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Intratympanic gentamicin treatmentfor disabling Meniere's disease:a preliminary report

S Asawavichianginda

K. Teerasut

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Intratympanic gentamicin treatment for disabling Meniere's disease : a preliminary report

Saowaros Asawavichianginda*
Kanchana Teerasut*

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Objective : *To examine the efficacy of intratympanic gentamicin instillation as the treatment for vertigo in unilateral, incapacitating Meniere's disease.*

Setting : *Neuro-otology Clinic, Department of Otolaryngology, Faculty of Medicine, Chulalongkorn University*

Design : *A prospective study*

Material & method : *Eight patients suffering from unilateral disabling Meniere's disease*

Results : *This preliminary report presents the result of follow-up 8 patients over 6-20 month periods. All patients had either complete (87.5%) or substantial (22.5%) control of their vertigo. After treatment, caloric excitability was reduced in all of the subjects. Disablity was also improved in all of the subjects (100%). Hearing was improved in 25.0%, unchanged in 25.0% and worse in 50.0% of the patients.*

* Department of Otolaryngology, Faculty of Medicine, Chulalongkorn University

Conclusion : *Chemical labyrinthectomy using intratympanic gentamicin offers an effective treatment for unilateral disabling Meniere's disease. In this preliminary review, the overall success rate of this treatment was 100% if control of the vertigo and improvements in disability levels were the criteria examined. Despite the effectiveness of the treatment, there is a consderable potential risk to hearing.*

Key words : *Meniere's disease, Ototoxic, Gentamicin.*

Reprint request : Asawavichianginda S, Department of Otolaryngology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

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เสาวรส อัศววิเชียรจินดา, กาญจนา ธีระสุต. การฉีดยา gentamicin เข้าไปในหูชั้นกลางเพื่อรักษาโรคเมเนียร์ : รายงานผลเบื้องต้น. จุฬาลงกรณ์เวชสาร 2541 มี.ค;42(3): 173-81

วัตถุประสงค์ : *เพื่อศึกษาถึงประสิทธิภาพของการรักษาโรคเมเนียร์ โดยใช้การฉีดยา gentamicin เข้าไปในหูชั้นกลาง*

สถานที่ทำการศึกษา : *คลินิกโสตประสาทวิทยา ภาควิชาโสต นาสิก ลาริงซ์วิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย*

วัสดุและวิธีการ : *ผู้ป่วยที่มารับบริการที่คลินิกโสตประสาท ซึ่งป่วยเป็นโรคเมเนียร์อย่างรุนแรง ไม่สามารถควบคุมอาการได้จากยา*

ผลการศึกษา : *ผลการศึกษาในผู้ป่วยเมเนียร์ 8 ราย โดยใช้การฉีดยา gentamicin เข้าไปในหูชั้นกลาง พบว่าสามารถควบคุมอาการเวียนศีรษะได้ดีมาก โดยผู้ป่วยจำนวน 7 รายที่หายจากอาการเวียนศีรษะ (87.5%) อีกหนึ่งรายมีอาการเวียนศีรษะเล็กน้อยในเดือนที่ 14 หลังให้การรักษา (22.5%) ผลการทดสอบการทรงตัว (caloric test) พบว่าหลังการรักษาการทดสอบนี้ได้ผลลดลงทุกราย หลังการรักษา ผู้ป่วยทุกราย สามารถทำงานและปฏิบัติภาระกิจประจำวันได้ดีขึ้น (100%) ผลกระทบต่อการได้ยิน พบว่าจำนวน 2 ราย (25.0%) มีการได้ยินที่ดีขึ้น, 2 ราย (25.0%) การได้ยินคงเดิม และอีก 4 ราย (50.0%) การได้ยินเลวลง*

สรุป : *การวิจัยนี้พบว่า การใช้ยา gentamicin ฉีดเข้าไปในหูชั้นกลาง เพื่อทำลายหูชั้นในในการรักษาโรคเมเนียร์ ได้ผลดีมากในการควบคุมอาการเวียนศีรษะ และทำให้ผู้ป่วยสามารถมีชีวิตอยู่ได้ตามปกติ อย่างไรก็ดีข้อควรระวังคืออาจมีผลกระทบต่อการได้ยินโดยทำให้เสื่อมมากขึ้น*

There are various therapeutic modalities for patients with Meniere's disease. The ideal treatment would eliminate vertigo, restore hearing, be simple and provide little risk for the patient. Vestibular neurectomy is the most effective therapy, however this technique involves the risk of a craniotomy, which limits its use. Surgical labyrinthectomy is another almost ideal treatment for controlling vertigo but its effects on hearing limits its use.

