

Intratympanic dexamethasone injection vs methylprednisolone for the treatment of refractory sudden sensorineural hearing loss

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Abstract

Background: During the past years various drugs have been used for sudden sensorineural hearing loss (SSNHL) treatment including steroids that are shown to be beneficial. Directed delivery of high doses of steroids into the inner ear is suggested for its potential and known as intratympanic steroids therapy (IST). Despite the use of dexamethasone and methylprednisolone as the traditional treatments, there are still debates about the optimal dosage, preferred drug, and the route of administration.

Materials and Methods: We performed a randomized clinical trial study in which 50 patients suffering from SSNHL and resistant to standard therapy were employed. Each patient took 0.5 ml methylprednisolone (40 mg/mg) along with bicarbonate or dexamethasone (4 mg/mL) through direct intratympanic injection. This method was performed and scheduled once every 2 days for three times only for the dexamethasone receiving group. Hearing test was carried out and the results were analyzed according to a four-frequency (0.5, 1.0, 2.0, 3.0 kHz) pure tone average (PTA) and Siegel's criteria.

Results: According to Siegel's criteria, three out of 25 (12%) dexamethasone receiving patients were healed in 1 and 4 (16%), 9 (32%) were respectively recovered in Siegel's criteria 2, 3, and 9 (32%) showed no recovery. In the group receiving methylprednisolone, recovery was found in 6 (24%), 8 (32%), 7 (28%) patients in the Siegel's criteria 1, 2, 3, respectively, and in 4 (16%) patients no recovery was recorded. In methylprednisolone group, hearing was significantly improved compared to the dexamethasone group ($P < 0.05$). The general hearing improvement rate was 84% in methylprednisolone receiving patients showing a significantly higher improvement than 64% in the dexamethasone group.

Conclusions: Topical intratympanic treatment with methylprednisolone is safe and an effective treatment approach for those SSNHL cases that are refractory to the common therapies by Dexamethasone.

Key Words: Dexamethasone, intratympanic injection, methylprednisolone, steroid therapy, sudden sensorineural hearing loss

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INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is a common emergency in Otolaryngology, known as an acute unilateral deafness, with a sharp onset (usually during 3 days), with more than 30 dB hearing loss at three subsequent frequencies.^[1,2] To observe the

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etiology of different diseases, various cases including autoimmune inflammation, viral cochleitis, and inner ear membrane rupture have been studied.^[3] The most convincing causes are viral and vascular etiologies. The natural background of SSNHL is still unknown; spontaneous recovery happens in almost 30% of cases and it will recover mostly during the first 2 weeks after its onset, and it contains partial response.

Many factors seem to influence recovery; the degree of hearing loss, the audiogram pattern, the existence of vertigo, and the duration between the onset and treatment of SSNHL are probably the most important factors.

Different therapies have been tried for SSNHL, none of which was effective. Hyperbaric oxygen, vasodilator drugs, agents that decrease blood viscosity and magnesium, are some examples of previously tested SSNHL treatments. Some studies present that steroids might be effective,^[1] while more results are needed. Systemic steroids with prompt administration increase the rate of hearing recovery.^[4] Needless to say that steroids in high doses can be followed by systemic effects; hence, it so cannot be used for all patients. Several mechanisms of action are recognized for corticosteroids including anti-inflammatory action, immune suppression, membrane stabilization, increased perfusion, and ion balance regulation.^[11] It has been shown that steroids can also be effective if no immune disorder is demonstrated.^[12]

The transtympanic route presents two main advantages: (1) it produces significantly higher perilymph concentrations of steroids than intravenous or oral administration; (2) it is possible to reduce the side effects due to systemic absorption. Effectiveness of local application of steroids in SSNHL, Ménière's disease, and in other inner ear conditions has been reported by many authors.^[2,5-10] Although dexamethasone and methylprednisolone were used traditionally but optimal dosage, drug, and route of administration still remain a matter of debate. Based on these considerations, we started treating SSNHL patients with transtympanic Dexamethasone versus methylprednisolone in order to better understand the real effectiveness of this treatment.

MATERIALS AND METHODS

In the randomized, clinical trial study, we enrolled 50 consecutive patients admitted to Otolaryngology Head and Neck Surgery Department of Isfahan Medical University in two hospital Kashani and

Al-Zahra between February 2012 and January 2013, all diagnosed with SSNHL and nonresponsive to standard therapy. Inclusion and exclusion criteria were: (1) 30 dB loss in three consecutive frequencies in <72 h, (2) normal otoscopic examination, (3) no history of chronic otitis media, (4) no history of trauma (head, acoustic, or barometric), (5) no history of Meniere's disease, hydrops, or fluctuating hearing loss, (6) no history of meningitis, (7) no history of prior ear surgery, (8) no history of radiation, (9) no exposure to ototoxic medications, (10) no response to conventional therapies included the systemic steroids therapy, neural nutrients administration, vascular dilator, anticoagulator, or hyperbaric oxygen therapy, and (11) no take any conventional therapies in two previous weeks.

