

Review

Intratympanic corticosteroids in Ménière's disease: A mini-review

Mitesh Patel

Division of Brain Sciences, Imperial College London, Charing Cross Hospital, London, W6 8RF, UK

Received 9 April 2017; revised 27 May 2017; accepted 1 June 2017

Abstract

This article reviews the effectiveness of intratympanic corticosteroids for vertigo control in Ménière's disease at 2-years follow-up according to the guidelines expressed by the American Academy of Otolaryngology-Head & Neck Surgery. Despite the increased use of intratympanic corticosteroids for vertigo control in Ménière's disease there is debate as to their effectiveness, particularly compared to gentamicin. Even so, after just a single course of injections, corticosteroids can reliably provide complete vertigo control (Class A) at 2-years in about 50% of cases as indicated in a recent double-blind randomized controlled clinical trial (Patel et al., 2016). But the effectiveness of intratympanic corticosteroids truly increases when treatment is provided 'as-needed', whereby complete vertigo control is established in up to 91% of cases. On the basis of available literature, there is good evidence to recommend the use of intratympanic steroid treatment for vertigo control in Ménière's disease, but patients must be monitored for non-response. The rationale for treating patients as-needed and the possible reasons for corticosteroid non-response are discussed.

Copyright © 2017, PLA General Hospital Department of Otolaryngology Head and Neck Surgery. Production and hosting by Elsevier (Singapore) Pte Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Keywords: Ménière's disease; Intratympanic; Corticosteroid; Dexamethasone; Methylprednisolone

Contents

1. Introduction	117
2. Methods	118
3. Results	119
3.1. Barrs, 2004	119
3.2. Garduno-Anaya et al., 2005	119
3.3. Boleas-Aguirre et al., 2008	119
3.4. Herraiz et al., 2010	120
3.5. Casani et al., 2012	120
3.6. Martin-Sanz et al., 2013a,b	120
3.7. McRackan et al., 2014	120
3.8. She et al., 2015	120
3.9. Albu et al., 2016	120
3.10. Patel et al., 2016	120
3.11. Leng et al., 2017	121
4. Discussion	121
5. Conclusion	122

E-mail address: Mitesh.Patel1@imperial.ac.uk.

Peer review under responsibility of PLA General Hospital Department of Otolaryngology Head and Neck Surgery.

6. Conflicts of interest	122
Acknowledgments	122
References	122

1. Introduction

Ménière's disease is associated with unstable or fluctuating levels of hearing and vestibular function from a failure of one or more of the inner ear mechanisms regulating endolymph and perilymph, afferent and efferent nerve signaling, intercellular signaling, metabolism and blood flow (Rauch, 2016). Consequently, hearing and balance functions become susceptible to a range of internal and external factors, such as stress, poor diet, hormonal variations, and barometric pressure changes (Rauch, 2010).

The active periods of Ménière's disease tend to occur in clusters of 6–11 per year, although remission may last several months or years (Phillips and Westerberg, 2011). The characteristics of Ménière's disease are well documented: episodic attacks of vertigo, a fluctuating and progressive hearing loss, tinnitus and aural fullness, but the most disabling feature is vertigo (Söderman et al., 2002). Episodes of vertigo tend to occur with higher frequency in the first few years after presentation and then decrease (Moffat, 1997).

Clinically, episodic vertigo can be quelled or reduced through intratympanic therapy (Sajjadi and Paparella, 2008) which involves the injection of either gentamicin or (cortico) steroid through the tympanic membrane into the middle ear space. The drug is absorbed into the inner ear perilymph primarily through the semi-permeable round window membrane, but also via the oval window annular ligament and the small lacunar mesh surrounding the inner ear (Phillips and Westerberg, 2011). The delivery of intratympanic gentamicin in Meniere's disease has been proven to quell the frequency and severity of vertigo attacks (Pullens and van Benthem, 2011), but, since the effect relies on ototoxic properties, patients are left with a permanent vestibular deficit and about 20% of patients experience hearing loss. Poor compensation from the acute vestibular loss can also result in persistent disequilibrium and postural unsteadiness. Corticosteroid, which does not ablate inner ear function, is sometimes used as a substitute to gentamicin in Meniere's disease (Itoh and Sakata, 1991; Sakata et al., 1986), but its efficacy has been contested (for review see (Lavigne et al., 2016)). Steroids would be preferred by many patients because they have no side-effects and unlike gentamicin are suitable in bilateral disease - but their effects can be short-lived (Atrache Al Atrache et al., 2016), injections can be painful and a positive response depends upon an inflammatory etiology (McCabe, 1979). However, evidence supporting the use of steroids in Meniere's disease include increased immune complexes (Brookes, 1986), complement (Xenellis et al., 1986), positive response to antigens (Suzuki et al., 1997), local

inflammation and vascular events (Espinosa-Sanchez and Lopez-Escamez, 2016) and a higher prevalence of autoimmune symptoms (Gazquez et al., 2011) in Meniere's disease patients over controls.

Compared to systemic steroid administration, intratympanic steroid results in 260× higher levels of steroid in the perilymph (Bird et al., 2011) as it bypasses the blood labyrinthine barrier. Although the action of steroids on the inner ear remains speculative, it may involve anti-inflammatory effects, immunosuppression and/or ion homeostasis (Hamid and Trune, 2008) as glucocorticoid receptors are present in vast numbers in the vestibular and cochlear systems. Via these receptors, steroids affect thousands of genes (Fukushima et al., 2002) and influence aquaporins (Fukushima et al., 2002; Pondugula et al., 2004), a family of small trans-membrane water transporters which play a role in regulating inner ear fluids, blood flow (Shirwany et al., 1998) and the endocochlear potential (Hamid and Trune, 2008).

