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Original article

Comparative Study between Intratympanic Methylprednisolone Injection versus Dexamethasone for the Treatment of Idiopathic Sudden Sensorineural Hearing Loss

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Abstract

Background: Idiopathic sudden sensorineural hearing loss (ISSHL) continues to be a medical mystery, both in terms of its cause and its therapy. Corticosteroids are supposed to aid ISSHL healing because of their anti-inflammatory effects. In this study, we compared the effectiveness of two steroid treatments for ISSHL: methylprednisolone (40 mg/mg) and dexamethasone (24 mg/ml). **Methods**: In a randomized, interventional study, we recruited 40 patients with ISSHL. Patients were randomly allocated to group (A) received injection of 1 ml Dexamethasone (24mg/ml) in the middle ear cavity and group (B) Injection of 1ml of Methylprednisolone (40 mg/ml) in the middle ear cavity, every patient in each group was injected 5 times in consecutive days and PTA and tympanometry done 3days,5 days, and 6weeks postoperatively.

Results: There was statistically insignificant higher complete and partial recovery in Methylprednisolone than Dexamethasone groups. In methylprednisolone group (17.4%) showed partial recovery compared to (16%) in dexamethasone group. Also, (21.7%) in methylprednisolone group showed complete recovery compared to (12%) in dexamethasone group. The mean speech discrimination after injection was 74.3%±19.3% in methylprednisolone group and 69.6%±31.6% in dexamethasone group. There was insignificant improvement in speech discrimination in both groups however, the absolute mean difference was higher in Methylprednisolone than Dexamethasone group. **Conclusions**: With a poor likelihood of recovery, idiopathic sudden sensorineural hearing loss continues to be a difficult clinical issue. Intratympanic steroid injection, however, is a comparatively efficient, secure, and well-tolerated method for the treatment of ISSHL. Results related to hearing loss strongly recommend using methylprednisolone intratympanic injection rather than dexamethasone.

1. Introduction:

An otological emergency, idiopathic sudden sensorineural hearing loss (ISSNHL) is characterized by the loss of hearing in at least three consecutive frequencies by 30 dB or more and occurring within 72 hours [1].

Acute SNHL occurs in 5–20 people per 100,000 annually. SSNHL may be more common than estimated because people who get well fast avoid seeking medical attention. Although it may affect people of any age, most cases occur in their thirties and forties. The incidence of SSNHL is the same in both sexes [2].

ISSHL's etiology may be idiopathic, but there are also additional reasons, such as viral infections, vascular problems, and immunologic disorders. A lack of agreement in the treatment of ISSHL was caused by the

challenge of determining the precise cause of hearing loss [3].

Because the origin of ISSHL is yet unknown, therapy regimens are not standardized. Vasodilators, diuretics, anticoagulants, plasma expanders, corticosteroids, and hyperbaric oxygen therapy are a few of the therapeutic options. Systemic steroids may cause major side effects, such as uncontrolled hyperglycemia, hypertension, gastrointestinal bleeding, and hip avascular necrosis, either alone or in combination. Intratympanic (IT) steroids enable the inner ear to reach high concentrations and minimize harmful effects brought on by systemic steroid treatment, in addition to the fact that side effects including sleeplessness, gastritis, flushing, and irritability are more common but less severe [3].

Patients with inner ear conditions including persistent Meniere's disease or idiopathic abrupt sensorineural hearing loss often get steroid therapy (ISSNHL). Intratympanic steroid (ITS) administration may be an acceptable substitute for systemic steroid treatment for certain individuals, yet, as it may be ineffective or contraindicated [2].

In order to treat inner ear disorders, steroids are increasingly often injected intratympanically. Since it is normally well tolerated and has been shown to give higher steroid concentrations in the perilymph without the risk of systemic side effects, it may be used as an alternative to or in addition to systemic steroid therapy [4].

The outcomes depend on a number of variables, including the kind and degree of hearing loss, the interval between the onset of symptoms and the start of therapy, the length of the treatment, and the method used to give the steroid. Corticosteroids, which may be given at various frequency and dosages, are the most widely used treatments for ISSHL despite all these changeable factors. To yet, it is unclear how corticosteroids affect the inner ear. However, corticosteroids' recognized methods of action are described as decreasing inner-ear inflammation, guarding against ischemia, boosting cochlear blood flow, and controlling end-cochlear potentials and protein synthesis [5].

