*The Journal of Laryngology & Otology*
June 2003, Vol. **117,** pp. 459–461

# Intratympanic gentamicin for Ménière's disease; a survey of current UK practice

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**Abstract**

Intratympanic gentamicin is increasingly used in the treatment of Ménière's disease. Many protocols have been published for its use, but there is little difference in outcome between them. The goal of the study was therefore to assess current UK practice in the use of intratympanic gentamicin.

A postal and e-mail survey of consultant ENT surgeons in the UK was conducted. Of 34 consultants who regularly used intratympanic gentamicin, 21 used a protocol based upon a single intratympanic dose of gentamicin via a needle through the tympanic membrane and repeated after at least a week. The remaining 13 used either a regime of more frequent administration or attempted a more complicated route of delivery in an effort to improve reliability and selectivity of action.

In the absence of evidence demonstrating benefit from regimens of increased complexity the majority of consultants are using the simplest possible protocol.

**Key words: Ménière's Disease; Aminoglycosides**

## Introduction

Intratympanic gentamicin is increasingly used in the treatment of Ménière's disease which is uncontrolled with medical therapy. The use of intratympanic aminoglycosides to treat Ménière's was initially reported in 1957 by Schuknecht,[1] who used streptomycin to perform a chemical labyrinthectomy. Gentamicin became available in 1964, and its successful intratympanic use was reported in 1977.[2] Gentamicin has replaced streptomycin as it is readily available and has a better ratio of vestibular to cochlear toxicity.[3] In order to facilitate the assessment of this treatment a suggested 'standard' protocol was published in 1992,[4] from which some protocols have been derived (Table I). Many protocols have been published, and analysis has suggested that there is little difference in outcomes between them.[5]

## Methods

A questionnaire (Appendix I) was e-mailed to all full members of the British Association of Otorhinolaryngologists – Head and Neck Surgeons (BAO-HNS) with e-mail addresses in the BAO-HNS handbook.

TABLE I
RECENT PROTOCOLS FOR THE USE OF INTRATYMPANIC GENTAMICIN[9–16]

| First author (year) | Delivery method | mg/ml | Regime | Volume (mls) | Repeated? |
|---|---|---|---|---|---|
| Longridge and Mallinson[9] | needle* | 26 | O.D., 2 days | 0.5 ml | Rpt. If symptomatic |
| Minor[10] | needle | 26 | O.D., repeat weekly | to fill, aspirated after 30 min | Until nystagmus* or SNHL |
| Kaasinen *et al.*[11] | needle | **30 | O.D. for 1–4 days, review 2–4/52 | 0.3–0.5 | Rpt. if symptomatic |
| McFeely *et al.*[12] | round window catheter | **26 | t.d.s. for 4 days | 1 over 10 min | Defined course |
| Pfleiderer[13] | catheter | **26 | t.d.s. for 4 days | 0.75 ml | Defined course |
| Corsten *et al.*[14] | ventilation tube | **18 | t.d.s. for 4 days | 1 ml | Defined course |
| Rauch and Oas[15] | needle | 40 | b.d. ×2, then b.d. 1 × /week | to fill | Until persistent dysequilibrium |
| Driscoll *et al.*[16] | needle | 40 | Once, review 2–4/52 | to fill | Rpt. if symptomatic |

*2nd perforation made anteriorly, **Spontaneous, head shaking induced or head thrust test (with Frenzel glasses)

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Accepted for publication: 3 October 2002.

TABLE II
REGIME USED

| Frequency | No. | Repeated? | No. | Endpoint (in the absence of SNHL) | No. |
|---|---|---|---|---|---|
| O.D. | 27 | once (then review) | 16 | Symptomatic improvement | 21 |
| B.D. | 1 | once/week 2–6× | 11 | Vertigo/dizzy/off balance/giddy | 4 |
| T.D.S. | 4 | 4–7 days | 4 | Absent caloric | 3 |
| Q.D.S. | 1 | 14 days | 1 | Set course | 6 |
| Continuous (10 days, 0.5 mg/hr) | 1 | b.d. until giddy | 1 | | |

In addition some further addresses were derived from a previous circular. Known otologists and those consultants whose names were mentioned in other replies as using this treatment were contacted again via e-mail and post. Results were entered on a database and the responses analysed.

