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Intratympanic vs. Oral Steroids for Treatment of Idiopathic Sudden Sensorineural Hearing Loss: A Randomized Controlled Study

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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Original Research Article

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ABSTRACT

Objective: To compare the efficacy of oral to intratympanicsteroids for treatment of idiopathic sudden sensorineural hearing loss (ISSHL).
Patients and Methods: A total of 39 ISSHL patients were included in this study. They were consecutively randomized into the "control" group, who received oral prednisone (started with 60 mg/day tapering over 14 days) or the "study" group, who received intratympanic methylprednisolone sodium succinate (four 1- mL doses of 40 mg/mL of methylprednisolone over 2 weeks, with a dose given every 3-4 days by injection through the tympanic membrane into the middle ear). Pure tone audiometry (PTA) was measured for all patients before injection as baseline. Patients were asked to come to the outpatient clinic after two weeks, one month and at the end of the second month to assess hearing, vital signs, otological examination and adverse events.
Results: At the last follow up visit, patients in the study group had significantly lower PTA than those in the control group (39.2±6.0 dB and 43.8±6.4 dB, respectively, p=0.027). Improvement in hearing was significantly higher among patients in the study group than those in the control group (32.1±6.9 dB and 27.5±6.5 dB respectively, p=0.041). Significantly higher proportions of patients in the control group had mood change (p=0.035), sleep change (p=0.044) and mouth dryness

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(p=0.020) than patients in the study group. On the other hand, a significantly higher proportion of patients in the study group had earache (p=0.030). Patients in both groups did not differ significantly as regard blood glucose problems, increased appetite, pain due to injection or weight gain. Patients' age correlated negatively with improvement in pure tone average (r= -0.267). However, this correlation was not statistically significant.

Conclusions: Treatment with intratympanic steroid injection is better than oral steroid treatment of patients with ISSHR. Adverse effects associated with intratympanic injections are less than those associated with systemic steroid therapy.

Keywords: Idiopathic sudden hearing loss; steroid therapy; pure tone audiometry; adverse events.

1. INTRODUCTION

Sudden hearing loss is defined as hearing reduction greater than 30 dB, over at least 3 contiguous frequencies, occurring over a period of 72 hours or less [1]. Idiopathic sudden sensorineural hearing loss (ISSHL) is an unexplained unilateral sensorineural hearing loss. It is not uncommon, with an estimated incidence rate of about 20 per 100, 000 persons per year [2]. http://jama.jamanetwork.com/article.aspx?articleid=900108 - ref-joc15047-1. It is typically seen among adults between 43 and 53 years of age, with equal sex distribution. Transient vestibular symptoms may be present in about half of patients [3-4].

The standard treatment for ISSHL is a tapering course of oral corticosteroids [5]. Several researchers demonstrated a statistically significant benefit of systemic corticosteroids for hearing recovery in patients with sudden sensorineural hearing loss [6-8]. Intratympanic corticosteroid treatment by direct injection into the middle ear has gained wide popularity, based on experimental studies in the guinea pig model that revealed significantly increased concentrations of corticosteroids at the target organ when administered intratympanically compared with systemic administration [9-10].

Intratympanic corticosteroid therapy for cases of ISSHL has the potential benefit over oral corticosteroid treatment of reduced systemic steroid exposure with its associated systemic adverse effects. Therefore, we performed a randomized controlled trial aiming to compare the efficacy of oral prednisone to intratympanic methylprednisolone for primary treatment of ISSHL.

2. PATIENTS AND METHODS

This study was conducted at the ORL-HNS Department at Muhayel Hospital. It is the highest tertiary care referral hospital in Muhayel City, Kingdom of Saudi Arabia. Eligibility criteria included adult patients, (aged above 18 years) and a unilateral sensorineural hearing loss that developed within 72 hours and was present for two weeks or less. Patients' pure tone average (PTA) must have been 50 dB or higher, and the affected ear must have been at least 30 dB worse than the contralateral ear in at least 1 of the 4 PTA frequencies (i.e., 500, 1000, 2000, and 4000 Hz).

Since the condition of interest in this study (i.e., sudden sensorineural hearing loss) is "idiopathic", all patients underwent thorough evaluation, including medical and otologic history and extensive systems review, head and neck and otologic and neurologic physical examination, audiometry, and imaging to rule-out structural or retrocochlear pathology.

Exclusion criteria included patients who indicated that their hearing has been asymmetric prior to the onset of ISSHL. Also excluded all patients who had pre-enrollment steroid usage, previous history of hearing loss, Meniere disease, or any chronic inflammatory or suppurative ear disease or cholesteatoma, otosclerosis, ear surgery (except ventilating tubes), hearing asymmetry prior to onset, congenital hearing loss, physical trauma or barotrauma to the ear immediately preceding hearing loss, history of genetic hearing loss with strong family history, or craniofacial or temporal bone malformations as revealed by computed tomographic scanning.