Given the ongoing debate as to intratympanic steroid use in Ménière's disease (Dodson et al., 2004; Doyle et al., 2004; Gabra and Saliba, 2013; Silverstein et al., 1998), herewith, I review published results on the effectiveness of intratympanic steroids in Meniere's disease for vertigo control. Only studies meeting 2-years follow-up are considered.

2. Methods

In March 2017, PubMed was searched for English-language studies with the terms “Ménière's disease”, “steroid”, “corticosteroid”, “methylprednisolone”, “dexamethasone” and “intratympanic”, meeting the criteria for definite Meniere's disease according to guidelines recommended by the American Academy of Otorhinolaryngology-Head and Neck Surgery and evaluation of treatment for at least 2-years (AAO-HNS, 1995). Definite Ménière's disease was two or more episodes of vertigo lasting 20-min or longer, significant unilateral sensorineural hearing loss, and either tinnitus or aural fullness after ruling out other otological or central conditions. Patients were unresponsive to conventional treatment (i.e., dietary/oral) for at least six months previous. Studies were not restricted to randomized controlled trials, blinded studies or unilaterality. However, only studies using the American Academy of Otorhinolaryngology-Head and Neck Surgery guidelines for reporting vertigo control (1995) at 2-years were considered.

The primary outcome measure was the percentage of patients with Class A vertigo control where the number of attacks of vertigo are categorized into Classes A–F: Complete

Control (A), Substantial Control (B), Limited Control (C), Insignificant Control (D), Worse Control (E) and Secondary treatment required (F) with the following formula:

$$\frac{\text{average number of attacks per month in the final six months of treatment}}{\text{average number of vertigo attacks per month for the six months before treatment}} \times 100$$

where, 0 = Complete Control, 1–40 = Substantial Control, 41–80 Limited Control, 81–120 Insignificant Control and >120 Worse Control of vertigo. Studies in which results are only available for Class A + Class B vertigo control have been marked as such.

3. Results

Twelve studies fulfilled inclusion criteria. As shown in Table 1, the median percentage of patients with complete (Class A) control after intratympanic steroids at 2-years was 71.7 (IQR 42.5–81.0%). Eight studies used an ‘as-needed’ protocol, but the number of injections for one course and drug concentration varied considerably. An as-needed protocol tended to be more beneficial than single-treatment, but figures for vertigo control varied. A brief description of each study is given below.

3.1. Barrs, 2004

In a retrospective study of 34 Ménière's disease patients after 4 consecutive weekly injections of dexamethasone,

complete vertigo control was achieved at 2-years in 8/34 patients (24%). Eighteen patients (53%) had no control of vertigo, as deemed by a relapse of vertigo or switching to

intratympanic gentamicin treatment after relapse. One patient experienced an improvement in hearing after dexamethasone, scoring better in speech discrimination than before treatment but there were no mean changes for hearing. Two patients experienced tympanic perforation after injection.

3.2. Garduno-Anaya et al., 2005

Garduno-Anaya and colleagues compared intratympanic dexamethasone (n = 11) to placebo (n = 11) over 2-years. The treatment protocol was one injection for five days at baseline. There was a significant improvement in complete vertigo control (dexamethasone: 82% vs. placebo: 57% achieving Class A), subjective functional level (90 vs. 42% achieving Level 1) and drop in dizziness handicap inventory scores (60.4 vs. 41.3 points) in the dexamethasone group over placebo. No patient in the dexamethasone group was deemed a treatment failure, whereas 5/11 patients were deemed failures in the placebo group. There was an improvement in subjective hearing in the dexamethasone group over controls (100% vs. 35%) but no difference for objective hearing measured with

Table 1

Summary of studies meeting inclusion criteria on the effectiveness of intratympanic steroid injections in Ménière's disease over 2-years. Class A (complete) vertigo control was used as the primary outcome in this Review.

Study	Steroid type	Conc. (mg/ml)	Treatment protocol	Further injections offered 'as-needed'	Study type	Sample size for steroid arm	Percentage of patients with Class A vertigo control (%)
Barrs, 2004	Dex	10	1 injection for 4 consecutive weeks	Yes	Retrospective	34	24
Garduno-Anaya et al., 2005	Dex	4	1 injection daily for 5 consecutive days	No	Prospective	11	82
Boleas-Aguirre et al., 2008	Dex	12	1 injection	Yes	Retrospective	129	91 ^a
Herraiz et al., 2010	Methylpred	40	1 injection for 3 consecutive days	Yes	Prospective	29	78
Casani et al., 2012	Dex	4	1 injection over 3 consecutive days	Yes	Prospective	28	43
Martin-Sanz et al., 2013a	Dex	4	1 injection weekly for 3 consecutive weeks	No	Prospective	53	15.1
Martin-Sanz et al., 2013b	Dex	4	1 injection daily for 3 consecutive days or 1 injection for 3 consecutive weeks	No	Retrospective	22/34	40.9/44.1
McRackan et al., 2014	Dex	24	1 injection, 3 doses delivered 10 min s apart	Yes	Retrospective	159	81.1 ^b
She et al., 2015	Methylpred	20	1 injection over 10 consecutive days	No	Retrospective	16	81
Albu et al., 2016	Dex	4	1 injection over 3 consecutive days or 1 injection over 3 consecutive days + high-dose betahistine	Yes	Prospective	32/30	44/73.3
Patel et al., 2016	Methylpred	62.5	1 injection fortnightly (1 course = 2 injections)	Yes	Prospective	30	70
Leng et al., 2017	Dex	5	1 injection for 4 consecutive days, over 4 consecutive weeks	Yes	Retrospective	23	73.9

Dex = Dexamethasone; Methylpred = Methylprednisolone.