An alternative method using ototoxic drug in the middle ear has been introduced. Schuknecht, in 1957, described the use of topical intratympanic streptomycin in eight patients.[1] Beck used low dose gentamicin in 118 patients and reported a 95% rate of vertigo improvement.[2,3]

At the Neuro-otology Clinic, Department of Otolaryngology, Faculty of Medicine, Chulalongkorn University, we used intratympanically gentamicin to treat 8 patients suffering from unilateral Meniere's disease. A prospective study was carried out and reported here.

Material and methods

Eight patients aged 27-57 years (mean 43) consisting of 2 men and 6 women who had suffered from the disease for 1-10 years (mean 4.75) were treated. All patients had a verified diagnosis of unilaterally active Meniere's disease based on clinical history (triad symptoms of fluctuating vertigo, tinnitus and hearing loss) and confirmed by audiologic and electronystagmographic testing. Their vertigo attacks were frequent and of considerable degree (vertigo interfered with empolyment and or quality of life). All patients were disabled by their disease and had failed to adequately respond to prior medical treatments including diuretics, vestibular suppressants and salt restriction.

The hearing in the affected ear was unserviceable in seven cases and caloric response was, as a rule, somewhat diminished. The patients were offered the gentamicin treatment in the hope of eliminating their vertiginous attacks. All of the patients were warned of the risk of hearing loss in the affected ear, some weeks of continued vertigo and unsteadiness after the treatment.

The patients were treated with intratympanic gentamicin as in-patients. Gentamicin was administered transtympanically through a No.5 infant nasogastric feeding tube with the tip designed in a trumpet shape. The catheter was placed into a posterior inferior myringotomy and sutured to the region of the tragal incisura and taped to the lobule.

A 1 ml-syringe was used for instillation of the gentamicin solution (40 mg/ml). The drug was injected until the fluid filled the catheter. Usually 0.6-0.8 ml was introduced each time. The residual gentamicin solution from the previous dose was emptied before each fresh injection. The nasogastric feeding tube has a volume of 0.2 ml, therefore, 0.4-0.6 ml of effective gentamicin was administered for each dose.

Three doses a day were given over three days resulting in a total of 9 doses.

The injection of gentamicin was done slowly with the patient lying supine with his head turned 45 degrees away from the treated side. This position was maintained for 30 minutes following the gentamicin administration to promote pooling of the drug in the round window niche.

Prior to each injection, patients were evaluated for the presence of vertigo, nystagmus and tandem gait (with eye open and closed) test. Treatment was terminated if there was presence of vertigo, nystagmus or deterioration of tandem gait ability. One patient had interruption of treatment because of a dizzy spell. No patient had their treatment interrupted due to the presence of nystagmus or an abnormal tandem gait test.

On discharge, the expected post treatment course (deafferentation symptoms) was noticed to each patient. If the patient had a vertiginous attack, he was advised to remain as active as possible and was given prescriptions for dimenhydrinate to be used if required.

Follow-up

The patients were seen at 1, 3, 6, 9, 12, 18 and 24 months post-treatment. All eight patients participated in follow-up visits. They have been checked for the presence of vertigo, persistent imbalance, status of tinnitus, as well as a general assessment as to disability. Their neurotologic examination was repeated as were audiologic evaluations and caloric tests.

Audiometric records were used to compare pre and post treatment hearing. Hearing parameter assessment included pure tone average (PTA) and speech discrimination scores (SDS). Each patient's post treatment hearing was classified as unchanged, improved or worse using AAO-HNS (American Academy of Otolaryngology-Head and Neck Surgery) criteria with the exception of the 24 months follow-up requirement.

Control of vertigo was classified as complete control, substantial control, limited control, insignificant control and worse using the AAO-HNS guideline as shown in table 1.

Table 1. 1985 AAO-HNS Criteria-Summary[6]

I. VERTIGO: Requires 6 months pretreatment observations and 24 months post-treatment follow-up

A. Vertigo control-numerical value:

$$\frac{\text{Average No. spells per month post-treatment (24 mo)}}{\text{Average No. spells per month pretreatment (6 mo)}} \times 100$$

Numerical value	score
= 0	complete control
= 1 - 40	substantial control
= 41 - 80	limited control
= 81 - 120	insignificant control
> 120	patient worse

B. Disability status:

0 = no disability

1 = mild disability - mild unsteadiness/dizziness that precludes working in a hazardous environment.

