Intratympanic Dexamethasone Delivery versus Placebo in Intractable Meniere Disease

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Abstract

Background: Numerous treatments strategies were used for Meniere disease (MD). In this study, we aimed to compare the efficacy of intratympanic dexamethasone versus intratympanic placebo in intractable MD.

Methods: This was a single-blinded randomized clinical trial. All patients with Intractable MD underwent ventilation tube insertion into tympanic membrane and were randomly allocated to two groups of 18-patients. The patients of the first group used dexamethasone base drop (placebo) every other day, the second group used dexamethasone drop for 3 months, and all patients were followed for 12 months.

Results: Control of vertigo and tinnitus with dexamethasone was more than the placebo, but there was no statistically significance difference between two groups ($P > 0.05$). Hearing function improvement and aural fullness resolution were higher in the placebo group, but there was no statistically significance difference, too ($P > 0.05$). Vertigo control in dexamethasone group in our study ranged from 72.2% to 83.3% of patients at different intervals. These figures ranged from 66.6% to 83.3% in placebo group. The highest rate of hearing function improvement in our study was 27.7% in placebo group. Tinnitus also followed the same pattern as hearing function.

Conclusions: Intratympanic dexamethasone for MD is very satisfactory if medical treatment fails with good vertigo control and no risk to hearing.

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Introduction

Meniere disease (MD) is a disorder the inner ear with a set of clinical features including fluctuating hearing loss, episodic vertigo, tinnitus, and aural fullness (1). MD is associated with endolymphatic hydrops with spinning and distention of the membranous, endolymph-containing parts of the labyrinthine system. The clinical features are subsequent to increased hydraulic pressure within the inner ear. This disease is idiopathic by definition but it is called MD in case of being secondary to various etiologies. These etiologies include trauma, endocrine abnormalities, electrolyte imbalances, autoimmune dysfunction, medication, parasitic infections, and hyperlipidemia (2-4).

The exact incidence of this condition is hard to establish but it is reported from 10 to 150/100000 persons (5). This condition usually occurs in patients between 20 and 40 years old. There is a positive family history in 20% of patients which can indicate the role of genetic predisposition. Uneven sexual distribution has not been reported in the literature (5,6).

Diagnosis of endolymphatic hydrops is established with clinical features (7). There is no specific test available for definite diagnosis of MD (8). All the patients with a history or clinical features indicating of MD should undergo neuro-otologic tests including pure tone audiometry (PTA)-tympanometry with acoustic reflex, auditory brainstem response, electronystagmography, and electrocochleography (9,10).

The treatment is focused on symptom alleviation and prevention of attacks. The majority of patients return to normal daily activities with medical management (11). Surgical treatment is reserved for refractory cases of MD (12,13). New techniques are evolving in the treatment of the disease including novel

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method for delivering medications with higher efficacy and less complications. One of the relatively new methods is intratympanic injection of medication (14). This method is conducted under local anesthesia. Advantages of intratympanic injection of steroids include less invasiveness, absence of systemic complications, providing the ability of prompt initiation of treatment, and higher concentration of steroids in comparison to oral or intramuscular ways of medication prescription. This technique is advised for patients who suffer from bilateral MD, who do not tolerate general anesthesia and who have good compliance for multiple sessions of injection (15). In this study, we evaluated the efficacy of intratympanic delivery of corticosteroids in intractable cases of MD through ventilation tube.

Materials and Methods

This was a single-blinded randomized clinical trial and was conducted from January 2013 through January 2014 in Tehran University of Medical Sciences (TUMS), Amiralam Hospital. All patients with MD were advised to have a low-sodium daily diet (daily intake of sodium equal to or < 1500 mg). Betahistine plus triamtrene-H was prescribed for all patients. On occasion, ant vertigo/antiemetic agents were used. This regimen was followed for 2 month. If improvement in symptoms did not occur, the patients were assigned as candidates for intratympanic delivery of corticosteroids. All candidates underwent ventilation tube insertion under local anesthesia in posterior-inferior quadrant of tympanic membrane. Patients were randomly allocated to two groups of 18-patients using block randomization. Patients of the first group used dexamethasone base drop (placebo) every other day, the second group used dexamethasone drop. All patients were unaware of the type of treatment and were blinded, but surgeon was not blinded. Subjects were instructed to be in the supine position with the head rotated 45° toward the contralateral side, keeping the treated ear up and not swallow for 20 minutes to assure enough time for the medication to be absorbed through round window niche. This process lasted for 3 months. Patients were evaluated on months 1, 3, 6, and 12 for recording possible improvements in symptoms.

