Very Low-Dose Intratympanic Gentamicin in Ménière's Disease

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Abstract

Background: Intratympanic gentamicin is widely used for vertigo control in patients with Ménière's disease refractory to conservative therapy. Dose titration aims to achieve vestibular ablation while preserving cochlear function. Aim: To evaluate the efficacy and safety of a very low-dose intratympanic gentamicin protocol in patients with endolymphatic hydrops and disabling vertigo. Methods: This prospective clinical case series included 27 patients with definite Ménière's disease who failed medical treatment. Gentamicin sulfate (5 mg/mL) was administered every 12 hours through a tympanostomy tube. Treatment was discontinued at the first subjective sign of ototoxicity. Mean duration of treatment approximately 9 days. Follow-up ranged from 6 months to 4 years. Primary outcome was vertigo control. Secondary outcomes included hearing level, tinnitus, and vestibular function. Results: Vertigo control was achieved in 96% (26/27) of patients. Hearing was preserved or improved in 92% (25/27). Tinnitus was unchanged or improved in 23 patients and worsened in four. Vestibular function was unchanged in four patients, reduced in 17, and absent in six. Conclusions: Very low-dose intratympanic gentamicin provides good vertigo control with a high rate of hearing preservation. It represents a simple, and cost-effective alternative to destructive surgical procedures in selected patients with refractory Ménière's disease.

Keywords: ***Ménière's disease, endolymphatic hydrops, intratympanic gentamicin, vertigo, hearing preservation***

1. Introduction

Ménière's disease is a chronic inner ear disorder characterized by recurrent episodes of spontaneous vertigo, fluctuating sensorineural hearing loss, tinnitus, and aural fullness [Lopez-Escamez et al., 2015; Basura et al., 2020]. The condition is strongly associated with endolymphatic hydrops, which is considered the principal pathological substrate underlying the disease process [Nakashima et al., 2016]. Despite advances in remains primarily clinical vestibular testing and magnetic resonance imaging techniques, diagnosis and is based on established international diagnostic criteria [Lopez-Escamez et al., 2015; Basura et al., 2020].

The natural course of Ménière's disease is highly variable. Recurrent fluctuations in vestibular function are believed

to impair central vestibular compensation and contribute to repeated vertigo attacks, whereas stable vestibular hypofunction facilitates adaptation and long-term symptom control [Huppert, 2010; Strupp et al., 2017]. Consequently, therapeutic strategies focus on reducing vestibular fluctuations while preserving residual auditory function whenever possible. Management is generally performed in a stepwise manner. Initial treatment includes dietary sodium restriction, lifestyle modification, betahistine therapy, diuretics, and vestibular suppressants during acute attacks [Basura et al., 2020,]. Although many patients achieve satisfactory symptom control with conservative measures, a subset continues to experience disabling vertigo despite prolonged medical treatment.

Historically, surgical procedures such as endolymphatic sac surgery, vestibular neurectomy, and labyrinthectomy have been employed in medically refractory cases [Koo, 2025; Patel et al., 2016]. While these interventions may provide excellent vertigo control, they are associated with hospitalization, surgical morbidity, and varying risks to residual hearing. Therefore, minimally invasive alternatives have become increasingly important in contemporary management [Casani et al., 2014; Gawęcki et al., 2012].

Intratympanic gentamicin therapy is currently one of the most widely accepted treatments for refractory unilateral Ménière's disease [Basura et al., 2020; Carey, 2004]. Gentamicin demonstrates preferential vestibulotoxicity relative to cochleotoxicity and diffuses into the inner ear through the round window membrane following transtympanic administration [Hirvonen et al., 2005; Nguyen et al., 2009]. The resulting reduction in vestibular function decreases abnormal vestibular input and facilitates central compensation, thereby reducing the frequency and severity of vertigo attacks [Salt & Plontke, 2018; Pullens & van Benthem, 2013].

