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MAIN ARTICLE

Is low-dose intratympanic gentamicin an effective treatment for Ménière's disease: the Birmingham experience

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Abstract

Background: Since the development of intratympanic aminoglycoside in the 1950s, otologists have been able to chemically ablate the vestibule. We present the results of using low-dose intratympanic gentamicin to treat Ménière's disease.

Method: A retrospective review was performed of all patients who underwent low-dose intratympanic gentamicin therapy over seven years. Data on gender, age, number of procedures, pure tone audiometry and symptom control were analysed.

Results: In all, 38 patients underwent low-dose intratympanic gentamicin therapy. These comprised 25 females and 13 males, with an average age of 58.4 years. Hearing was preserved in 87.5 per cent of patients, with no significant difference before and after treatment ($p = 0.744$). In all, 85.7 per cent of patients had complete or substantial symptom control (classes A and B, respectively).

Conclusion: Low-dose intratympanic gentamicin therapy was effective in controlling the symptoms of Ménière's disease patients, while preserving hearing.

Key words: Ear, Inner; Vertigo; Hearing; Gentamicin; Ménière's Disease; Treatment

Introduction

Ménière's disease is a debilitating condition that results in a triad of tinnitus, rotational vertigo and fluctuating sensorineural hearing loss. The development of intratympanic aminoglycoside therapy in the 1950s by Schuknecht provided otologists with the ability to chemically ablate the vestibule prior to undertaking surgical procedures.[1]

Although intratympanic gentamicin is now an accepted treatment method for Ménière's disease, no consensus exists on the best application method (direct injection or instilling via tympanostomy tube, microcatheter or Silverstein Microwick™) or dosing schedule.[2–4]

Some authors favour a high-dose regime in which multiple daily or weekly doses are given for four weeks, while others prefer to use a continuous or titration regimen in which daily or weekly doses are given until vestibular symptom onset, a change in vertigo symptoms, or hearing loss occurs. Many authors, however, argue that the low-dose method, in which intratympanic gentamicin is given (with repeat treatment reserved for recurrent symptoms), is a safer approach for preserving hearing.[5]

This study compared the results of low-dose intratympanic gentamicin therapy for refractory Ménière's disease with those of recent reports.

Materials and methods

A retrospective review was performed of the case notes of all the patients who underwent low-dose intratympanic gentamicin therapy to control Ménière's disease from 2005 until 2012. Data on gender, age, number of procedures, pure tone audiometry results, and symptom control before and after the procedure were collected.

Pure tone audiometry

The lowest air conduction average at 0.5, 1, 2, 4 and 8 kHz was recorded before and, where possible, three months after treatment. Hearing improvement or deterioration was defined as a change of more than 10 dB. Speech discrimination scores were not recorded.

Vertigo control

Control of vertigo symptoms was described as class A (complete control), class B (substantial control),

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TABLE I
AAOHNS SYMPTOMATIC CONTROL CLASSIFICATION

Class	Score*
A	0
B	1–40
C	41–80
D	81–120
E	>120

*Score = average number of spells per month post-treatment ÷ average number of spells per month pre-treatment × 100; AAOHNS = American Academy of Otolaryngology Head and Neck Surgery

class C (limited control), class D (insignificant control) or class E (worse symptoms), as defined by the American Academy of Otolaryngology Head and Neck Surgery Committee on Hearing and Equilibrium guidelines published in 1995 (Table I).

Statistical analysis

Statistical analysis was performed by the Medical Statistical Department at the University of Birmingham using IBM SPSS statistics software version 19 (IBM, Armonk, New York, USA).

Treatment method

Written informed consent was obtained from all patients prior to treatment. A volume of 0.5 ml gentamicin (40 mg/ml) was injected through the tympanic membrane using the operating microscope and a fine-bore spinal needle. Prior to this, the tympanic membrane was anaesthetised using a topical agent (a eutectic mixture of local anaesthetics, containing 2.5 per cent each lidocaine and prilocaine) or local anaesthetic. The gentamicin solution can be buffered using 0.5 ml 8.4 per cent sodium bicarbonate and 0.5 ml local anaesthetic to reduce middle-ear discomfort. However, we did not find this to be necessary and currently inject the solution unaltered. After injection, the patient was instructed to lie supine with the head turned to the contralateral side and to maintain this position for half an hour.

