

Intratympanic gentamicin for Ménière's disease: effect on quality of life as assessed by Glasgow benefit inventory

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Abstract

Objectives: To evaluate patients' quality of life after receiving intratympanic gentamicin as treatment for Ménière's disease.

Design: Retrospective study using the Glasgow benefit inventory scale (GBI) questionnaire.

Participants: Patients diagnosed with Ménière's disease, according to the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) diagnostic criteria (refractory to medical management), who were treated with intratympanic gentamicin injection.

Materials and methods: This retrospective study included all patients diagnosed with Ménière's disease (according to AAO-HNS criteria; refractory to medical management) undergoing gentamicin labyrinthectomy in our unit over the preceding three years. Other causes of hearing loss were ruled out as all patients underwent magnetic resonance imaging, electronystagmography and sway magnetometry. Patients underwent gentamicin infiltration at a concentration of 2 ml of 30 mg/ml and were reviewed six weeks later and received a repeat injection if no benefit was evident. Six months after their last follow up, they were sent a GBI questionnaire. Twenty-one questionnaires were posted, and the response rate was 81 per cent.

Results: As per the responses received, the total benefit of intratympanic gentamicin injection was found to be +30.3. The three components of GBI were analysed separately; it was found that general benefit was greatest (+33.3), followed by physical benefit (+28.1) and social benefit (+21.6).

Conclusion: This study suggests that gentamicin definitely improves quality of life in patients with Ménière's disease and should be the first line of treatment if medical management fails.

Key words: Meniere's Disease; Gentamicin; Quality of Life

Introduction

Ménière's disease was described by Prosper Ménière in 1861 thus: 'A syndrome consisting of continuous or intermittent head noise accompanied by diminution of hearing and intermittent attacks of vertigo, uncertain gait and falling accompanied by nausea, vomiting and syncope'. The American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) in 1995 defined Ménière's disease as a clinical disorder/idiopathic syndrome of endolymphatic hydrops. For clinical purposes, the presence of endolymphatic hydrops can be inferred during life by the presence of the following: recurrent, spontaneous episodic vertigo; hearing loss; aural fullness; and tinnitus. Either tinnitus or aural fullness (or both) must be present on the affected side to make the diagnosis, for reporting purposes, under these guidelines.¹ The disability of Ménière's syndrome is characterized by

vertigo (96 per cent), hearing loss (87.7 per cent), blocked ear sensation (74.1 per cent) and tinnitus (91.1 per cent).

There are no definite final pathways for Ménière's disease. Gibson and Arenberg suggest that a narrowed endolymphatic duct becomes obstructed by debris, which is cleared by a combination of the secretion of hydrophilic proteins within the endolymphatic sac and a hormone, saccin, that increases the volume of endolymph within the cochlea. It is proposed that sudden restoration of longitudinal flow initiates the attacks of vertigo.²

The work of Masutani *et al.*³ and Kimura⁴ regarding the role of the dark cell is gaining importance. Dark cells have the important role of active transport of electrolyte in the vestibular labyrinth and are correlated with production of endolymph. They lie at the periphery of the macula of the utricle and cristae of

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the semicircular canals. Abnormal dark cells are implicated in endolymphatic hydrops in Ménière's disease cases.⁵

It is theorized that gentamicin delivered via middle-ear instillation may diminish dark cell production of endolymph by causing structural changes, in the form of a widened intercellular space, less osmophilic cytoplasm and irregular-shaped basal portion,⁶ thereby providing chemical control of Ménière's disease.

The current concept in treatment of intractable cases of Ménière's disease is to accept the endolymphatic hydrops while attempting to eliminate the vertigo response, with stabilization of hearing (Figure 1).

Fowler⁷ was the first to prescribe systemic streptomycin to treat patients with bilateral Ménière's disease. Shuknecht⁸ was the first to prescribe intratympanic injection of aminoglycosides.

Intratympanic gentamicin in low doses has been shown to reduce the labyrinthine response while controlling and preserving cochlear function.⁹ Ablative surgery results in complete vestibular loss. Moreover, labyrinthectomy techniques are always associated with deafness in the treated ear, and vestibular neurectomy requires a craniotomy, with potentially life-threatening complications.

In treating Ménière's disease with gentamicin, two primary philosophies exist: chemical ablation versus chemical alteration. Ablation results in highly successful control of vertigo but at the cost of increased risk of hearing loss, while alteration is potentially less effective in vertigo control but, more importantly, has less chance of adverse side effects (i.e. hearing loss). We employed the latter method.

