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INTRATYMPANIC INJECTION OF DEXAMETHASONE FOR TREATMENT OF TINNITUS OVER ORAL DRUGS

Otolaryngology

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ABSTRACT

INTRODUCTION: Tinnitus is a self debilitating symptom of a cochlear dysfunction. Various treatment outlines have been used since time immemorial for its treatment. Intratympanic steroid injection for the treatment of tinnitus has been tried for over fifteen years. Several studies have been done to bring forward various treatment aspects of tinnitus. Various drugs like Alprazolam and vitamins, like Vitamin B 12 have also been used in the treatment of tinnitus.

METHODOLOGY: A clinical based experimental study was carried out in ENT OPD of State Medical College, among patients visiting with tinnitus. Out of the 120 patients, 60 were given intratympanic dexamethasone, once every week for 4 weeks, and the rest 60 were given oral drugs for a month. The patients were followed up after 1 month and 3 months respectively. All the patients were asked to fill a questionnaire (Tinnitus Handicap Inventory severity scale) before starting the treatment and were compared with the results of the questionnaire after the treatment was over.

RESULTS: Patients who were treated with IT dexamethasone, significant improvement was seen (p= 0.00) as compared to those who were given oral drugs (p= 0.621).

CONCLUSION: Intratympanic injection has significant role for treatment of tinnitus . Early the intervention better is the outcome. Patient with severe degree of tinnitus showed minimum improvement.

KEYWORDS

Intratympanic, Dexamethasone, Tinnitus, Tinnitus Handicap Inventory Severity Scale.

INTRODUCTION:

Tinnitus is in itself a debilitating symptom of a cochlear dysfunction. Various treatment outlines have been used since time immemorial for its treatment. Intratympanic (IT) steroid injection has been used increasingly in various inner ear diseases. Systemic steroids are known to improve hearing levels in sudden sensorineural hearing loss. In 1996 [1]Sakata et al treated patients with chronic otitis media (COM), labyrinthine syphilis, Meniere's disease, vertigo, sudden SNHL, streptomycin intoxication, acoustic trauma, head injury, or other otological diseases by infusing a dexamethasone solution into their middle ear. 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 [2,3]. Second, many glucocorticoid receptors and mineralocorticoid receptors have been found in the inner ear structures [4-6]. After these studies, a large-scale prospective study demonstrated IT-steroid injection treatment was not inferior to oral steroid treatment on sudden SNHL in humans[7] .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 [8,9]. 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.

IT steroid injection for the treatment of tinnitus has been tried for over fifteen years. Sakata et al. [10] reported that tinnitus improved in 75% of 3,978 ears immediately after four IT-steroid injections and in 68% after 6 months. Cesarani et al.[11] reported 13.5% cure rate and 24% improvement rate 8 weeks after nine injections of dexamethasone. However, those studies were single arm studies without controls. In 2005 Araújo *et al.* in a randomized single-blind study showed no difference between intratympanic injection of dexamethasone and saline in patients with severe, disabling tinnitus[13].

Recent clinical studies have demonstrated that gadolinium can readily diffuse through the round window membrane[1415].

Although the pathophysiological mechanism of tinnitus in the central auditory system is still unclear, the majority of tinnitus is believed to be triggered by cochlear damage. Tinnitus subjects with normal audiograms do not necessarily indicate the absence of cochlear damage. Several studies have demonstrated that tinnitus subjects with normal audiograms show increased hearing thresholds at extended high frequencies above 8 kHz compared to normal-hearing subjects without tinnitus[15, 16]. Some investigators found subtle damage to the outer hair cells that alters otoacoustic emissions can cause tinnitus.[18-20] Cochlear damage from numerous causes such as noise, ototoxic agents, endolymphatic hydrops, viral infection, and vascular ischemia are commonly related to inflammatory cytokines and production of reactive oxygen species. Anti-inflammatory and immunosuppressive actions of glucocorticoid could play a key role to both prevent and recover from the cochlear damage [21].

Tinnitus has much comorbidity, which is often exacerbated by the incessant phantom sound. Oftentimes, individuals have accompanying symptoms including: frustration, irritability, anxiety, depression, hearing difficulties, hyperacusis, insomnia and concentration difficulties. In addition, severe depression can aggravate tinnitus[22]. Due to the co-occurrence of anxiety and tinnitus, certain benzodia zepines have been administered as possible tinnitus treatment options. Alprazolam has been prescribed as an anxiolytic and antidepressant. A double-blind study conducted showed the effects of Alprazolam on 40 subjects who took 0.25mg to 0.5mg for one week at bedtime [23]. In addition to pharmacological medications, certain studies have looked at the use of vitamins to treat tinnitus.

