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ORIGINAL RESEARCH

Transtympanic Gentamicin and Fibrin Tissue Adhesive for Treatment of Unilateral Menière's Disease: Effects on Vestibular Function

Augusto Casani, Daniele Nuti, Stefano Sellari Franceschini, Elisa Gaudini, and **Iacopo Dallan,** Siena and Pisa, Italy

OBJECTIVE: To determine the effects of transtympanic injections, with a mixture composed of gentamicin and fibrin tissue adhesive (FTA), on vestibular function of patients with intractable unilateral Menière's disease.

STUDY DESIGN: This was an open, prospective study.

SETTING AND PATIENTS: The study was performed at 2 tertiary referral centers. Twenty-six patients affected by "definite" unilateral Menière's disease, unresponsive to medical therapy for at least 6 months, were enrolled.

INTERVENTION: A buffered gentamicin solution mixed with FTA was injected in the middle ear until the development of bedside vestibular hypofunction signs and/or caloric weakness in the treated ear.

MAIN OUTCOME MEASURE: Vestibular function was evaluated by 3 bedside vestibular tests (observation of spontaneous nystagmus, head shaking test, and head thrust test) and by a caloric test. Tests were performed on days 10 and 30 after completion of treatment. Tests were also performed 3, 6, and 12 months from completion of the gentamicin-FTA protocol. The effects of treatment were also assessed in terms of hearing levels, control of vertigo, and disability status.

RESULTS: In 22 of the 26 patients, only 1 gentamicin-FTA injection was necessary to obtain 1 or more signs indicating a reduction of the vestibular function in the treated ear. Four patients needed another treatment because of the persistence of their incapacitating symptoms during the follow-up. Four patients needed more than 1 injection to obtain a vestibular hypofunction. None of the patients who received 1 or 2 injections presented hearing loss in direct temporal relationship to the treatment.

CONCLUSIONS: A mixture of gentamicin and fibrin glue makes it possible to considerably reduce the number of administrations in patients with intractable unilateral Menière's disease. Spontaneous nystagmus, post head shaking nystagmus, and a head thrust sign are the clinical signs that indicate onset or progression of unilateral vestibular hypofunction. These signs were obtained with only 1 injection in 81% of patients.

EBM RATING: C

Menière's disease (MD) is a distressing disorder characterized by fluctuating hearing loss, tinnitus, aural fullness, and episodic vertigo. In about 5%-10% of patients, medical treatment is not able to control the symptoms, and patients suffer from frequent and serious vertigo spells with vomiting, which considerably limits their relational life. For these medically intractable patients, ablative surgery was recommended (labyrinthectomy, vestibular neurectomy) to obtain a complete loss of function of the pathologic labyrinth. The presence of possible disadvantages due to intracranial surgery (hearing loss, pain, facial palsy, and other, even more serious effects) has led to a renewal of the use of a therapeutic option employed in past years: chemical labyrinth ablation through aminoglycoside antibiotics, that is, gentamicin.[1,2,3,4,5,6,7]

This technique is virtually complication free compared with ablative surgical treatment such as labyrinthectomy or vestibular nerve section, and now it can be considered the treatment of choice for patients with unilateral MD in whom medical therapy has failed.[6,7]

Gentamicin is known to damage the cochlear epithelium less than the vestibular epithelium,[8,9] even though not all the evidence supports this statement.[10,11]

From the Department of Otorhinolaryngology, University of Siena (Drs Nuti and Gaudini) and the Department of Otorhinolaryngology, University of Pisa (Drs Casani, Franceschini, and Dallan), Italy.

Reprint requests: Dr. Augusto Casani, Department of Neuroscienze, ENT Section, Università degli Studi di Pisa, Via Savi, 10, 56126 Pisa, Italy.

E-mail address: a.casani@med.unipi.it.