^a No further treatments were needed or asked for.

^b Vertigo control outcome was customized (Class A + Class B control), but the study was of sufficient quality to merit inclusion.

pure-tone audiometry or speech discrimination. Although there was a subjective improvement in tinnitus (48%) and aural fullness (48%) in the dexamethasone group, there was no difference between groups for tinnitus handicap inventory scores or grading of tinnitus severity.

3.3. *Boleas-Aguirre et al., 2008*

In a retrospective study of intratympanic dexamethasone delivered as-needed in 129 Ménière's disease patients over 2-years, vertigo control (meaning no further treatments were needed or asked for) was achieved in 117/129 (91%) patients. A single injection of dexamethasone was required in 48 cases (37%), two injections in 26 cases (20%), three injections in 18 cases (14%), four injections in 15 cases (21%) and more than four injections in 15 cases (21%). Twelve patients were dissatisfied and opted for intratympanic gentamicin treatment. Of these 12 failures, 9 switched to gentamicin within the first 6-months after baseline treatment. Hearing was unchanged after intratympanic dexamethasone.

3.4. *Herraiz et al., 2010*

The effectiveness of intratympanic methylprednisolone in 29 Ménière's disease patients was studied prospectively after 3 consecutive daily injections at baseline and thereafter as-needed. Seventy-eight percent of cases (22/29) were free of vertigo (Class A vertigo control), and 96% had none or 1 spell at 2-years. Because of relapsing vertigo, 12 patients (35.2%) required re-treatment over the 2-year period. Two patients (6.25%) required intratympanic gentamicin after experiencing no vertigo control (at 14 and 18-months). There was no overall effect of methylprednisolone on hearing but tinnitus relief was achieved in 78% of the patients. Two patients experienced tympanic perforation after injection. Burning and pain after injection were minimal and lasted no more than 2-h.

3.5. *Casani et al., 2012*

In an open-label, randomized trial comparing intratympanic dexamethasone (n = 28) to gentamicin (n = 32) over 2-years, Casani and colleagues treated unilateral Ménière's disease patients with 3 injections over consecutive days (one course). Thereafter, patients with relapsing vertigo were offered further intratympanic treatment (i.e., as-needed). The authors found that complete vertigo control (Class A) after intratympanic dexamethasone was achieved in 12/28 patients (43%) and good control in 5 patients (18%) at 2-years. Four dexamethasone patients received two courses (14.3%) and 5 dexamethasone patients received three courses (17.9%). Two dexamethasone patients experienced no vertigo control and were switched to intratympanic gentamicin. Gentamicin established complete vertigo control in 26/32 (81%) of cases. There were no changes to pure-tone hearing or speech discrimination after intratympanic dexamethasone, but there

was a significant loss in speech discrimination in the gentamicin group.

3.6. *Martin-Sanz et al., 2013a,b*

Martin-Sanz conducted a prospective study on the effectiveness of one intratympanic dexamethasone injection delivered for three consecutive weeks at baseline in 53 Ménière's disease patients. At 2-years, complete control (Class A) was achieved in 15.1% and an overall level of good control (Class A + B) in 32.1% (*Martin-Sanz et al., 2013a*). However, a retrospective study of patients by the same authors after 1 dexamethasone injection for 3 consecutive days (n = 22) or 1 dexamethasone injection for 3 consecutive weeks (n = 34) showed complete control at 2-years in 40.9 and 44.1% respectively (*Martin Sanz et al., 2013b*).

3.7. *McRackan et al., 2014*

McRackan and colleagues conducted a ten-year retrospective study of 159 Ménière's disease patients treated with intratympanic dexamethasone after 3-perfusions, 10-min apart, at baseline and then delivered as-needed i.e., if symptoms worsened or persisted patients were re-treated. Overall, 129/159 patients (81.1%) experienced complete or good vertigo control (Classes A + B) at 2-years follow-up. Most symptoms were abated with five or fewer treatments (73.6%) and for each treatment there was a 20% decrease in the likelihood of further treatment. Only one treatment was needed in 24.5% of patients. One patient required tympanoplasty following tympanic membrane perforation. The outcome measure in this study did not distinguish between Class A and Class B control, but because there is sufficient clarity and quality, the study has been included in this Review.

3.8. *She et al., 2015*

She and colleagues conducted a 2-year retrospective analysis of 16 Ménière's disease patients after intratympanic methylprednisolone delivered once daily for 10 consecutive days at baseline (10 injections). Complete vertigo control (Class A) was achieved at 2-years in 13/16 (81%) cases. Two patients continued to experience severe vertigo episodes and switched to intratympanic gentamicin treatment at 12 and 18-months. One patient experienced tympanic membrane perforation four years after treatment but there were no other adverse events. There was no significant change in hearing after intratympanic methylprednisolone and 2/16 patients (12%) experienced a reduction in tinnitus. No patient experienced a worsening of tinnitus. Functional activity scores improved after treatment by 87% over 2-years.

