International Journal of Otorhinolaryngology and Head and Neck Surgery
Shetty S et al. Int J Otorhinolaryngol Head Neck Surg. 2019 Jul;5(4):1056-1060
http://www.ijorl.com
pISSN 2454-5929 | eISSN 2454-5937

DOI: http://dx.doi.org/10.18203/issn.2454-5929.ijohns20192729

Original Research Article

Efficacy of intratympanic injection of dexamethasone in the treatment of subjective idiopathic tinnitus

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Received: 26 March 2019
Revised: 02 June 2019
Accepted: 04 June 2019

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ABSTRACT

Background: To study the efficacy of intratympanic injection of dexamethasone in cases of subjective idiopathic tinnitus.
Methods: Prospective interventional study at the Department of ENT, JSS Medical College and Hospital, Mysore, in which 45 patients diagnosed clinically as subjective idiopathic tinnitus, for a duration of 2 years from October 2016 were included in the study. The patients were subjected to 3 intratympanic injections of dexamethasone once in a week for 3 weeks. They received a 0.5 ml intratympanic injection of 4mg/ml dexamethasone solution. After topical anaesthesia, using a 2 ml syringe and a spinal needle no. 22, the assigned solution was administered under direct vision using an endoscope in the postero- inferior quadrant of the tympanic membrane. They were followed up at the end of 1 and 3 months from the last injection. Tinnitus handicap inventory was repeated during the follow up and was compared to the value at presentation.
Results: There was a statistically significant improvement in the THI at the first follow up compared with the baseline THI. Whereas there was no statistically significant change in improvement rate from the 1st follow up to the 2nd follow up (p=0.7), however there is decrease in the improvement, which means the improvement is temporary, and starts reverting by the second visit to some extent.
Conclusions: It was observed that the improvement in the tinnitus was for a short term after intratympanic injection of dexamethasone.

Keywords: Intratympanic injection, Dexamethasone, Subjective idiopathic tinnitus, Tinnitus handicap inventory, Tinnitus

INTRODUCTION

Subjective idiopathic tinnitus might be defined as the experience of noises in the ears or head without both aberrant etiology and external stimuli. It is derived from the latin word tinnire, which means 'to ring'. The sound perception or noise emanating from the ears or head ranges from a barely noticeable annoyance to a debilitating chronic condition, which can interfere with a person's quality of life and may be extremely annoying.[1]

Although tinnitus is a significant health and economic problem, there are no FDA approved drugs to treat tinnitus, and few drugs reliably suppress or eliminate chronic tinnitus in the majority of patients. The lack of drug therapies is in part due to a limited understanding of the biological basis of tinnitus, the heterogeneity of the tinnitus population, the wide range of medical conditions that appear to cause tinnitus, and the huge cost associated with developing drugs to specifically treat tinnitus.[1]

One of the principal advantages of intratympanic therapy is the ability to deliver therapeutic concentrations of the drug in a highly targeted manner to the inner ear, thus avoiding systemic side effects. Compared with IT doses much higher systemic doses are required when action is intended on the inner ear, which is an end organ with blood- brain barrier.[1]

Corticosteroid administration has been widely used as the empirical treatment for various inner ear diseases such as sudden sensorineural hearing loss (SSNHL), Meniere's disease, and autoimmune-induced hearing loss for a long time. After Sakata et al first tried intratympanic (IT) steroid injection to control Meniere's disease, IT steroid injection treatment has been used as an alternative option to systemic steroid treatment over the last two decades.[2]

Two major lines of evidence support the feasibility of IT steroid injection treatment and explaining its mechanism of action. First, injected steroid into the middle ear cavity can penetrate the round window membrane and diffuse into the inner ear fluid. Second, many glucocorticoid receptors and mineralocorticoid receptors have been found in the inner ear structures. Moreover, there is a theoretical advantage that IT steroid injection could increase the concentration into the target organ while it could also reduce the systemic steroid exposure; therefore the use of IT steroid injection has become widespread in a short time.[2]

Animal studies have demonstrated markedly higher concentration of corticosteroids in the endolymph and perilymph of the cochlea when delivered via the intratympanic route in comparison with systemic administration.[2]

Recent literature recommends IT-steroid injection not only as an alternative to oral steroid in vulnerable subjects such as diabetic patients, but also for a salvage therapy after failure of initial therapy.[2]

METHODS

Source of the data

45 patients diagnosed clinically by prospective interventional study as subjective idiopathic tinnitus presenting to our Department of ENT, JSS Medical College and Hospital, Mysore for a duration of 2 years from October 2016.