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The intent of gentamicin treatment for refractory unilateral MD is to stop or reduce the severity and frequency of vertigo spells while preserving hearing. This outcome can be obtained because gentamicin reduces the vestibular function or because, probably, it reduces endolymph secretion.[12,13]

According to the literature, the way of administration is not crucial to the result; instead, the concentration of the drug and the number and frequency of injections seem to be more important. In fact, it seems proven that predetermined and prolonged regimens of administration, aim for a complete ablation of the vestibular function, are linked to a high percentage of hearing loss.[1,2,3,6] It is now generally accepted that, to obtain satisfactory vertigo control, complete ablation of the vestibular function is not necessary.[13] Therefore, the number and the frequency of gentamicin injections and also the concentration of gentamicin in the injected solution must be reduced to the essential minimum so as to minimize the risk of hearing loss.[2,7,13,14,15]

The ideal end point of gentamicin treatment is difficult to establish. Some physicians[4,16,17] discontinue the treatment if spontaneous nystagmus, unsteadiness, or worsening of hearing arises. Others continue the treatment until persistent dizziness or dysequilibrium develops.[5] Minor[13] has established a protocol based on weekly injections of gentamicin, which were administered up to the onset of 1 or more of the 3 clinical signs of unilateral vestibular hypofunction.

To the extent of reducing the amount of drug administration to the minimum, we decided to mix a gentamicin-buffered solution with a "glue" to protract drug permanency in the middle ear and hence allow higher absorption in the inner ear. In this report, we present the effects of a treatment with transtympanic gentamicin mixed with a human fibrin tissue adhesive (FTA) on vestibular function in patients with intractable unilateral MD. We also evaluated the effects on cochlear function and vertigo control, even if the short-term follow-up does not permit us to draw definitive conclusions about the functional results.

PATIENTS AND METHODS

Patients

Our study reports data about 26 patients with medically intractable MD seen at the Division of Otolaryngology of the University of Pisa (Pisa, Italy) and of the University of Siena (Siena, Italy) during the period September 2000 to June 2001. These subjects were followed up by means of regular controls for 12 months. All the patients were affected by definite MD, according to the criteria of the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) Committee on Hearing and Equilibrium[18]; they had also been through medical therapy (diuretics, betahistine, low salt diet) for at least 6 months.

Criteria for inclusion in the study were the following:

- unilateral MD;
- recurrent vertigo spells despite medical therapy for 6 months;
- serviceable hearing and vestibular function in the unaffected ear;
- absence of signs and symptoms suggesting an involvement of the central nervous system;
- normal MRI with gadolinium

Patients with previous otologic surgery on the affected ear were not included. Each patient gave us informed consent. The institutional review board of each local hospital approved the treatment protocol.

METHODS

Pretreatment Evaluation

Patients underwent a complete otoneurologic evaluation, caloric testing, audiogram, and impedance audiometry before beginning the study. Vestibular function was assessed by bithermal (30°C and 44°C) and ice water test when indicated. Caloric nystagmus was evaluated by recording the frequency and the maximum velocity of the slow phase with a video-based system (VNG-Ulmer). An asymmetry greater than 20% between the responses of the 2 sides was considered as a unilateral weakness. The "bedside" vestibular tests (inspection for spontaneous nystagmus, horizontal head shaking test, and head thrust test in the horizontal plane) were performed to identify any sign of "clinical" unilateral vestibular paresis.

Information about the number and severity of vertigo episodes was also obtained, and the functional level scale, according to the AAO-HNS, was assessed. Pure tone hearing acuity was calculated as the average threshold of the 4 frequencies 0.5, 1, 2, and 3 kHz.

Treatment Protocol

Human FTA (Tissucol Pronto Uso, Baxter AG, Vienna, Austria) is a 2-component biologic sealant compounded with (1) thrombin solution—calcium chloride and (2) Tissucol-aprotinin solution, which contains clotting human plasma proteins, that is, fibrinogen, factor XIII, plasminogen, fibronectin, and aprotinin. The biologic fibrin sealant is provided frozen in 2 ready-to-use syringes, which have to be thawed by bringing them to body temperature before use. The Tissucol package includes 2 syringes, which contain the 2 sealant components and 2 tips already inserted in a "Duploject" device that allows them to mix adequately.

