

Efficacy of Intratympanic Injection of Methyl Prednisolone in Improving Idiopathic Subjective Tinnitus: A Major Leap in the Treatment of Idiopathic Subjective Tinnitus

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Abstract

Aims: In this study, we have made an attempt to study the efficacy of intratympanic injection of methylprednisolone in the management of idiopathic subjective tinnitus.

Materials and Methods: A prospective study was conducted in the ENT department, PMCH, Patna from May 2019 to March 2020. The patients irrespective of their age, gender and duration of tinnitus, were included in this study after a detailed history taking and thorough clinical examination, to exclude any cause of subjective tinnitus. The severity of tinnitus in the patients was assessed using visual analogue scale and THI scores.

Results: A total of 50 individuals with age ranging from 23 years to 60 years participated in the study. Complete resolution of symptom was seen in 12 patients (24% of cases). Improvement in VAS scores seen in each age group was calculated. The average duration of tinnitus in patients, who got completely relieved from tinnitus was found to be ~2.6 months.

Conclusion: From this study, we concluded that early intervention showed much better results. Maximum improvement in VAS scores seen in each age group was calculated. From this study data, we found that earlier intervention in younger patients, with intratympanic methylprednisolone injections gave better results in the treatment of patients with idiopathic subjective tinnitus.

Keywords: Tinnitus, Methylprednisolone, Intratympanic Injection, Idiopathic Subjective Tinnitus.

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Introduction

Tinnitus is the perception of sound that does not arise from an external source. Its mechanism is poorly understood and its pathophysiology remains unclear [1]. The sounds heard can be ringing, buzzing or hissing, or a combination and can be continuous, intermittent or pulsatile, which can be too annoying for the patient and can affect the quality of life [2].

Tinnitus can be subjective or objective. Objective tinnitus can be detected by an

observer by a stethoscope or an ear canal microphone. These somatosounds reflect the perception of internally generated sounds from joints, muscles, turbulent blood flow or rarely, otoacoustic emissions. Whereas, subjective tinnitus is inaudible to an observer, which remains the most common form.

Tinnitus can persist for many years, leading to insomnia, inability to concentrate and depression [3]. As tinnitus

is seen more commonly in patients with hearing loss, an association with cochlear lesion is suggested. It is considered that tinnitus is triggered in the initial stage of cochlear lesion. Hence, it is considered that we could eliminate tinnitus, if intervention is attempted when the cochlear damage is reversible [4].

Corticosteroid has been widely administered as empirical treatment for various inner ear diseases. Intratympanic steroid therapy has been used as an alternative to systemic steroid therapy, over the last two decades. There are two main reasons for the emergence of intratympanic steroid injection as a modality of treatment. Firstly, the steroid injected into the middle ear can penetrate the round window membrane and diffuse into the inner ear fluid [5]. And secondly, many glucocorticoid and mineralocorticoid receptors have been found in the inner ear structures [6,7,8]. In addition, there is a theoretical advantage of increase in the concentration of drug in the target organ, when administered via intratympanic injections, thereby reducing the systemic steroid exposure, which has made intratympanic steroid injection widespread, in a short period of time.

Cochlear damage from many causes namely noise, ototoxicity, endolymphatic hydrops, viral infections and vascular ischemia are mostly related to inflammatory cytokines and reactive oxygen species production. Anti-inflammatory and immunosuppressive actions of glucocorticoid could play a significant role in preventing and recovering from the cochlear damage [9].

Methylprednisolone is a synthetic corticosteroid, which acts similarly as naturally occurring glucocorticoids. It is five times more potent in its anti-inflammatory properties, when compared to hydrocortisone [10]. Its clinical use is mainly due to its anti-inflammatory and immunosuppressive activity in the human body.

Methyl prednisolone moves across cell membrane by passive diffusion and binds to intracellular glucocorticoid receptor. This complex translocates into the nucleus, where it interacts with specific DNA sequences, resulting in either enhancement or suppression of particular gene transcription. The methyl prednisolone-glucocorticoid receptor complex binds and blocks the promoter sites of pro inflammatory genes [11], promotes expression of anti-inflammatory gene products [12] and inhibits cytokine synthesis, mainly by blocking the function of transcription factors, such as nuclear factor- kappa- B (NF-kB) [13].