Vitamin B12 deficiency is associated with axonal degeneration, demyelination, and neuronal death. Berkiten *et al*. [24] investigated the relationship among hearing loss, tinnitus, and B12 deficiency.

MATERIALS AND METHODS:

Type of study:

A clinical based experimental and interventional study was taken up among the patients visiting the ENT OPD of a State Medical College and Hospital. Only consenting candidates were considered for the study and predesigned and pretested proforma was be used for data collection.

Study design:

Longitudinal

Subjects:

120 subjects were taken in the study with 60 subjects given an

intratympanic injection of dexamethasone and rest 60 given oral drugs like Alprazolam and vitamin B complex.

INCLUSION CRITERIA:

1. All patients attending OPD with tinnitus.
2. With an intact tympanic membrane.

EXCLUSION CRITERIA:

1. Patients unwilling for injection in ear
2. Suspected CP angle tumour.
3. Presbyacusis.
4. Conductive hearing loss
5. Retro cochlear lesions

Procedure:

60 patients were given injection of dexamethasone in a lying down position and the drug was infused into the middle ear through the tympanic membrane. To allow maximum contact of the drug with the round window, the patient was positioned and kept silent at rest for 20 minutes. Every patient was given 2-4 mg of intratympanic injection dexamethasone once every week, for 4 weeks and then followed up after 1 month and 3 months respectively.

The rest 60 patients were given oral drugs (Alprazolam and Vitamin B complex) for a duration of 1 month and followed up after 1 month and 3 months respectively.

ANALYSIS OF THE RESULTS:

A proforma (Tinnitus Handicap Inventory Questionnaire) was filled up by the candidates before the treatment was started and the same questionnaire was filled up subsequently after the treatment was completed and after one month and three months subsequently. The scores were calculated as per the proforma filled up by the candidates and outcomes compared. SPSS 20.0 software was used for analysis of the results.

Tinnitus Handicap Inventory SEVERITY SCALE:

INSTRUCTIONS:

The purpose of this questionnaire is to identify difficulties that you may be experiencing because of your tinnitus. Please answer every question. Please do not skip any questions.

1. Because of your tinnitus, is it difficult for you to concentrate?
   Yes Sometimes No
2. Does the loudness of your tinnitus make it difficult for you to hear people?
   Yes Sometimes No
3. Does your tinnitus make you angry?
   Yes Sometimes No
4. Does your tinnitus make you feel confused?
   Yes Sometimes No
5. Because of your tinnitus, do you feel de sperate?
   Yes Sometimes No
6. Do you complain a great deal about your tinnitus?
   Yes Sometimes No
7. Because of your tinnitus, do you have trouble falling to sleep at night?
   Yes Sometimes No
8. Do you feel as though you cannot escape your tinnitus?
   Yes Sometimes No
9. Does your tinnitus interfere with your ability to enjoy your social activities (such as going out to dinner, to the movies)?
   Yes Sometimes No
10. Because of your tinnitus, do you feel frustrated?
    Yes Sometimes No
11. Because of your tinnitus, do you feel that you have a terrible disease?
    Yes Sometimes No
12. Does your tinnitus make it difficult for you to enjoy life?
    Yes Sometimes No
13. Does your tinnitus interfere with your job or household responsibilities?
    Yes Sometimes No
14. Because of your tinnitus, do you find that you are of t en irritable?
    Yes Sometimes No
15. Because of your tinnitus, is it difficult for you to read?
    Yes Sometimes No
16. Does your tinnitus make you upset?
    Yes Sometimes No
17. Do you feel that your tinnitus problem has placed stress on your relationships with members of your family and friends?
    Yes Sometimes No
18. Do you find it difficult to focus your attention away from your tinnitus and on other things?
    Yes Sometimes No
19. Do you feel that you have no control over your tinnitus?
    Yes Sometimes No
20. Because of your tinnitus, do you often feel tired?
    Yes Sometimes No
21. Because of your tinnitus, do you feel depressed?
    Yes Sometimes No
22. Does your tinnitus make you feel anxious?
    Yes Sometimes No
23. Do you feel that you can no longer cope with your tinnitus?
    Yes Sometimes No
24. Does your tinnitus get worse when you are under stress?
    Yes Sometimes No
25. Does your tinnitus make you feel insecure?
    Yes Sometimes No

