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Presumed reduction of vestibular function in unilateral Menière's disease with aminoglycoside eardrops

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Abstract

We report the first case in the world literature of deliberate ablation of vestibular function in unilateral Menière's disease with aminoglycoside eardrops (Garasone).

These findings give conclusive proof that Garasone eardrops, and by implication, all topical aminoglycoside ear drops can be vestibulotoxic in the presence of a tympanic membrane defect. The lower concentration of gentamicin in Garasone, in comparison to the standard intratympanic preparations for chemical ablation of vestibular function, may also offer a reduction in the potential risk of cochleotoxocity.

Key words: Aminoglycosides; Menière's disease; Vertigo; Disease management

Introduction

Incapacitating vertigo is the most disabling symptom of Menière's disease. Ablation of vestibular function in the affected ear offers an effective means of controlling this symptom in patients with unilateral disease who have remained refractory to conservative management.

The technique of intratympanic instillation of aminoglycosides as a treatment for unilateral Menière's disease has evolved since Schuknecht first described it in 1957 (Schuknecht, 1957). Streptomycin successfully abolished vestibular function but was found to be highly cochleotoxic. In 1978, the first report of intratympanic gentamicin as a method of controlling vertigo was published (Beck and Schmidt, 1978) and subsequent studies have documented the efficacy of this procedure (Moller *et al.*, 1988; Lange, 1989; Yamazaki *et al.*, 1991; Nedzelski *et al.*, 1993; Rauch and Oas, 1997). Intratympanic gentamicin is also associated with the risk of sensorineural hearing loss and the trend recently is more conservative with instillations of gentamicin separated by one to two weeks in order to limit the risk of this complication (Driscoll *et al.*, 1997).

There have been very few cases of ototoxicity from aminoglycoside eardrops reported in the English literature with most focussing on the incidence of sensorineural hearing loss (Tommerkup and Moller, 1984; Lind and Kristiansen, 1986; Podoshin *et al.*, 1989; Hui *et al.*, 1997). However, the vestibulotoxic nature has not been well investigated even though gentamicin is the active ingredient in many of these preparations. More recently, increasing evidence has been put forward of vestibulotoxicity induced by aminoglycoside eardrops in the presence of tympanic membrane perforations (Longridge, 1994; Wong and Rutka, 1997; Marais and Rutka, 1998).

This report describes a case of chemical ablation of vestibular function using topical Garasone drops via a ventilation tube in a patient with unilateral Menière's disease.

Case report

A 49-year-old woman presented with a two-year history of intermittent vertigo with episodes lasting for 30 minutes or longer. The attacks were associated with decreased hearing, increased tinnitus and a feeling of pressure affecting her right ear. Between these episodes, she had a continuous feeling of unsteadiness and light-headedness.

Examination showed normal tympanic membranes. Cranial nerve and cerebellar function was fully intact. She had normal Romberg's, Unterberger's and heel-toe gait tests. There was no evidence of nystagmus and smooth pursuit was normal, as were saccadic eye movements. The Halmagyi head thrust test and the headshake test were normal. The Hallpike positional test was normal and hyperventilation for one minute did not reproduce her symptoms. An initial audiogram was within normal limits and her speech recognition threshold was 25 dB on the

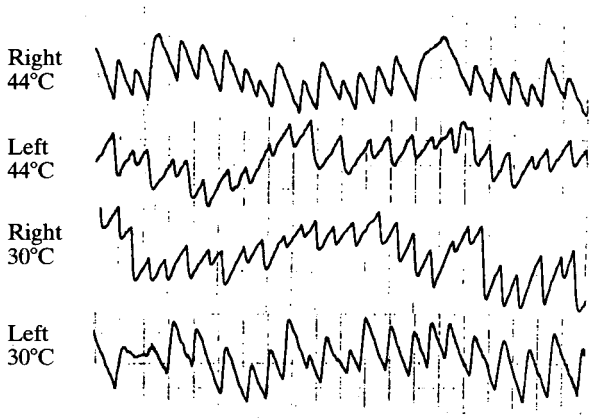

FIG. 1

Electronystagmographic tracing of bithermal caloric responses. Symmetrical responses recorded at 44°C and 30°C.