Methyl prednisolone, just like other corticosteroids, also suppresses the cyclooxygenase (COX)-2 synthesis, which is responsible for the production of prostaglandins in the damaged tissue, leading to the inflammation cascade [14]. Methyl prednisolone reverses capillary permeability, thereby inhibiting the migration of fibroblasts and polymorphonuclear leukocytes, controlling the rate of protein synthesis and stabilising lysosomes at the cellular level and hence, preventing inflammation as well.

In this study, we have made an attempt to study the efficacy of intratympanic injection of methylprednisolone in the management of idiopathic subjective tinnitus.

Materials and Methods

A prospective study was conducted in the Department of ENT, Patna Medical College and Hospital, Patna. The study was conducted in patients with idiopathic subjective tinnitus, who attended the outpatient department from May 2019 to March 2020. A total of 57 patients were included as study subjects, out of which 7 were lost to follow up. And hence, these study results have been derived from 50 patients.

The patients irrespective of their age, gender and duration of tinnitus, were included in this study after a detailed history taking and thorough clinical examination, to exclude any cause of subjective tinnitus. The presence of any systemic disorders, such as thyroid dysfunction or hypertension and any other complaints of ear disease in the last 6 months or any abnormality in contrast enhanced MRI were excluded. Those who were included had normal hearing thresholds within 25 dB.

A properly informed written consent was taken from the patients, who were willing to be included in this study. The severity of tinnitus in the patients was assessed using Visual Analogue Scale (VAS questionnaire) and Tinnitus Handicap Inventory severity scale (THI scores).

VAS questionnaire included 5 parameters, i.e., loudness of tinnitus, annoyance, effect on work, effect on social life and awareness of tinnitus. These parameters were graded from 0 to 10, 0 being noted for no symptoms and 10 denoted most severe symptoms, and calculated to a total of 100%, with 20% being assigned for each parameter.

THI scores were calculated using patients' responses to 25 questions of the questionnaire and graded accordingly.

VAS scores and THI scores were calculated prior to administration of intratympanic injections. Every patient received weekly intratympanic injections of methyl prednisolone, a maximum of six injections or till he/ she got relieved of symptoms, whichever being the earliest. The patients were assessed 2 weeks after the administration of last intratympanic injection. VAS scores and THI scores were reassessed and improvement was measured by reducing the post treatment score from the pre-treatment score. Relative improvement in VAS scores and THI scores were also evaluated.

Procedure of Intratympanic injection of methyl prednisolone

Patient was made to lie in supine position and tympanic membrane was visualized under operating microscope. A gauze soaked in 4% Lignocaine was placed over the tympanic membrane for about 10 minutes, for surface anaesthesia. A sterile 25 gauge spinal needle was attached to a 2mL syringe and 0.5mL of Methylprednisolone suspension of 40mg/mL concentration was injected into the anteroinferior quadrant of tympanic membrane, which was almost enough to completely fill up the middle ear cavity. Patient was instructed not to swallow or speak, to prevent the leak of injected drug through the eustachian tube [15] and to keep his/ her head turned $\sim 45^\circ$ towards the opposite side [4] and to maintain this position for the next 15 minutes after injection [16].

Results

A total of 50 individuals (37 men and 13 women) with age ranging from 23 years to 60 years participated in the study. There were a total of 12 patients in the age group of 20 to 30 years, out of which 8 were males and 4 were females. However, there were 16 patients in the age group of 30 to 40 years, of which 11 were males and 5 were females. Whereas, there were 13 patients in the age group of 40 to 50 years, of which 11 were males and 2 were females. And there were 9 patients in the age group of 50 to 60 years, of which 7 were males and 2 were females. Male to female ratio was found to be 2.86:1.

Complete resolution of symptoms was seen in 12 patients (24% of cases), out of which 5 patients belonged to the age group of 20 to 30 years, 3 patients belonged to the age group of 30 to 40 years, 3 patients belonged to the age group of 40 to 50 years and 1 patient belonged to the age group of 50 to 60 years.