## Results

One hundred and twenty-eight replies were received. Thirty-four otologists use this treatment. The results are summarized in Tables II, III and IV. Twenty-one delivered the dose via a needle through the tympanic membrane, nine via a tympanostomy tube. Of the remaining four, three performed a tympanotomy and placed gentamicin-soaked pledgets in the round window niche and one injected directly through the round window or fenestrated the lateral semicircular canal and injected into that.

The regimen used is clearly dictated to an extent by the method of application. Twenty-six clinicians used a single dose, that was repeated after a week by six clinicians. Three repeated the dose three times a day and one four times a day, and the frequent dose regimes involved ongoing treatment for four to seven days or until dizzy (Nedzelski or Pfleiderer regime).[6] One utilized a diesetronic pump to provide a continuous infusion to the round window niche at 0.5 mg/hr for 10 days. Those utilizing a single dose used predominantly 40 mg/ml or 30 mg/ml preparations (19 and six clinicians respectively), those using multiple doses used lower concentrations.

## Discussion

Gentamicin is a relatively vestibular-specific ototoxic agent. Ablation of the vestibular sensory cells relieves the vertigo associated with endolymphatic hydrops. When applied to the middle ear gentamicin will diffuse via the round window into the scala tympani and hence to the scala vestibuli and vestibular labyrinth. In the vestibular system hair cell loss first occurs on the crest of the cristae and in the striolar regions of the maculae, spreading outwards as damage progresses.[7] Aminoglycosides enter the endolymph and perilymph slowly, and once in the endolymph may be present for days. They may persist for up to a year in lysosomal-like bodies within the hair cells, which may predispose hair cells to subsequent damage. There is genetic variability in susceptibility to aminoglycosides, with a distinct group of highly susceptible individuals carrying a mutation of the 12s ribosomal RNA gene, nucleotide 1555A–G. This is mitochondrial RNA and therefore maternal history is significant. It has been observed that these patients may develop hearing loss, thought to be secondary to aminoglycoside use, some years later.[8] To what extent the dose response curve is linear in the rest of the population is unclear.

Variations in the technique of application have been described, primarily in an effort to increase the specificity and reliability of vestibular ablation and hence hearing preservation. Another point of concern has been the variation in absorbed dose if gentamicin is simply injected into the middle ear, that ought to depend on factors such as volume of the middle-ear cleft and eustachian tube patency. Analysis of published results has however shown little difference in success.[5]

The choice of technique of application is therefore influenced by: the theoretical benefit of improved vestibular specificity, the reliability of dose delivery and the ease of execution and expense.

Our results suggest that the majority of consultants fall into one of two categories, those that continue to utilize a relatively complicated technique for its theoretical benefit and those who, in the light of analysis showing little difference, use the simplest and easiest technique available. While such variation in techniques remain it is unlikely to be possible in the short-term to prove the superiority of any one technique. The widespread adoption of a single dose regimen doubtless reflects the ease of this approach.

TABLE III
DOSE USED

| Mg/ml | Number |
|---|---|
| 40 | 17 |
| 26–30 | 11 |
| 20 | 1 |
| 10 | 2 |
| 3 | 3 |

TABLE IV
DELIVERY METHOD USED

| Route | Number |
|---|---|
| Tympanostomy tube/catheter | 8 |
| Injection – needle/TM | 21 |
| Pledgets to round window | 3 |
| Silverstein wick | 1 |
| Other | 1 |

https://doi.org/10.1258/002221503321892299 Published online by Cambridge University Press

