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Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)
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Are intratympanic corticosteroids effective for Ménière's disease?

Authors: Ángela Chuang-Chuang**[1,2]**, María A Baeza**[2,3]**

Affiliation:
[1] Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile
[2] Proyecto Epistemonikos, Santiago, Chile
[3] Departamento de Otorrinolaringología, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

E-mail: angelesbaezaa@gmail.com

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Abstract

Ménière's disease affects the inner ear and its main symptoms are vertigo, hearing loss and fluctuating aural symptoms. Nowadays, there are many therapeutic alternatives, being the use of intratympanic corticosteroids one that has become popular. To answer this question, we searched in Epistemonikos database, which is maintained by screening multiple databases. We identified four systematic reviews including 15 studies overall, of which seven were randomized trials. We extracted data and generated a summary of findings table using the GRADE approach. We concluded intratympanic corticosteroids probably do not decrease tinnitus, and might not decrease vertigo, hearing loss or aural fullness sensation in Ménière's disease. Intratympanic corticosteroids probably do not cause important adverse effects.

Problem

Ménière's disease affects the inner ear and it is characterized by episodes of recurrent vertigo, fluctuating sensorineural hearing loss and aural symptoms (such as tinnitus and aural fullness), being its main characteristic the fluctuation of its symptoms [1],[2]. The objective of the treatment is to reduce the intensity of the cardinal symptoms, to decrease the number of acute vertigo crises and to prevent the progression of the disease. Nowadays there are many therapeutic alternatives, including dietary sodium restriction, antivertiginous drugs, diuretics, intratympanic injection of drugs and even surgery. There is no consensus regarding the best intervention, nonetheless, one of the alternatives that has gained popularity in the last years is the injection of intratympanic corticosteroids [1].

Ménière's disease is supposed to be an immunological disorder of the endolymphatic sac, with mechanisms involved at many levels. In this way, the injection of corticosteroids would have a role when absorbed towards the perilymph [1]. Its advantage would be achieving a higher concentration of corticosteroids in the inner ear, and avoiding adverse effects associated to systemic use. Also, it is a procedure that can be performed in an ambulatory setting [1]. However, there is a low risk of persistent tympanic perforation, dysgeusia, vertigo and pain; the latter two are generally self-limited [3].

Methods

We used Epistemonikos database, which is maintained by screening multiple databases, to identify systematic reviews and their included primary studies. With this information we generated a structured summary using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

Key messages
- Intratympanic corticosteroids might not decrease vertigo, hearing loss nor aural fullness sensation in Ménière's disease, but the certainty of this evidence is low.
- Intratympanic corticosteroids probably do not decrease tinnitus in Ménière's disease.
- Intratympanic corticosteroids probably do not cause important adverse effects.

About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	We found four systematic reviews [1],[4],[5],[6] that include 15 primary studies reported in 17 references [7],[8],[9],[10],[11],[12],[13],[14],[15],[16],[17],[18],[19],[20],[21], among them seven randomized controlled trials [7],[8],[10],[11],[12],[13],[14], from which four compare the intervention against placebo or no treatment, which correspond to the question of this summary [7],[8],[12],[13]. This table and the summary in general are based on the latter.
What types of patients were included	The four trials included patients with the diagnosis of Ménière's disease with failure to medical treatment. The diagnostic criteria of the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) for the diagnosis of definite Ménière's disease were used in two trials [8],[12]. None of the systematic reviews specified the criterion used for the remaining two trials [7],[12].
What types of interventions were included	The trials assessed intratympanic injection of dexamethasone in different protocols: • Dexamethasone 4 mg/ml in one injection and dexamethasone 12 mg/ml in one injection [7] • Dexamethasone 4 mg/ml in one daily injection for five consecutive days [8] • Dexamethasone 8 mg/ml in one injection daily for three days [12] (none of the reviews provided data regarding the interval between injections) • Dexamethasone 0.2 mg/ml [13], (none of the reviews provided data regarding the interval between injections) Three trials compared against intratympanic injection of placebo [7],[8],[12] and one against medical treatment [13].
What types of outcomes were measured	The outcomes where grouped as follows: • Vertigo • Hearing loss • Tinnitus • Aural fullness • Adverse effects of treatment • Other outcomes: electrophysiological study with electronystagmography, extratympanic electrocochleography and visual analogue scale for pain.