Patients were reviewed in the clinic after six weeks. If stable, they were reviewed again after a further six weeks and audiography was performed to assess hearing. If they were still symptomatic, they received a further intratympanic gentamicin injection.

Results

Patient demographics

A total of 38 patients underwent low-dose intratympanic gentamicin therapy from 2005 until 2012. These comprised 25 females and 13 males, with an average age of 58.4 years (range 23–81 years). A total of 48 procedures were carried out over this period, with 29 patients undergoing 1 procedure, 8 patients requiring 2 procedures and 1 patient requiring 3 procedures to control the symptoms. The average period between multiple procedures was 7 months (range 2–77 months).

Audiology results

Figure 1 summarises the post-treatment hearing results in which hearing levels had changed by more than 10 dB in either direction. The mean hearing threshold of the whole group (excluding those with profound hearing loss) was 60.5 dB prior to treatment and 59.9 dB after treatment. No significant decline in hearing was detected between tests (Paired t-test, $p = 0.744$).

Vertigo control

Of the 38 patients who received treatment, 3 were lost to follow up. The remaining 35 patients were followed up for an average of 22.4 months (5–54 months). Figure 2 shows the rate of vertigo control in patients receiving single and multiple treatments, as well as the overall outcome.

One patient with a class C outcome had an average hearing threshold of 93.3 dB and went on to undergo

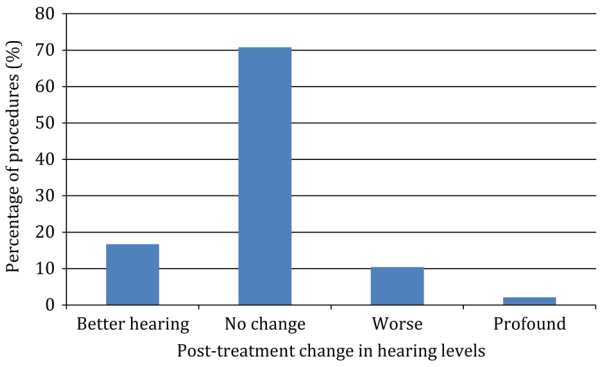

FIG. 1
Graph summarising the hearing results after low-dose intratympanic gentamicin treatment. *Progressive disease with an average threshold of 83.3 dB prior to treatment.

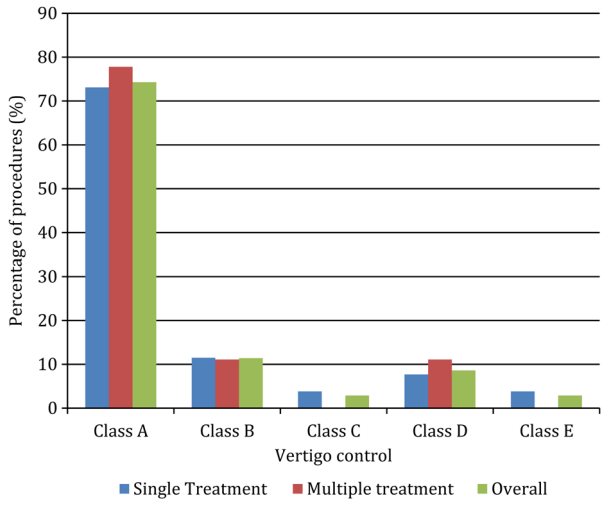

FIG. 2
Graph showing symptomatic vertigo control after low-dose intratympanic gentamicin.