**References**

1 Schuknecht H. Ablation therapy in Ménière's disease. *Acta Otolaryngol (Stockh)* 1957;**132**(suppl):1–42
2 Lange G. Die intratympanale Behandlung des Morbus Meniere mit ototoxishen Antibiotica. *Laryngo-Rhino-Otol* 1977;**56**:409–14
3 Blakley BW. Clinical forum: a review of intratympanic therapy. *Am J Otol* 1997;**18**:520–6
4 Nedzelski JM, Schessel DA, Bryce GE, Pfleiderer AG. Chemical labyrinthectomy: local application of gentamicin for the treatment of unilateral Ménière's disease. *Am J Otol* 1992;**13**:18–22
5 Blakley BW. Update on intratympanic gentamicin for Ménière's disease. *Laryngoscope* 2000;**110**:236–40
6 Nedzelski JM, Chiong CM, Fradet G, Schessel DA, Bryce GE, Pfleiderer AG. Intratympanic gentamicin instillation as treatment of unilateral Ménière's disease: update of an ongoing study. *Am J Otol* 1993;**14**:278–82
7 Wright T. Ototoxicity. In: Wright T, Ludman H (eds.): *Diseases of the Ear*. London: Arnold, 1997,504–15
8 Fischel-Ghodsian N, Prezant TR, Chaltraw WE, Wendt KA, Nelson RA, Arnos KS, *et al.* Mitochondrial gene mutation is a significant predisposing factor in aminoglycoside ototoxicity. *Am J Otol* 1997;**18**:173–8
9 Longridge NS, Mallinson AI. Low-dose intratympanic gentamicin treatment for dizziness in Ménière's disease. *J Otol* 2000;**29**:35–9
10 Minor LB. Intratympanic gentamicin for control of vertigo in Ménière's disease: vestibular signs that specify completion of therapy. *Am J Otol* 1999;**20**:209–19
11 Kaasinen S, Pyykko I, Ishizaki H, Aalto H. Intratympanic gentamicin in Ménière's disease. *Acta Otolaryngol Head Neck Surg* 1998;**118**:294–8
12 McFeely WJ, Singleton GT, Rodriguez FJ, Antonelli PJ. Intratympanic gentamicin treatment for Ménière's disease. *Otolaryngol Head Neck Surg* 1998;**118**:589–96
13 Pfleiderer AG. The current role of local intratympanic gentamicin therapy in the management of unilateral Ménière's disease. *Clin Otolaryngol* 1998;**23**:34–41
14 Corsten M, Marsan J, Schramm D, Robichaud J. Treatment of intractable Ménière's disease with intratympanic gentamicin: review of the university of Ottowa experience. *J Otolaryngol* 1997;**26**:361–4
15 Rauch SD, Oas JG. Intratympanic gentamicin for treatment of intractable Ménière's disease: a preliminary report. *Laryngoscope* 1997;**107**:49–55
16 Driscoll CLW, Kasperbauer JL, Facer GW, Harner SG, Beatty CW. Low dose intratympanic gentamicin and the treatment of Ménière's disease: preliminary results. *Laryngoscope* 1997;**107**:83–9

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Mr R. Obholzer takes responsibility for the integrity of the content of the paper.
Competing interests: None declared

## Appendix I The questionnaire distributed

**Intratympanic gentamicin for ménières disease**

Do you use intratympanic gentamicin for the treatment of Ménières disease?
Do you follow a protocol?
Is your protocol published?
I so, where?

What do you actually do?

Mode of delivery:
Injection through tympanostomy tube/catheter –
Injection – needle through tympanic membrane –
eustachian tube catheter –

Concentration injected:
>> Genticin® injection (Roche) = 40 mg/ml
>> Genticin® drops (Roche) = 3 mg/ml
>> Gentisone HC® 3% = 3 mg/ml
>> Isotonic Gentamicin injection (Baxter) = 800 mcg/ml
>> Non-proprietary gentamicin = 40 mg/ml
>> Cidomycin® (Hoechst Marion Roussel) injection 40 mg/ml
>> Paediatric injection 10 mg/ml
>> Intrathecal injection 5 mg/ml

Volume injected: >>

Frequency: o.d., b.d., t.d.s., q.d.s.

For how many days?

Number of cycles:
Set number/Until symptomatic improvement/Until hearing loss

Total dose:
Approximately how many patients do you treat per year?
Thank you doing this, your time is greatly appreciated.