

Intratympanic Methylprednisolone Injection as First Line Therapy for Idiopathic Sudden Sensorineural Hearing Loss

Mukul Patar,¹ Rupanjita Sangma¹

ABSTRACT

Introduction

Steroid therapy is considered to be the gold standard for sudden sensorineural hearing loss (SSNHL). Delivering steroids by intratympanic injection is more efficient than systemic injections with minimum or no side effects. The present study was aimed to evaluate the efficacy and safety of intratympanic methylprednisolone injections as initial first line therapy for unilateral idiopathic SSNHL and the ease of giving it by otoendoscopy.

Materials and Methods

A prospective analysis was performed for the patients diagnosed as unilateral idiopathic SSNHL from April 2014 to April 2016 and receiving intratympanic steroids injections as first line therapy. Patients with unilateral sensorineural hearing loss of at least 30 dB at 3 contiguous frequencies occurring within a period of not more than 3 days are only included. All of the intratympanic steroid (ITS) injections were administered as OPD procedures. Each patient was treated by 3 injections given at 3 days interval.

Results

A total of 22 patients who underwent primary intratympanic steroid (ITS) injection for unilateral SSNHL during the study period were included in the study. The mean age was 42.22 years (± 9.79) and age ranged from 27 to 68 years. Patients included in our study came within 2nd to 27th day of occurrence of deafness and the mean duration (days) from onset of disease to start of ITS was 7.86 days. The average hearing gain in our study was 44.22 dB. In the present study 11 patients (50%) showed complete hearing improvement and 10 cases (45.45%) had partial and one (4.54%) showed no hearing recovery at 3 weeks follow up period.

Conclusion

Minimal systemic absorption with minimum or no systemic effects and high percentage of success rate encouraged the surgeons to prefer ITS as primary therapy for idiopathic unilateral SSNHL. It is effective, cheap, well-tolerated and can be performed as OPD procedure.

Keywords

Hearing Loss, Sensorineural; Injection, Intratympanic; Methylprednisolone

Sudden sensorineural hearing loss (SSNHL) was first described by De Kleyn in 1944 and defined by Wilson et al¹ as sudden decline in hearing over < 3 days affecting ≥ 3 frequencies by > 30 dB with no identifiable etiology. There is always high degree of patient frustration and little evidence to suggest the viral infection, bacterial infection, vascular occlusion or vasculitis as the sole etiological factor. In the past patients were given all available treatments at once due to multiple possible etiologies and limited time

to treat. Old treatment regimens for SSNHL included steroids, carbogen inhalation, oral papaverine, aspirin & hydrochlorothiazide. Steroid therapy is considered to be the gold standard for SSNHL and this treatment method

1 - Department of ENT, Jorhat Medical College, Jorhat, Assam

Corresponding author:

Dr Mukul Patar
email: patarmukul@gmail.com

has been accepted and efficacy has been proven with randomized clinical studies. Intratympanic steroid (ITS) injection is usually used as a rescue therapy for patients with SSNHL who do not benefit from systemic steroid therapy. It is said that physician who does not give steroids may have violated standard of care but physician is also at risk if steroid is given and complications occur. Delivering steroids by intratympanic injection is more efficient than systemic injections and decreases chances of side effects related to systemic steroid injections.² The rationale for intratympanic corticosteroids treatment is that by intratympanic injections steroid reach in high concentration in the inner ear compared to oral or IV injection.³

Erichsen et al⁴ has demonstrated corticosteroid receptors in the inner ear of mice. In intratympanic injections, steroids target these receptors in inner ear, decrease inflammation, improve blood flow, protect against ischaemia, increase stria vascularis function and morphology, prevent loss of spiral ganglion neurons, modulate sodium/potassium in endolymph and regulate RNA transcriptional factors. Till date, majority of studies were conducted concerning the use of ITS as rescue therapy in SSNHL after failure of systemic steroids.^{5,6} Only few studies have evaluated the efficacy of ITS as initial and only treatment for SSNHL. Silverstein et al² in 1996 first reported on intratympanic steroids for SSNHL.

The present study aimed to evaluate the efficacy and safety of intratympanic methylprednisolone injections as initial first line therapy for unilateral idiopathic SSNHL and the ease of giving ITS injections by otoendoscopy.

Materials and Methods

A prospective analysis was performed for the patients diagnosed as unilateral idiopathic SSNHL from April 2014 to April 2016 and receiving ITS injections as first line therapy. Patients with unilateral sensorineural hearing loss of at least 30 dB at 3 contiguous frequencies occurring within a period of < 3 days are only included.

Patients with identified causes were excluded from this study and only idiopathic cases were investigated.

Bilateral cases were also not included in this study. Patients with lesions found on imaging like vestibular schwannoma or inner ear malformation with associated SSNHL or recent use of ototoxic medications were excluded from the study.

