Hearing Outcome of Intra-tympanic Methylprednisolone in Patients with Sudden Sensorineural Hearing Loss-A cross-sectional study at Patan hospital

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ABSTRACT

Background

Intratympanic Steroid, even in low dose causes effective therapeutic concentration in inner ear fluid and hence is emerging in the treatment of Sudden Sensorineural Hearing Loss for its lower systemic side effects. Guidelines still recommends it for the salvage therapy so lacks consensus on its use as an initial therapy.

Objective

To evaluate the hearing outcome of initial intratympanic methylprednisolone injection in Sudden Sensorineural Hearing Loss.

Method

This is a retrospective chart review of the patients who received intratympanic injections of methylprednisolone for Sudden Sensorineural Hearing Loss from January 2020 to January 2023 at department of ENT-HNS, Patan Academy of Health Sciences (PAHS), Lalitpur, Nepal. Hearing outcome of patients who presented within 15 days of onset of symptoms (group I) and after that (group II) were evaluated.

Result

Total of 50 patients, who received intratympanic methylprednisolone were included, 43 in group I and seven in group II. There was statistically significant hearing improvement with mean difference of 18.744dB, 29.184dB and 36.682dB after 1st, 2nd and 3rd injection respectively in group I. In group II hearing improvement with mean difference of 13.000dB, 17.143dB, 22.143dB was seen with no statistical significance. Similarly, in group I, 26,23 and four had complete, partial and no recovery respectively and in group II one had complete recovery and four and three had partial and no recovery after the 3rd dose of injection. Only one case reported severe ear ache post injection which was managed with oral analgesics.

Conclusion

Intra tympanic steroid can be considered as the initial treatment for Sudden Sensorineural Hearing Loss without complication with good hearing outcome.

KEY WORDS

Intratympanic injections, Methylprednisolone, Sudden sensorneural hearing loss, Steroid therapy

INTRODUCTION

Steroid has been the most effective treatment for the Sudden Sensorineural Hearing Loss (SSNHL) till date.[1-3] Studies have shown that intratympanic steroid (ITS), even low dose causes effective therapeutic concentration in the inner ear fluid enabling direct penetration through round window membrane.[4] So, low dose ITS has been emerging in the treatment of SSNHL for its lower side effect with no systemic absorption and hence can be used where systemic corticosteroid is contraindicated.[5]

Several studies have compared ITS over systemic steroid: one showed that ITS was non-inferior to systemic steroids, while another did not find any advantage of ITS over systemic.[6,7] Despite this guidelines still recommend that ITS only be used as a salvage therapy i.e. after 15 days of onset or when other treatments fail.[8] The reasons for not using ITS is fear of pain and permanent perforation and lack of clarity in the extent of benefit when ITS is administered early or later.[7,8]

Though we have been regularly administering ITS as initial therapy for SSNHL, outcomes have not been documented. IT steroid as an initial therapy for SSNHL is debatable and lacks consensus. Therefore this study aims to evaluate the hearing outcome of IT methylprednisolone injection as an initial therapy in SSNHL in term of hearing improvement with respect to the interval between first dose of IT methylprednisolone and time of onset of symptom, dosing interval between two IT injections, and in different effected frequencies and also find out the proportion of patients who made complete, partial or no recovery.

METHODS

This is a retrospective study conducted at Patan Academy of Health Sciences a tertiary referral center, department of ENT & HNS. Upon receiving approval from the Institutional Review Committee (IRC reference number: drs2401121833), documents of all the patients who received IT methylprednisolone as an initial therapy for SSNHL between January 2020 to January 2023 were reviewed and recorded. Patients receiving IT steroid other than methylprednisolone and those with bilateral SSNHL or preexisting hearing loss in the opposite ear were excluded.

As per department protocol all diagnosed cases of SSNHL who had been injected IT methylprednisolone as initial therapy were subjected to PTA on the 3rd day of post IT injections and injections were repeated up to three doses if no complete recovery. Those with complete recovery within any of the doses were not subjected to further injections.

The cases were divided into two groups according to the first treatment from the day of onset of symptoms as primary or group I i.e. within 15 days of SSNHL and salvage or group II after 15 days of SSNHL group, as recommended by the clinical guide line on IT steroid injections for SSNHL of American academy of otolaryngology.[8]

Recovery was defined as per the recommendation of American Academy of Otolaryngology–Head and Neck Surgery (AAOHNS) outcome assessment

1. Unless a previous asymmetry of hearing was known or suspected, the unaffected ear should be used as the standard against which recovery should be compared.