Auditory tests were conducted in 500, 1000, 2000, and 4000 Hz frequencies for all patients. We considered 10 dB change in at least 2 frequencies in PTA and presence of vertigo as significant findings. For all patients, these parameters were measured just before treatment initiation and 12 months after treatment. All patients were asked about type, frequency and duration of vertigo. Tinnitus and aural fullness were recorded too. Informed consents were obtained from all patients, and the study was approved by the Ethics Committee of TUMS and the National Medical Ethics Committee considering the Declaration of Helsinki. SPSS software (Version 16; SPSS, Inc., Chicago, IL, USA) was used for data analysis.

Results

Patients were recruited for 3 months and after follow-up sessions, 36 patients completed the study in two 18-patient groups 16 patients (44.4%) were males while 20 patients (55.5%) were females. The most frequent age group in our study was 30-39 years group. The detailed information of sexual distribution, age distribution, and disease duration are presented in table 1.

Table 1. Basic characteristics of patients

Characteristics	N (%)
Gender	
Male	16 (44.4)
Female	20 (55.5)
Age (years)	
10-19	2 (5.5)
20-29	4 (11.1)
30-39	13 (36.1)
40-49	8 (22.2)
50-59	7 (19.4)
60-69	2 (5.5)
Disease duration	
0-1	12 (33.3)
1-2	8 (22.2)
2-3	6 (16.6)
3-4	3 (8.3)
4-5	3 (8.3)
> 5	4 (11.1)

Vertigo control: In placebo group, vertigo was controlled in 15 patients (83.3%) at the first month. In further evaluations 13 patients (72.2%), 12 patients (66.6%), and 12 patients (66.6%) were vertigo-controlled at months 3, 6, and 12, respectively. There was no case of vertigo worsening detected.

In dexamethasone group, vertigo was controlled in 15 patients (83.3%) at the first month. Next follow-ups showed 15 (83.3%), 16 (88.8%), and 13 (72.2%) vertigo-controlled patients at 3, 6, and 12 months, respectively. No case of vertigo worsening was detected. There was no statistically significant difference between two groups for vertigo control (all $P > 0.05$). Detailed information of vertigo presentation is presented in table 2.

Hearing improvement: In placebo group, hearing improved in 3 (16.6%), 3 (16.6%), 4 (22.2%), and 5 (27.7%) patients at months 1, 3, 6, and 12, respectively. In dexamethasone group, hearing improvement was seen in 2 (11.1%), 1 (5.5%), 4 (22.2%), and 4 (22.2%) patients at months 1, 3, 6, and 12, respectively. There was no significant difference seen in hearing improvement between two groups (all $P > 0.05$).

Table 2. Vertigo control in two placebo and dexamethasone groups

Variables	Dexamethasone group (months)				Placebo group (months)			
	1	3	6	12	1	3	6	12
A (%)	2 (11.1)	1 (5.5)	4 (22.2)	4 (22.2)	3 (16.6)	3 (16.6)	4 (22.2)	5 (27.7)
B1 (%)	11 (61.1)	12 (66.6)	8 (44.4)	5 (27.7)	6 (33.3)	7 (38.3)	4 (22.2)	4 (22.2)
B2 (%)	2 (11.1)	2 (11.1)	4 (22.2)	4 (22.2)	4 (22.2)	2 (11.1)	3 (16.6)	2 (11.1)
C (%)	0	0	0	0	2 (22.2)	1 (5.5)	1 (5.5)	1 (5.5)
D (%)	0	0	0	0	0	0	0	0
E (%)	3 (16.6)	3 (16.6)	2 (11.1)	5 (27.7)	3 (16.6)	5 (27.7)	6 (33.3)	6 (33.3)
F (%)	0	0	0	0	0	0	0	0

A: At least 10 dB improvement in comparison to the best hearing threshold before treatment + absence of recurrent vertigo; B1: No change in hearing threshold in comparison to the best hearing threshold before treatment + absence of recurrent vertigo; B2: Hearing threshold between the best and the worst hearing threshold before treatment + absence of recurrent vertigo; C: Hearing threshold equal to the worst hearing threshold before treatment + absence of recurrent vertigo; D: Hearing threshold worse than the worst hearing threshold before treatment + absence of recurrent vertigo; E: A or B criteria + recurrent vértigo; F: C or D criteria + recurrent vertigo

Tinnitus control: In placebo group, tinnitus improvement was in 1 patient (9%) and 1 patient (9%) at months 6 and 12, respectively. In dexamethasone group, improvement was seen in 1 (7.1%), 2 (14.2%), 2 (14.2%), and 4 (28.4%) patients at months 1, 3, 6, and 12, respectively. There was no significant difference in tinnitus control between two groups (all $P > 0.05$) (Table 3).