Although the effectiveness of intratympanic gentamicin is well established, the optimal dosing strategy remains controversial. Early protocols frequently employed repeated high-dose injections intended to achieve complete vestibular ablation. While effective for vertigo control, these regimens were associated with significant rates of hearing deterioration [Carey, 2004; Nguyen et al., 2009]. More recent investigations have demonstrated that low-dose and titration-based protocols can achieve comparable vertigo control while substantially reducing cochlear toxicity [Harcourt et al., 2014; Gawęcki et al., 201;, Scarpa et al., 2019; vanSonsbeek et al., 2022].

The rationale of the present protocol is based on administering multiple very small doses that can be discontinued immediately at the first indication of vestibular or cochlear toxicity. This approach aims to maximize vertigo control while minimizing cumulative cochlear exposure to gentamicin. Success in vertigo control after intratympanic gentamicin (ITG) should ideally be assessed using the , which remain widely used in Ménière's disease studies.

The aim of this prospective clinical study was to evaluate the efficacy and safety of a very low-dose intratympanic gentamicin protocol in patients with definite Ménière's disease who remained symptomatic despite conventional medical treatment.

2. Materials and Methods

This prospective case series included 27 patients with definite Ménière's disease diagnosed according to accepted clinical criteria [Basura et al., 2020; Lopez-Escamezet et al., 2015]. All patients had long-standing disabling vertigo and had failed adequate medical therapy, including dietary modification and conservative treatment. Intratympanic gentamicin was offered before destructive surgical intervention.

All patients provided informed consent after receiving detailed information and counseling regarding the expected benefits and potential risks of treatment, including hearing deterioration and prolonged vestibular dysfunction.

2.1 Patient Selection

Twenty-seven patients with definite Ménière's disease were diagnosed based on accepted clinical criteria of the Bárány Society and AAO-HNS [Patel et al., 2016], including:

- Recurrent spontaneous episodes of rotational vertigo lasting between 20 minutes and 12 hours.
- Fluctuating low- to medium-frequency sensorineural hearing loss documented by audiometry.
- Tinnitus and/or aural fullness in the affected ear.
- Exclusion of alternative vestibular disorders.

All patients had persistent disabling vertigo despite at least six months of conservative management, including dietary sodium restriction, betahistine therapy, and vestibular suppressants during acute attacks.

Patients with bilateral active disease, previous ablative vestibular procedures, retrocochlear pathology, chronic middle ear disease, or inability to complete follow-up were excluded.

2.2 Pre-treatment Evaluation

Before treatment, all patients underwent otologic and neurologic evaluation, including:

- Detailed medical history.
- Microscopic otologic examination.
- Pure-tone audiometry.
- Tympanometry.
- Caloric vestibular testing.
- Neurological evaluation when indicated.

Pure-tone average (PTA) was calculated using hearing thresholds at 0.5, 1, 2, and 4 kHz.
The frequency and severity of vertigo attacks during the six months preceding treatment were documented.

2.3 Intratympanic Gentamicin Protocol

Under local anesthesia, a tympanostomy tube was inserted into the tympanic membrane of the affected ear.
Gentamicin sulfate solution (5 mg/mL) was administered through the tympanostomy tube at a dose of 1 mL every 12 hours. Following administration, patients remained in the supine position with the treated ear facing upward for approximately 30 minutes to facilitate diffusion across the round window membrane. Duration of treatment was 7-16 days (mean 9 days). The total dose of Gentamycine used was from 70 mg-160 mg depending on the patient.

Clinical monitoring including audiologic and vestibular evaluation followed the treatment on daily basis. Treatment was discontinued immediately upon the appearance of any subjective or objective indication of ototoxicity, including:

- New imbalance or disequilibrium.
- Worsening tinnitus.
- Subjective hearing deterioration.
- Objective audiometric threshold shift.

The total number of administered doses varied according to individual response.
There were no specific criteria used to determine the duration of the treatment.