Systemic administration may be constrained by the blood-labyrinth barrier, which reduces the exchange of fluid between plasma and the inner ear as a result. Local intratympanic administration often seems to be preferable because the cochlea is one of the most difficult organs to access for drug delivery [6].

A needle is used to inject steroids through the tympanic membrane into the middle ear space, where they are then absorbed and

diffused into the perilymph of the inner ear primarily through the semi-permeable round window membrane, but also through the oval window annular ligament and small lacunar mesh. The semi-permeable circular window membrane hinders the entry of most medicines and other substances into the inner ear somewhat. Drugs supplied via the round window will reach hair cells and nerve cells quickly thanks to the communication network between the scala tympani, the organ of Corti, and spiral ganglion [7].

Intratympanic steroids have minimal morbidity; however, there are some potential complications or side effects that must be considered and thoroughly discussed with the patient before undergoing the procedure such as transient dizziness, injection pain, a burning sensation, tinnitus, post-injection vertigo, and a small perforation of the eardrum [8]. In this study, we aimed to compare the effectiveness of two steroid treatments for ISSHL: methylprednisolone (40 mg/mg) and dexamethasone (24 mg/ml).

2. Patients and Methods:

Setting Study design

This study was a randomized interventional cohort study performed on 40 cases; it is a single blind study. This study was performed at the Otorhinolaryngology department, Beni-Suef University Hospital to compare the therapeutic efficacy of different Intra-tympanic Injection of steroids including Methylprednisolone (40mg/ml) and dexamethasone (24mg/ml) in the treatment of ISSHL.

Subjects

Patient diagnosed with idiopathic sudden sensorineural hearing loss presented to the Otorhinolaryngology department, Beni-Suef University Hospital through 12 months from the start of January 2022 till the end of December 2022. The total number of cases was 40 cases. Patients were randomly allocated into 2 groups: **Group A:** 20 cases treated with intratympanic injection of Methylprednisolone (40 mg /ml). **Group B:** 20 cases treated with intratympanic injection of Dexamethasone (24 mg/ml).

Inclusion Criteria:

Patients must meet all of the following criteria to be eligible for enrollment in the study, Patients with sudden SNHL (patients with sudden hearing loss, drop in air and bone conduction curves in their PTA) for 2 weeks or less.

Exclusion Criteria:

Patients who meet any of the following criteria are not eligible for inclusion in the study, Patients with SNHL due to a known cause such as intratympanic tumor or cerebellopontine angle lesions diagnosed by

CT or MRI. Patients with sudden SNHL for more than 2 weeks. Patients with acute otitis externa and otitis media. Patients started other medications like systemic steroids or just observation as a primary treatment.

Full history taking including age, sex, onset of hearing loss, history of trauma, viral infections and other causes of SNHL. Examination of tympanic membrane of both ears, Weber and Rinne tests and neurological assessment. Pure tune audiometry and tympanometry. It is obligatory to provide patient education and consent before performing the procedure. Use a binocular otology microscope and speculum to visualize the postero- inferior quadrant of the tympanic membrane, Wax and debris in the external auditory canal may need to be removed to ensure good visualization of the entire tympanic membrane. Position of patients: supine with their heads tilted at a 45° angle to the opposite ear. Injection of 1ml of Methylprednisolone (40mg/ml) in the middle ear cavity of the first group (A) (20 patients) using the syringe with a 25-gauge spinal needle passing through the Postero-inferior part of the tympanic membrane. Injection of 1ml of Dexamethasone (24mg/ml) in the middle ear cavity of the other group (B) (20 patients) using the syringe with a 25-gauge spinal needle passing through the Postero-inferior part of the tympanic membrane. Every patient in each group was injected five times in consecutive days.

The primary outcome assessed the pure tone audiometry (PTA) and tympanometry, it was done 3 days, 5 days and 6 weeks post operatively. If there is no improvement or slight or partial recovery after the injection 5 times; systemic steroids were started immediately unless contraindicated. Evaluation of the efficacy of treatment according to the Modified Siegel's criteria.