Tinnitus Handicap Inventory SEVERITY SCALE

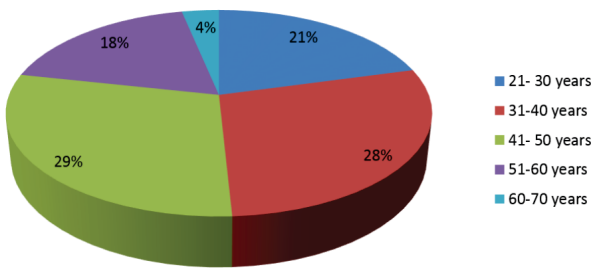
Grade	Score	Description
1	0-16	Slight: Only heard in quiet environment, very easily masked. No interference with sleep or daily activities.
2	18-36	Mild: Easily masked by environmental sounds and easily forgotten with activities. May occasionally interfere with sleep but not daily activities
3	38-56	Moderate: May be noticed, even in the presence of background or environmental noise, although daily activities may still be performed
4	58-76	Severe: Almost always heard, rarely, if ever, masked. Leads to disturbed sleep pattern and can interfere with ability to carry out normal daily activities. Quiet activities affected adversely
5	78-100	Catastrophic: Always heard, disturbed sleep patterns, difficulty with any activity.

RESULTS:

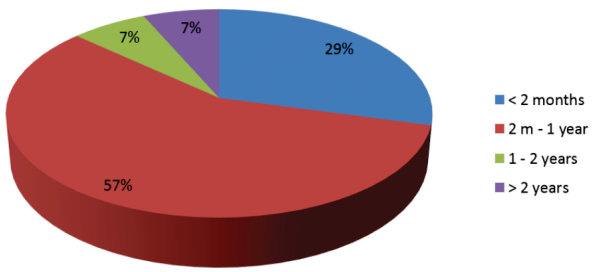
Improvement was considered with a decreasing grade of tinnitus post treatment as compared to the pre treatment status as calculated by the Tinnitus Handicap Inventory Severity Scale.

Out of the 120 patients taken in our study, 67 were males and 53 females.

Age of presentation of the patients



Duration of symptoms at the time of presentation



Aetiology according to the patient				
	Frequency	Percent	Valid Percent	Cumulative Percent
Idiopathic	83	69.2	69.2	69.2
Traumatic	4	3.3	3.3	72.5
Noise induced	4	3.3	3.3	75.8
CVA	4	3.3	3.3	79.2
Chronic diseases	8	6.7	6.7	85.8
Probably meniere's	11	9.2	9.2	95.0
Infective origin	6	5.0	5.0	100.0
Total	120	100.0	100.0	

Most of the patients (83) had an idiopathic cause, 4 patients with a traumatic cause, 4 with noise induced, 8 patients with a chronic disease like a heart disease, 6 patients following fever or other infective etiology and 11 patients with probably meniere's disease.

If associated with SNHL				
	Frequency	Percent	Valid Percent	Cumulative Percent
Yes,severe	45	37.5	37.5	37.5
Yes,moderate	30	25.0	25.0	62.5
Yes,mild	16	13.3	13.3	75.8
High frequency	10	8.3	8.3	84.2
Normal hearing	19	15.8	15.8	100.0
Total	120	100.0	100.0	

111 patients had association with various grades of SNHL where as 19 patients had a normal hearing.

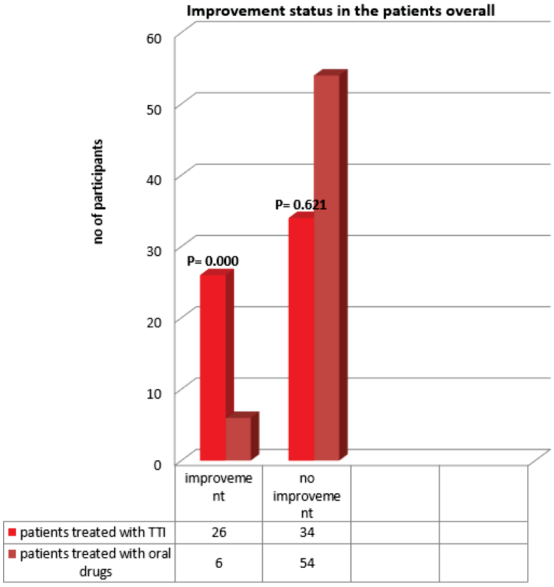
Improvement in patients who were given Intratympanic dexamethasone:

	Frequency	Percent %	Valid Percent	Cumulative Percent
1	26	43.3	43.3	43.3
2	34	56.7	56.7	100.0
Total	60	100.0	100.0	

Out of the 60 patients who were given TTI of dexamethasone 26 show improvement (shift from a higher grade to lower grade)

Improvement in p atients who received or al drugs:				
	Frequency	Percent%	Valid Percent	Cumulative Percent
1	6	10.0	10.0	10.0
2	54	90.0	90.0	100.0
Total	60	100.0	100.0	

Out of the 60 patients who were given oral drugs, 6 showed improvement where as the rest don't show any improvement.