2. A complete recovery requires return to within 10 dB HL of the unaffected ear and recovery of WRSs to within 5% to 10% of the unaffected ear.

3. Partial recovery should be defined in two ways based on whether or not the degree of initial hearing loss after the event of SSNHL rendered the ear non-serviceable (based on the AAO-HNSF definition).

4. Anything less than a 10 dB HL improvement should be classified as no recovery.

Methylprednisolone was chosen as it is the only steroid available in the maximum effective dose per ml i.e. 40 mg/ml in our country. All the patients had received intratympanic injection of 1 ml of methylprednisolone in the dose of 40 mg/ml in the anteroinferior quadrant via 25 Gauge spinal needle under local anesthesia i.e. 15% xylocaine spray 1 puff in each ear. The patients position were maintained in the head turned to opposite side with 30° head end elevation. Then the patients were kept in the same position for 30 minutes.

Data was entered, edited and coded in Microsoft Excel. The data was then imported to statistical software JASP version 0.19.0 for further analysis. The categorical variables were summarized using count and percent while continuous variables were summarized using mean and standard deviation. Association of duration of symptoms and outcomes were tested using a Chi Square test and Fisher Exact test as appropriate. Association of duration of symptoms with PTA at different intervals were tested using student t-test. The level of significance was set at 5%.

RESULTS

A total of 55 patients had received IT methylprednisolone injections for SSNHL during the study period. Five were excluded, two for bilateral hearing loss and three for not completing 3 doses of IT injection even without complete recovery. Among the 50 included 24 (48%) were male and 26 (52%) were female with mean age of 37.34 years ranging from 79 to 4 years. There were 43 (86%) patients in group I (duration of symptoms ≤ 15 days) and 7 (14%) in group II (duration of symptoms > 15days). The sex and age distribution had no any statistically significant difference in both the groups.

The interval of each injections in group I and group II were similar with no any statistical significance (Table 1). However the interval was lesser in group I, between each injections as compared to group II.

Table 1. Comparison of distribution of age, sex and duration in two groups.

Characteristics	Primary (Group I)	Salvage (Group II)	P-value
Male	19 (44.17%)	5 (71.43%)	0.181
Female	24 (55.81%)	2 (28.57%)	
Age mean ± sd years	37.56 ± 15.67	36.00 ± 28.84	0.829
Interval of injection (mean ± sd)			
Between 1st and 2nd	5.12 ± 3.72	7.00 ± 4.36	0.231
Between 2nd and 3rd	4.58 ± 4.75	7.43 ± 4.75	0.142

The baseline mean Pure Tone Average (PTA) among all the participants was 68.12 ± 29.28 dB. After the first IT injection the mean PTA improved to 50.18 ± 29.12dB with a mean paired differences of 17.94 dB (95% CI: 12.419 to 23.461; t = 6.530; p < 0.001). Similarly there were progressive improvement with statistical significance in hearing with PTA average of 48.35 ± 28.86dB and 49.10 ± 29.92dB with the mean difference of 34.690 dB (95% CI: 19.518 to 34.413; t = 7.336; p < 0.001) and 34.690 (95% CI: 25.029 to 44.350; t = 7.356; p < 0.001) after the 2nd and 3rd IT injections respectively as shown in table 2. Paired sample t-tests were conducted to evaluate the within-subject differences in PTA values after each IT application compared to baseline. There was statistically significant progressive improvement in hearing thresholds observed across each IT injections.

Similarly, among the participants of group I, i.e. those presenting within 15 days of onset of hearing loss, the baseline mean Pure Tone Average (PTA) was 64.21 ± 28.44 dB. After the first IT injection the mean PTA improved to 45.47 ± 26.93dB with a mean paired differences of 18.744 dB (95% CI: 12.460 to 25.028; t = 6.019; p < 0.001). Similarly there were statistically significant progressive improvement in hearing with PTA average of 42.33 ± 25.86dB and 42.46 ± 25.81dB the mean difference of 29.184 dB (95% CI: 20.493 to 37.874; t = 6.858; p < 0.001) and 38.682 (95% CI: 27.176 to 50.188; t = 6.991; p < 0.001) after the 2nd and 3rd IT injections respectively (Table 3).

Among the participants of group II i.e. those presenting after 15 days of onset of symptoms we observed progressive improvement across each interventions. Table 4 shows that the baseline mean Pure Tone Average (PTA) was 92.14 ± 23.52dB. After the first IT injection the mean PTA improved to 79.14 ± 26.67dB with a mean paired differences of 13.000 dB (95% CI: 2.455 to 23.543; t = 3.017; p < 0.05). Similarly there were progressive improvement in hearing with PTA average of 75.00 ± 27.87dB and 70.00 ± 34.27dB the mean difference of 17.143dB (95% CI: 3.390 to 30.896; t =3.050; p < 0.05) and 22.143 (95% CI: 3.398 to 40.888; t = 2.890; p < 0.05) after the 2nd and 3rd IT injections respectively.

