeks following initial therapy. A 20-dB gain in pure-tone audiometry or a 20% improvement in speech discrimination score was considered a significant improvement. The results of both groups were compared and tested for statistical significance.

## Results

The recovery rate in the systemic group was 65%, whereas the recovery rate in the intratympanic group was 56%; the overall results were comparable over different frequencies. Failure to improve was observed equally in both groups in 21% of patients.

## Conclusion

No statistically significant difference was observed between both the groups. Intratympanic steroid injection as a primary treatment of idiopathic sensorineural hearing loss is an effective alternative to systemic therapy.

## Keywords:

deafness, local, sudden, steroid

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## Introduction

Idiopathic sudden sensorineural hearing loss (SSNHL) usually arises unilaterally and indicates rapid dysfunction of the hearing sense organs; tinnitus usually presents in about 85% of cases whereas vertigo presents in up to 30%. Unilateral hearing loss impairs the localization of sound and the comprehension of spoken language [1–5].

SSNHL is a medical emergency affecting the quality of life of patients and continues to be a diagnostic and management challenge for physicians. It is defined as sudden loss of 30 dB or more in three successive frequencies in pure-tone audiometry (PTA) over a period of 3 days [6–11].

The proposed theory for the pathophysiologic mechanism implicated in inner ear dysfunction is centered on increased secretion of the neurotransmitter glutamate in the synapse between the inner hair cell and the first

neuron of the auditory pathway, which leads to loss of synapses between the inner hair cell and the afferent neuron, with the final outcome being impairment of the electrical transduction [7–9].

The extent of hearing loss and the affected audiogram frequencies are a function of the number and location of the hair cells that are lost. Hearing loss of this type is, in principle, reversible, especially when the mechanism of injury is withdrawn [10].

SSNHL is also defined as hearing loss occurring over no longer than 3 days, with a decrease of 30 dB at three or more frequencies [12].

Systemic steroids remains the most common form of therapy for the treatment of SSNHL; patients who receive systemic therapy shown an overall statistically significant higher recovery rate of hearing than those treated with placebo [13].

The side effects associated with systemic steroid therapy have long been associated with hyperglycemia, hypertension, hypokalemia, peptic ulcer disease, osteoporosis, and immune suppression [14].

Intratympanic steroids have been utilized as a therapeutic option in idiopathic SSNHL, applied mainly as a form of salvage therapy after attempts to recover hearing using systemic steroids have failed [15,16].

Several studies have utilized intratympanic steroids solely as a salvage therapy, whereas others have evaluated their efficacy at presentation. In a study evaluating the concurrent administration of systemic steroids and intratympanic dexamethasone for profound SSNHL, Battista [17] concluded that no significant hearing recovery was achieved with the treatment regimen.

Few studies have compared the primary use of intratympanic steroids with systemic steroids from the onset of hearing loss. This study was carried out to compare both forms of therapy in idiopathic SSNHL

## Methods

A retrospective double-blind, randomized study was carried out in the otolaryngology department of the Suez Canal University Hospital (Ismailia, Egypt) from 2007 to 2011.

Forty-six patients with a diagnosis of unilateral SSNHL (inclusion criteria included  $\geq 20$  dB of loss on PTA over three contiguous frequencies in less than 3 days) [18]. Patients who attended the outpatient unit with a sudden onset in the last 72 h without any medical treatment were included in our study.

Exclusion criteria included a history of head trauma, use of ototoxic medications, acoustic trauma, Ménière's disease, previous ear surgery, perilymph fistula, and barotraumas. Neoplastic disorders such as cerebellopontine angle tumors were excluded on the basis of an MRI study.

Audiological testing with PTA, speech reception threshold, and speech discrimination score (SDS) was carried out in all patients.

MRI with gadolinium was carried out (to exclude cerebellopontine angle tumors) with a laboratory evaluation that included assessment of complete blood count, electrolyte, erythrocyte sedimentation rate, thyroid function testing, fasting blood sugar, and lipid profile.

Patients were divided randomly into two groups:

- (1) In the first group [systemic methylprednisolone acetate (SMPA)], 23 patients received methylprednisolone acetate (1 mg/kg/day) with a tapering effect for 15 days with a maximum dose of 60 mg/day. The total duration of therapy was 30 days [18].
- (2) In the second group [intratympanic methylprednisolone acetate (IT-MPA)], 23 patients received

IT-MPA (40 mg/ml) with a 21-G needle, four times, over 30 days [19].

Follow-up for all patients using PTA and SDS was carried out twice weekly for 2 weeks and the improvement was defined as an improvement in PTA of at least 15 dB [18].