3.9. *Albu et al., 2016*

In a comparative effectiveness study between intratympanic dexamethasone delivered once on three consecutive days and

intratympanic dexamethasone with daily high dose betahistine (144 mg/day), complete vertigo control (Class A) for the steroid only group was achieved in 14/32 (44%) patients whereas combined steroid and betahistine therapy achieved complete vertigo control in 22/30 (73.3%) at 2-years. Substantial vertigo control or better (Class A + B) was indicated in 21/32 patients (65.6%) in the single therapy group and in 27/30 patients (90%) in the combined therapy group. Injections were repeated as-needed. In the intratympanic steroid group, 5 patients received one additional injection (15%) and 6 patients (18%) received two additional injections. In the combined intratympanic steroid and betahistine group, 4 patients received one additional injection (12%) and 3 patients received two additional injections (10%). One patient from both groups experienced no control of vertigo and both were subsequently scheduled for intratympanic gentamicin. Hearing and tinnitus were unchanged. Functional level scores mimicked the level of vertigo control.

3.10. Patel et al., 2016

Intratympanic methylprednisolone (n = 30) was compared to intratympanic gentamicin (n = 30) in a double-blind, controlled, randomized comparative effectiveness study over 2-years. Unilateral Ménière's disease patients were treated at baseline with two injections and thereafter further courses were given as-needed. In the methylprednisolone group, complete vertigo control (Class A) was achieved in 21/30 patients (70%) compared to 25/30 (83.3%) in the gentamicin group. After methylprednisolone, 22 patients (73.3%) experienced an improved Functional Level score and 8 patients (26.7%) better pure-tone hearing and speech discrimination. There were also reductions for tinnitus, dizziness and aural fullness. Fifteen patients (50%) required further courses of methylprednisolone. Two patients were deemed treatment failures and were assigned intratympanic gentamicin treatment. The study showed no significant difference between the methylprednisolone and gentamicin for the control of vertigo, total number of injections, number of patients with relapsing vertigo or for the amount of pain from injection but better speech discrimination after methylprednisolone. Two patients in the methylprednisolone group experienced post-injection ear infections.

3.11. Leng et al., 2017

Leng and colleagues conducted a retrospective study of intratympanic dexamethasone in 51 MD patients delivered at baseline and then as-needed. One complete course was four injections administered on a weekly basis for 4 consecutive weeks (16 injections). Twenty-three Ménière's disease patients were followed-up for at least 2-years (24–77 months). At 2-years, 17/23 (73.9%) achieved complete vertigo control (Class A). Eleven patients (21%) required re-treatment and three patients failed to respond to intratympanic dexamethasone. Hearing was unchanged but there was a dramatic improvement in Functional Level scores (from mean 5 to 2).

4. Discussion

Although poorly understood, inflammatory and autoimmune processes appear to be linked to the development of Meniere's disease (Gazquez et al., 2011; Greco et al., 2012; Riente et al., 2004). Support for this is the successful reduction of vertigo and hearing symptoms after steroid treatment. However, for a subset of patients, steroid offers no relief and this has led to debate as to its overall effectiveness. Results here (see Table 1) support the use of intratympanic steroid for vertigo control in Ménière's disease, especially when delivered as-needed (median 71.7% complete control). Moreover, steroid injections as-needed seem to be equally effective to gentamicin for vertigo control in unilateral Ménière's disease (Patel et al., 2016; Sennaroglu et al., 1999), but because steroid is non-ablative, it could be considered first-choice for many patients.

Due to the fluctuating nature of symptoms and poor understanding of disease etiology, treatment of Meniere's disease is challenging. This is further complicated by data showing that vertigo resolves in 57% of patients after 2-years and 71% after 8-years with the disease (Silverstein et al., 1989). Moreover, as bilateral involvement increases with disease progression, ablative treatment must be given with caution. However, until recently, only ablative treatment had been proven to achieve significant vertigo control under strict scientific conditions. A randomized double-blind clinical trial has now shown that intratympanic steroid can fulfill this requirement especially when patients are treated as-needed (Patel et al., 2016), a result that is supported by other non-controlled studies (e.g., Boleas-Aguirre et al., 2008; McRackan et al., 2014). This finding is particularly welcome because intratympanic steroid carries few adverse effects and Cochrane Reviews have found insufficient evidence to support the use of betahistine (James and Burton, 2001), diuretics (Thirlwall and Kundu, 2006), positive pressure treatment (van Sonsbeek et al., 2015) or endolymphatic sac surgery (Pullens et al., 2013). The below discusses the rationale for treating patients with intratympanic steroid as-needed and the possible reasons for non-response.

As can be seen in Table 1, the reported success of intratympanic steroid for vertigo control in Meniere's disease varies widely, presumably because the benefits of steroid are temporary and relatively short-lived (Miller and Agrawal, 2014). Crucially, patients with an autoimmune variant of the disease are likely to respond better to steroid treatment. Remarkably, this subgroup of Meniere's disease patients is one of five identified (Frejo et al., 2016, 2017). Despite this, one course of intratympanic steroid quells vertigo episodes over 2-years in about 25–50% of patients (Barrs, 2004; McRackan et al., 2014; Patel et al., 2016). However, in some patients, intratympanic steroid treatment must be repeated but the response to treatment seems to improve with each further injection (McRackan et al., 2014) and may provide complete control of vertigo in up to 91% of cases at 2-years. Rather than a one-off treatment like intratympanic gentamicin, intratympanic steroid appears to be more effectively delivered as-needed.