First we mixed 2 mL of gentamicin (40 mg/mL) with 1 mL of sodium bicarbonate in order to obtain a 6.4 pH solution with 26.7 mg/mL concentration. Then 0.9 mL of thrombin was taken from a syringe and replaced with the same quantity of physiologic solution. Then 0.75 mL of diluted thrombin solution was replaced with the same amount of gentamicin bicarbonate to obtain 1 mL of preparation. The final concentration of gentamicin obtained was

equal to 20 mg/mL. The syringe containing the solution (gentamicin-bicarbonate-thrombin) was connected again to Duploject; with an insertion of a 27-gauge needle for a transtympanic injection, the device assemblage was complete.

Local anesthesia was obtained by filling the external ear with a lidocaine/procaine cream. The buffered gentamicin and the fibrin glue solution (0.3/0.6 mL) were injected through the midposterior aspect of the tympanic membrane to fill the middle ear. The 2 solutions, contained in the respective syringes, were at the time of the injection completely mixed, producing a viscous solution that rapidly formed an elastic white mass. The solidification process of this mixture resembled the last coagulation phase and took about 25-30 seconds from the start of administration. Patients remained in the supine position with the affected ear up for half an hour and then were dismissed.

Posttreatment Evaluation

After 10 days, pure tone audiometry and bedside vestibular examination were performed. After a further 20 days, patients returned for assessment of hearing acuity, bedside examination, and caloric testing. The treatment was considered to be complete when any of the bedside vestibular tests gave positive results at the time of the return visit. If 1 or more of the bedside tests were positive before the patient's being given a gentamicin-FTA injection, treatment was considered to be effective only if tests indicated a reduction of vestibular function.

One month after the injection, if patients had not developed signs of vestibular hypofunction or a significant reduction of the caloric response, a reinjection was immediately administered, and the patient was invited to come back after 1 month. If PTA in the affected ear increased more than 10 dB, the patient was informed about the risk of further hearing loss if an additional injection was needed.

Clinical evaluation of the vestibular system, caloric testing, and PTA were performed again 3, 6, and 12 months after completion of the gentamicin-FTA protocol unless patients' necessities or requests arose. Auditory function was evaluated by a comparison of audiometric tests pretreatment and posttreatment.

We considered PTA differences significant if they exceeded 10 dB. Information about the number and severity of vertigo episodes was again obtained, and the functional level scale was reassessed.

RESULTS

Thirty-one patients were treated with transtympanic gentamicin and FTA with this protocol from September 1, 1999, to June 30, 2001. Five patients were lost in the follow-up. We report the results of 26 patients who could be followed by means of regular controls for 12 months.

The 26 included 13 men and 13 women with an average age of 58 years (range, 38-80 years). The left ear was affected in 11 patients and the right ear in 15. Symptoms of unilateral MD were experienced for an average of 49 months (range, 20-151 months).

Assessment of Vestibular Function

Table 1 summarizes the age, number of injections, pretreatment and posttreatment vestibular signs, and pretreatment and posttreatment caloric results.

Most patients became symptomatic 6-10 days after the first gentamicin-FTA injection. Most of them developed mild unsteadiness and dysequilibrium, and only a few complained of the typical symptoms of acute unilateral vestibular hypofunction.

In 22 of the 26 patients, only 1 gentamicin-fibrin glue injection was sufficient to obtain 1 or more signs indicating a reduction of vestibular function. In 1 of these (no. 11), only the caloric response was reduced at the first follow-up (1 month) without any new vestibular sign. Two patients (nos. 12 and 19) obtained the vestibular hypofunction by means of 2 injections, and 2 (nos. 20 and 26) needed more than 2 injections.

Six patients (nos. 9, 13, 15, 16, 20, and 26) were retreated during the follow-up because, even if a vestibular hypofunction was obtained, they complained of recurrences of their symptoms (severe vertigo spells lasting hours).