Auditory function was determined by pure-tone audiometry; the mean hearing levels were expressed as the average of hearing thresholds at 0.5, 1, 2, and 3 kHz (4-tone average) (PTA), according to the guidelines of the Committee on Hearing and Equilibrium of the American Academy of Otolaryngology — Head and Neck Surgery. Auditory measurements were performed before and 1 month after the treatment, according to Siegel's criteria for hearing improvement.^[14] 'Complete recovery' was defined as more than 30 dB hearing gain and as final hearing better than 25 dB, 'partial recovery' as more than 15 dB hearing gain and as final hearing between 25 and 45 dB, 'slight improvement' as more than 15 dB hearing gain but with a final hearing poorer than 45 dB, and 'no improvement' as less than 15 dB hearing gain and final hearing poorer than 75 dB. The operative procedure of intratympanic steroid injection was performed under a microscope and with patient in supine position. After the surgeon confirmed the intact tympanic membrane and middle ear status, topical anesthesia was administered with a cotton ball soaked with lidocaine 10% pump spray (Xylocaine), which was applied on the tympanic membrane for 20 min. While the patient tilted the head 45° to the healthy side, a 25-gauge spinal needle was introduced into the posteroinferior portion of membrane and 0.5 ml of methylprednisolone (40 mg/ml) with bicarbonate or dexamethasone (4 mg/ml) was instilled through this site in each group, respectively. This procedure was carried out three times, once every 3 days, only for the dexamethasone group. The patient was instructed to avoid swallowing or moving for 30 min, remaining in the same position.

Statistical tests were performed using Mann-Whitney U test for categorical variables and Student's t-test for continuous variables (SPSS ver. 14.0, SPSS Inc., Chicago, IL, USA).

RESULTS

The demographics and audiological data of the patients are summarized in Table 1. There were 29 men (58%) and 21 women (42%). The mean age at enrolment for all patients was 45.88 +/- 14.97 years and ranged from 16 to 70 years. The mean age for the men was 47.24 +/- 15.6 years and for the women was 44 +/- 14.21 years. Age, sex, degree of initial hearing loss, and the time delay between onset of hearing loss and treatment were not statistically significant different between the dexamethasone and methylprednisolone group [Table 1].

Final hearing improvement on the basis of Siegel's criteria is shown in Figure 1. For statistical analysis, improvement was defined as hearing results categorized as I, II, and III of Siegel's criteria and no improvement was defined as hearing results categorized as IV of Siegel's criteria.

Three of twenty-five patients (12%) in dexamethasone group were recovered in Siegel's criteria I and 4 (16%),

9 (32%) were, respectively, recovered in Siegel's criteria II and III and 9 (32%) were not recovered. In the methylprednisolone group, 6 (24%), 8 (32%), 7 (28%) patients were recovered in the Siegel's criteria I, II, III, respectively, and 4 (16%) patients were not recovered. Statistical analysis shows a significant difference between dexamethasone and methylprednisolone groups based on Siegel's criteria ($P < 0.05$). The overall hearing improvement rate was 64% in the dexamethasone group, which was significantly higher than 84% in the methylprednisolone group. No unexpected adverse events and worsening in hearing occurred during the injection or follow-up period.

CONCLUSIONS

Clinically SSNHL, a common otologic emergency, has possibility of high spontaneous recovery, but all reports describing treatments indicate that early initiation of treatment will undoubtedly lead to improved prognoses. Because the etiology of SSNHL is not fully understood, there is no universal treatment modality.

Because of spontaneous recovery in SSNHL, it is difficult to determine if any therapeutic intervention actually improves the hearing. The natural history of untreated patients with SSNHL states that the recovery rates varies from 31% to 65%,^[13,14,16,17] while the hearing recovery in treated patients ranges from 35% to 89%.^[15,16] These results may be related to different factors: the patient data, the type of steroid administration, the length of therapy, the severity of hearing loss, the duration from onset of symptoms to start of treatment, the variable treatment protocols, and the method of statistical analysis. At this time, steroids systematic administration is considered to be the most commonly accepted treatment for SSNHL.