The age, gender, affected side, routine blood tests including CBC, basic biochemical parameters, time period from onset of hearing loss and start of treatment, associated tinnitus and vestibular symptoms and comorbidities like diabetes, hypertension were recorded. Patients were grouped according to their ages – age less than 20 years, between 20 and 40 years, between 40 and 60 years and those more than 60 years. Audiometric evaluation of all the patients were done by pure tone audiometry and hearing thresholds at 250, 500, 1000, 2000, 4000 and 8000 Hz frequencies were obtained. Pure tone average was determined by calculating the arithmetic mean of 500, 1000, 2000 and 4000 Hz frequencies. The patients were informed about the treatment procedure and the possible benefits and risks. Informed consents were obtained from all the patients, who agreed with the treatment procedure. Audiometric findings were recorded in all the cases before treatment and three weeks and three months after treatment. Hearing gain after ITS treatment was calculated from pre-treatment and post treatment hearing thresholds in different frequencies.

Intervention:

All of the ITS injections were administered as OPD procedure assisted by otoendoscopy with 0° otoendoscope. The advantages that we got using an endoscope was that the procedure of ITS can be performed as OPD procedure in the clinic and can be performed more precisely with a clear endoscopic visualisation of tympanic membrane (TM) without an operating microscope. Patient was placed in the supine position with the affected ear directed upwards and head tilted at 45 degree. The external ear and tympanic membrane visualised with the 0° otoendoscope and any debris present in external canal were cleaned.

A small cotton ball soaked in 10% local anaesthetic solution placed carefully over the tympanic membrane for surface anaesthesia. A 23 gauge spinal needle was

angled for proper visualisation of puncture site and 40 mg/ml sterile aqueous suspension of methylprednisolone warmed to body temperature was injected into the postero-inferior quadrant of the tympanic membrane using a 2ml syringe. 0.3-0.5 ml of the solution was gradually injected, till the middle ear cavity was completely filled. Patient was instructed to avoid swallowing and speaking and kept in supine position with affected ear up for 30 minutes to provide maximal absorption of medications through round window and to prevent drug leakage through the Eustachian tube. Each patient was treated by 3 injections given at 3 days interval.

Hearing Evaluation:

Pure tone audiometric finding in unaffected ear was presumed as pre-morbid baseline hearing in the affected ear. Evaluation was done before each injection and 3 weeks and 3 months after completion of steroid injection. Mean value of pre-treatment and post treatment audiometric findings were calculated as the mean value from 6 frequencies (250, 500, 1000, 2000, 4000, 8000 Hz). Post treatment hearing recovery was defined as complete recovery when the final pure tone audiometry finding within 10 dB of baseline hearing.

Data Collection:

Review of medical records was undertaken for all patients who underwent ITS injection from April 2014 to April 2016. These data were composed of both pretreatment and post treatment audiometric findings and recorded in decibels (dB) of hearing loss.

Results

A total of 22 patients who underwent primary ITS for sudden unilateral SNHL during the study period were included in the study. Patients who received ITS as secondary treatment after failure of primary treatment with oral or systemic steroids, patients using ototoxic drugs were not included in this study. There were 14 males and 8 females.

The mean age was 42.22 years (± 9.79) and age ranged from 27 to 68 years. Patients included in our study came for treatment within 2nd to 27th day of occurrence of deafness. The mean duration (days) from onset of disease to start of ITS was 7.86 days. The left ear of 15 patients and the right ears of 7 patients were affected. Depending on medical history and medical records, all the patients were assumed to have normal hearing before SSNHL as none of them had an audiogram performed previously. The profiles of the patients are summarized in the table 1.

All the patients received 3 injections of ITS at the interval 3 days. Four patients with idiopathic unilateral SSNHL had diabetes mellitus (DM) and 7 patients had hypertension as co morbid conditions. 16 patients (72.72%) experienced pain at the time of injection that disappeared within minutes to hours, 6 patients (27.27%) described dizziness and 4 (18.18%) had tinnitus lasting for few hours only. No serious complications developed in any patient during and after treatment. Patients with DM receiving ITS were kept under coverage of oral antibiotics during the treatment period.

The improvements of hearing threshold at 250, 500, 1000, 2000, 4000 and 8000 Hz were calculated from post treatment pure tone audiometry findings. It was observed that significant improvement were there in all the frequencies with recovery in mean pure tone by 44.22 dB.