The advantages of using intratympanic gentamicin are: no systemic side effects, local delivery, minimal invasiveness, the high concentration obtained and the fact that it can be performed as an out-patient procedure.

As with other chronic diseases, two models or conceptual frameworks can be used to describe the non-fatal outcome of Ménière's disease: the assessment of impairment, disability and handicap; and the evaluation of health-related quality of life (QOL). Kenny *et al.* found that disease may cause more emotional than physical disability.¹⁰ The AAO-HNS criteria regarding reporting treatment outcome are more disease specific, while QOL reporting is more patient oriented.

There is little evidence currently available for the specific social, professional and personal problems caused by vestibular disorders. The Glasgow benefit inventory (GBI) is a validated, generic QOL questionnaire designed for measuring outcome after ENT procedures.¹¹ It has been found to be sensitive to changes in health and is patient-oriented. It measures QOL in three domains: social, general and physical. There are 18 questions in the GBI; 12 relate to general QOL improvement while three each relate to social and physical improvement. Each question has five possible responses, wherein a score of five denotes most favourable outcome and one least favourable outcome. A score of three

denotes no change. In our study, the GBI¹¹ was the tool used to measure the QOL of patients with Ménière's disease treated with intratympanic gentamicin injection.

Materials and methods

In our study, all patients had diagnosed cases of Ménière's disease, according to AAO-HNS diagnostic criteria, which were not responding to regular medical management. Other causes of hearing loss were ruled out as all patients underwent magnetic resonance imaging, electronystagmography and sway magnetometry. Of the studied patients who responded, the youngest was 32 years old and the oldest 77 years (mean age, 54 years). Eight patients were suffering from left-sided disease and nine from right-sided disease.

Initially, 23 patients were included in our study and were sent postal questionnaires based on the GBI. Two patients did not receive gentamicin therapy as they had responded to grommet insertion alone and hence were later excluded from the study. Out of the 21 eligible patients who received questionnaires, 17 (80.9 per cent) responded (15 women and two men). A second letter was sent to those patients who did not respond the first time but no further replies were received.

This retrospective study included all patients who had undergone gentamicin labyrinthectomy in our unit over the preceding three years. Patients were sent the questionnaire six months after their last follow up.

All the patients had failed trials of standard medical therapy as per the management protocol followed in our unit (Figure 2). The treatment rationale and all possible outcomes of gentamicin therapy were explained to each patient.

Patients underwent gentamicin infiltration using buffered gentamicin (30 mg/ml) warmed to body temperature to avoid caloric effect. The solution was injected through a grommet by the same doctor on each occasion. The various reported methods and regimes for gentamicin infiltration, including those employed in this series, are shown in Table I.

The numbers of infiltrations in this series are shown in Table II.

Results

The total benefit of intratympanic gentamicin injection was found to be +30.3 (on the GBI scale, +100 denotes the best possible result and -100 the worst possible result or outcome). When the three components of the GBI were analysed separately, it was found that general benefit was the greatest (+33.3), followed by physical benefit (+28.1) and social benefit (+21.6)(Table III).

Discussion

Outcome research is now an accepted concept in clinical medicine as it reinforces the fact that the patient plays a central role in modern clinical

TABLE I
INTRATYMPANIC GENTAMICIN INTERVENTIONS REPORTED

Study	Delivery	Regime	Volume	Concentration (mg/ml)
Corsten <i>et al.</i> (1997)	Ventilating tube	TDS for 4 days	1 ml	18
Driscoll <i>et al.</i> (1997) ⁹	Needle	Once, review in 2–4 wks	To fill	40
Kaasinen <i>et al.</i> (1998)	Needle	OD for 1–4 days, review in 2–4 wks	0.3–0.5 ml	30
Longridge <i>et al.</i> (2000)	Needle	OD for 2 days	0.5 ml	26
McFeely <i>et al.</i> (1998)	Round window catheter	TDS for 4 days	1 ml	26
Minor <i>et al.</i> (1999)	Needle	OD, repeat weekly	To fill	26
Pleiderer <i>et al.</i> (1998)	Catheter	TDS for 4 days	0.75 ml	26
Rauch & Oas (1997)	Needle	BD for 2 days then BD for 1 wk	To fill	40
Current study (2006)	Ventilating tube	BD over 2 days, review at 6 wks	To fill	30

Adapted from Obholzer and Wareing¹² with permission. TDS = thrice daily; OD = once daily; BD = twice daily

TABLE II
NUMBER OF GENTAMICIN INFILTRATIONS USED PER PATIENT

Infiltrations (n)	Patients (n)
1	4
2	1
3	3
4	3
5	3
6	0
7	2
8	1

practice. Quality of life questionnaires measure functional capacity, psycho-social well-being and symptomatic relief, which are of utmost importance to the patients.

