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Instrumental head impulse test changes after intratympanic gentamicin for unilateral definite Ménière's disease: A systematic review and meta-analysis

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ABSTRACT

Objective: To estimate how much could intratympanic gentamicin (ITG) interfere with the vestibular-ocular reflex (VOR) parameters on instrumental head impulse test (HIT), either with scleral search coil or video head impulse test and, eventually, foresee the control of vertigo crisis in unilateral intractable Ménière's disease (MD).

Methods: A literature search was conducted in PubMed, Scopus, Web of Science and Cochrane search engines. The search terms used were "vestibular ocular reflex", "head impulse test", "gentamicin," and "Meniere's disease". Limitations included text availability to be full text, species to be humans and language to be English. All study types were included. 89 articles were screened identifying four eligible studies were identified. Studies were included after consensus of the authors. Meta-analysis was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Data was analysed using Review Manager software.

Results: Instrumental HIT, after ITG for MD, demonstrated, in the treated ear, a decreased gain in the horizontal, posterior and superior semicircular canals (SCC), of 0.36 (0.26; 0.47; 95% CI), 0.35 (0.22; 0.48; 95% CI) and 0.28 (0.21; 0.35; 95% CI), respectively. Gain asymmetry increases between the treated and non-treated ear of 23.78 (7.22; 40.35; 95% CI), 32.01 (12.27; 51.76; 95% CI) and 17.49 (9.99; 24.99; 95% CI), were similarly detected in the horizontal, posterior and superior SCC, respectively. Significantly smaller gain values after the first treatment were observed for a single injection group versus multiple injection group in the horizontal ($p = 0.002$) and superior SCCs ($p = 0.016$).

Conclusions: Instrumental HIT is effective in evaluating the SCC function after ITG for intractable unilateral MD. VOR gain changes in the direction of the treated ear in the three SCC have been clearly registered. An increased reduction of the VOR gain in the horizontal and anterior SCC also seemed to foresee the control of vertigo crisis. Still, after meta-analysis, the small number of patients' data available did not allow to define a treatment end-point value. This review also indicated that further and better-designed studies are warranted.

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1. Introduction

Ménière's disease (MD) is characterized by episodic vertigo associated with low/medium-frequency sensorioneural hearing loss and fluctuating symptoms – hearing loss, tinnitus, pressure and/or fullness – in the afflicted ear [1]. So far, the precise ethiopathogenesis remains unclear and the current therapy aims to control the symptoms of the condition, namely the severity and frequency of the vertigo attacks. Despite the large number of studies available, an effective evidence-based medical therapy has yet to be established [2–4].

Intratympanic administration of aminoglycosides, such a gentamicin, has been considered an effective and economical approach for the treatment of medically intractable MD, aiming to control vertigo attacks on the basis of a partial/total ablation of the vestibular end-organ [5,6]. However, the precise mechanism underlying aminoglycosides in the control of vertigo and the optimal dose remain unclear [7]. As with any other ototoxic drug, an excessive dose or a particularly aggressive administration protocol will induce potentially harmful and not totally predictable cochleotoxic and vestibulotoxic side effects [8]. Distinct protocols have been tried in an effort to achieve the best control of vertigo against the least damage to the hearing, but there is currently no widely accepted standardized procedure.

The vestibular response change after treatment has been used in some protocols to try to identify the end-of-treatment point, as well as the probability in obtaining a complete control of the vertigo. For those purposes different methods have been tried: bedside vestibular signs [9], caloric tests [10], vestibular evoked myogenic potentials [11,12] and video head impulse test (vHIT) [13].

The evaluation of semicircular canal (SCC) function has been traditionally performed by caloric tests since Robert Barany seminal studies, in 1914. More recently, the head impulse test (HIT), introduced in 1988 by Curthoys and Halmagyi, has also consistently proved to be an effective tool in this domain [14]. The ocular response to a sudden and abrupt head impulse, with an high acceleration, in particular when the very initial response (<100 ms) is analyzed, is an expression of the correct function of the vestibular receptors in the ampulla of the specific SCC, in the plane of the stimulus [15]. In that circumstance the saccadic system and the smooth-pursuit are not fully available to compensate for the retinal position error [16]. This makes HIT a pure test of the angular vestibular ocular reflex (VOR). When analyzing this response with either video-based (vHIT) or scleral search coils (SSC) systems, a precise and detailed measurement of the vestibular function can thus be undertaken and registered [15]. In recent times vHIT has been taking over the caloric test as the first test for patients with suspected vestibular disorders [17,18]. It is fast, innocuous, repeatable and provides objective quantitative data about each of the SCC [16].

Considering that intratympanic gentamicin (ITG) administration acts mainly by cell damage in the peripheral vestibular receptor [19,20], it is thus predictable to produce changes in VOR. This appears to be consistently evaluated by vHIT, in which changes in the function of the horizontal SCC canal and its inherent relation to the control of vertigo crises have been reported, namely when VOR gains are considered [13].

Against this background, it seemed desirable to evaluate the current status of medical literature in regard to a diagnostic tool, which may define objectively, the end-point dose for this vestibulotoxic treatment and therefore reduce the risk of overtreatment with undesirable cochleotoxic consequences.

The aim was to determine how much could ITG interfere with the VOR parameters on instrumental HIT, either with SSC or vHIT and, eventually, foresee the control of vertigo crisis. Taking into consideration the limited number of studies on the analysis of the parameters of instrumental HIT, the technique of meta-analysis was employed to try to better assimilate the results from the selected studies.

2. Material and methods

A literature search using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [21] was performed independently by two authors (PM and JS) to identify all studies that evaluated, in an instrumental fashion, the head impulse test (SSC and vHIT) after intratympanic gentamicin for uncontrolled unilateral definite MD.

The subject headings, "vestibular ocular reflex", "head impulse test", "gentamicin," and "Meniere's disease" were entered into PubMed, Scopus, Web of Science and Cochrane search engines in different combinations. Search was limited to English language studies. Inclusion criteria included all types of studies. Further inclusion criteria included: patients with definitive diagnosis of MD using, when possible, the 1995 American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) criteria [22]; patients who failed conventional therapy (dietary modification, diuretics and beta-histine) and patients who had not received other surgical intervention or invasive procedures besides ITG were included.

The publications' abstracts were reviewed, and those fulfilling the criteria were obtained and its references further reviewed to identify other relevant articles. The outcome measures examined included: vestibular ocular reflex gains (defined as the ratio of eye velocity to head impulse velocity [14]), gain asymmetry, control of vertigo crisis. The mean, standard deviation, and range were recorded for each parameter. Each selected article was assigned a level of evidence by two of the authors (PM, JS) using guidelines published by the Oxford University Centre for Evidence-Based Medicine (CEBM) (http://www.cebm.net). Any dispute in the assignment of the levels was resolved after discussion and mutual agreement.

2.1. Statistical analysis

Statistical evidence of effects is presented as described in the original studies. We compared the groups using random effects meta-analysis weighted by the mean difference of individual studies to estimate the global mean difference and 95% confidence intervals (95% CI). When testing a hypothesis about continuous variables, nonparametric tests were used as

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