Reasons for having to repeat steroid injections could include low steroid concentration or lower overall cumulative dosage. Indeed, there seems to be a trend between higher steroid concentration or dosing and the percentage of patients with complete vertigo control, a finding that has been pointed out previously (Albu et al., 2015). One of the best results was shown by Hamid (Hamid and Trune, 2008), who after treating patients with 24 mg/ml dexamethasone, found complete vertigo control and hearing improvement in 90% of Ménière's patients at 2-years, with no significant side-effects. Similarly, Shea and Ge (Shea and Ge, 1996) delivered dexamethasone in a combination of intratympanic, intravenous and oral forms in 28 Ménière's disease patients which established complete vertigo control in 63% of patients, reduced dizziness in 96.4% and improved hearing in 35%. Although these results support the conclusion that a high dose of steroid is effective, the optimal treatment protocol is yet to be properly established. This is a challenging task because there is considerable variation in symptoms across patients and over time, but more concerning is the subset of patients who do not respond to treatment at all. With numerous homeostatic mechanisms required for normal ear function (Trune and Canlon, 2012) and five disease subtypes (Frejo et al., 2016, 2017), it is not so surprising that steroid does not work for all cases of Ménière's disease. Many channels within the inner ear linked to the production of hydrops (Salt and Plontke, 2010) are influenced by steroids other than glucocorticoids (Trune, 2010), indicating a self-limiting sensitivity to corticosteroid treatment. Another consideration is that about 25–35% of migrainers experience episodic attacks of vertigo (Kayan and Hood, 1984) and sensorineural hearing loss (Lee et al., 2000), which could cloud the diagnosis of Ménière's disease. Furthermore, the prevalence of migrainous vertigo in Ménière's disease is as high as 31% (Wladislavosky-Waserman et al., 1984; Shin et al., 2013), which may bias a patient's assessment of disease-related vertigo attacks.

The need for further injections would normally be considered a drug failure under the American Academy's criteria (AAO-HNS, 1995), but as steroid treatment is accepted to be short-lasting, these criteria have to be adjusted. The results of recent studies in Ménière's disease have accommodated for this problem by stating the number of re-injections, number of patients changing treatment (failures) and the class of vertigo control without regard to re-treatment. In the case of intratympanic steroid, the reasons to continue with treatment may include reduction in the frequency or severity of vertigo attacks, reduced aural fullness or tinnitus, risk of hearing loss or disequilibrium from other therapies or bilateral involvement. Repeated injections of steroid may seem disadvantageous due to the burden of possible relapse, especially compared to intratympanic gentamicin (Boleas-Aguirre et al., 2008). However, a significant proportion (22%) of patients treated with intratympanic gentamicin require further injections to control vertigo (Minor, 1999), and in a double-blind randomized controlled trial comparing intratympanic steroid to gentamicin, the number of patients requiring further injections and the overall number of injections was not significantly

different between treatment groups (Patel et al., 2016). A second consideration is the type of steroid. Methylprednisolone is considered superior to dexamethasone as peak concentrations are higher and remain within the perilymph for longer (Parnes et al., 1999). But data in this Review suggest that both methylprednisolone and dexamethasone are equally effective.

This Review has limitations. The main focus of this Review was the percentage of patients with Class A vertigo control. Although Class B vertigo control may be adequate to some patients, it may still be very debilitating for others. Hearing outcomes were not addressed in this Review, but no study showed a significant drop in hearing after steroid.

The beneficial effects of steroid treatment in Ménière's disease were not limited to studies meeting inclusion criteria for this Review. Various studies did not meet the full 2-years follow-up (Hirvonen et al., 2000; Paragache et al., 2005; Ren et al., 2015) or the AAO-HNS guidelines for reporting vertigo control (AAO-HNS, 1995) but showed successful control of vertigo after intratympanic steroid. An example is a recent study by Atrache Al Attrache et al. (2016), which showed a dramatic reduction in the number of vertigo spells after intratympanic dexamethasone over 2-years. Furthermore, in a particularly elegant study, steroid treatment alongside endolymphatic sac shunting established complete control of vertigo in 93% of cases at 18-months (Wick et al., 2017). Steroid also appears to abate drop attacks. In a crucial retrospective study, Liu et al. (2016) investigated whether intratympanic dexamethasone (delivered once a week for 4 consecutive weeks) is effective in the treatment of drop attacks in Ménière's disease. Remarkably, the authors showed that 6/7 patients experienced total abolition of drop attacks after either just a single course (5 patients) or after two (1 patient). Although one patient experienced no improvement, this finding is particularly important because drop attacks can cause serious injury and the current gold-standard treatment is aggressive intratympanic gentamicin or vestibular nerve section.

5. Conclusion

If Ménière's disease patients continue to experience attacks of vertigo despite dietary management or oral medication, intratympanic steroid may be used as an as-needed therapy. With steroid, there is little risk of hearing loss, chronic symptoms of dizziness resulting from the fixed vestibular loss or adverse events. As many patients with Ménière's disease are frail or experience anxiety that complicates ablative therapy, intratympanic steroid is an excellent option. That said, clinicians must decide the appropriate treatment in concordance with the patient's expectation as intratympanic steroid treatment may need to be repeated periodically.