It is always difficult to define outcome measures for any disease, and this is even more so with chronic conditions such as Ménière's disease; even if the patient responds to treatment with an objective improvement (e.g. a quantitative hearing improvement), there may be no change in the patient's perception of their illness.

After failure of symptomatic medication, and before consideration of destructive surgery, there is an increasing recognition of the usefulness of aminoglycosides (with their vestibular toxic side effects) in treating this condition. Recently, great interest has been generated in treating this condition with gentamicin,^{13,14} and many studies have been published suggesting the efficacy of this drug in controlling Ménière's disease.

The AAO-HNS criteria are more treatment specific than patient specific. A literature search

TABLE III
QUALITY OF LIFE BENEFITS OF GENTAMICIN INFILTRATION

GBI benefit domain	GBI score	CI
Total	+30.3	17–49
General	+33.3	20–43
Social support	+21.6	6–37
Physical health	+28.1	14–43

GBI = Glasgow benefit inventory; CIs = confidence intervals

revealed one previous QOL study which suggested that medical and surgical management did not significantly influence hearing results and that patients thus treated had greater emotional disability than physical disability.¹⁰ Soderman *et al.* (2001)¹⁵ and Soderman *et al.* (2002)¹⁶ studied different modalities of treatment of Ménière's disease and suggested that gentamicin allowed greater control of vertigo but that patients' overall QOL did not differ with different treatment modalities. We are not aware of any other study addressing the QOL impact of this form of therapy in isolation.

The GBI is a useful measure of patient benefit from ENT interventions. It fulfils three requirements: it is patient oriented; it is sensitive to changes in health status resulting from an intervention; and it enables comparison between different interventions. In the GBI scoring, +100 denotes the best possible result and –100 the worst possible result or outcome of an intervention.

The GBI provides an overall score, which usefully enables comparison of results of different interventions, as well as profiles scores, which provide

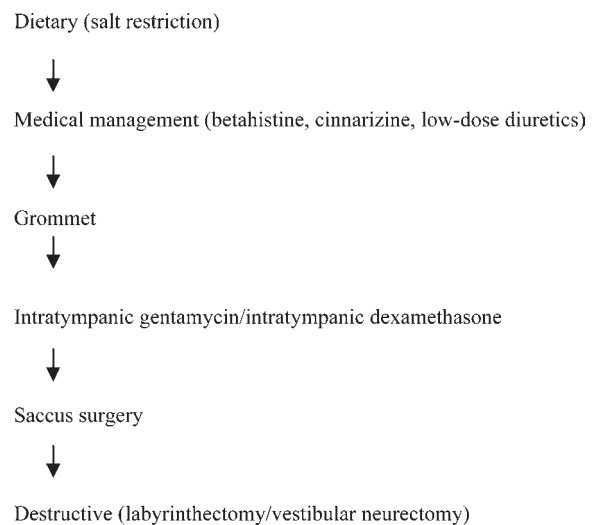


FIG. 1

Treatment protocol for patient with Ménière's disease.