While the mean PTA values among all the participants and both group I and group II, suggest overall trend towards improvement, the reported mean differences were derived using paired analysis, reflecting within subject changes. The numerical difference between baseline and follow-up means do not directly correspond to the paired differences due to variations in number of available participants,

Table 2. Comparison of mean PTA at various intervals of IT steroids application among all the study participants. (n = 50) (paired sample t-test)

Interval (Mean ± SD)	Number of participant (N)	Comparison (Mean ± SD)	Mean Difference	95% CI of mean diff.		T value	P value
				Lower	Upper		
Baseline PTA (68.12 ± 29.28) (N=50)	50	PTA after 1st IT application (50.18 ± 29.12)	17.940	12.419	23.461	**6.530**	**< 0.001***
	38	PTA after 2nd IT application (48.35 ± 28.86)	26.966	19.518	34.413	**7.336**	**< 0.001***
	27	PTA after 3rd IT application 49.10 ± 29.92)	34.690	25.029	44.350	**7.356**	**< 0.001***

Table 3. Comparison of mean PTA at various intervals of IT steroids application among study participants who reported symptoms before 15 days. (n =43) (paired sample t-test)

Interval (Mean ± SD)	Number of participant (N)	Comparison (Mean ± SD)	Mean Difference	95% CI of mean diff.		T value	P value
				Lower	Upper		
Baseline PTA (64.21 ± 28.44) (N=43)	43	PTA after 1st IT application (45.47 ± 26.93)	18.744	12.460	25.028	**6.019**	**<0.001***
	31	PTA after 2nd IT application (42.33 ± 25.86)	29.184	20.493	37.874	**6.858**	**<0.001***
	20	PTA after 3rd IT application 42.46 ± 25.81)	38.682	27.176	50.188	**6.991**	**<0.001***

Table 4. Comparison of mean PTA at various intervals of IT steroids application among study participants who reported symptoms after 15 days. (n = 07) (paired sample t-test)

Interval (Mean ± SD)	Number of participant (N)	Comparison (Mean ± SD)	Mean Difference	95% CI of mean diff.		T value	P value
				Lower	Upper		
Baseline PTA (92.14 ± 23.52 (N=7)	7	PTA after 1st IT application (79.14 ± 26.67)	13.000	2.455	23.545	**3.017**	0.023
	7	PTA after 2nd IT application (75.0 ± 27.87)	17.143	3.390	30.896	**3.050**	0.023
	7	PTA after 3rd IT application (70.0 ± 34.27)	22.143	3.398	40.888	**2.890**	0.028

Table 5. Hearing recovery in two groups after each injection.

Groups	Group I			Group II			P value (Fisher's Exact Test)
Recovery	Complete Recovery	Partial Recovery	No recovery	Complete	Partial	No recovery	
Overall	26 (60.46%)	13 (30.23%)	4 (9.30%)	1 (14.29%)	3 (42.86%)	3 (42.86%)	0.045
After 1st Injection	12 (27.90%)	20 (46.51%)	11 (25.58%)	0 (0.00%)	4 (57.14%)	3 (42.86%)	0.19
After 2nd Injection	11 (35.48%)	16 (51.61%)	4 (12.90%)	0 (0.00%)	5 (71.43%)	2 (28.57%)	0.21
After 3rd injection	3 (15.00%)	13 (65.00%)	4 (20.00%)	1 (14.29%)	3 (42.86%)	3 (42.86%)	0.60

p value is significant when < 0.05

as those participants who recover completely were not subjected to further injections. This indicates that the improvements are more accurately captured through individual-level comparisons rather than group averages alone.

Recovery of Sudden SNHL

The recovery of participants were as per the recommendation of American Academy of Otolaryngology–Head and Neck Surgery (AAOHNS).

Overall outcome

In group I, 26 (60.46%) had complete recovery and 13 (30.23%) and 4 (9.30%) had partial and no recovery respectively as shown in table 5. Similarly, in group II 1 (14.29%) recovered completely, whereas 3 (42.86%) and 3 (42.86%) had partial and no recovery respectively. Participants in group one showed statistically significant better outcome with P value < 0.05. (p= 0.045) (Table 5). (In this place I have omitted value and the fischer exact test)

Outcome after 1st injection

In group I, 12 (27.90%) and 20 (46.51%) had complete recovery and partial recovery respectively. While 11 (25.58%) did not recover. Similarly, in group II none had complete recovery. Partial recovery was observed in 4 (57.14%) and 3 (42.86%) did not recover. The result is not statistically significant with P value > 0.05 (p=0.19) (Table 5).

