



## Our experiences on intratympanic dexamethasone usage to vertigo control in ménière disease

### Meniere hastalığında vertigo kontrolünde intra timpanik deksametazon kullanımı ile ilgili tecrübelerimiz

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#### Abstract

**Objective:** Ménière disease is a disorder defined with vertigo and disequilibrium attacks and followed by a considerable normal equilibrium until to the next vertigo attack. The frequency of these attacks changes not only patient to patient but also in particular patient himself/herself in varying degree. Although there are studies about intratympanic corticosteroid injection treatment for the disease in the literature, the long-term efficacy of this minimally invasive treatment modality is obscure regarding with this issue. In this study, we aimed to verify long-term results in the use of intratympanic dexamethasone in patients with Ménière disease.

**Materials and Methods:** This is a retrospective study that was performed in a tertiary referral center in which eleven patients with vertigo due to Ménière disease were evaluated. Intratympanic dexamethasone was infiltrated to diseased ear of these patients. The ratio between the number of vertigo episodes in the 6 months prior to treatment and the number of episodes in the six months between the 18th and 24th month after treatment (according to the norms of the American committee for the hearing and the equilibrium, 1995) were examined.

**Results:** All patients improved significantly. Treatment was repeated after one year in one of the patients.

**Conclusion:** Similarly with the published literature, the use of intratympanic dexamethasone may be useful to control vertigo due to Ménière disease to avoid or to be a prior step to other more invasive treatments.

**Keywords:** Intratympanic Dexamethasone; Ménière Disease; Vertigo.

#### Öz

**Amaç:** Ménière hastalığı vertigo ve denge bozukluğu ataklarını takiben yeni bir vertigo atağına kadar nispeten normal dengenin olduğu bir hastalık olarak açıklanmaktadır. Bu atakların sıklığı hastadan hastaya olduğu kadar, hastanın bizzat kendisinde de farklı derecelerde değişiklik gösterir. Literatürde bu hastalığın tedavisinde intratimpanik kortikosteroid enjeksiyonu tedavisi ile ilgili çalışmalar mevcut olmasına rağmen, bu konuyla ilgili olarak bu minimal invazif tedavinin uzun dönem faydası belirsizdir. Bu çalışmada Ménière hastalarına intratimpanik dexamethasone kullanımının uzun dönem sonuçlarını tetkik etmeyi amaçladık.

**Gereç ve Yöntemler:** Ménière hastalığına bağlı olarak vertigo şikayeti olan 11 hastanın değerlendirildiği bu retrospektif çalışma bir üçüncü basamak sağlık merkezinde yapılmıştır. Bu hastalarda, hasta olan kulağa intratimpanik dexamethasone enjeksiyonu uygulanmıştır. Tedavi öncesi 6 aylık dönemdeki vertigo ataklarının sayısı ile tedavi sonrası 18. ve 24. aylar arasındaki 6 aylık dönemdeki vertigo atakları sayısı arasındaki oran (Amerika İşitme ve Denge Komitesinin normlarına göre, 1995) değerlendirilmiştir.

**Bulgular:** Bütün hastalarda belirgin iyileşme elde edildi. Hastalardan birinde 1 yıl sonra tedavi tekrar edildi.

**Sonuç:** Literatür ile benzer olarak, intratimpanik dexamethasone kullanımı daha invazif tedavi yöntemlerinde bir önceki basamak olarak veya bunlardan kaçınmak için Ménière hastalığına bağlı vertigonun kontrolünde faydalı olabileceğini göstermektedir.

**Anahtar Kelimeler:** İntratimpanik Dexamethasone; Ménière Hastalığı; Vertigo.

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## INTRODUCTION

After McCabe determined the effect of steroid treatment of autoimmune inner ear diseases, there has been performed many studies about *Ménière* disease (MD) that is evidenced as an immune mediated disorder of endolymphatic sac (1-6). Experimental reports of corticosteroid receptors within the inner ear and histological changes to the stria vascularis by corticosteroids have confirmed an important role of corticosteroids in the inner ear physiology (7). These findings have provided important background to the belief of using systemic or intratympanic steroids to treat inflammatory inner ear conditions.

The drug transport from middle ear to inner ear is dependent on the semipermeable capability of the round window membrane. Other routes of admission include the annular ligament of oval window and the small lacunar mesh in the bone wall nearby the inner ear (8).

Intratympanic *dexamethasone* injection (ITDI) has been recommended in the literature as a safe and effective procedure to control of vertigo symptom in patients with MD, especially to those who failed to response to previous management with diuretics and low-salt diet (9). There are several articles on IT steroids for MD have been published exhibiting positive (10-13) or negative results (14-18), but, these studies are difficultly comparable for they differ from each other in terms of study design, dose of the drug used, protocol, and time of follow-up.