2.4 Follow-up Evaluation

Patients were evaluated at 1 month, 3 months, 6 months, and annually thereafter.
At each visit, the following were assessed:

- Frequency and severity of vertigo attacks.
- Pure-tone audiometry.
- Tinnitus status.
- Vestibular symptoms.
- Caloric vestibular testing

Follow-up duration ranged from 6 months to 4 years.

2.5 Outcome Measures

The primary outcome measure was vertigo control.
Secondary outcome measures included:

- Change in hearing thresholds.
- Change in tinnitus severity.
- Vestibular function assessed by caloric testing.
- Need for additional treatment.

Treatment was considered clinically sucessful when complete or substantial control of vertigo was achieved without requiring destructive surgical intervention.

3. Results

3.1 Patient Characteristics

Twenty-seven patients fulfilled the inclusion criteria and completed follow-up. The study population consisted of 15 men and 12 women, with a mean age of 53 years (range: 34–72 years).

The mean duration of Ménière's disease before intratympanic treatment was approximately 5.8 years (range: 1–18 years). All patients reported frequent disabling vertigo attacks despite prolonged medical management.

The right ear was affected in 16 patients and the left ear in 11 patients.

3.2 Treatment Administration

All patients successfully completed the intratympanic gentamicin protocol. The number of doses administered varied according to individual clinical response and the appearance of early signs of vestibular toxicity.

No patient experienced persistent tympanic membrane perforation, middle ear infection, or other procedure-related complications. Duration of treatment was 7-16 days depending on each patient.

3.3 Vertigo Control

Vertigo control was achieved in 26 of 27 patients (96%).

Twenty-three patients experienced complete cessation of disabling vertigo attacks during follow-up. Three patients reported rare mild residual episodes that did not interfere with daily activities.

Only one patient continued to experience recurrent vertigo and was considered a treatment failure. This patient subsequently underwent alternative management.

Most patients reported improvement within several weeks after treatment completion.

3.4 Hearing Outcomes

Pre-treatment pure-tone audiometry demonstrated fluctuating sensorineural hearing loss consistent with Ménière's disease.

At final follow-up, hearing thresholds remained stable or improved in 25 patients (92%).

Two patients experienced measurable hearing deterioration. In both cases, hearing loss was mild and did not progress further during follow-up.

The overall change in mean pure-tone average for the study population was minimal, indicating good cochlear preservation.

3.5 Tinnitus Outcomes

Before treatment, all patients reported tinnitus in the affected ear.

At final follow-up:

- Tinnitus improved in 14 patients.
- Tinnitus remained unchanged in 9 patients.
- Tinnitus worsened in 4 patients.

No patient required additional treatment specifically for tinnitus.

3.6 Vestibular Function

Caloric testing after treatment demonstrated varying degrees of vestibular hypofunction.

Post-treatment responses were:

- Unchanged in 4 patients (15%).
- Reduced in 17 patients (63%).
- Absent in 6 patients (22%).

Patients with preserved caloric responses frequently achieved excellent vertigo control, indicating that complete

vestibular ablation was not necessary for therapeutic success.

3.7 Long-Term Follow-up

Follow-up ranged from 0.5 to 4 years.

Vertigo control remained stable throughout the observation period in the majority of successfully treated patients (class A and B according to AAO-HNS 1995 criteria)

A small number of patients experienced transient disequilibrium during the early post-treatment period, which gradually resolved through central vestibular compensation.

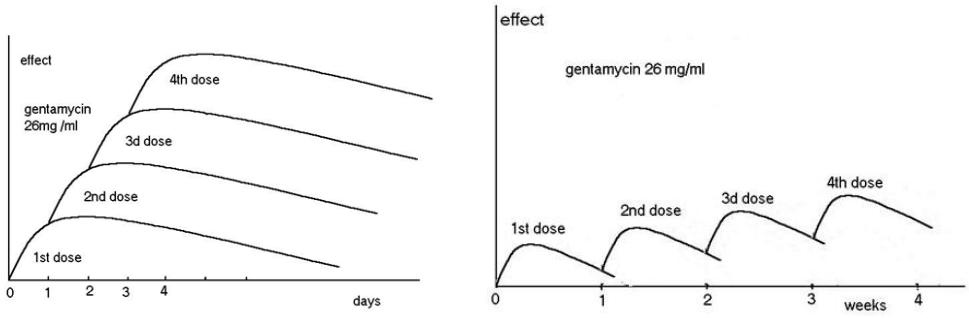
No patient developed bilateral vestibular failure or severe long-term balance disability.