Data collection and analysis:

IBM-SPSS version 27 was used to do the coding, data entry, and analysis of the data gathered in a master sheet. Pearson's Chi-square test for independence of attributes/exact Fisher's test was used to compare groups based on categorical variables represented as numbers of patients or percentages of patients. The independent T test was used to compare the means of continuous variables between the different groups while Mann Whitney U test was used to compare between non parametric scale variables. Wilcoxon signed rank test was used to follow up nonparametric scale variables within the same group. A significant level of less than 0.05 was used.

Ethical considerations:

A detailed informed consent was signed by the eligible patients before recruitment in the study and confidentiality of all data was assured. The researcher introduced himself to all participants included in the study and demonstrated all steps of the procedures and the possible benefits and risks of the study. The Beni-Suef University school of medicine's research ethics committee gave its approval to the study plan No. FMBSUREC/09012022/Ahmed. All patients gave an informed consent, and the study was done according to Helsinki declarations.

3. Results:

This randomized controlled trial was conducted on 40 cases to compare the therapeutic efficacy of different Intratympanic Injection of steroids including Methylprednisolone (40mg/ml) and dexamethasone (24mg/ml) in the treatment of ISSHL. There were 8 cases with bilateral ISSHL so, the total number of ears were 48 ears distributed as follows: Methylprednisolone 23 ears (47.9%), Dexamethasone 25 ears (52.1%). There was no statistically significant difference between Methylprednisolone and Dexamethasone groups regarding the age, sex, laterality of affection (P-value>0.05) (P-value>0.05) (both groups were matched) as showed in Table 1.

Table (1): Age, sex distribution, and laterality of the affected sides of the studied patients.

Items	Methylprednisolone (no of ears=20)	Dexamethasone (no of ears=20)	P-value
Age (mean±SD)	33.1±11.6	33.6±12.3	0.906
Sex **Male** **Female**	 9(45.0%) 11(55.0%)	 13(65.0%) 7(35.0%)	0.204
Affected side **Right** **Left**	 10(43.5%) 13(56.5%)	 13(52.0%) 12(48.0%)	0.555
Laterality **Unilateral** **Bilateral**	(no=20) 17(85.0%) 3(15.0%)	(no=20) 15(75.0%) 5(25.0%)	0.695

This table shows that there was no statistically significant difference between Methylprednisolone and Dexamethasone groups regarding pretreatment grade of ISSHL (P-value>0.05) (both groups were matched) (Table 2).

Table (2): Pretreatment grade of affection of ISSHL and baseline speech discrimination in the studied patients.

Items	Methylprednisolone (no of ears=23)	Dexamethasone (no of ears=25)	P-value
Grade pre ttt			0.466
Grade II	10(43.5%)	11(44.0%)	(ET)
Grade III	10(43.5%)	7(28.0%)	
Grade IV	3(13.0%)	5(20.0%)	
Grade V	0(0.0%)	2(8.0%)	

Outcomes of the study

There was statistically insignificant higher complete and partial recovery in Methylprednisolone than Dexamethasone groups (P-value>0.05) Table 3.

Table (3): Recovery of ISSHL in the studied patients after complete injection.

Items	Methylprednisolone (no of ears=23)	Dexamethasone (no of ears=25)	P-value
Recovery			
No	14(60.9%)	15(60.0%)	0.388
Slight	0(0.0%)	3(12.0%)	
Partial	4(17.4%)	4(16.0%)	
Complete	5(21.7%)	3(12.0%)	

There was statistically insignificant difference between Methylprednisolone and Dexamethasone groups regarding the speech discrimination before injection (P-value>0.05). There was insignificant improvement in speech discrimination in both groups however the percentage of increase was higher in Methylprednisolone than Dexamethasone group (P-value>0.05) (Table 4).