The aim of this study is to demonstrate the efficacy of intratympanic *dexamethasone* through an intratympanic injection in the control of vertigo attacks in patients suffering from unilateral MD as summarized by the American Academy of Otolaryngology–Head and Neck Surgery Committee on Hearing and Equilibrium in 1995 (AAO-HNS 1995) (19). ). In this study, we did not focus on the tinnitus and hearing loss before and after intratympanic injection.

## MATERIALS and METHODS

The retrospective research protocol was approved by the Local Ethic committee. A retrospective, minimum 2-year follow-up study was achieved between 2000 and November 2010. Patients with unilateral MD on the basis of the criteria of the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) (19) who failed to respond to previous medical treatment with diuretics (*Diazomid; asetazolamid 250 mg tb, Sanofi Aventis İlaçları Ltd.Şti, İstanbul, Türkiye*); betahistin (*Betaseric: betahistin HCL 24 mg tb, Abbott Laboratuvarları İthalat İhracat Tic. Ltd. Şti., Paris, France*); and low-salt diet for at least 6 months are included in current study. According to the diagnostic criteria of the AAO-HNS, we included to the study if the patients have 20 min or longer at least two spontaneous vertigo episodes, hearing loss, tinnitus or aural fullness, and if other causes were excluded. If the patient has central or

other vestibular disorder, middle ear diseases such as chronic otitis media or otosclerosis, bilateral *Meniere* diseases, previous intratympanic treatments or surgical treatment for vertigo excluded from the study. Complete otoneurological examination, caloric testing, audiogram, pure tone audiometry, impedance audiometry, speech discrimination scores, spontaneous nystagmus, head shaking test, and head impulse test were performed in all patients. Vertigo control was analyzed according to the AAO- HNS 1995 guidelines (class A-F) (19).

Under the otomicroscope, patients were placed in supine position with the head turned to the unaffected ear. Local anesthesia was achieved by filling the external ear canal with Emla cream (*Emla; lidocaine 2.5% and prilocaine 2.5%, AstraZeneca Türkiye ilaç San. Tic. Ltd. Şti., İstanbul, Türkiye*) for five minutes. Using a 22-gauge spinal needle and 2 ml syringe, *dexamethasone (Decort; 8 mg/2 ml, IM/IV, Deva Holding A.Ş., İstanbul, Türkiye)* was infiltrated through the posteroinferior part of the eardrum to fill the tympanic cavity. The infiltration was administered slowly; the patient was educated to stay in the supine position for one hour with no talking and swallowing as little as possible. Side effects were also recorded. The injection was repeated 3 times at intervals of every 3 days. After each day's procedure the patient returned to normal daily activities.

Response to treatment about vertigo control was evaluated clinically. The number of episodes among the 24 month of after treatment, comparing with the number of episodes before treatment (according to the norms of the AAO-HNS,1995) were analyzed.

### Statistical Analysis

Statistical Packages for the Social Sciences (SPSS) 18.0 (*IBM, New York, USA*) was used for statistical analysis of the gained data in current study. A Kaplan-Meier time-to-event method was used to evaluate the percentage of the subjects who had enough control of their vertigo over time after initial IT *dexamethasone* injection.

## RESULTS

Eleven patients, 7 women and 4 men, aged ranging between 19 and 58 years (mean age 40.9 years) participated in this study (table 1). Patients who are included in the study had neither previously experienced surgical treatment on the ear nor had any other drug infiltrated in the tympanic cavity. The *dexamethasone* injection was repeated 3 times at intervals of every 3 days. Follow-up period was at least 24 months in all patients.

Vertigo control required 3 *dexamethasone* infiltrations in 10 patients (90.9%), and 6 infiltrations were required in only one patient (9.09%) in the follow-up period. There was no need for an additional treatment to control vertigo attacks (e.g. sac decompression, vestibular nerve section) in any patients. No tympanic membrane, middle ear or drug complications were identified regarding with the procedure.

All of the patients stated that obvious improvement in their vertigo symptoms after the intratympanic treatment. Five patients (45%) expressed >90 benefit (A), while 1 patient (9%) stated ≥75 benefit (B), and 4

patients (36%) stated ≥40 benefit (C). In only one patient (9%) showed < 40 benefit (D) after the procedure, and the same procedure repeated in that patient (table 1).

**Table 1.** The patients underwent intratympanic dexamethasone injection treatment

Patient	Age	Sex	Number of injections	Number of vertigo attacks in the 6 month before treatment	Number of vertigo attacks between 18-24 months after treatments	Benefits ratio (%)	Class (Criteria of the AAO-HNS)
AM	35	M	3	2	1	50	C
YA	48	M	3	3	0	100	A
DD	47	F	3	3	0	100	A
SK	53	F	3	5	2	40	C
MC	30	M	3	4	1	75	B
AK	33	F	3	4	0	100	A
ZC	46	F	3	3	0	100	A
ZO	40	F	3	2	1	50	C
NK	19	F	3	3	1	66,6	C
FK	41	F	3	3	0	100	A
ANB	58	M	3 + 3	3	2	33,3	D

The criteria of the AAO-HNS is based on a ratio between the number of vertigo attacks in the 6 months prior to treatment and the number of episodes in the six months between the 18th and 24th month after treatment. According to this scale, five patients belonged to class A (complete control of the vertigo) and one to class B (important control of the vertigo).