Overall treatment success was maintained throughout follow-up, and no patient required destructive surgical procedures after successful gentamicin therapy.

4. Discussion

The study shows that a very low-dose intratympanic gentamicin protocol can provide excellent control of disabling vertigo while preserving hearing in the majority of patients with medically refractory Ménière's disease. Vertigo was controlled in 96% of cases, (class A and B according to AAO-HNS 1995 criteria) and hearing remained stable or improved in 92% of patients. The results add to evidence that complete vestibular ablation is not required for effective vertigo control and that carefully titrated gentamicin can minimize cochlear toxicity.

In advanced Ménière's disease, the main therapeutic objective is to eliminate or substantially reduce recurrent vertigo, the symptom most responsible for social limitation,work impairment, and reduced quality of life. In this cohort, only one patient did not achive satisfactory control, yielding a success rate comparable to or higher than rates reported with conventional intratympanic gentamicin protocols. Previous studies generally report vertigo control rates of 80% to 95%, depending on dose, follow-up duration, and patient selection [Chia et al., 2004; Gawęcki et al., 2012; Scarpa et al., 2024].

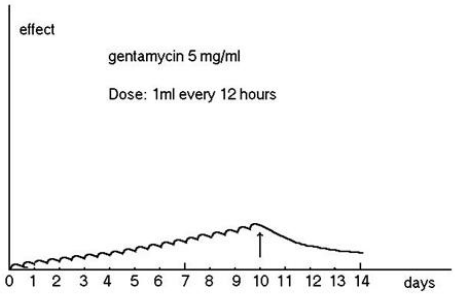


The mechanism of vertigo control after gentamicin treatment is still being clarified. Traditionally, benefit was attributed to selective vestibular hair-cell damage and consequent vestibular ablation. More recent data suggest that gentamicin may also affect dark cells and secretory mechanisms involved in endolymph regulation [Hirvonen et al., 2005; Nguyen et al., 2009; Salt & Plontke, 2018; Pullens & van Benthem, 2013]. By reducing inner-ear fluid fluctuations without necessarily causing complete vestibular loss, this effect may explain why some patients retain measurable caloric responses while achieving excellent vertigo control. A key finding of this study is the high rate of hearing preservation. Cochlear toxicity remains the major concern limiting broader use of intratympanic gentamicin [Casani et al., 2014; Scarpa et al., 2019; Webster et al., 2023]. Earlier protocols often used repeated high-dose injections or continued treatment until clear vestibular symptoms developed. Although these approaches were effective for vertigo control, some series reported hearing deterioration rates of 20%–35% [van Sonsbeek et al., 2022]. This concern has led to low-dose and titration-based regimens designed to preserve cochlear function while maintaining strong vertigo control [Nguyen et al., 2009; Zheng & Lin, 2024; Scarpa et al., 2024].

The present protocol differs from many published regimens by using an extremely low gentamicin concentration,

administered every 12 hours under close clinical surveillance. Treatment was stopped at the first subjective sign of toxicity. This approach has two potential advantages: it reduces cumulative cochlear exposure and individualizes therapy according to each patient's sensitivity rather than relying on a fixed number of injections. The favorable hearing outcomes in this cohort support the value of this conservative strategy.

Its durable effect may also permit repeat treatment if vertigo recurs.



These findings are consistent with the view that gentamicin may exert a stronger effect on the posterior labyrinth, possibly because of its proximity to the oval window [Basura et al., 2020]. At very low concentrations, the drug may preferentially influence vestibular and endolymph-regulating structures without causing complete labyrinthine ablation, thereby supporting central compensation and sustained symptom control.