Patients were evaluated by certified audiologists using the standard protocol for pure-tone threshold audiometry [20,21].

Pure-tone average was calculated at thresholds of 250, 500, 1000, 2000, 4000, and 8000 Hz.

## Statistical analysis

Data collected were processed using SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as means  $\pm$  SD, whereas qualitative data were expressed as numbers and percentages. The student *t*-test was used to compare the significance of difference for quantitative variables that followed a normal distribution.

## Results

Forty-six patients (28 women and 18 men) with unilateral SSNHL who fulfilled the previous inclusion criteria, mean age 46.7 years, were divided randomly into two main groups: SMPA group and IT-MPA group.

All patients were subjected to PTA as shown in Table 1; most of the SSNHL varied from mild to profound in 2, 4, and 8 kHz.

The mean SDS was 80.2% (SD  $\pm$  3.23).

In the SMPA group, 23 patients received methylprednisolone acetate (1 mg/kg/day) with a tapering effect for 15 days with a maximum dose of 60 mg/day [18].

Complete recovery occurred in 15 patients (65%), whereas three patients showed mild improvement subjectively with audiometric changes of about 5 dB in the affected frequencies. Finally, five patients reported no improvement at all subjectively, with no changes in PTA, as shown in Table 2.

Results showed a marked improvement in 2, 4, and 8 kHz, which was statistically significant. The mean change in SDS ranged from 81.2 to 84.4%.

IT-MPA was administered in 23 patients (40 mg/ml) with a 21-G needle, four times, over 15 days [19].

Complete recovery occurred in 13 patients (56%), whereas five patients showed a mild improvement subjectively, with audiometric changes about 5 dB in affected frequencies. Finally, five patients reported no improvement at all subjectively, with no changes in PTA, as shown in Table 3.

The results showed a marked improvement in 2, 4, and 8 kHz, with a statistical significance. The mean change in SDS ranged from 79.9 to 81.2%.

**Table 1 Mean intensity among patients with SSNHL**

Frequency	Mean intensity [dB (n=46)]	SD
250	12.1	2.024
500	11.4	3.502
1	10.5	1.311
2	50.9	5.035
4	61.9	7.035
8	72.1	6.036

N, number of patients; SSNHL, sudden sensorineural hearing loss.

**Table 2 Pre-SMPA and post-SMPA hearing threshold**

Frequency	Mean intensity (dB)		P
	Pre-SMPA (n=23)	Post-SMPA (n=23)	
250	13.6	13.6	NS
500	10.9	10.9	NS
1	11.2	11.2	NS
2	52.4	29.1	S
4	60.8	31.4	S
8	69.9	35.9	S

N, number of patients; S, significant; SMPA, systemic methylprednisolone acetate.

**Table 3 Pre-IT-MPA and post-IT-MPA hearing threshold**

Frequency	Mean intensity (dB)		P
	Pre-IT-MPA (n=23)	Post-IT-MPA (n=23)	
250	12.9	12.9	NS
500	11.9	11.9	NS
1	9.8	9.8	NS
2	49.5	33.2	S
4	63.1	36.1	S
8	74.2	39.4	S

IT-MPA, intratympanic methylprednisolone acetate; N, number of patients; S, significant.

The mean SDS in both groups varied from 80.2 to 82.8%, without any significant changes.

Comparison between both groups did not indicate any statically significant changes in post-treatment recovery as shown in Table 4 and Fig. 1.

## Discussion

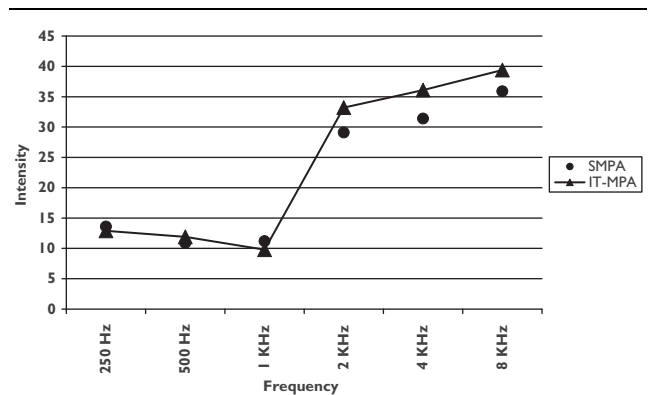
SSNHL is defined as hearing loss occurring over no longer than 3 days, with a decrease of 30 dB at three or more frequencies [12]. Systemic steroids are the main form of therapy for the treatment of SSNHL worldwide. In 1980, Wilson *et al.* [13] carried out a double-blind study, in which patients were administered systemic steroids or placebo, and there was an overall statistically significant recovery rate of hearing in 61% of patients treated with steroids versus 32% with placebo.