2 = moderate disability - unsteadiness/dizziness that results in necessity for a sedentary occupation

3 = severe disability - symptoms exclude gainful employment

II. HEARING:

A. Pure-tone average (PTA):

$$\frac{\text{Average threshold}}{\text{0.5, 1, 2, 3 KHz}}$$

B. Pretreatment audiogram:

$$\frac{\text{Worst PTA and Speech Discrimination (SD)}}{\text{6 mo prior to therapy}}$$

C. Post-treatment audiogram:

$$\frac{\text{Worst PTA and SD}}{\text{24 mo post-treatment}}$$

Hearing	PTA	SD
Unchanged	$\pm$10 dB	or $\pm$ 15%
Improved	> 10 dB decrease	or 15% increase
Worse	> 10 dB increase	or 15% decrease

Results

Seven patients received the full nine-dose course of gentamicin.One had a vertiginous attack after 8 doses of gentamicin injection. All patients experienced vertigo or ataxia after treatment, however, most were improved at the first follow-up visit.

In this study we followed the AAO-HNS criteria for evaluating our results except that in this preliminary report the 24 months follow-up data was not yet available. Our observation period is thus 20 months.

The vertigo was completely controlled with no further attacks in all of the patients except one (87.5%) who had a mild dizzy spell at 14 months after treatment. Disabilities were was absent in all patients.

A reduction in ipsilateral caloric response was achieved in all patients (100%). Caloric response change, as well as treatment effectiveness, vertigo control, and disability status are noted in table 2.

Table 2. Vestibular outcome of gentamicin treatment of unilateral Meniere's disease.

No.	Vertigo control Varbal	Vertigo control Numeric	Pretreatment caloric difference	Post-treatment caloric difference (6 mo after treatment)	Disability status	Period of follow up (mo)
1	Complete	0	18.6%	96%	No	12
2	Complete	0	39.5%	100%	No	20
3	Complete	0	12.0%	88%	No	17
4	Substantial	1	40.0%	77%	No	7
5	Complete	0	31.0%	47%	No	12
6	Complete	0	100%	100%	No	6
7	Complete	0	100%	100%	No	10
8	Complete	0	38.0%	100%	No	8

Hearing outcome is reported in table 3. Hearing was improved in 2 of 8 patients (25%), unchanged in 2 patients (25%) and worse in 4 patients (50%). Of the four patients whose hearing decreased, one had partial, one nearly complete and two had complete ablation of caloric excitability. There was no other complication such as bleeding or infection.

Table 3. Hearing outcome of gentamicin treatment of unilateral Meniere's disease.

No	Pretreatment PTA (dB)	Post-treatment PTA (dB) (6 mo after treatment)	Pretreatment SDS	Post-treatment SDS (6 mo after treatment)	Hearing Status
1	58	68	80%	40%	Worse
2	60	80	56%	44%	Worse
3	43	33	80%	100%	Improved
4	53	35	36%	60%	Improved
5	76	96	28%	0%	Worse
6	78	70	20%	20%	Unchanged
7	83	90	60%	0%	Worse
8	63	60	12%	12%	Unchanged

PTA = Pure tone average

SDS = Speech discrimination score

Discussion

On preliminary review, intratympanic gentamicin was successful in controlling disabling vertigo in all patients. One patient developed a recurrence of a dizzy spell after a symptom free 14 months post-treatment interval which indicates that the full two-year follow up period is required prior to drawing final conclusions. The overall treatment success rate in our study was 87.5%, compared to 90% reported by J.M. Nedzelski (1992)[4] and 87.5 % in 16 patients by Odkvist (1984)[5] and 91% by Beck (1986).[2,3]

One of the most important limitations of intratympanic gentamicin treatment of Meniere's disease is its potential for causing hearing loss. The partial hearing loss seen in four of our patients and the hearing improvement seen in two may due to the usual fluctuation of hearing caused by this disease. However, the treatment definitely has considerable effects on hearing. In our study, almost all of the patients had unserviceable ears before treatment, therefore, there were no complaints of a decreasing hearing following treatment. Our experience with hearing loss (50%) is more than that reported by Nedzelski[4] (15%) and Odkvist[5] (31%).

The unsatisfactory hearing outcome in this study may be due to the gentamicin overdose. The application of more sensitive cochlear status monitoring i.e. electro-cocheography, otoacoustic emission test during treatment may be required in order to detect the ototoxic effect of gentamicin.

Performing daily audiograms may not be sensitive enough to detect changes in hearing status since the toxic effect of gentamicin appears to be at its maximum 3-5 days following the administration of the drug.[7,8]

The weekly dose regimen of intratympanic gentamicin reported by Adam A (1995)[9] may reduce the incidence of hearing loss.

We conclude that gentamicin induced chemical labyrinthectomy offers a useful alternative to other types of treatment of disabling Meniere's disease. However, it should not be used in people with a diminished ability for a central nervous system compensation and prior to treatment the patient should be warned that hearing in the treated ear is at risk.

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