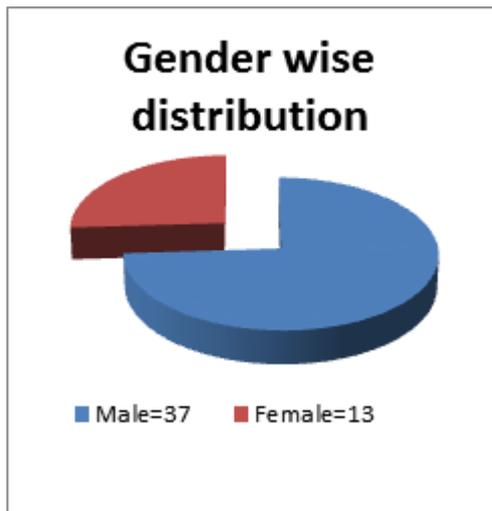


Figure 1: Gender wise distribution

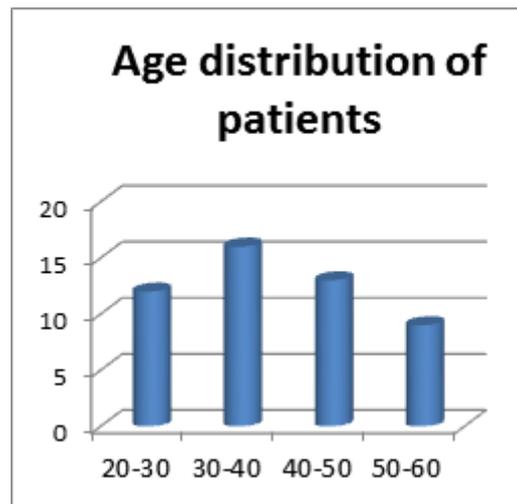


Figure 2: Age wise distribution

Average improvement in VAS Scores, i.e. the difference in VAS scores before the injections and 2 weeks after the completion of intratympanic injections was calculated for all age groups. The average improvement in VAS scores in the age groups 20 to 30 years, 30 to 40 years, 40 to 50 years and 50 to 60 years were found to be 43.83%, 40.25%, 37.54% and 30.67% respectively. From this study, we found that younger patients responded much better than older patients, as the

patients of 20 to 30 years age group showed better improvement in VAS scores following intratympanic methyl prednisolone injections.

The average improvement in THI scores were also calculated for the age groups 20 to 30 years, 30 to 40 years, 40 to 50 years and 50 to 60 years and were found to be 42, 39.25, 37.38 and 30 respectively. These results supported the findings derived from VAS score assessment of improvement in tinnitus severity.