Conflicts of interest

The author has no conflicts of interest.

Acknowledgments

This study was supported by the National Institute for Health Research (NIHR) Imperial Biomedical Research Centre. The views expressed are those of the author and not necessarily those of the NIHR.

References

- AAO-HNS, 1995. Committee on hearing and equilibrium guidelines for the diagnosis and evaluation of therapy in Ménière's disease. American Academy of Otolaryngology-Head and Neck Foundation, Inc Otolaryngol. Head. Neck Surg. 113 (3), 181–185.
- Albu, S., Chirtes, F., Trombitas, V., Nagy, A., Marceanu, L., Babighian, G., Trabalzini, F., 2015. Intratympanic dexamethasone versus high dosage of betahistine in the treatment of intractable unilateral Ménière disease. Am. J. Otolaryngol. 36 (2), 205–209.
- Albu, S., Nagy, A., Doros, C., Marceanu, L., Cozma, S., Musat, G., Trabalzini, F., 2016. Treatment of Ménière's disease with intratympanic dexamethasone plus high dosage of betahistine. Am. J. Otolaryngol. 37 (3), 225–230.
- Atrache Al Atrache, N., Krstulovic, C., Pérez Guillen, V., Morera Pérez, C., Pérez Garrigues, H., 2016. Response over time of vertigo spells to intratympanic dexamethasone treatment in Ménière's disease patients. J. Int. Adv. Otol. 12 (1), 92–97.
- Bars, D.M., 2004. Intratympanic injections of dexamethasone for long-term control of vertigo. Laryngoscope 114 (11), 1910–1914.
- Bird, P.A., Murray, D.P., Zhang, M., Begg, E.J., 2011. Intratympanic versus intravenous delivery of dexamethasone and dexamethasone sodium phosphate to cochlear perilymph. Otol. Neurotol. 32 (6), 933–936.
- Boleas-Aguirre, M.S., Lin, F.R., Della Santina, C.C., Minor, L.B., Carey, J.P., 2008. Longitudinal results with intratympanic dexamethasone in the treatment of Ménière's disease. Otol. Neurotol. 29 (1), 33–38.
- Brookes, G.B., 1986. Circulating immune complexes in Ménière's disease. Arch. Otolaryngol. Head. Neck Surg. 112 (5), 536–540.
- Casani, A.P., Piaggi, P., Cerchiai, N., Seccia, V., Franceschini, S.S., Dallan, I., 2012. Intratympanic treatment of intractable unilateral Ménière disease: gentamicin or dexamethasone? A randomized controlled trial. Otolaryngol. Head. Neck Surg. 146 (3), 430–437.
- Dodson, K.M., Woodson, E., Sismanis, A., 2004. Intratympanic steroid perfusion for the treatment of Ménière's disease: a retrospective study. Ear Nose Throat J. 83 (6), 394–398.
- Doyle, K.J., Bauch, C., Battista, R., Beatty, C., Hughes, G.B., Mason, J., Maw, J., Musiek, F.L., 2004. Intratympanic steroid treatment: a review. Otol. Neurotol. 25 (6), 1034–1039.
- Espinosa-Sanchez, J.M., Lopez-Escamez, J.A., 2016. Ménière's disease. Handb. Clin. Neurol. 137, 257–277.
- Frejo, L., Soto-Varela, A., Santos-Perez, S., Aran, I., Batuecas-Caletrio, A., Perez-Guillen, V., Perez-Garrigues, H., Fraile, J., Martin-Sanz, E., et al., 2016. Clinical subgroups in bilateral Ménière disease. Front. Neurol. 7, Article 182.
- Frejo, L., Martin-Sanz, E., Teggi, R., Trinidad, G., Soto-Varela, A., Santos-Perez, S., Manrique, R., Perez, N., Aran, I., et al., 2017. Extended phenotype and clinical subgroups in unilateral Ménière disease: a cross-sectional study with cluster analysis. Clin. Otolaryngol. <http://dx.doi.org/10.1111/coa.12844> (in press).
- Fukushima, M., Kitahara, T., Uno, Y., Fuse, Y., Doi, K., Kubo, T., 2002. Effects of intratympanic injection of steroids on changes in rat inner ear aquaporin expression. Acta Otolaryngol. 122 (6), 600–606.
- Gabra, N., Saliba, I., 2013. The effect of intratympanic methylprednisolone and gentamicin injection on Ménière's disease. Otolaryngol. Head. Neck Surg. 148 (4), 642–647.
- Garduño-Anaya, M.A., Couthino De Toledo, H., Hinojosa-González, R., Panebianese, C., Ríos-Castañeda, L.C., 2005. Dexamethasone inner ear perfusion by intratympanic injection in unilateral Ménière's disease: a two-year prospective, placebo-controlled, double-blind, randomized trial. Otolaryngol. Head. Neck Surg. 133 (2), 285–294.