Inclusion criteria

The patients for study were selected based on the following criteria:

- Patients with subjective idiopathic tinnitus.
- Patients who can give informed consent.

Exclusion criteria

- Age less than 15 years and more than 60 years.
- Patients with secondary causes for tinnitus.

Methods of collection of data

Data was collected in a pretested proforma which met the objective, inclusion and exclusion criteria of the study. Detailed history taking and clinical ENT examination including otoscopic examination was carried out to rule out other ear diseases. Then the patients were subjected to pure tone audiometry, impedence audiometry including tympanometry and acoustic reflex testing, speech audiometry and tinnitus handicap inventory. Brainstem evoked response audiometry was done when a retrocochlear lesion was suspected. Those patients suspected to have any neurological illness was send to the neurology department for a detailed examination to rule out any neurologic illness. Informed consent was taken. The patients were subjected to 3 intratympanic injections of dexamethasone once in a week for 3 weeks. They received a 0.5 ml intratympanic injection of 4 mg/ml dexamethasone solution. The patient was placed in a supine position with the head turned about 45 degrees to the unaffected ear. Topical anaesthesia of the tympanic membrane was administered using 10% lignocaine spray, complete clearance of which will be done using suction after 2-3 minutes. Using a 2 ml syringe and a spinal needle no. 22, the assigned solution was administered under direct vision using an endoscope in the postero-inferior quadrant of the tympanic membrane. The patient was asked to remain in the described position for about 30 minutes. The patients were followed up at the end of 1 month and 3 months from the last injection. Tinnitus handicap inventory was repeated during the follow up.

Statistical analysis

The analysis will be done using appropriate statistical tests.

RESULTS

Age

Of the 45 patients in our study, the mean age was found to be 38.6 years with a standard deviation of 13.5. Majority of the patients were found to be between 30 to 60 years of age.

Gender distribution

Of the 45 patients in our study, 24 were females (24.53%) and 21 patients were men (21.47%).

Duration of tinnitus

Of the 45 patients, 25 (55.6%) presented with tinnitus with a duration less than 6 months, 17 with a duration

between 7-12 months and 12 with a duration more than 12 months as shown in Table 1. The mean duration of tinnitus was found to be 8.9 months with a standard deviation of 10.1.

Table 1: Duration of tinnitus (DOT).

		Count	Percentage (%)
DOT months	<6 months	25	55.6
	7-12 months	13	28.9
	>12 months	7	15.6

Table 2: Mean THI.

	Mean	SD	P value	P value
Baseline THI	40.44	9.76		
1st follow up THI	36.76	8.47	<0.0001	<0.0001
2nd follow up THI	34.33	8.31	<0.0001	

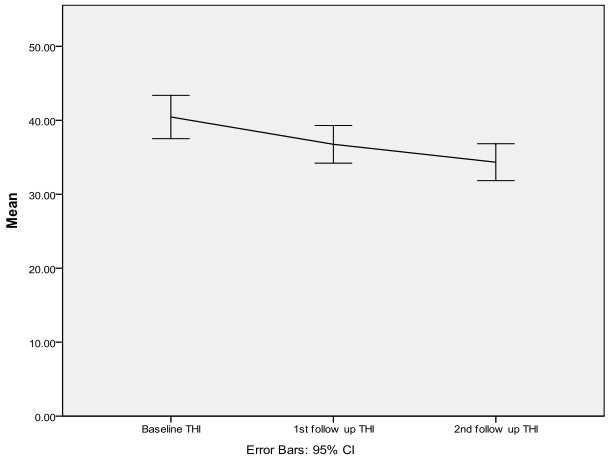

Figure 1: Changes in THI over time.