Table 1: Distribution of patients

Age Group	Male	Female
20-30	8	4
30-40	11	5
40-50	11	2
50-60	7	2

Table 2: Maximum improvement in VAS score in each age group

Age Group	Maximum improvement
20-30	58%
30-40	48%
40-50	44%
50-60	42%

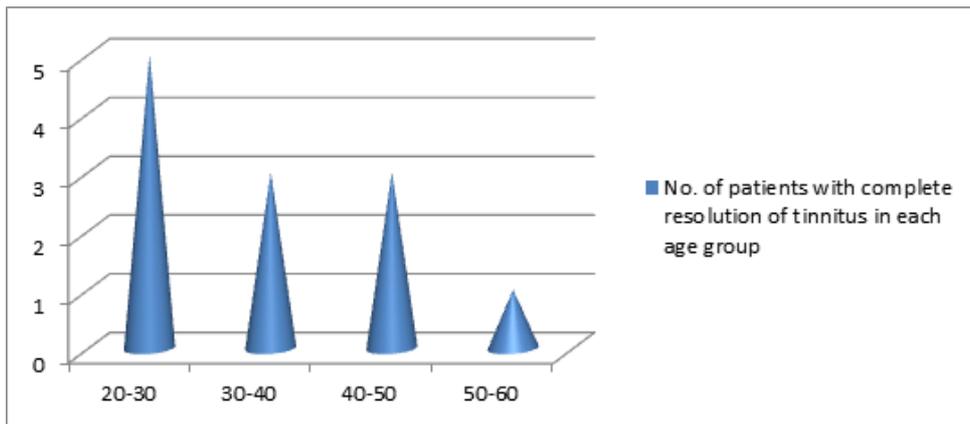


Figure 3: No. of patients with complete resolution of tinnitus in each age group

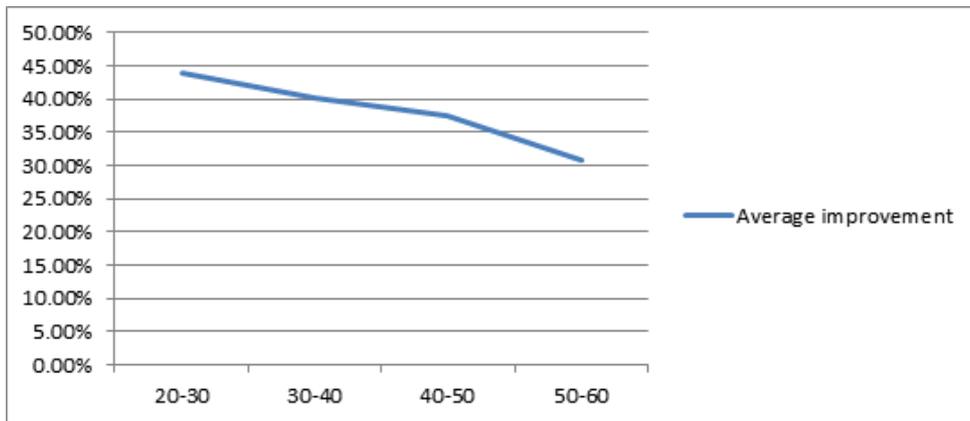


Figure 4: Average improvement in VAS in each age group

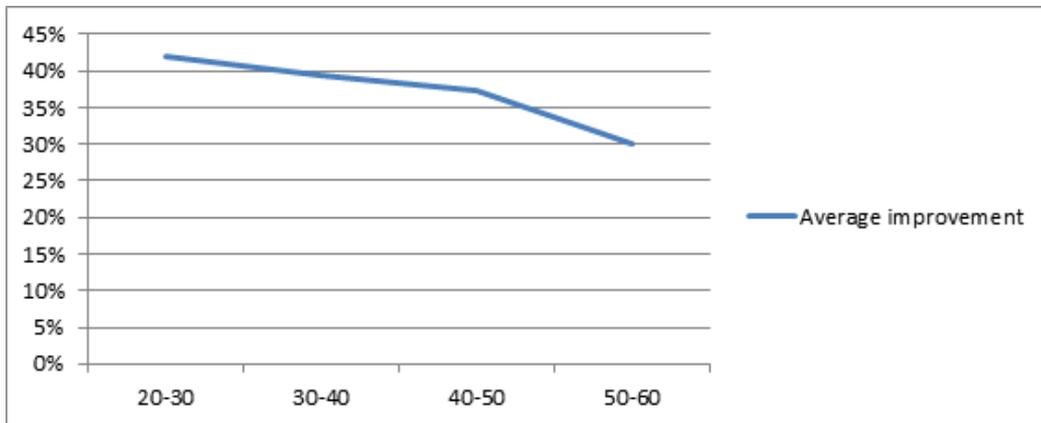


Figure 5: Average improvement in THI score in each group

Tinnitus severity was graded as per THI scores and down gradation following therapy was assessed. Average down gradation in tinnitus severity following intratympanic methyl prednisolone therapy for age groups 20 to 30 years, 30 to 40 years, 40 to 50 years and 50 to 60 years were calculated to be 2.08, 1.94, 1.85 and 1.44 respectively. These results also strengthened our belief that younger

patients responded well to the therapy. In patients of age group 20 to 30 years, we found a reduction of more than 2 grades in the severity of tinnitus, which was a very much appreciable finding.

Maximum improvement in VAS scores in age groups 20 to 30 years, 30 to 40 years, 40 to 50 years and 50 to 60 years were found to be 58%, 48%, 44 % and 42 %

respectively. From this study, we found that younger patients showed much better response than elderly patients.

Relative improvement in VAS scores was also calculated. It was measured by the formula,

$$\left(\frac{\text{improvement in VAS scores following therapy}}{\text{VAS score prior to therapy}} \right).$$

It is a much better indicator of response to intratympanic methyl prednisolone therapy. In this study, the patients in the age group 20 to 30 years showed a relative improvement in VAS scores of 86.29%, whereas those in the age group 50 to 60 years showed a relative improvement in VAS scores of only 66.33%, supporting our finding that younger patients showed better results with intratympanic methyl prednisolone therapy.