Aural fullness: In placebo group, aural fullness was decreased from 8 (100%) patients at baseline to 1 patient (12.5%) at month 12. In dexamethasone group, there was no aural fullness at month 12. There was no significant difference found between two groups for aural fullness ($P > 0.05$). Detailed information is seen at table 4.

Complications: There was just one case of chronic infection with tympanic membrane perforation without resolution after treatment, which was underwent tympanoplasty surgery.

Discussion

Our study showed that control of vertigo and tinnitus with dexamethasone was more than the placebo, but there was no statistically significance difference between two groups. Hearing function improvement and aural fullness resolution were higher in the placebo group, but there was no statistically significance difference, too.

The causes of MD are not thoroughly understood yet. Due to this lack of knowledge on definite underlying cause of the disease, various therapeutic approaches have developed including intratympanic steroid injection, intratympanic gentamicin injection, endolymph sac decompression, vestibular neurectomy, and labyrinthectomy surgery.

However, some reports have acclaimed the role of viral infections and autoimmune components in the MD development. The idea of immune basis of Meniere was first introduced by Ryan (16) afterward; there was a growing bulk of evidence indicating various aspects of autoimmune activity in MD. Reports of higher levels of antibodies against antigens of inner ear (6,17-21) and higher incidence of other autoimmune diseases in MD patients (22-24) emphasize the role of autoimmune processes in the development of MD. These pieces of evidence provide rationale for administration of steroids in the treatment of MD. Systemic steroids are used widely and easily but long-term complications raise concerns about abundant prescription of these agents for MD, so the idea of intratympanic delivery of steroids was developed. This method with the same basis was performed in different ways. Middle ear injection, labyrinth perfusion after myringotomy with laser and ventilation tube insertion have been some types of this method. Using intratympanic steroid in topical from through ventilation tube seems feasible and practical (25).

Vertigo control in dexamethasone group in our study ranged from 72.2% to 83.3% of patients at different intervals. These figures ranged from 66.6% to 83.3% in placebo group. Itoh and Sakata (26) found similar results with intratympanic injection of dexamethasone. A systematic review on efficacy of intratympanic steroids in controlling symptoms of MD reported that 90% improvement in vertigo symptom was seen (15).

Table 3. Tinnitus status in two groups of placebo and dexamethasone treatment

Variables	Dexamethasone group (months)				Placebo group (months)			
	1	3	6	12	1	3	6	12
None (%)	5 (27.7)	6 (33.3)	6 (33.3)	8 (44.4)	7 (38.8)	7 (38.8)	8 (44.4)	8 (44.4)
Mild (%)	8 (44.4)	7 (38.8)	9 (50)	7 (38.8)	5 (27.7)	8 (44.4)	8 (44.4)	8 (44.4)
Moderate (%)	5 (27.7)	4 (22.2)	1 (5.5)	2 (11.1)	6 (33.3)	3 (16.6)	2 (11.1)	2 (11.1)
Severe (%)	0	1 (5.5)	2 (11.1)	0	0	0	0	0
Worst attack ever (%)	0	0	0	1 (5.5)	0	0	0	0

Table 4. Aural fullness frequency in two groups of placebo and dexamethasone treatment

Parameter	Baseline	Dexamethasone group (months)				Baseline	Placebo group (months)			
		1	3	6	12		1	3	6	12
Frequency (%)	8 (100)	0	0	1 (12.5)	0	8 (100)	0	2 (25)	0Q	1 (12.5)

Montandon et al. (27) reported that ventilation tube decreased vertigo attacks from 71% to 11% with its placebo effect. This finding is consistent with our findings which strongly suggest placebo effect of ventilation tube insertion.

The highest rate of hearing function improvement in our study was 27.7% in placebo group. Our findings regarding hearing function improvement are not as high as previous studies. Shea and Ge (28) reported a 68% improvement in hearing; Silverstein et al. (29) also reported a 43% improvement rate. Garduno-Anaya et al. (30) findings are near our study with 35% improvement in hearing function. Tinnitus follows the same pattern; while in our study, tinnitus showed maximum improvement rate of 28.4%, other reports declare rates around 45-82 percent.

Conflict of Interests

Authors have no conflict of interests.

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