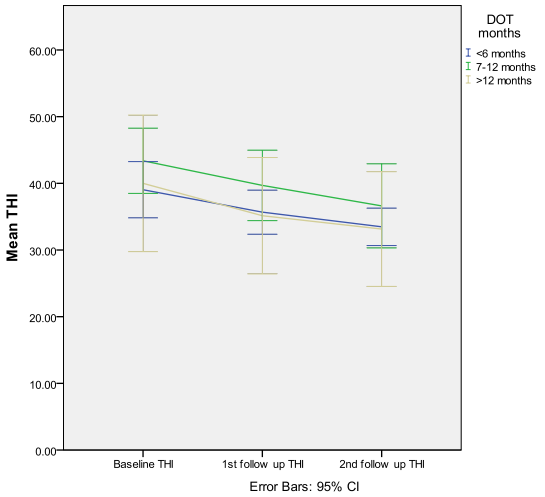

Figure 2: Changes in THI over time with respect to duration of tinnitus.

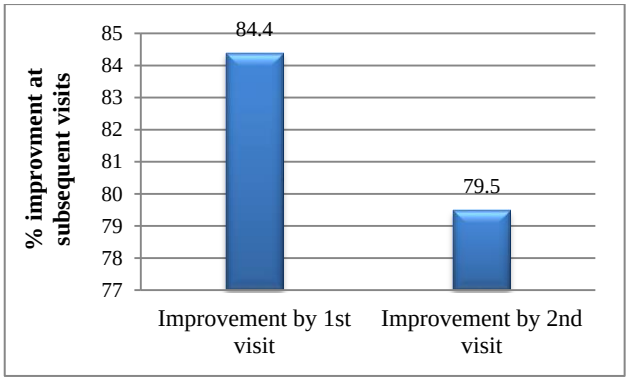

Figure 3: Improvement in THI at subsequent visits.

Laterality

Of the 45 patients, it was observed that 24 patients presented with ringing sensation in the left ear (53.3%) and 21 presented with ringing sensation in the right ear.

Audiometry

The mean Pure tone audiometry of the 45 patients was found to be 28.98 with a standard deviation of 13.91.

Tinnitus handicap inventory (THI)

The mean baseline THI was 40.44. At the first follow up (after 1 month), the mean THI was 36.76 with a p value less than 0.0001, showing that there was a statistically significant reduction in the tinnitus following 3 injections of intratympanic dexona. At the second 2nd follow up (after 3 months), it was found that there was again a statistically significant decrease in the mean THI to 34.33 with a p value less than 0.0001.

With respect to the gender of the patient, there was no statistically significant change in the THI from the baseline to the first and second follow ups (p=0.8). With respect to the side of the ear affected, there was no statistically significant change in the THI from the baseline to the first and second follow ups (p=0.8). With respect to the duration of the tinnitus the patient presented with, there was no statistically significant change in the THI from the baseline to the first and second follow ups (p=0.7), as shown in Figure 2.

Improvement

Out of the 45 patients in our study, 38 patients (84.4%) had an improvement by the first visit and 35 patients (79.5%) had an improvement by the second visit as shown in Figure 3.

There was a statistically significant improvement in the THI at the first follow up compared with the baseline THI. Whereas there was no statistically significant change in improvement rate from the 1st follow to the

2nd follow up (p=0.7), however there is decrease in the improvement, which means the improvement is temporary, and starts reverting by the second visit to some extent.

DISCUSSION

In our study of 45 patients with subjective idiopathic tinnitus, we found that after giving three doses of intratympanic injection of dexamethasone, at the first follow up (i.e., after one month following the last injection) there was a significant improvement in the tinnitus. Whereas at the second follow up (i.e., three months later) the improvement compared to the first follow up was not significant.

In our study factors like age, sex, duration of tinnitus and laterality did not have any significant influence on the improvement in tinnitus.

Mahmoud and Hafize reported a significant difference between the study group and the control group (tinnitus patients without IT dexamethasone injection) for the two parameters, loudness level and minimal masking level, and concluded that the tinnitus matching test could be used as a subjective evaluation for tinnitus and outcome measure of the therapy. THI scores were also improved significantly after the therapy. Most of the patients changed from severe and catastrophic handicap to slight, mild, and moderate handicap; however, none of the tinnitus patients showed full recovery of tinnitus.[3]

An et al also reported that the mean THI scores were significantly reduced at 3 months after IT dexamethasone injection.[4]

In our study no patient had full recovery from tinnitus. However, Cesarani and colleagues reported 34% full recovery of the tinnitus. This could be attributed to the difference in the inclusion criteria of their study group in which the duration of tinnitus did not exceed 3 months.