## DISCUSSIONS

There is not a consensus about which treatment method and schedule is best to succeed vertigo control in MD. There are various results of ITDI in controlling vertigo and few studies focused on hearing recovery in MD. There are no studies comparing ITDI results to the natural history of MD. Itoh and Sakata (10) reported that after dexamethasone 2 mg (0.5 mL) injection for a total of 4 or 5 times at intervals of 1 or 2 weeks, vertigo attacks responded well in 49 of 61 patients (80%) according to the criteria of the AAO-HNS 1985. Shea (20) found that 96.4% improvement of vertigo at 1 year and 76% at 2 years of follow-up by perfusion plus intravenous and oral *dexamethasone*. Sennaroglu et al reported that 72% of vertigo control using *dexamethasone* in 3 months via a ventilation tube in patients with *Ménière* disease (21). Same author said that the ventilation tube insertion has only a placebo effect and his results are parallel to Montandon et al, who avoided in 71% the vertigo attacks and deducted the frequency in 11% with placed a ventilation tube on the tympanic membrane. Barrs showed a full recovery of vertigo in 52% of 21 patients with *Ménière* disease at 3 months of follow-up and 43% at 6 months of follow-up, secondary to intratympanic injection once a week for 4 consecutive weeks (15). We showed recovery in vertigo with same way in 74% only using intratympanic injections, without placing ventilation tube which is similar to the many results of the ITE in the literature.

Minimum 2-year follow-up is required for enough assessment of treatment efficacy according to the AAO-HNS 1995 guidelines in *Ménière* disease (19). By the

same way, Anaya et al said that the basis of the corticosteroid use is reduction of inflammation secondary to immune-mediated dysfunction (8). The response of systemic pharmacologic therapy agents depends upon the concentration that this dose modulates or alters only the vestibular neuroepithelium as it is known. It could impact improving symptom in a sustained form just by concentrating the *dexamethasone* solution (8). For example, one author found vertigo control in 90% of 60 patients with *Ménière* disease via 24 mg/ml *dexamethasone* doses. This is the best result with respect to controlling the recurrence of vertigo attacks in *Ménière* disease without significant secondary side effects (9). We used 4 mg/ml *dexamethasone* to control of vertigo attacks in our all patients.

We believe that the intratympanic approach is a simple, practical, and cheap method. Middle ear exploration or placing ventilation tube is not necessary if there is no pathologic middle ear like obstructed round window. Anaya et al said that for patients with obstructions, lysis of adhesions should be reserved, perhaps could be passed by the drug (8). We don't have any patient with middle ear pathology or complication such as tympanic membrane perforation, deterioration in vertigo secondary to injection way and doses, 4 mg/ml.

*Dexamethasone* is the most potent and the longest acting corticosteroid (8). The potential risks of systemic corticosteroids; in particular the risk of avascular necrosis of the femoral head, susceptibility to infection, diabetes, osteoporosis, peptic ulcer, ocular effects, and decreased wound healing. It seems reasonable that the intratympanic *dexamethasone* treatment avoids all troublesome secondary effects (22). Pharmacokinetic studies have revealed that *dexamethasone* applied to the round window will result in considerably higher drug levels in the inner ear fluids when compared with systemic delivery, clearly related with the benefit of the absence of many undesirable side effects or contraindications (23).

Our vertigo control result is not lower than the many outcomes of the endolymphatic sac surgery in the literature as like Jackson et al 46%, Silverstein et al 67%, Paparella and Sajjadi 70%, Portmann 77%, Soderman et al 82% (24). So we believe, as like Sennaroglu, the position of ITDE should be initiated before surgical treatment, because this method is the most practical, minimal invasive and ablative treatment. We think as like to Anaya et al, and Sennaroglu algorithm that initially should try to low salt-caffeine diet and conservative medical treatment should recommended in this patients (8, 24). After 6 months, if vertigo is continues, ITDE could be started; after 3 months, if there is vertigo, undergo ITGE. Patients with normal hearing ESD can be recommended. If ESD also fails in patients with normal hearing, vestibular nerve section may be advised.

## CONCLUSIONS

In this study we obtained a complete control of vertigo in 74% of subjects by intratympanic *dexamethasone* injection, for this reason we advise this method in the treatment of *Ménière's* disease, especially after the failure of low-salt and caffeine diet and use of conservative medical treatment such as vasodilators and diuretics before any surgical treatment. Because this method is a safe, practical, minimal invasive, and also this method avoids the side effects that is related with the use of systemic approach. Even though the follow-up period is long enough, the weakness of this study is the small number of cases. The following aim is going to be carried out a wide prospective study with more cases to offer clearer sign in favor of the use of this protocol.

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