Table (4): Following up speech discrimination in the studied patients.

speech discrimination (%)	**Methylprednisolone (no of ears=23)**	**Dexamethasone (no of ears=25)**	**P-value**
Pretreatment **Median (IQR)** **Mean±SD**	 72% (60%,79%) 68.1%±16.8%	 72% (62%,80%) 64.9%±29.6%	0.618 (MW)
Postreatment **Median (IQR)** **Mean±SD**	 80% (66.5%, 88%) 74.3%±19.3%	 80% (62%, 92%) 69.6%±31.6%	0.601 (MW)
P-value (pre vs post in each group)	0.226	0.374	--------
% of increase **Mean±SD** **Median(IQR)**	 9±12.5 0(0,19)	 7.6±12.1 0(0,13.3)	0.710 (MW)

Percent of increase=[(Post-Pre)/Pre] X 100, MW: Mann-Whitney, IQR: interquartile range

Subgroup analysis of bilateral cases in each group

There was insignificant difference between right and left ears in bilateral cases regarding the speech discrimination before and after complete injection and their percentage of change (P-value>0.05) (Table 5).

Table (5): Comparison between right and left ears regarding the speech discrimination before and after and their percentage of change.

Drug			**N**	**Mean**	**Std.Deviation**	**P-value**
Methylprednisolone	**Speech discrimination before**	**Rt**	**3**	70.6667%	18.03700%	0.478
		Lt	**3**	61.3333%	10.06645%	
	Speech discrimination after	**Rt**	**3**	76.0000%	22.27106%	0.754
		Lt	**3**	70.6667%	16.16581%	
	Percentage of change	**Rt**	**3**	6.7340	5.91865	0.480
		Lt	**3**	14.8148	16.97250	
Dexamethasone	**Speech discrimination before**	**Rt**	**5**	59.6000%	35.05424%	>0.999
		Lt	5	59.6000%	35.05424%	
	Speech discrimination after	**Rt**	5	61.2000%	35.93327%	>0.999
		Lt	5	61.2000%	35.93327%	
	Percentage of change	**Rt**	4	2.7778	5.55556	>0.999
		Lt	4	2.7778	5.55556	

None of the patients included in the study developed any of the possible complications of intratympanic injection.

4. Discussion:

Hearing loss of at least 30 dB at least three consecutive frequencies within 72 hours is considered idiopathic sudden sensorineural hearing loss (ISSHL). The impact of ISSHL on patients' daily lives is substantial [9].

Idiopathic sudden sensorineural hearing loss (ISSHLpathophysiology)'s has been linked to autoimmune conditions, viral infections, and microcirculation issues, among other things. However, it is yet unknown what causes ISSHL. As a result, there is still debate regarding the best treatment option for ISSHL. Combination therapy, which combines topical systemic steroids and vasodilator medications, has been employed as the main treatment among several all-encompassing strategies. However, despite

intensive systemic steroid therapy, the spontaneous recovery rate only reaches between 30% and 60% [10].

To yet, it is unclear how corticosteroids affect the inner ear. However, corticosteroids' established methods of action include decreasing inner ear inflammation, guarding against ischemia, boosting cochlear blood flow, and controlling protein synthesis and endocochlear potentials. Corticosteroids also lessen the amount of the deteriorated area of the stria vascularis without affecting the function of the outer hair cells [11].

The most popular corticosteroids for this mode of administration are dexamethasone and methylprednisolone since they can both effectively pass the round window to the perilymph following intratympanic injection at low plasmatic concentration levels. Since methylprednisolone has a higher concentration and longer half-life in the perilymph and endolymph than dexamethasone and hydrocortisone, it was the corticosteroid of choice for intratympanic injection [12].

Our study found that there was statistically insignificant higher complete and partial recovery in Methylprednisolone than Dexamethasone groups. In methylprednisolone group (17.4%) showed partial recovery compared to (16%) in dexamethasone group. Also, (21.7%) in methylprednisolone group showed complete recovery compared to (12%) in dexamethasone group. As regards the speech discrimination, according to the grade of ISSHL, the majority of patients in both groups were grade II and III with a mean speech discrimination 68.1%±16.8% for methylprednisolone group and 64.9%±29.6% for dexamethasone group. There was no statistically significant difference between both groups regarding pretreatment grade of ISSHL. The mean speech discrimination after injection was 74.3%±19.3% in methylprednisolone group and 69.6%±31.6% in dexamethasone group. There was statistically insignificant difference between Methylprednisolone and Dexamethasone groups regarding the speech discrimination after injection. There was insignificant improvement in speech discrimination in both groups however the absolute mean difference was higher in Methylprednisolone than Dexamethasone group. Also, there was statistically insignificant difference between Methylprednisolone than Dexamethasone groups regarding the percentage of increase of the speech discrimination after injection however it was higher in Methylprednisolone.