The overall improvement in our study was 65% among patients treated with systemic steroids, whereas 56% of the patients improved on receiving primary intratympanic therapy. This is comparable with the earlier published literature.

**Table 4 Comparison of the hearing threshold level after SMPA and IT-MPA**

Frequency	Mean intensity (dB)		P
	Post-SMPA (n=23)	Post-IT-MPA (n=23)	
250	13.6	12.9	NS
500	10.9	11.9	NS
1	11.2	9.8	NS
2	29.1	33.2	NS
4	31.4	36.1	NS
8	35.9	39.4	NS

IT-MPA, intratympanic methylprednisolone acetate; N, number of patients; SMPA, systemic methylprednisolone acetate.

**Figure 1**

Comparison between hearing threshold levels after systemic methylprednisolone acetate (SMPA) and intratympanic methylprednisolone acetate (IT-MPA).

Several authors have also investigated combined therapies (antiviral with steroids) [22–25]. However, no definitive conclusions have been reached and the use of systemic steroids for the treatment of SSNHL remains a common form of treatment and the standard of practice in North America.

Systemic steroid therapy has long been associated with several side effects including hypertension, diabetes, hypokalemia, peptic ulcer disease, osteoporosis, and immunosuppression [14]. It is not uncommon to encounter cases with strict contraindications to systemic steroid therapy; therefore, the need for alternative effective routes of administration emerged.

Intratympanic amino glycosides and intratympanic steroids have been used as a therapeutic option for Ménière's disease. Itoh *et al.* [26] first described the intratympanic delivery of steroids for use in Ménière's disease, with 80% of treated patients experiencing improvement in vertigo.

In a study evaluating the concurrent administration of systemic steroids and intratympanic dexamethasone for profound SSNHL, Battista [17] concluded that there was no significant recovery in hearing with the treatment regimen; however, they suggested the possibility of improvement in hearing if treatment is initiated early (within 11 days of hearing loss).

We reported success in 56% of patients when intratympanic steroids were used as early as within 3 days of the onset of SSNHL. Similarly, a prospective, nonrandomized study comparing patients who received systemic steroids with concurrent intratympanic methylprednisolone with another group of patients who received systemic steroids alone did not show a significant difference in hearing outcome [27]. This is in agreement with the current study, in which no significant difference was found among both the groups.

No studies published to date have reached a definitive conclusion that primary intratympanic therapy should be started and not used as salvage therapy as the current practice indicates.

Another study that examined intratympanic methylprednisolone in 20 patients after failed systemic therapy found that 55% of patients showed a statistically significant improvement in pure-tone average of 10 dB or greater or speech discrimination of greater than 12% improvement [16].

On reviewing the results of our study, it can be concluded that primary intratympanic steroid therapy in the form of methylprednisone acetate may lead to a reasonable improvement in SSNHL patients; it is a slightly over 50% chance of giving the patient a useful hearing results. It should be kept in mind that this figure is based on early treatment ( $\leq 3$  days).

In real life, the presentation of SSNHL is delayed because of several factors; in developing countries, where advanced medical care is beyond the reach of many patients, and deficient competent otolaryngology with audiologist services. Systemic steroids for the above-mentioned reasons will continue to remain the standard therapy.

The duration of systemic therapy is a subject of debate in the literature; dosing schedules are markedly different among reports and no standard guidelines exist. Most reports agree on an overall 1-month duration from the start to tapering and most agree on a total daily dose of 60 mg.

For intratympanic therapy, several approaches have been described: injection, perfusion, microwick, and catheters have all been reported to yield successful outcomes.

The simplest form of intratympanic medication delivery is injection into the tympanic membrane either directly with a long needle or through a myringotomy with or without tube placement. We utilized a spinal needle and found it to be very convenient for use; it can be easily bent as desired and coupled to a standard sterile syringe. This form of delivery is quick, can be performed in the clinic setting, and is currently in widespread use.

Repeated injections can be administered on a weekly basis and, if required, beyond that period a tube should be placed; this may lead to a small risk of persistent perforation or otorrhea [28,29].

## Conclusion

Sixty-five percent of patients showed marked improvement in SDS or PTA after systemic treatment compared with 56% in the intratympanic group when the criterion of 20-dB PTA or 20% was considered to define improvement. No patient showed significant benefit from intratympanic steroids after 5 weeks. No statistically significant difference was observed between both groups. Intratympanic steroid injection as a primary treatment of idiopathic SSNHL is an effective alternative to systemic therapy.

## Acknowledgements

### Conflicts of interest

There are no conflicts of interest.

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