Pure tone audiometry (PTA) was calculated according to the American Speech-Language-Hearing Association [11], as the arithmetic mean of the hearing thresholds at 4 studied PTA frequencies in the affected ear. Recruitment of cases took place for four years, during the period from January 2011 till December 2014. Participant patients were first seen and diagnosed by the researcher at the Otolaryngology Outpatient Clinic.

After screening for eligibility, a total of 39 ISSHL patients could be recruited within the study period. They were consecutively randomized into the "control" group, who received oral prednisone (60 mg/d tapering over 14 days) or the "study" group, who received intratympanic methylprednisolone sodium succinate (four 1-mL doses of 40 mg/mL of methylprednisolone over 2 weeks, with a dose given every 3-4 days by injection through the tympanic membrane into the middle ear). The researcher was not blinded to the treatment group but the audiologists were blinded to it.

Intratympanic injections were given by the researcher using an operating microscope. Anesthesia was obtained with topical phenol. Patients were positioned supine with the affected ear slightly up and remained in this position for 30 minutes after the injection. They were instructed to keep water out of the treated ear for the duration of treatment.

Patients in the study group were asked to come to the clinic at times of their intratympanic steroid injections, while all patients were asked to come to the outpatient clinic after two weeks, one month and then at the end of the second month to assess hearing level by PTA, vital signs, otological examination, and to check if any adverse events.

The primary end point of this study was the change in hearing threshold, calculated as the difference between the PTA at baseline and the last follow-up visit (2 months after recruitment). Secondary outcome measures included adverse events at the last follow up visit.

3. RESULTS

Table 1 shows that males constituted 47.4% of the study group and 45% of the control group. The mean age of participants in the study group was comparable to that of the control group (49.8±5.9 years vs. 49.7±7.3 years, respectively). The main associated symptoms among patients in the study and control groups were tinnitus (42.1% and 45%, respectively), dizziness (21.1% and 25%, respectively) and vertigo (21.1% and 20%, respectively). All differences in patients' characteristics according to their group were not statistically significant.

Table 2 shows that patients' pure tone average (PTA) at baseline did not differ significantly according to their group. However at the two months follow up visit, patients in the study group had significantly lower PTA than those in the control group (39.2±6.0 dB and 43.8±6.4 dB, respectively, p=0.027). Moreover, improvement in hearing was significantly higher among patients in the study group than those in the control group (32.1±6.9 dB and 27.5±6.5 dB respectively, p=0.041).

Table 1. Personal characteristics of patients in both study groups

Characteristics	Study group (n=19)	Control group (n=20)	p-value
Gender			
• Male	9 (47.4%)	9 (45.0%)	
• Female	10(52.6%)	11(55.0%)	0.882
Age (Mean+SD)	49.8±5.9	49.7±7.3	0.994
Associated symptoms			
• Tinnitus	8 (42.1%)	9 (45.0%)	0.855
• Dizziness	4 (21.1%)	5 (25.0%)	0.770
• Vertigo	4 (21.1%)	4 (20.0%)	0.935

Table 2. Pure tone average (dB) at baseline and follow up

Pure tone average	Study group (n=19)	Control group (n=20)	p-value
At baseline	71.3±5.9	71.3±6.9	0.986
At two months	39.2±6.0	43.8±6.4	0.027
Improvement	32.1±6.9	27.5±6.5	0.041

Fig.1. shows that patients' age correlated negatively with improvement in pure tone average (r= -0.267), i.e., as patients get older, the improvement in hearing after treatment becomes less. However, this correlation was not statistically significant.

Table (3) shows that significantly higher proportions of patients in the control group had mood change (p=0.035), sleep change (p=0.044) and mouth dryness (p=0.020) than patients in the study group. On the other hand, a significantly higher proportion of patients in the study group had earache (p=0.030). Patients in both groups did not differ significantly as regard blood glucose problems, increased appetite, pain due to injection or weight gain.

4. DISCUSSION

Steroids are the only proven drugs for the treatment of ISSHL [12]. Intratympanic steroids are increasingly used in the treatment of patients with sudden sensorineural hearing loss [13].

In the present study, the outcome of ISSHL patients who received intratympanic corticosteroids (n=19) was compared with those who received systemic corticosteroids by the oral route (n=20).

Table 3. Adverse events among ISSHL patients in both groups

Adverse events	Study group (n=19)	Control group (n=20)	p-value
Mood change	2 (10.5%)	8 (40.0%)	0.035
Blood glucose problem	3 (15.8%)	6 (30.0%)	0.292
Sleep change	1 (5.3%)	6 (30.0%)	0.044
Increased appetite	1 (5.3%)	5 (25.0%)	0.088
Earache	4 (21.1%)	0 (0.0%)	0.030
Pain due to injection	2 (10.5%)	0 (0.0%)	0.136
Mouth dryness/ thirst	0 (0.0%)	5 (25.0%)	0.020
Weight gain	0 (0.0%)	3 (15.0%)	0.079

Results of the present study showed almost equal proportions of male and female patients. The mean age of participants was approaching 50 years. The main associated symptoms were tinnitus, dizziness and vertigo.