Outcome after 2nd injection

Eleven patients, i.e.35.48% of patients in group I further recovered completely with 2nd injection while none had complete recovery in group II. In group I, 16 (51.61%) and 4 (12.90%) had partial and no recovery. In group II,5 (71.43%%) showed partial recovery and 2 (28.57%) did not recover. This was not statistically significant as P value is > 0.05 (p=0.21) (Table 5).

Outcome after 3rd injection

Only 27 patients were further subjected to 3rd dose of injection for not having complete recovery. Among them in group I, 3 (15.00%) further recovered completely, 13 (65.00%) and 4 (20.00%) had partial and no recovery respectively. In group II, I (14.29%), 3 (42.86%) and 3 (42.86%) had complete, partial and no recovery respectively. Both group showed similar proportion of complete and partial recovery. However, this difference was statistically not significant (p = 0.60) (Table 5).

Hearing improvement as per the effected frequencies

The differences in the average PTA threshold of the pre injection and after the complete recovery or completion of 3rd dose of IT injections of each frequencies were calculated to find out the improvement in hearing in each frequency. As shown in figure 1, there is a rising trend in the improvement of PTA average with peak at 2000Hz and falling trend towards 8000kHz.

Complication: There were no major complication reported by the patient. Only one case reported severe earache post IT and was managed with oral analgesics. None of our patients developed tympanic membrane perforation, dizziness, vertigo.

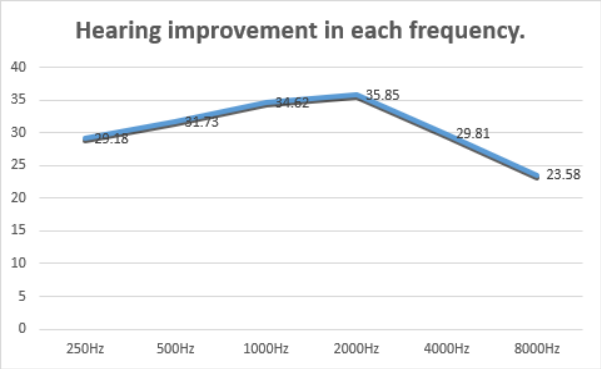

Figure 1. Hearing improvement after completion of 3rd dose of IT injection in various frequencies of pure tone audiometry.

DISCUSSIONS

Steroid therapy (ST) whether systemic or intratympanic has been the most accepted and established medical treatment for SSNHL. Though there has been various debate on the better outcome of both, various studies have proved that both have equivocal outcome.[10,11] Intratympanic steroid (ITS) has been recommended as an initial therapy for SSNHL, in those where the systemic steroid is contraindicated or as a salvage therapy.[8] We had administered IT steroid to all the patients with SSNHL as an initial therapy, with the advocacy that if it is recommended to those with comorbidities and systemic steroid therapy (SST), which is also a poor prognostic indicators, it shall definitely have good outcome and can be used in all the cases.[1]

Studies also debate that systemic steroid has more wider coverage with its systemic effect, which decreases the inflammatory mediators, by decreasing the circulating blood leukocytes.[12] Yang et al. in his study found out that dexamethasone was not effective in reduction of inflammatory infiltrates in the inner ear.[13] Studies also have shown that steroid lack access to the more central cochlear nerve hence leading to the inadequate treatment of cochlear nerve disease in internal auditory canal and cerebellopontine angel.[13]

With all these consideration, in our study, with ITS as a initial therapy, overall 27 (54%), had good outcome, i.e complete recovery and of the rest, 17 (34%) had partial recovery, showing good response with initial ITS. Among them, result was better in group I with 26 (52%) vs 1 (2%) in group II with complete recovery. Our result of the complete recovery is comparable to the other studies of both systemic, combined and IT steroid therapy. Fitzgerald et al. in his study where he injected 0.4 ml of 62.5 mg/ml methylprednisolone had 67% response rate with better response rate of 91% in "prompt treatment" group.[10] His study showed that early treatment is the only variable significant in the outcome, favoring our result.[10] Similarly, in the study of Sergey et al. IT dexamethasone had better result (88% vs 48% and 56% improvement) compared to the oral and IV dexamethasone group in one months.[11] IT dexamethasone had even better results with complete recovery rate of 60% compared to 20% in the other two groups at the end of 6 month.[11] Our cases however did not have long term follow up of more than one months to see the long term results. Many studies have shown good results with IT steroid in terms of hearing gain ranging from 24% to 52.7%.[5,14,15] Lyu et al. in their study of IT injections for pregnant ladies with SSNHL had curative rate of 57.1%, and all of them delivered healthy full-term neonates.[16] This not only showed the effectiveness of IT steroid but the safety too.[16] Superiority of ITS in comparison to the systemic steroid therapy is also emphasized by the meta-analysis done by Yang et al. In their meta-analysis ITS had better results in terms of hearing gain and recovery rate regardless of type of steroid and mode of administrations.[17] Ng et al. also emphasized the effectiveness of ITS in managing SSNHL by his meta- analysis of ITS as a salvage treatment and concluded that ITS had significant improvement in hearing threshold as compared to the no treatment group.[18]