She et al compared the efficacies of IT prednisolone injection, IT dexamethasone injection, and carbamazepine by means of oral administration for subjective tinnitus. The effective rate of the prednisolone group, dexamethasone group, and the carbamazepine group was 48.6, 33.3, and 44.0%, respectively, and the control rate half a year after the treatment was 45.7, 27.8, and 36.0%, respectively. They reported that prednisolone may be better than dexamethasone in IT perfusion for subjective tinnitus. They concluded that IT steroid injection has a positive effect on subjective tinnitus and may be considered to be an alternative treatment to it.[5]

The advantage of prednisolone over dexamethasone was explained by Parnes et al who showed that methylprednisolone had a higher concentration and longer duration in the perilymph after transtympanic administration compared with hydrocortisone or dexamethasone.[6]

However, Hamid reported that dexamethasone is more effective, because it is absorbed faster than other steroids; he used a higher concentration of dexamethasone (24 mg/ml) in his study.[7]

In contrast, Araujo et al studied the effectiveness of IT dexamethasone injection as a treatment for severely disabling cochlear tinnitus, in their randomized, prospective, single-blind study. They concluded that there was no advantage in IT injections of dexamethasone over saline solution in the treatment of severely disabling tinnitus, and both solutions produced a placebo-like improvement in about 30–40% of patients. They attributed their results to the inclusion of patients with severely disabling tinnitus, which is different from common forms of tinnitus; the symptoms are intense, with a high annoyance level and an affective component that renders the patient incapable of performing daily tasks efficiently.[8]

In 1989, House severed the cochlear nerves of patients with Ménière's disease who were undergoing vestibular nerve section and who also had severe tinnitus. Considering that tinnitus in Ménière's disease certainly has a cochlear origin, it was surprising to learn a large percentage of these patients continued to experience the unaltered symptom after the cochlear nerve was severed. Somehow, the central auditory pathways kept the symptom of tinnitus alive after cochlear deafferentation. A lack of central suppression of spontaneous auditory pathways could explain the noise permanence. The central component of severely disabling tinnitus even when of cochlear origin, makes the IT injections of dexamethasone inefficient in some group of patients, especially in those with severely disabling tinnitus.[9]

Parelkar et al reported that, although IT therapy is a highly efficacious and tempting mode of drug delivery, IT dexamethasone injections are not effective for refractory tinnitus and do not alter the hearing loss; this study was also conducted on patients with severely disabling tinnitus. They also referred the failure of IT injection in a group of patients to the poor round window membrane permeability. The mechanism of action of this therapeutic modality is multifactorial, including anti-informatory effects, a metabolic improving effect, an edema-relieving effect, and suppress the irritated or hypersensitive hair cells in the inner ear, which are believed to cause tinnitus.[10]

Pondugula et al pointed at other mechanism of action for IT dexamethazone injection in tinnitus patients, which suggest that steroid perfusion of labyrinthine tissues can affect sodium and fluid transport *in vitro* studies.[11]

The choice of an IT route in the treatment of tinnitus has two advantages: first, high perilymph levels are attained

as a result of providing a direct passage through the oval window membrane, and, second, adverse effects of systemic administration of the drug are avoided.[12]

Local side effects, may include injection-site pain, dizziness, caloric vertigo, infection, persistent tympanic membrane perforation, or possible vasovagal or syncopal episodes during injection. In our study, no side effects were noted.[13]

Sufficient warming of the drug, the use of fine needles and appropriate local anaesthesia, a gentle rate of injection, and avoidance of excessive injection volumes seem to be key factors for good local tolerance.[14]

CONCLUSION

There was a statistically significant improvement in the THI at the first follow up compared with the baseline THI. Whereas there was no statistically significant change in improvement rate from the 1st follow to the 2nd follow up, however there is decrease in the improvement, which means the improvement is temporary, and starts reverting by the second visit to some extent. Hence, it was observed that the improvement in the tinnitus was for a short term.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Shetty S, George A, Chandrashekar S, Prakash BG. Efficacy of intratympanic injection of dexamethasone in the treatment of subjective idiopathic tinnitus. Int J Otorhinolaryngol Head Neck Surg 2019;5:1056-60.