Discussion

The rationale for intratympanic corticosteroid treatment is that it delivers a high concentration of drug to the target tissue i.e. inner ear through diffusion from the round window membrane with minimal systemic exposure. Many researchers studied ITS treatment for SSNHL and reported positive results.⁷

It was also found that the highest corticosteroid concentrations with longest duration were obtained with hydrocortisone, dexamethasone and methylprednisolone.⁸ But data to support the use of ITS as primary therapy are currently limited to case series, reporting success rates similar to those reported with oral therapies.³ Dexamethasone was the

most common steroid used for ITS use^{5,9,10} followed by methylprednisolone.¹¹ But methylprednisolone presented the best absorption profile in both perilymph and endolymph after transtympanic administration.³

Table II: Recovery of Hearing 3 weeks after completion of ITS injections

	RESULTS
Hearing gain 3 weeks after treatment (ITS)	Mean \pm SEM: 44.22 dB \pm 6.47 Range: 0 - 67dB
Complete hearing recovery	11 (50%) cases
Partial hearing recovery	10 (45.45%) cases
No hearing recovery	1 (4.54%) case

SEM = Standard Error of Mean

We used methylprednisolone (40mg/ml) for intratympanic therapy and 0.3 - 0.5 ml injected through the TM towards round window at the interval of 3 days. Literatures described different methods of drug delivery into the middle ear like transtympanic needle injection^{5,9,11,12} delivery through a myringotomy¹⁰ and through a myringotomy tube.¹¹

In our study, 11 cases (50%) showed complete hearing improvement and 10 cases (45.45%) had partial hearing improvement and one female patient (4.54%) showed no hearing recovery at 3 months follow up period (Table 2). Study conducted by Banerjee⁸ and Parnes³ reported successful hearing improvement in 50% (mean PTA improvement was 27 dB) when ITS methylprednisolone was used as a primary treatment. Ljiljana C et al¹³ reported absolute hearing gain between the initial audiogram and final audiogram in IT MP group as 50.7dB, mean relative recovery was 78% following primary ITS therapy.

In the present study we injected ITS to four diabetic patients with ISSHL and blood sugar was within normal limits at the time of each injection and we achieved

partial hearing improvement in all the cases (mean PTA improvement was 37.3 db). Ljiljana et al¹³ compared a group of 10 diabetic patients who were treated with ITS dexamethasone and showed successful hearing improvement in 70%. Hypertension was detected in seven cases and BP was controlled before starting the ITS without any serious complications.

The average hearing gain between the initial audiogram and the final audiogram in our study was 44.22 dB + 6.47 (SEM) and it seems high compared to reports of spontaneous recovery rates. Main limitation of our study was no control group with any other treatment. It is also not clear whether the improvement was actually from ITS or due to natural course of disease. Wilson et al¹ reported 29 of 52 non treated patients regained normal hearing ability (56%). Our study is based on small sample sizes but we need larger sample sizes to establish the valid conclusion of ITS as primary therapy of idiopathic SSNHL.

Complications during and after ITS have been rare and included pain, vertigo, otitis media, TM perforation, dysguesia, chronic otitis media and further hearing loss.^{3,9,12} Pain at the time of injection can be reduced by surface anaesthesia with Lidocaine 10% solution (cotton ball soaked), similar procedure was also used by Onur Gundogan et al.¹⁹ Kakehata et al,¹² in their case control study mentioned less toxicity with initial intratympanic steroids therapy than systemic steroids. Possible ototoxic effect of IT steroids has been ruled out by some clinical studies.^{14,15,16} Dallan I et al¹⁷ has reported one patient with worsening of hearing after repeated injections of methylprednisolone. Pain and a burning sensation around the ear were the frequently encountered side effects of ITS of methylprednisolone and resolved over a period of 10-20 minutes after the injection.¹⁸ In the present study 6 (27.27%) patients complained of dizziness that resolved within minutes and 4 patients complained of tinnitus immediately after the injections but resolved within 24 hours. In our study we have used 23 gauge spinal needle curved to have a good visualization of TM and because of smaller size of needle the hole at TM heals up without any post treatment iatrogenic perforation. We have not found any unexpected major adverse event during treatment or follow up period.

Some issues relating to ITS injections that may need further study are – amount of loss by Eustachian tube, unknown whether absorbed systemically, unknown whether vehicle should be highly viscous or less viscous, would product with high viscosity maintain round window contact better, presence of air bubbles in round window niche and round window adhesions, concentration gradient needed to maintain the therapeutic effect.

Conclusion

Controversy still exists among the ENT practitioners regarding the treatment of idiopathic SSNHL by ITS injections. Many of ENT surgeons still prefer ITS as a rescue therapy instead of primary. Results from different studies showed encouraging results of primary ITS therapy.

Minimal systemic absorption with minimum or no systemic effects and high percentage of success rate encouraged the surgeons to prefer ITS as primary therapy instead of systemic steroids. Moreover it is effective, cheap, well-tolerated and can be performed as OPD procedure with no serious side effects.

Low complications, successful hearing improvement in diabetic and hypertensive patients were also encouraging. Limitation of our study is that it has no control group and study was conducted in a small number of patients. Controlled studies in a large group of patients will further confirm the benefits of ITS as a primary treatment of choice for idiopathic SSNHL.

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