Bar chart showing the results of a PAIRED T TEST on both the samples individually. Patients who were treated with Intratympanic dexamethasone show improvement with a p value of 0.00 , whereas patients treated with oral drugs (Alprazolam and Vitamin B complex) show no improvement , with a p value of 0.621

Relationship With Duration Of Symptoms:

Duration of symptoms	Improved	No improvement
<2months	11(45.8%)	13
2m–1year	10(50%)	10
1–2years	3(33%)	6
>2years	2 (28%)	5

Chart showing relationship of symptom improvement with duration of presentation in patients who were given Intratympanic dexamethasone. Patients who presented earlier, show a better chance of improvement.

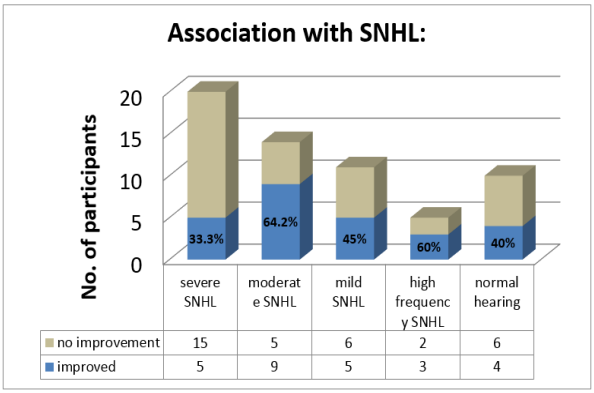


Chart showing maximum improvement in patients showing high and normal hearing, followed by moderate hearing loss and mild hearing loss.

ETIOLOGYACCORDING TOTHEPATIENT	IMPROVED	NO IMPROVEMENT
IDIOPATHIC	20(50%)	20
TRAUMATIC	0	2
NOISEINDUCED	2(100%)	0
CVA	0	2
CHRONICDISEASES	1(25%)	3
PROBABLYMENIERE'S	2(33%)	4
INFECTIVEORIGIN	1(25%)	3

Table showing maximum improvement in patients with noise induced hearing loss, followed by idiopathic, probably meniere's and those associated with chronic diseases or tinnitus following any infective cause.

DISCUSSION:

Of the 120 patients taken in our study, 67 were male and 53 females, showing almost no sex preponderance. Patients presented to our OPD with tinnitus were in an age group of 21-67 years with maximum patients between 41 – 50 years. Most of the patients presented between 2 months to 1 year of the symptoms. Among the patients who were treated with intratympanic dexamethasone, significant improvement was seen in 26 of them, with a p value of 0.00 as compared to those who were given oral drugs, in which only 6 showed improvement, with a p value of 0.621.The improvement of the symptoms is significantly related with the duration of the symptoms in our study. Out of the 60 patients who were given Intratympanic dexamethasone,44 patients presented within 1 year of the symptom duration. 45.8% who presented within 2 months of the symptoms showed improvement, and 50% of those presenting between 2 months to 1 year showed improvement. Patients presenting with severe SNHL was the commonest with 38%, but had the least improvement (33.3%). 40% of the patients who had a normal hearing also showed improvement and 60% of patients with high frequency SNHL showed improvement. Maximum patients presented to us as an idiopathic case of tinnitus, out of which 50 % got improvement following dexamethasone injection. 2 patients among the patients who received injection dexamethasone show improvement in the symptoms.

RESEARCH AND DEVELOPMENT CONSIDERATIONS:

Lack of clinical trials with double blinding are lacking in the field of tinnitus. Tinnitus is a comparatively unexplored arena of our subject. There is still limited understanding of tinnitus because of inadequate animal models and lack of serendipitous discoveries. There is no standardized protocol for FDA approval; therefore, the first drug to prove effective will have to pave the way through the approval and legalization process.

CONCLUSION:

Intratympanic dexamethasone can be considered as a good alternative for improvement of symptoms of tinnitus. Reassurance and psychological management of the patients have not been looked for in our research paper. Earlier presentation has got better chances of improvement. Patients presenting as idiopathic cases have a maximum improvement chance. The patients who presented in association with severe SNHL had a worse prognosis as compared to those with a normal hearing and mild, moderate or high frequency SNHL.

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