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labyrinthectomy. One of the three patients with a class D outcome and a hearing threshold of 43.3 dB went on to undergo saccus decompression; the remaining two patients received the best supportive and medical care. One patient with a class E outcome and a hearing threshold of 52.5 dB went on to undergo labyrinthectomy

Discussion

The vestibulotoxic effect of aminoglycosides used to treat vertigo was first described by Fowler in 1948.[6] In 1956, Schuknecht became the first person to use intratympanic streptomycin for unilateral Ménière's disease patients. His success rate for controlling vertigo was 62 per cent but almost all patients had resulting sensorineural hearing loss.[1] In the 1970s, Beck and Schmidt used intratympanic gentamicin to better effect.[7] This is currently an accepted alternative treatment for symptomatic Ménière's disease that has not responded to dietary and medical treatment prior to embarking on surgical procedures.[8]

Although intratympanic gentamicin is an acceptable treatment, an effective evidence-based approach to treatment has not been established because Ménière's disease has a fluctuating natural course, thus making evaluation difficult. Controversy remains about how regularly gentamicin should be instilled to control symptoms. Some surgeons favour the low-dose approach in which gentamicin is instilled once and any further treatments are reserved for recurrent symptoms. Others prefer the high-dose, continuous or titration method in which gentamicin is instilled on a daily or weekly basis or continuously (via a microcatheter) until electronystagmography shows vestibular weakness. Many authors argue that intermittent dosing with long intervals between the two injections to check whether hearing loss has occurred is a safer approach to preserving hearing.

As reviewed by Chia *et al.*, the titration method (daily or weekly doses until the onset of vestibular symptoms, change in vertigo or hearing loss) demonstrated significantly better complete (81.7 per cent) and effective (96.3 per cent) vertigo control compared with the low-dose method (66.7 per cent and 86.8 per cent, respectively). However, the multiple daily method led to significantly greater overall hearing loss (34.7 per cent) compared with other methods.[5]

Carey *et al.* reported that titration therapy with intratympanic gentamicin offers vertigo control in 87 per cent (range 75–100 per cent) of unilateral Ménière's disease patients. The risk of additional hearing loss was about 21 per cent (range 0–37 per cent). Vertigo reoccurred, however, in nearly one third of patients.[9]

Similarly, in a Cochrane review of two prospective, double-blinded, placebo-controlled, randomised clinical trials, Pullens *et al.* reported that the low-dose approach resulted in complete vertigo control with no hearing loss, whereas the weekly dose led to no vertiginous attacks in 9 out of 16 patients after a year, although 25 per cent of patients had an increased hearing loss of greater than 20 dB.[8]

In contrast, Cohen-kerem *et al.* concluded that the success rate was not affected by the gentamicin treatment regimen (fixed vs titration), and that hearing level and word recognition were not adversely affected by gentamicin treatment, regardless of the regimen.[10]

At our institute, the low-dose intratympanic gentamicin regimen is preferred with the aim of controlling symptoms with minimum risk to hearing. Only patients with definite Ménière's are offered this treatment, and a conservative approach is adopted for those with possible or probable disease. Ablation is not considered necessary and treatment is provided according to the frequency and severity of vertigo symptoms. Gentamicin injection is not used for controlling fluctuating hearing, tinnitus or aural pressure symptoms.

Using low-dose intratympanic gentamicin, we obtained effective vertigo control (class A and B results) in 85.7 per cent of patients, with hearing improvement or preservation in 87.5 per cent of procedures. Our results are similar to those reported in a meta-analysis performed by Chia *et al.* These authors concluded that the low-dose delivery method demonstrated effective vertigo control in 86.8 per cent of procedures (with complete control in 66.7 per cent). Their rate of profound hearing loss after treatment (2.4 per cent of patients) is similar to our rate of 2.1 per cent.[5]

- **Intratympanic gentamicin is used to chemically ablate the vestibule in Ménière's disease patients**
- **There is no consensus on delivery method or dosing regime**
- **High-dose gentamicin is better for controlling symptoms**
- **However, there is a higher risk of sensorineural hearing loss**
- **Low-dose gentamicin has less risk to hearing and has been used successfully to treat Ménière's disease patients**

Quaglieri *et al.*, Casani *et al.* and de Beer *et al.* recently reported the effective control of vertigo symptoms using low-dose gentamicin in 80.7–93.5 per cent of patients and hearing deterioration of more than 10 dB in 12.5–15.8 per cent. Again, these rates are similar to our rates of 85.7 per cent and 10.4 per cent, respectively.[11–13]

Conclusion

In our experience, low-dose intratympanic gentamicin is effective at controlling the symptoms of Ménière's disease patients, while preserving hearing. Our results are consistent with those of other studies using a similar approach.

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