Summary of findings

The information regarding the effects of intratympanic corticosteroids in Ménière's disease is based on four randomized trials that include 126 patients [7],[8], [12],[13]. All of the trials reported vertigo, hearing loss and tinnitus. Aural fullness was reported only by one trial [13] and the adverse effects were reported in two trials [7],[8].
The summary of findings is the following:

- Intratympanic corticosteroids might not decrease vertigo in Ménière's disease, but the certainty of the evidence is low.
- Intratympanic corticosteroids might not decrease hearing loss in Ménière's disease, but the certainty of the evidence is low.
- Intratympanic corticosteroids might not decrease aural fullness sensation in Ménière's disease, but the certainty of the evidence is low.
- Intratympanic corticosteroids probably do not decrease tinnitus in Ménière's disease. The certainty of the evidence is moderate.

- Intratympanic corticosteroids probably do not cause important adverse effects. The certainty of the evidence is moderate.

Intratympanic Corticosteroids in Ménière's disease		
Patients	Ménière's disease with failure to medical treatment without history of surgery or corticosteroid treatment	
Intervention	Intratympanic injection of corticosteroids	
Comparison	Intratympanic injection of placebo or medical treatment	
Outcomes	**Effects**	**Certainty of the Evidence (GRADE)**
Vertigo	Three trials did not find differences in the control of vertigo [13], the reduction of number of days of vertigo per month [7] or electronistagmography [12]. Nevertheless, one trial [8] evidenced differences in the control of vertigo, with 82% (with corticosteroids) versus 57% (without corticosteroids) achieving Class A (complete control). This same trial showed greater decrease in the Dizziness Handicap Inventory (DHI) * score in the corticosteroids group.	⊕⊕◯◯ [1,2,3] Low
Hearing loss	No trial found differences in hearing loss measured with pure tone average [8], [12] or with speech discrimination [8], [12], [13] **. One trial [8] showed benefit of intratympanic corticosteroids in the subjective perception of hearing loss, with improvement in 35% of the patients (with corticosteroids) versus 10% (without corticosteroids).	⊕⊕◯◯ [1,2,3] Low
Aural fullness	One trial [12] did not show difference in aural fullness sensation.	⊕⊕◯◯ [1,3] Low
Tinnitus	None of the four trials [7], [8], [12], [13] found differences in the control of tinnitus. This was measured with the Tinnitus Handicap Inventory (THI)* in two trials [7], [8] and the modality of measurement was not specified in the other two [12], [13].	⊕⊕⊕◯ [1,2] Moderate
Adverse effects of treatment	The information about adverse effects identified in the trials is imprecise and inconsistent; one trial [8] did not report adverse effects or complications from the treatment, and other trial [7] reported a total of eight tympanic perforations among which only one did not resolve by the end of the trial. However, there is abundant evidence that supports its safety in other contexts [5].	⊕⊕⊕◯ [4] Moderate

GRADE: evidence grades of the GRADE Working Group (see later in this article).

* Dizziness Handicap Inventory (DHI) and Tinnitus Handicap Inventory (THI) are questionnaires that measure the degree of disability caused by vertigo and tinnitus respectively. Both consist of 25 questions with scores of 0, 2 or 4 points, being 0 points the minimum score (no perceived disability) and 100 points the maximum (maximum perceived disability).

**For one trial [7], it was not specified in the systematic reviews how the hearing loss was measured.

[1] Three of the four trials had low risk of bias and one had important limitations. The certainty of the evidence was not reduced for this factor given that it probably does not influence the conclusions, except for the aural fullness outcome which is only reported in one trial with high risk of bias.
[2] The certainty of evidence was reduced for inconsistency, because the trials reached very different conclusions.
[3] The certainty of evidence was reduced for imprecision. Although a meta-analysis could not be conducted, the total number of patients is limited.
[4] The certainty of the evidence was reduced for indirect evidence, since it comes from other conditions.

About the certainty of the evidence (GRADE)*

⊕⊕⊕⊕
High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕◯
Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate

⊕⊕◯◯
Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕◯◯◯
Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.
† Substantially different = a large enough difference that it might affect a decision.

Other considerations for decision-making

To whom this evidence does and does not apply

- This evidence applies to patients with Ménière's disease with failure to medical treatment.
- It does not apply to patients with Ménière's disease who have received previous surgical or corticosteroid treatment.

About the outcomes included in this summary

- The outcomes selected for this summary correspond to those that have more impact in the therapeutic decision-making and in the quality of life of patients, according to the opinion of the authors.

Balance between benefits and risks, and certainty of the evidence

- It is an intervention with uncertain benefits, but on the other side the adverse effects or complications secondary to the treatment are not severe (risk of residual tympanic perforation which generally resolves spontaneously).
- It is not possible to adequately balance the benefits and risks because of the existing uncertainty.

