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Review

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

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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.

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

Contents

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

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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 Attrache 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

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