No improvement was seen in 1 patient, who was 60 years old male and had been having tinnitus since past 2 years. Complete relief from tinnitus was seen in 12 patients. The average duration of tinnitus in patients, who got completely relieved from tinnitus was found to be ~2.6 months. From this study, we concluded that early intervention in patients with idiopathic subjective tinnitus showed much better results when compared to late presenting cases.

From our study, we concluded that earlier intervention in younger patients, with intratympanic methyl prednisolone injections gave better results in the treatment of patients with idiopathic subjective tinnitus.

In our study, we didn't encounter any patient complaining of vertigo following intratympanic injection. 16 patients (32%) complained of mild pain at the time of injection, which got relieved in few minutes.

A study conducted by Diao El Din M. El Hennawi et al in 2017, observed minor side effects such as mild dizziness and mild otalgia in 13 % of cases [13].

We also observed pin point perforations at the injection site in 2 cases (4%), which got healed spontaneously within a maximum of 1 month of the last injection. Similarly, in a study conducted by YanluLyu et al in 2018, they also observed that 4.9% of patients had small perforations that recovered in 6 months follow up period [17].

Discussion

This study assessed the efficacy and safety of intratympanic methyl prednisolone injection in the management of idiopathic subjective tinnitus of duration ranging from 1 month to 2 years.

In our study, we observed that the maximum improvement of VAS scores in age groups 20 to 30 years, 30 to 40 years, 40 to 50 years and 50 to 60 years were found to be 58%, 48%, 44% and 42% respectively. From this study, we found that younger patients showed much better response than elderly patients.

Our findings were similar to the findings in similar studies conducted in the recent years as well.

In a study conducted by Diao El Din M et al, in 2017, they found a clinical improvement of about 56.5% with intratympanic methyl prednisolone injections [18]. While, a study conducted by She et al. found an improvement of 48.6% with intratympanic prednisolone therapy [19].

In this study, the patients in the age group 20 to 30 years showed a relative improvement in VAS scores of 86.29%, whereas those in the age group 50 to 60 years showed a relative improvement in VAS scores of only 66.33%, supporting our finding that younger patients showed better results with intratympanic methyl prednisolone therapy.

The average improvement in VAS scores in the age groups 20 to 30 years, 30 to 40 years, 40 to 50 years and 50 to 60 years

were found to be 43.83%, 40.25%, 37.54% and 30.67% respectively.

Average improvement in THI scores were also calculated for the age groups 20 to 30 years, 30 to 40 years, 40 to 50 years and 50 to 60 years and were found to be 42, 39.25, 37.38 and 30 respectively.

From this study, we found that younger patients responded much better than older patients, as the patients of 20 to 30 years age group showed better improvement in VAS scores and THI scores following intratympanic methyl prednisolone injections.

Average down gradation in tinnitus severity following intratympanic methyl prednisolone therapy for age groups 20 to 30 years, 30 to 40 years, 40 to 50 years and 50 to 60 years were calculated to be 2.08, 1.94, 1.85 and 1.44 respectively. These results also strengthened our belief that younger patients responded well to the therapy. Tinnitus severity showed more than 2 grades reduction in patients of age group 20 to 30 years, which was a very much appreciable finding.

No improvement was seen in 1 patient, who was 60 years old male and had been having tinnitus since past 2 years. Complete relief from tinnitus was seen in 12 patients. The average duration of tinnitus in patients, who got completely relieved from tinnitus was found to be ~2.6 months. From this study, we concluded that early intervention in patients with idiopathic subjective tinnitus showed much better results when compared to late presenting cases.

A study conducted by Diaa El Din M. El Hennawi in 2017, also supported the finding by stating that the effects of methyl prednisolone acetate decreases as tinnitus moves from the acute to the chronic phase [19]. Shim et al also stated that the intratympanic steroid injection was effective in the treatment of newly developed tinnitus [4].

Complete resolution of symptoms was seen in 12 patients (24% of cases), out of which 5 patients belonged to the age group of 20 to 30 years, 3 patients belonged to the age group of 30 to 40 years, 3 patients belonged to the age group of 40 to 50 years and 1 patient belonged to the age group of 50 to 60 years.

Another study conducted on 54 patients, showed complete resolution of tinnitus by intratympanic steroid therapy in about 34% of cases [20].

Conclusion

From our study, we concluded that earlier intervention in younger patients, with intratympanic methyl prednisolone injections gave better results in the treatment of patients with idiopathic subjective tinnitus.

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