We observed increasing improvement in the hearing threshold with overall mean difference from initial PTA to final PTA of 34.69dB by the end of 3rd injection, and 26.96dB and 17.94dB after the 2nd and 1st injection. The improvement in hearing was better in group I with mean gain of 38.68dB compared to 22.14dB in group II by the end of 3rd injection. This is similar to the gain in the study of Kara et al. where there was improvement of 31.38 and 37.55 in the tenth day and second months in the ITS group compared to 19.35 and 20.68dB in systemic group.[19] Similarly, Bhandari et al. in their study had significant hearing gain in low, medium and high frequency proving the efficacy of ITS.[20] They also found that ITS had better outcome if given within four days of onset of symptoms. Thus, supporting our result.[20]

There is considerable variability in the dosing interval and number of injections in studies with ITS as both salvage and initial therapy. We had injected total of three ITS in both the group with no further injection if the recovery is complete. And there was no significant difference of dosing interval between groups in between the doses. Studies have ranges of doses of upto maximum 9 to 3 and the interval also ranging from 1 to 7 days between the doses.[5,9,15,21] In a study by Kwak et al. where he injected total 4 does of IT dexamethasone for every 1, 2, 3 and 4 days, one who received daily injection had significantly higher complete recovery rate than the others.[15] Similarly, Wang et al. had highest rate of hearing recovery in the group receiving six IT injections, and also concluded that number of IT injections as the only independent factor with positive association with the hearing recovery.[9] In contrast to this, Andrianakis et al. studied two groups with 3 and 4 numbers of ITS as a salvage therapy and found no statistically significant difference in the result. He also concluded that lesser injections showed lesser complications. Similarly, Andrianakis et al. studied the effect of intratympanic steroid injection frequency in idiopathic SSNHL and concluded that earlier time of initiation of the treatment had higher rate

of improvement, whereas frequency did not significantly affect the hearing recovery.[21] Thus, supporting our result where group I had better recovery rate as well as better improvement in hearing.

In our study, the end point of the treatment was complete recovery of the hearing as per AAOHNS guideline. To our knowledge there are no such studies which compared the outcome in each injections. Till date all the studies we found have evaluated their result at the end of the treatment. In our study it showed that even the single dose of steroid seem to improve a significant number of the cases with complete recovery. These patients were not subjected to further injection, thus reducing the financial burden and chances of complications related to the IT injection. This could be due to the natural history of the disease where certain cases, improve by themselves.[1]

We also evaluated the hearing gain in each frequency, which showed rising curve with maximum gain of 35.85dB at 2000 Hz and again decreasing curve till 8000Hz. This was contradictory to the other studies where there is maximum gain at the low frequency with lesser improvement in higher frequency.[1,20]

We had only one complication where the patient had severe pain post injection for about 24 hours, which was managed with oral analgesics and no other complications were noted. There are studies reporting complications like, pain, vertigo, tympanic membrane perforation, which increased with the increase in the number of injection.[9,15,21]

The study being a retrospective study we lack data of long term follow up of all the patients. None of the patient had speech discrimination scores. There was no equal distribution of the cases in both the group, only seven in Group II.

CONCLUSION

ITS can be the first line therapy of SSNHL, thus avoiding the side effect of systemic steroid even in the patients with no contraindication of systemic steroid. The only concern is about the complications, which can be avoided by choosing the regime as total of 3-4 injections, each injections per week, as per our study and the review of literature. This can reduce complications especially the tympanic membrane perforation, which seem to increase with the increasing number of injection. We recommend for the repeat PTA after each injection, to avoid unnecessary further injection in those who have completely recovered and start the treatment as soon as possible. For the better evidence we recommend further prospective studies with equal distribution of cases in both the group.

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