Matching with our study was a study by Yang et al. (2010), 47 participants were treated for acute sensorineural hearing loss and the effects of intratympanic dexamethasone or methylprednisolone were examined. Patients got methylprednisolone or dexamethasone treatment lasting at least 7 days. They demonstrated that intratympanic dexamethasone or methylprednisolone may be helpful in the treatment of individuals with acute sensorineural hearing loss, although there was no discernible difference in the benefit of the two drugs [13].

Similarly, Tarkan et al., (2018) who compared intratympanic methylprednisolone (20mg/ml) and dexamethasone (4mg/ml) for the management of idiopathic sudden sensorineural hearing loss in 46 patients ,one dosage per day for 5 consecutive days, evaluations were performed pretreatment, daily in inpatient clinics, and in the first week and second month after discharge, and revealed that the therapeutic success rate was 62.5% (complete improvement 16.7% and marked improvement 45.8%) in the methylprednisolone group, whereas it was 54.6% (complete improvement 27.3% and marked improvement 27.3%) in the dexamethasone group. The methylprednisolone group had a greater rate of therapeutic effectiveness; however, it was not statistically significant. The methylprednisolone group showed more progress in speech discrimination; however, the difference was not statistically significant. However, they claimed that their patients had greater recovery rates [14].

Choi et al., (2020) evaluated the response of injection of intratympanic dexamethasone in profound idiopathic sudden sensorineural hearing loss. They retrospectively reviewed 115 patients with profound ISSNHL, combination or systemic steroid therapy was used as the first line of treatment for all patients. On patients who exhibited little to no progress in accordance with Siegel's criteria, we then applied salvage ITDI treatment. It only showed a partial recovery in 12.6% of instances and a full recovery in 7.8% of cases. In 43.7% of instances, there was a marginal improvement [15].

As a treatment for idiopathic sudden sensorineural hearing loss, Sang et al. (2019) assessed and compared the efficacy of intratympanic high doses of dexamethasone (24 mg/mL) and methylprednisolone (125 mg/mL). The dexamethasone group included 20 patients (7 receiving primary ITD), and the methylprednisolone group included 10 patients (1 receiving primary ITM). The remaining patients received IT steroids as a salvage therapy after three weeks of oral

prednisolone therapy. Over the course of four treatment sessions, each group got 1 mL of the appropriate steroid via ventilation tubes once a week. Clinical response was assessed by pure tone audiometry every week for the first month, at six months, and at twelve months (PTA). Within 10 dB of the unaffected ear, 20% of the hearing loss (HL) in the ITM group in the affected ear fully recovered. In 50% of the instances, there was a partial recovery, but in 30% of the cases, there was no meaningful improvement. Only one participant in the ITD group had symptoms of partial recovery [16].

50 patients with refractory sudden sensorineural hearing loss were studied by Berjis et al., 2016; they were randomly assigned to receive either intratympanic dexamethasone (4 mg/mL) injection or methylprednisolone (40mg/mg) injection once every 2 days for three times; auditory measurements were taken before and 1 month after treatment; and the researchers found that the methylprednisolone group had a significantly higher overall hearing improvement. According to Siegel's criterion for hearing improvement, the methylprednisolone group had a 24% full recovery rate, whereas the dexamethasone group had a 14% recovery rate [17].

The study of Gupta et al., (2022) about intratympanic steroid therapy for treatment of ISSHL using an aqueous solution of dexamethasone and methylprednisolone, this study consists of 110 patients with refractory ISSHL and also found that 60 patients (54.5%) showed improvement, 46(41.8%) had no change in hearing, and 4(3.6%) worsened [18]. The study of Alil et al., (2020) compared oral steroids (prednisolone) 1mg/kg body weight for first seven days, it was reduced by half strength weekly and continued for four weeks to intratympanic steroids (Dexamethasone), a total 60 patients of ISSHL was selected for the study. PTA was repeated every two weeks over duration of two months for documentation of improvement of hearing and found that recovery was more with middle ear injection group in 18 patients (60%) in comparison to oral steroids in 14 patients (46.66%) [19].