These findings are in accordance with those of Byl [14], who noted that in ISSHL, males are equally affected as females. The average age at onset ranges from 46 to 49 years with increasing incidence with age. Mattox and Simmons [15] added that tinnitus is usually reported in patients with sudden hearing loss and vestibular symptoms are present in about 40% of cases.

Our study showed that, at the last follow up visit, improvement in hearing was significantly higher among patients in the study group (who received intratympanic steroids) than those in the control group (who received oral steroids).

Several studies have demonstrated better outcomes in cases of sudden hearing loss treated with intratympanic than those treated with systemic steroids. Rauch [16]) concluded that using the continuous intratympanic dexamethasone is effective, safe and efficient for treatment of ISSHL. Ahn et al. [17] reported that intratympanic corticosteroids salvaged hearing in 40% of patients when given to patients with sudden sensorineural hearing loss within 1-2 we Kara et al. [12] found that, on the second month after treatment, improvement in PTA among patients who received intratympanic steroids was better than that among patients who received oral steroids (37.55 dB and 20.68 dB, respectively).

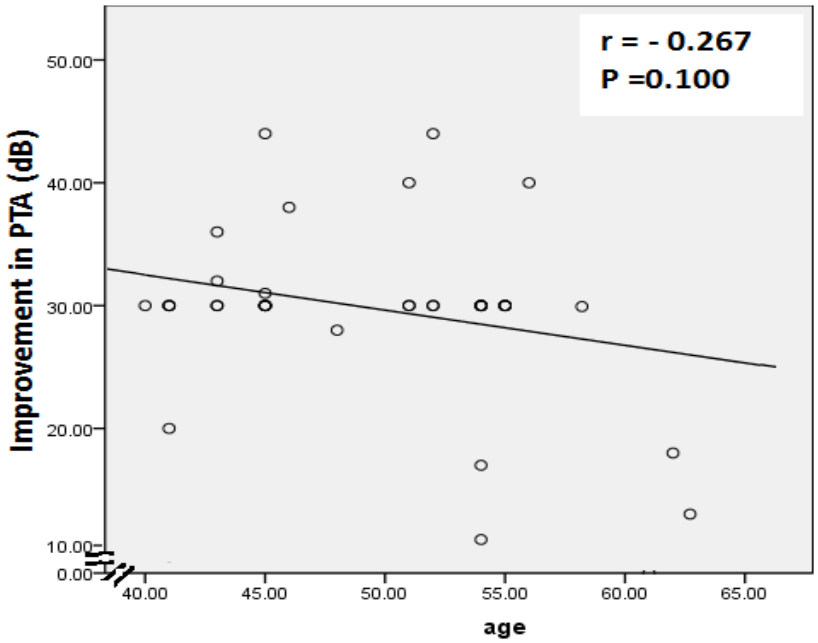

Fig. 1. Correlation coefficient (r) and linear regression between age and improvement in PTA among patients with idiopathic sudden sensorineural hearing loss

The superiority of results achieved by intratympanic steroids has been explained by that steroids delivered through the intratympanic route attain higher perilymph levels, resulting in better hearing outcomes [12]. Moreover, intratympanic corticosteroids increase cochlear blood flow, prevent aminoglycoside toxicity and improve ionic homeostasis, which are necessary for adequate cochlear function [18].

However, some studies reported that the outcome of treatment with intratympanic does not differ from that of systemic steroids [19]. A meta-analysis study concluded that there is no difference between systemic steroids and intratympanic corticosteroid treatment for management of sudden sensorineural hearing loss cases [20].

Differences in reported outcomes may be due to the inconsistency regarding the dose, number of intratympanic injections and the duration of treatment of steroids used across different studies [18].

In this study, a negative correlation has been noticed between patients' age and the achieved improvement in their hearing after two months. Nevertheless, this correlation was not statistically significant.

This finding is in agreement with that reported by Raymundo et al. [18], who reported no significant correlations between age and improvement after intratympanic corticosteroids therapy in patients with ISSHL.

In the present study, significantly higher proportions of ISSHL patients receiving oral steroids had mood changes, sleep changes and dryness of mouth than patients receiving intratympanic steroids, while a significantly higher proportion of patients receiving intratympanic steroids had earache.

These findings have been explained by Chandrasekhar [10], who noted that adverse events among patients receiving oral steroids include change in appetite, mood, or sleep pattern; weight gain; and increased thirst. However, local steroid administration to the ear does not produce significant circulating drug levels.

Ho et al. [21] added that intratympanic steroid therapy provides organ-specific treatment, with high doses applied over the round window membrane, thereby avoiding the possible adverse effects of systemic steroid therapy.

5. CONCLUSION

In conclusion, treatment with intratympanic steroid injection is better than oral prednisone of patients with ISSHR. Adverse effects associated with intratympanic injections are less than those associated with systemic steroid therapy.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The authorhereby declares that this study has been examined and approved by the appropriate ethics committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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