What would patients and their doctors think about this intervention

- Based on the evidence presented in this summary, most patients and clinicians should be inclined against its use.
- Nonetheless, taking into account the lack of better therapeutic alternatives in patients with failure to medical treatment, it is expected that those doctors or patients who value more the possible benefit, although small, would incline in favor of the intervention. Those who value more the certainty of the evidence, the costs or the possible risks, possibly would lean against its use.

Resource considerations

- Even though it is a procedure that requires little time and can be performed in an outpatient context, the costs can be high because it is conducted by a specialist, repeatedly, and supplies are needed.
- It is not possible to provide an adequate costs/benefit balance given the existing uncertainty.

Differences between this summary and other sources

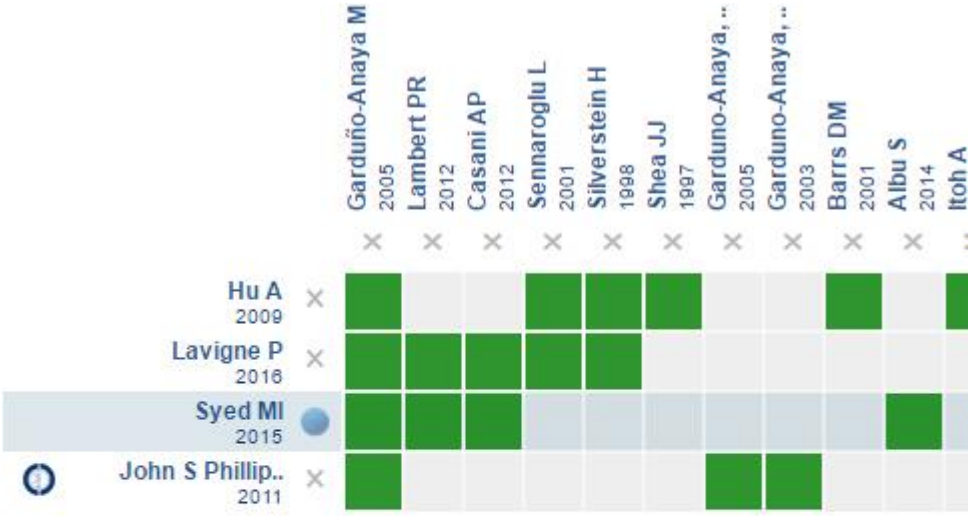
- The different reviews identified differ in their conclusions. Two reviews conclude it could be beneficial on some outcomes [4],[6], other propose it could be beneficial but the evidence is limited [1] and other concludes it is not possible to draw conclusions given the low quality of the evidence [5].
- We did not identify relevant clinical practice guidelines in this area.

Could this evidence change in the future?

- The probability that the evidence presented in this summary changes with future evidence is high given the existing uncertainty.
- We did not identify published trials not included in the analized reviews, but there is an ongoing systematic review that will evaluate the multiple existing treatments in these patients, which could provide relevant information [22].

How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database.
The author of the matrix can select relevant information for a specific health question (typically in PICO format) in order to display the information set for the question.
The *rows* represent systematic reviews that share at least one primary study, and *columns* display the studies.
The boxes in green correspond to studies included in the respective reviews.

Follow the link to access the **interactive version:** Intratympanic steroids for Ménière's disease

Notes

The upper portion of the matrix of evidence will display a warning of "new evidence" if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier. After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

The details about the methods used to produce these summaries are described here http://dx.doi.org/10.5867/medwave.2014.06.5997.

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database (www.epistemonikos.org).

These summaries follow a rigorous process of internal peer review.

Conflicts of interest
The authors do not have relevant interests to declare.

Referencias

1. Phillips JS, Westerberg B. Intratympanic steroids for Ménière's disease or syndrome. Cochrane Database Syst Rev. 2011 Jul 6;(7):CD008514 | CrossRef |
2. Lopez-Escamez JA, Carey J, Chung WH, Goebel JA, Magnusson M, Mandalà M, et al. [Diagnostic criteria for Menière's disease. Consensus document of the Bárány Society, the Japan Society for Equilibrium Research, the European Academy of Otology and Neurotology (EAONO), the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) and the Korean Balance Society]. Acta Otorrinolaringol Esp. 2016 Jan-Feb;67(1):1-7 | CrossRef | PubMed |