- Gazquez, I., Soto-Varela, A., Aran, I., Santos, S., Batuecas, A., Trinidad, G., Perez-Garrigues, H., Gonzalez-Oller, C., Acosta, L., Lopez-Escamez, J.A., 2011. High prevalence of systemic autoimmune diseases in patients with Ménière's disease. PLoS One 6 (10), e26759.
- Greco, A., Gallo, A., Fusconi, M., Marinelli, C., Macri, G.F., de Vincentiis, M., 2012. Ménière's disease might be an autoimmune condition? Autoimmun. Rev. 11 (10), 731–738.
- Hamid, M., Trune, D., 2008. Issues, indications, and controversies regarding intratympanic steroid perfusion. Curr. Opin. Otolaryngol. Head. Neck Surg. 16 (5), 434–440.
- Herraiz, C., Plaza, G., Aparicio, J.M., Gallego, I., Marcos, S., Ruiz, C., 2010. Transtympanic steroids for Ménière's disease. Otol. Neurotol. 31 (1), 162–167.
- Hirvonen, T.P., Peltomaa, M., Ylikoski, J., 2000. Intratympanic and systemic dexamethasone for Ménière's disease. ORL J. Otorhinolaryngol. Relat. Spec. 62 (3), 117–120.
- Itoh, A., Sakata, E., 1991. Treatment of vestibular disorders. Acta Otolaryngol. Suppl. 481, 617–623.
- James, A.L., Burton, M.J., 2001. Betahistine for Ménière's disease or syndrome. Cochrane Database Syst. Rev., CD001873, 1.
- Kayan, A., Hood, J.D., 1984. Neuro-otological manifestations of migraine. Brain 107 (Pt 4), 1123–1142.
- Lavigne, P., Lavigne, F., Saliba, I., 2016. Intratympanic corticosteroids injections: a systematic review of literature. Eur. Arch. Otorhinolaryngol. 273 (9), 2271–2278.
- Lee, H., Lopez, I., Ishiyama, A., Baloh, R.W., 2000. Can migraine damage the inner ear? Arch. Neurol. 57 (11), 1631–1634.
- Leng, Y., Liu, B., Zhou, R., Liu, J., Liu, D., Zhang, S.L., Kong, W.J., 2017. Repeated courses of intratympanic dexamethasone injection are effective for intractable Ménière's disease. Acta Otolaryngol. 137 (2), 154–160.
- Liu, B., Leng, Y., Zhou, R., Liu, J., Liu, D., Zhang, S.L., Kong, W.J., 2016. Intratympanic steroids injection is effective for the treatment of drop attacks with Ménière's disease and delayed endolymphatic hydrops: a retrospective study. Medicine (Baltimore) 95 (52), e5767.
- Martin-Sanz, E., Luzardo, C.Z., Riesco, L.R., Patino, T.M., Sanz, R., 2013a. The use of electrocochleography to monitor the response of Ménière's disease patients to intratympanic steroids. Acta Otolaryngol. 133 (11), 1158–1164.
- Martin Sanz, E., Zschaeck, C., Christiane, Z.L., Gonzalez, M., Manuel, G.J., Mato, T., Rodríguez, L., Barona, R., Sanz, R., 2013b. Control of vertigo after intratympanic corticoid therapy for unilateral Ménière's disease: a comparison of weekly versus daily fixed protocols. Otol. Neurotol. 34 (8), 1429–1433.
- McCabe, B.F., 1979. Autoimmune sensorineural hearing loss. Ann. Otol. Rhinol. Laryngol. 88 (5 Pt 1), 585–589.
- McRackan, T.R., Best, J., Pearce, E.C., Bennett, M.L., Dietrich, M., Wanna, G.B., Haynes, D.S., Labadie, R.F., 2014. Intratympanic dexamethasone as a symptomatic treatment for Ménière's disease. Otol. Neurotol. 35 (9), 1638–1640.
- Miller, M.W., Agrawal, Y., 2014. Intratympanic therapies for Ménière's disease. Curr. Otorhinolaryngol. Rep. 2 (3), 137–143.
- Minor, L.B., 1999. Intratympanic gentamicin for control of vertigo in Ménière's disease: vestibular signs that specify completion of therapy. Am. J. Otol. 20 (2), 209–219.
- Moffat, D.A., 1997. Endolymphatic mastoid shunt surgery in unilateral Ménière's disease. Ear Nose Throat J. 76 (9), 642–643, 647–648, 650–641.
- Paragache, G., Panda, N.K., Rangunathan, M., Sridhara, 2005. Intratympanic dexamethasone application in Ménière's disease-Is it superior to conventional therapy? Indian J. Otolaryngol. Head. Neck Surg. 57 (1), 21–23.
- Parnes, L.S., Sun, A.H., Freeman, D.J., 1999. Corticosteroid pharmacokinetics in the inner ear fluids: an animal study followed by clinical application. Laryngoscope 109 (7 Pt 2), 1–17.
- Patel, M., Agarwal, K., Arshad, Q., Hariri, M., Rea, P., Seemungal, B.M., Golding, J.F., Harcourt, J.P., Bronstein, A.M., 2016. Intratympanic methylprednisolone versus gentamicin in patients with unilateral Ménière's