The precise mechanism through which steroids may improve hearing remains unknown; both glucocorticoid and mineralocorticoid receptors may be found in the inner ear.^[18,19] The main roles of steroids in the treatment of SSNHL are: (1) the protection of cochlea from the harmful effects of inflammatory mediators, such as the tumor necrosis factor (TNF- α and NF- κ B) and cytokines (interleukin 1 and 6), which is elevated in infection and inflammation;^[20-22] (2) increasing cochlear blood flow^[20] thereby avoiding cochlear ischemia;^[23] (3) avoiding noise-induced hearing loss;^[24] (4) regulating protein synthesis in the inner ear.^[25] There the vascular stria regulates Na/K secretion in order to maintain endocochlear potential; it is the most frequent site of injury in the SSNHL.^[26] Systemic steroid therapy improves vascular stria function and may preserve its morphology and therefore it has potential for recovering from SSNHL.^[27]

Table 1: General characteristics of patients

	Dexamethasone Group	Methylprednisolone Group	P Value
Age	42.48 +/- 16.4	49.28 +/- 12.82	0.109
Male: Female	13: 12	16: 9	0.284
Right: Left	11: 14	9: 16	0.387
Duration (days)*	17.16 +/- 12.64	20.24 +/- 13.30	0.406
Initial PTA (dB HL) †	65.07 +/- 25.44	54.53 +/- 21.99	0.124

*days between onset and start of treatment, initial pure tone average (PTA) at 500, 1000, 2000, and 3000 Hz hearing thresholds

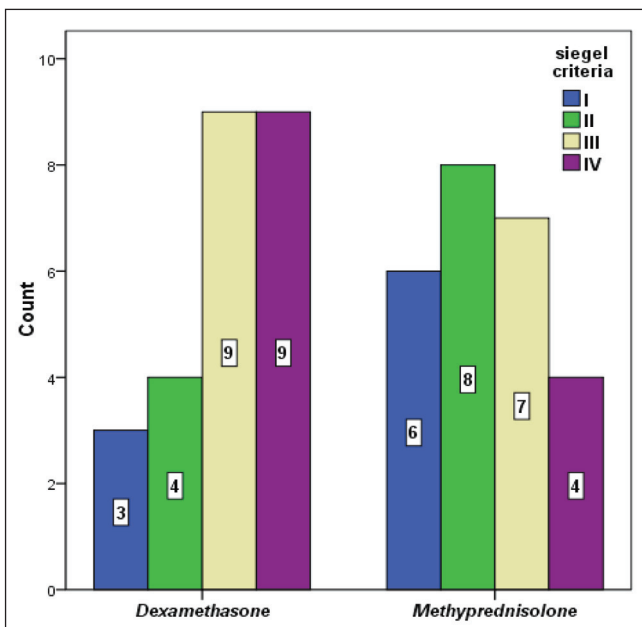


Figure 1: Hearing improvement based on Siegel's criteria in Dexamethasone and Methylprednisolone groups

For the first time, Silverstein showed intratympanic steroids therapy (IST) was effective in the treatment of SSNHL^[28] that followed by several other reports.^[29-38] It was demonstrated that intratympanic infusion of steroids leads to a much higher perilymphatic concentration, as compared to the systemic route.

Usually, intratympanic steroids are used in three main aims: (1) initial treatment, (2) adjuvant therapy given concomitantly with systemic steroids, and (3) salvage treatment after failure of standard therapy. However, according to several clinical trials,^[31-34] IST, as first-line therapy, seems to be a valuable solution in refractory SSNHL, at least as effective as systemic steroids and can be a reasonable alternative for patients who are in the failure of intravenous treatment or cannot tolerate systemic therapy.^[38-39]

The overall hearing improvement was observed in 21 of 25 methylprednisolone received patients (84%), which was significantly higher than 64% of 25 patients in dexamethasone group ($P < 0.05$). Dallan *et al.* reviewed the medical records of patients diagnosed with SSNHL and nonresponsive to standard therapy. These patients were treated with intratympanic methylprednisolone. They showed that 15 (55%) of 27 patients presented a useful improvement in the hearing status.^[43] In the other study, Yang *et al.* investigate the effect of intratympanic dexamethasone or methylprednisolone on treatment of sudden sensorineural hearing loss in 47 subjects. patients received an at least 7-day dexamethasone (5 g/l/d) or methylprednisolone (40 g/l/d) course. They showed Intratympanic dexamethasone or methylprednisolone can be beneficial in treatment on patient with sudden sensorineural hearing loss, however, there was no significant difference in the effect between dexamethasone and methylprednisolone.^[40-44]

In our study based on Siegel's criteria complete recovery in the methylprednisolone group was significantly better than the dexamethasone group (24% vs 12% respectively). It means that according to our results, intratympanic methylprednisolone therapy shows better hearing recovery for sudden sensorineural hearing loss patients without early response to systemic treatment rather than dexamethasone. Both topical intratympanic application of dexamethasone and methylprednisolone are safe and effective methods for the treatment of SSNHL cases that are refractory to conventional therapies.

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