3. González R, Caro J. Corticoides intratimpánicos: una revisión sistemática. Rev. Otorrinolaringol. Cir Cabeza Cuello [online]. 2007;67(2):178-185 | CrossRef |
4. Syed MI, Ilan O, Nassar J, Rutka JA. Intratympanic therapy in Meniere's syndrome or disease: up to date evidence for clinical practice. Clin Otolaryngol. 2015 Dec;40(6):682-90 | CrossRef | PubMed |
5. Hu A, Parnes LS. Intratympanic steroids for inner ear disorders: a review. Audiol Neurootol. 2009;14(6):373-82 | CrossRef | PubMed |
6. Lavigne P, Lavigne F, Saliba I. Intratympanic corticosteroids injections: a systematic review of literature. Eur Arch Otorhinolaryngol. 2016 Sep;273(9):2271-8 | CrossRef | PubMed |
7. Lambert PR, Nguyen S, Maxwell KS, Tucci DL, Lustig LR, Fletcher M, et al. A randomized, double-blind, placebo-controlled clinical study to assess safety and clinical activity of OTO-104 given as a single intratympanic injection in patients with unilateral Ménière's disease. Otol Neurotol. 2012 Sep;33(7):1257-65 | CrossRef | PubMed |
8. Garduño-Anaya MA, Couthino De Toledo H, Hinojosa-González R, Pane-Pianese C, Ríos-Castañeda LC. 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. 2005 Aug;133(2):285-94 | PubMed |
9. Barrs DM, Keyser JS, Stallworth C, McElveen JT Jr. Intratympanic steroid injections for intractable Ménière's disease. Laryngoscope. 2001 Dec;111(12):2100-4 | PubMed |
10. Casani AP, Piaggi P, Cerchiai N, Seccia V, Franceschini SS, Dallan I. Intratympanic treatment of intractable unilateral Meniere disease: gentamicin or dexamethasone? A randomized controlled trial. Otolaryngol Head Neck Surg. 2012 Mar;146(3):430-7 | CrossRef | PubMed |
11. Sennaroglu L, Sennaroglu G, Gursel B, Dini FM. Intratympanic dexamethasone, intratympanic gentamicin, and endolymphatic sac surgery for intractable vertigo in Meniere's disease. Otolaryngol Head Neck Surg. 2001 Nov;125(5):537-43 | PubMed |
12. Silverstein H, Isaacson JE, Olds MJ, Rowan PT, Rosenberg S. Dexamethasone inner ear perfusion for the treatment of Meniere's disease: a prospective, randomized, double-blind, crossover trial. Am J Otol. 1998 Mar;19(2):196-201 | PubMed |
13. Paragache G, Panda NK, Ragunathan M, Sridhara. Intratympanic dexamethasone application in Meniere's disease-Is it superior to conventional therapy? Indian J Otolaryngol Head Neck Surg. 2005 Jan;57(1):21-3 | CrossRef | PubMed |
14. Albu S, Chirtes F, Trombitas V, Nagy A, Marceanu L, Babighian G, et al. Intratympanic dexamethasone versus high dosage of betahistine in the treatment of intractable unilateral Meniere disease. Am J Otolaryngol. 2015 Mar-Apr;36(2):205-9 | CrossRef | PubMed |
15. Itoh A, Sakata E. Treatment of vestibular disorders. Acta Otolaryngol Suppl. 1991;481:617-23 | PubMed |
16. Boleas-Aguirre MS, Lin FR, Della Santina CC, Minor LB, Carey JP. Longitudinal results with intratympanic dexamethasone in the treatment of Ménière's disease. Otol Neurotol. 2008 Jan;29(1):33-8 | CrossRef | PubMed |
17. Barrs DM. Intratympanic injections of dexamethasone for long-term control of vertigo. Laryngoscope. 2004 Nov;114(11):1910-4 | PubMed |
18. Hillman TM, Arriaga MA, Chen DA. Intratympanic steroids: do they acutely improve hearing in cases of cochlear hydrops? Laryngoscope. 2003 Nov;113(11):1903-7 | PubMed |
19. Sennaroğlu L, Dini FM, Sennaroğlu G, Gursel B, Ozkan S. Transtympanic dexamethasone application in Ménière's disease: an alternative treatment for intractable vertigo. J Laryngol Otol. 1999 Mar;113(3):217-21 | PubMed |
20. Arriaga MA, Goldman S. Hearing results of intratympanic steroid treatment of endolymphatic hydrops. Laryngoscope. 1998 Nov;108(11 Pt 1):1682-5 | PubMed |
21. Shea JJ Jr. The role of dexamethasone or streptomycin perfusion in the treatment of Meniere's disease. Otolaryngol Clin North Am. 1997 Dec;30(6):1051-9 | PubMed |
22. van Esch BF, van der Zaag-Loonen HJ, Bruintjes TD, van Benthem PP. Interventions for Menière's disease: protocol for an umbrella systematic review and a network meta-analysis. BMJ Open. 2016 Jun 9;6(6):e010269 | CrossRef | PubMed |

Author address:
[1] Facultad de Medicina
Pontificia Universidad Católica de Chile
Diagonal Paraguay 476
Santiago Centro
Chile.