- disease: a randomised, double-blind, comparative effectiveness trial. *Lancet* 388 (10061), 2753–2762.
- Phillips, J.S., Westerberg, B., 2011. Intratympanic steroids for Ménière's disease or syndrome. *Cochrane Database Syst. Rev.*, CD008514, 7.
- Pondugula, S.R., Sanneman, J.D., Wangemann, P., Milhaud, P.G., Marcus, D.C., 2004. Glucocorticoids stimulate cation absorption by semicircular canal duct epithelium via epithelial sodium channel. *Am. J. Physiol. Ren. Physiol.* 286 (6), F1127–F1135.
- Pullens, B., van Benthem, P.P., 2011. Intratympanic gentamicin for Ménière's disease or syndrome. *Cochrane Database Syst. Rev.*, CD008234, 3.
- Pullens, B., Verschuur, H.P., van Benthem, P.P., 2013. Surgery for Ménière's disease. *Cochrane Database Syst. Rev.*, CD005395, 2.
- Rauch, S.D., 2010. Clinical hints and precipitating factors in patients suffering from Meniere's disease. *Otolaryngol. Clin. North Am.* 43 (5), 1011–1017.
- Rauch, S.D., 2016. Ménière's disease: damaged hearing but reduced vertigo. *Lancet* 388 (10061), 2716–2717.
- Ren, H., Yin, T., Lu, Y., Kong, W., Ren, J., 2015. Intratympanic dexamethasone injections for refractory Meniere's disease. *Int. J. Clin. Exp. Med.* 8 (4), 6016–6023.
- Riente, L., Bongiorno, F., Nacci, A., Migliorini, P., Segnini, G., Delle Sedie, A., Ursino, F., Tommasi, S., Fattori, B., 2004. Antibodies to inner ear antigens in Meniere's disease. *Clin. Exp. Immunol.* 135 (1), 159–163.
- Sajjadi, H., Paparella, M.M., 2008. Meniere's disease. *Lancet* 372 (9636), 406–414.
- Sakata, E., Kitago, Y., Murata, Y., Teramoto, K., 1986. Treatment of Ménière's disease. Middle ear infusion with lidocaine and steroid solution. *Auris Nasus Larynx* 13 (2), 79–89.
- Salt, A.N., Plontke, S.K., 2010. Endolymphatic hydrops: pathophysiology and experimental models. *Otolaryngol. Clin. North Am.* 43 (5), 971–983.
- Sennaroglu, L., Dini, F.M., Sennaroglu, G., Gursel, B., Ozkan, S., 1999. Transtympanic dexamethasone application in Ménière's disease: an alternative treatment for intractable vertigo. *J. Laryngol. Otol.* 113 (3), 217–221.
- She, W., Lv, L., Du, X., Li, H., Dai, Y., Lu, L., Ma, X., Chen, F., 2015. Long-term effects of intratympanic methylprednisolone perfusion treatment on intractable Ménière's disease. *J. Laryngol. Otol.* 129 (3), 232–237.
- Shea, J.J., Ge, X., 1996. Dexamethasone perfusion of the labyrinth plus intravenous dexamethasone for Ménière's disease. *Otolaryngol. Clin. North Am.* 29 (2), 353–358.
- Shin, J.E., Kim, C.H., Park, H.J., 2013. Vestibular abnormality in patients with Meniere's disease and migrainous vertigo. *Acta Otolaryngol.* 133 (2), 154–158.
- Shirwany, N.A., Seidman, M.D., Tang, W., 1998. Effect of transtympanic injection of steroids on cochlear blood flow, auditory sensitivity, and histology in the guinea pig. *Am. J. Otol.* 19 (2), 230–235.
- Silverstein, H., Isaacson, J.E., Olds, M.J., Rowan, P.T., Rosenberg, S., 1998. Dexamethasone inner ear perfusion for the treatment of Meniere's disease: a prospective, randomized, double-blind, crossover trial. *Am. J. Otol.* 19 (2), 196–201.
- Silverstein, H., Smouha, E., Jones, R., 1989. Natural history vs. surgery for Meniere's disease. *Otolaryngol. Head. Neck Surg.* 100 (1), 6–16.
- Suzuki, M., Krug, M.S., Cheng, K.C., Yazawa, Y., Bernstein, J., Yoo, T.J., 1997. Antibodies against inner-ear proteins in the sera of patients with inner-ear diseases. *ORL J. Otorhinolaryngol. Relat. Spec.* 59 (1), 10–17.
- Söderman, A.C., Bagger-Sjöbäck, D., Bergenius, J., Langius, A., 2002. Factors influencing quality of life in patients with Ménière's disease, identified by a multidimensional approach. *Otol. Neurotol.* 23 (6), 941–948.
- Thirlwall, A.S., Kundu, S., 2006. Diuretics for Ménière's disease or syndrome. *Cochrane Database Syst. Rev.*, CD003599, 3.
- Trune, D.R., 2010. Ion homeostasis in the ear: mechanisms, maladies, and management. *Curr. Opin. Otolaryngol. Head. Neck Surg.* 18 (5), 413–419.
- Trune, D.R., Canlon, B., 2012. Corticosteroid therapy for hearing and balance disorders. *Anat. Rec. (Hoboken)* 295 (11), 1928–1943.
- van Sonsbeek, S., Pullens, B., van Benthem, P.P., 2015. Positive pressure therapy for Ménière's disease or syndrome. *Cochrane Database Syst. Rev.*, CD008419, 3.
- Wick, C.C., Manzoor, N.F., McKenna, C., Semaan, M.T., Megerian, C.A., 2017. Long-term outcomes of endolymphatic sac shunting with local steroids for Meniere's disease. *Am. J. Otolaryngol.* 38 (3), 285–290.
- Wladislawosky-Waserman, P., Facer, G.W., Mokri, B., Kurland, L.T., 1984. Meniere's disease: a 30-year epidemiologic and clinical study in rochester, mn, 1951–1980. *Laryngoscope* 94 (8), 1098–1102.
- Xenellis, J., Morrison, A.W., McClowskey, D., Festenstein, H., 1986. HLA antigens in the pathogenesis of Ménière's disease. *J. Laryngol. Otol.* 100 (1), 21–24.