Eski et al., (2020) compared the efficiencies of hyperbaric oxygen therapy and intratympanic steroid treatment using dexamethasone (8 mg/2 mL). A total of 136 patients who were treated for ISSHL were reviewed from the medical records. All of the patients were given systemic steroid therapy. Among them, 33 patients received hyperbaric oxygen therapy (100% O_2 and 2.5atm) for 20 minutes (total of 10 sessions) and 36 patients

received 0.3–0.5 mL of dexamethasone (8 mg/2mL) once a day for 1 week treatment following systemic steroid therapy. Hearing measurements at the end of the first month after treatment. The time to recovery was higher in the ITS treatment cohort (40%) than in the hyperbaric oxygen therapy cohort (17%). The starting time for dexamethasone treatment was 4 days (range: 1–30) and that for hyperbaric oxygen therapy was 8 days (range: 3–30) [20].

Keseroğlu et al., (2020) evaluated the addition of intratympanic steroids to systemic steroids using dexamethasone and methylprednisolone and found that the overall success rate was (58%) and only (7.5%) showed complete recovery and marked improvement [21].

For the intratympanic steroids group, full recovery was attained in 56 of 235 patients, according to Mirian & Ovesen's systematic review and meta-analysis of the intratympanic versus systemic corticosteroids in first-line therapy of idiopathic acute sensorineural hearing loss (24 percent). Numerous factors, including the medication dose, duration, interval, method of administration, and individuals with primary and/or refractory ISSHL, might be used to explain the disparate findings from these trials. It is challenging to design standardized treatment regimens due to the abundance of variables. The majority of the patients who were treated with methylprednisolone were females, with a mean age of 33.1±11.6. (55 percent). Similarly, dexamethasone patients were mostly male and had a mean age of 33.6±12.3 years (65 percent). The majority of instances (85%) in the methylprednisolone group affected the left ear in 56.5 percent of cases, while (75%) in the dexamethasone group affected the right ear in cases (52 percent) [22].

Tarkan et al., (2018) compared intratympanic methylprednisolone and dexamethasone for the treatment of idiopathic sudden sensorineural hearing loss and reported that the two study groups were classified as the IT methylprednisolone group (n=24, mean age: 50.0±12.4 year) and the IT dexamethasone group (n=22, mean age: 47.3±14.6 years). The majority of cases were males in both groups with no significant differences between them as regards to age and sex. Also, the majority of cases showed unilateral affection affecting mainly the right ear with no significant differences between both groups [14].

The study of Amarillo et al., (2019) about the efficacy of intratympanic corticosteroid as a treatment in idiopathic sudden sensorineural

hearing loss reported a mean age of 48.95±1.67 and most of them were females (57.9%) [12]. Chew & MK, (2020) revealed in their study about the efficacy of steroids in management of ISSHL that (90%) of patients presented with unilateral ISSHL involvement [23].

Also, Xiong et al., (2022) reported near results to our study and found that the mean age of the 188 enrolled patients was 50.15 ± 13.46 years (range: 18–80 years). There were 107 women and 81 men with equal numbers of left and right affected ears in 94 cases only [24].

5. Conclusion:

Idiopathic Sudden Sensorineural Hearing Loss remains a challenging clinical problem and emergency case with low recovery rate. However, the use of intratympanic steroid injection is relatively an effective, safe and well-tolerated procedure for the treatment of ISSHL. Outcomes regarding hearing loss advocate the use of intratympanic injection of Methylprednisolone rather than dexamethasone.

Recommendations:

For individuals who report with idiopathic acute sensorineural hearing loss, methylprednisolone and dexamethasone are advised as the first line of therapy, with a small benefit to using methylprednisolone rather than dexamethasone. To verify the findings of our study, more research with a bigger sample size should be conducted. It is advised that future research assess the usefulness of systemic and intratympanic steroids administered together. Further research may examine the relationship between the severity of hearing loss and treatment response as well as comparisons between various dosages to determine the ideal dose.

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