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FIG. 2

Electronystagmographic tracing of air-caloric stimulation at 10°C using the Dundas-Grant method. The left ear was stimulated for 15 seconds and the right ear for 30 seconds. No vestibular response present on the right.

right and 15 dB on the left. However, sequential audiograms showed fluctuation of the low frequency thresholds in her right ear. Electronystagmography (ENG) caloric testing was normal (Figure 1). A CT scan of her head, one month prior to her consultation, arranged by her family doctor was normal and a diagnosis of right Menière's disease was made.

Initial management consisted of Diazide® (50 mg triamterene and 25 mg hydrochlorothiazide) (one tablet p.o. daily) and Serc® (betahistine) (8 mg p.o. t.i.d.). However, the patient became incapacitated by her attacks of vertigo and was keen to undergo chemical ablation of the vestibular function of her right ear. A ventilation tube was inserted into the right tympanic membrane and she was instructed to instill Garasone eardrops® (1 ml contains 3.0 mg gentamicin sulphate and 1.0 mg betamethasone sodium phosphate) (two drops b.d.) into that ear using tragal pressure for three weeks. During this period, the patient continued to experience intermittent episodes of vertigo associated with decreased hearing and increased tinnitus in her right ear.

Having finished the course of eardrops her attacks of vertigo stopped. An air caloric test performed two months after finishing the course of Garasone ear drops revealed absent vestibular function on the right side with normal function on the left (Figure 2). This was confirmed clinically by a positive Halmagyi head thrust to the right. An audiogram showed that her hearing was unaffected. She has had no further episodes of vertigo and remains happy with her current status.

Discussion

Anatomical and physiological studies have shown that the human round window membrane is permeable to a wide variety of substances (Kwabata and Paparella, 1971; Goycoolea *et al.*, 1988). Topical aminoglycosides appear to enter the perilymph at this site relatively slowly (Tran Ba Huy *et al.*, 1983). However, its clearance from the inner ear appears slower than its entry rate. Therefore, with repeated applications of aminoglycosides to the round window area, the concentration may rise within the perilymph to reach toxic levels. Animal experiments and human case reports have shown that all aminoglycosides cause ototoxicity, although it appears that the site of ototoxic damage is dependent on each specific drug. For example, gentamicin and streptomycin appear to be predominantly vestibulotoxic, whereas amikacin and neomycin are more cochleotoxic.

The selective vestibulotoxic nature of topical aminoglycoside preparations when instilled into the middle ear has been used to ablate vestibular function in order to control the vertiginous episodes associated with Menière's disease for over 20 years (Beck and Schmidt, 1978; Moller *et al.*, 1988; Lange, 1989; Yamazaki *et al.*, 1991; Nedzelski *et al.*, 1993; Rauch and Oas, 1997). The technique has evolved throughout this period to ensure that undesirable side-effects, primarily sensorineural hearing loss, are reduced. The initial method of intratympanic gentamicin used concentrations of about 30 mg/ml administered several times per day until vestibular toxicity developed. This invariably occurred three to five days after their treatment started but may be delayed by up to two weeks. However, due to concern regarding the variability in dose response between patients, treatment modalities have become more conservative with 'low-dose' intratympanic gentamicin becoming more common. This tends to involve instillations of topical gentamicin separated by one to two weeks (Driscoll *et al.*, 1997).

In this case, we have made use of this potential vestibular toxicity to ablate the vestibular function with definite proof as shown by caloric responses that were normal prior to treatment and abolished after treatment. There was no evidence of cochlear damage. To our knowledge, deliberate ablation of vestibular function using topical aminoglycosides eardrops has not been previously reported. This may offer a reduction in the risk of cochlear toxicity in the treatment of patients wishing to undergo vestibular ablation with unilateral Menière's disease. However, it also acts as an important warning of the inherent risks of using topical aminoglycosides in the treatment of ear infections in the presence of tympanic membrane perforations or ventilation tubes that provide ready access of these preparations to the middle ear.

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