The main limitations are the small sample size and lack of a control group. Nonetheless, the consistency of the outcomes and the extended follow-up period support the clinical relevance of the findings.

Vestibular testing showed outcomes ranging from preserved responses to complete caloric abolition. Notably, vertigo control was successful in many patients with residual vestibular function, further supporting the idea that complete vestibular destruction is not essential for clinical benefit. Stabilizing abnormal vestibular input may be sufficient to enable central compensation and prevent recurrent attacks. Similar findings have been reported by investigators who observed a weak correlation between caloric weakness and clinical vertigo control [van Sonsbeek et al., 2022; Zheng & Lin, 2024].

Tinnitus outcomes were generally favorable, with most patients reporting stable or improved symptoms. Although intratympanic gentamicin is not primarily a tinnitus treatment, reduced vestibular fluctuation and improved inner-ear stability may indirectly lessen tinnitus in some patients. Worsening in a small subgroup may reflect progression of the underlying disease rather than direct treatment-related toxicity.

Low-dose intratympanic gentamicin also has practical advantages. The procedure can be performed in an outpatient setting, requires limited equipment, and avoids the risks of hospitalization and surgery [Koo et al., 2025; Patel et al., 2016]. Compared with vestibular neurectomy or labyrinthectomy, it is less invasive, less costly, and associated with lower morbidity. Because its effect develops gradually, treatment may also be repeated if symptoms recur, offering flexibility in long-term management.

Several limitations should be considered. The cohort was relatively small, and the absence of a control group limits direct comparison with other treatments. Vestibular assessment relied mainly on caloric testing, which evaluates only part of vestibular function. Modern tests, including video head impulse testing (vHIT) and vestibular-evoked myogenic potentials (VEMPs), could provide more detailed information about the vestibular effects of low-dose gentamicin. Even so, the prospective design, standardized protocol, and long follow-up strengthen the reliability of the results.

Future randomized controlled studies should compare very low-dose regimens with contemporary single-injection and on-demand gentamicin protocols. Additional evaluation with modern vestibular testing may further clarify the mechanisms that allow durable vertigo control while preserving hearing.

Overall, these results support very low-dose intratympanic gentamicin as an effective, hearing-preserving option for patients with refractory Ménière's disease. Its combination of strong vertigo control, low morbidity, and favorable hearing outcomes makes it a practical alternative to destructive surgical procedures.

5. Conclusions

The findings of this prospective case series demonstrate that a very low-dose intratympanic gentamicin protocol (5 mg/mL administered every 12 hours with individualized dose titration) is an effective and safe treatment option for patients with medically refractory unilateral Ménière's disease. The protocol achieved excellent long-term vertigo control in 96% of patients while preserving or improving hearing in 92%, with only minimal treatment-related morbidity. These results support the concept that successful symptom control (meaning excellent vertigo control with preservation of useful hearing and acceptable vestibular compensation) can often be achieved without complete vestibular ablation, suggesting that stabilization of abnormal vestibular input may be sufficient to promote central vestibular compensation and durable relief from recurrent vertigo.

An important strength of this approach is the individualized titration strategy, whereby treatment is discontinued at the earliest clinical evidence of vestibular or cochlear toxicity. This minimizes cumulative gentamicin exposure and may substantially reduce the risk of cochlear damage while maintaining excellent therapeutic efficacy. In addition to its favorable safety profile, the procedure is simple to perform, is inexpensive, and avoids the morbidity associated with destructive surgical procedures such as vestibular neurectomy or labyrinthectomy. The possibility of repeating treatment in cases of recurrent symptoms further enhances its clinical usefulness.

6. Acknowledgements

6.1 AI Use Statement

The authors declare that artificial intelligence tools were used during the preparation of this manuscript. Specifically, AI-assisted tools were used for language editing, grammar correction, and improvement of clarity. The intellectual content, analysis, interpretation of results, and final approval of the manuscript remain the sole responsibility of the authors.

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