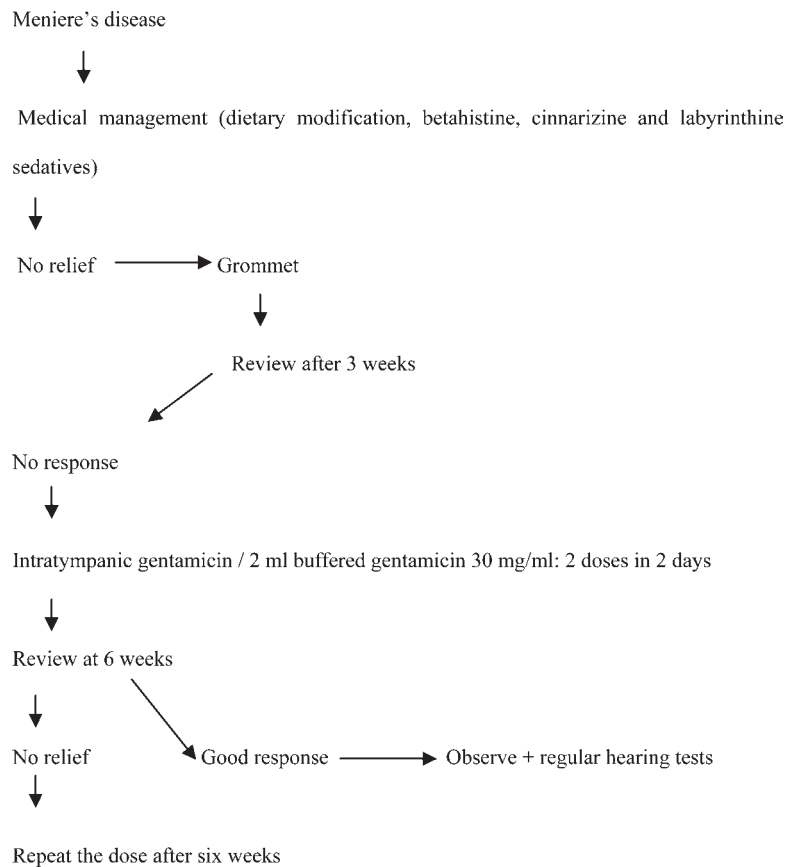


FIG. 2

Standard management protocol followed at our unit. Hearing was monitored closely throughout.

additional information on the nature of patient benefit associated with the ENT intervention.

In this study, analysis of the total mean benefit measured by the GBI showed that gentamicin injection improved the QOL in 80 per cent of patients. The overall total score, +30, clearly suggests that the procedure was beneficial. These results were compared to those obtained following bone-anchored hearing aid (BAHA) implantation and middle-ear surgery (Figure 3).

- This retrospective study included all patients diagnosed with Ménière's disease (according to the American Association of Otolaryngology-Head and Neck Surgery criteria; refractory to medical management) undergoing gentamicin labyrinthectomy in an otolaryngology unit over the preceding three years
- All patients were sent a questionnaire based on the Glasgow benefit inventory
- This study suggests that gentamicin definitely improves quality of life in patients with Ménière's disease and should be the first line of treatment if medical management fails

On comparing the three GBI QOL domains following middle-ear surgery for ear activity,¹¹ BAHA

implantation¹⁷ and intratympanic gentamicin for Ménière's disease (our series), our patients fared better than those in the middle-ear surgery group in all domains (and these are both difficult-to-define conditions in which intervention is required).

When the three domains of the GBI applicable to this study were analysed separately, the general benefit was found to be greatest, followed by the physical benefit and then the social benefit.

The general benefit subscale score was +33; this proves that patients felt better. The social benefit

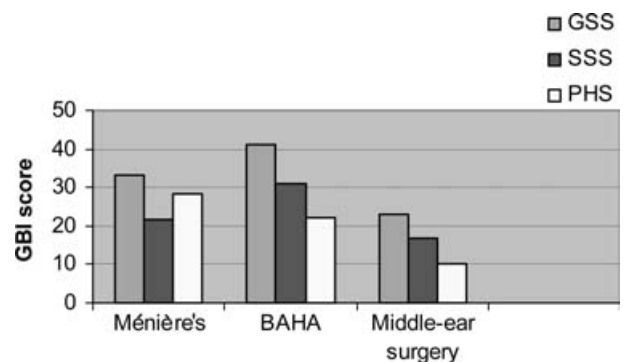


FIG. 3

Glasgow benefit inventory (GBI) scores for different ENT diseases. GSS = general subscale; SSS = social support subscale; PHS = physical health subscale; BAHA = bone-anchored hearing aid

score was high, indicating that patients were more confident in their day-to-day life. This is a very interesting outcome, as our study group was self-selected, refractory to treatment and had poor outcome measures before the studied treatment. Therefore, a positive result suggests that intratympanic gentamicin was a good mode of treatment for a difficult condition, which improved patients' overall QOL; in addition, compared with patients undergoing BAHA implantation, our patients showed a significant improvement in social benefit.

Ménière's disease can cause significant physical disability; vertigo may persist for days to weeks. An improvement in the GBI physical health benefit score is a good indicator of increased feelings of well-being. Our study obtained a GBI physical health benefit score of +28.1, indicating that intratympanic gentamicin for Ménière's disease improved patients' physical well-being, suggesting a good outcome of the procedure.

Conclusion

This study suggests that intratympanic gentamicin definitely improves the QOL of patients with Ménière's disease and is relatively safe regarding preservation of hearing. It should be considered as the first line of treatment if medical management fails.

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