Vestibular Signs

At the first follow-up evaluation, performed about 10 days after the injection, new "bedside" vestibular signs were detectable in 21 patients after 1 injection and in 2 patients after 2 injections: spontaneous nystagmus alone in 2 patients; paretic head shaking nystagmus in 3; head thrust sign in 2; spontaneous nystagmus and paretic head shaking nystagmus in 1; spontaneous nystagmus and head thrust sign in 4; paretic head shaking nystagmus and head thrust sign in 4; and spontaneous nystagmus, head shaking nystagmus, and head thrust sign in 7.

In 3 patients, no new sign was detected after treatment. Patient no. 11 received 1 injection, and a caloric test, performed 1 month after the injection, showed a 35% unilateral weakness. No further injections were given, and an examination 3 months after the injection revealed a head-shaking-induced nystagmus and head thrust sign, indicative of vestibular hypofunction in the treated ear, and the caloric response diminished (67%). After 1 year this patient was asymptomatic, the caloric response was still reduced, and only head shaking nystagmus was detectable. Patient no. 20 received 3 gentamicin-FTA injections before developing a reduction of the caloric response (30%) without any clinical sign of vestibular hypofunction. After 4 months he had new episodes of disabling vertigo and received 2 further injections at a distance of 1 month. At the 1-year examination, the caloric response had further diminished (27%), but no sign of unilateral hypofunction developed.

Table 1
Pretreatment and posttreatment signs and caloric results

		Pretreatment evaluation			Posttreatment evaluation					
					Signs			Caloric		
Patient no. (initials)	Age and sex	Signs	Caloric	Injections (no.)	10 days-1 month	3 months	12 months	1 month	3 months	12 months
1 (CP)	75 F	sn,ht	50%uw	1	Sn,hs,ht	hs,ht	hs,ht	nr	nr	np
2 (DR)	50 M	nl	32%uw	1	Sn,hs,ht	hs,ht	hs,ht	nr	iw	iw
3 (MI)	63 F	nl	40%uw	1	Sn,hs,ht	hs,ht	hs,ht	38%uw	iw	iw
4 (SD)	70 F	hs	26%uw	1	Sn,hs,ht	hs,ht	nl	nr	85%uw	78%uw
5 (ME)	80 M	hs,ht	41%uw	1	Sn,hs,ht	hs,ht	hs,ht	58%uw	90%uw	iw
6 (CA)	39 M	nl	nl	1	Sn,hs,ht	hs,ht	hs,ht	nr	iw	iw
7 (PT)	45 M	hs	30%uw	1	Sn,hs,ht	hs,ht	hs,ht	iw	iw	88%
8 (LM)	58 M	nl	38%uw	1	Sn,hs,ht	hs	hs	nr	nr	np
9 (BN)**	47 M	nl	32%uw	1 + 1	hs,ht	hs,ht	hs,ht	55%uw	nr	nr
10 (FP)	50 F	nl	nl	1	Sn,hs,ht	nl	nl	67%uw	42%uw	40%uw
11 (CG)	56 M	nl	nl	1	nl	hs,ht	hs	35%uw	67%uw	57%uw
12 (TE)*	38 M	nl	nl	2	hs,ht	hs,ht	hs,ht	nl	nr	nr
13 (AC)**	72 F	nl	nl	1 + 1	hs	hs	hs,ht	50% uw	33% uw	iw
14 (FD)	77 F	hs	35%uw	1	hs,ht	hs,ht	hs,ht	iw	nr	iw
15 (VG)**	66 F	nl	51%uw	1 + 1	hs,ht	sn,hs,ht	hs,ht	78%uw	nr	nr
16 (BI)**	71 F	nl	28%uw	1 + 1	hs,ht	hs	hs,ht	55%uw	nr	nr
17 (CE)	57 F	nl	31%uw	1	sn,hs	hs	hs	67%uw	51%uw	40%uw
18 (FM)	55 F	nl	55%uw	1	Sn,hs,ht	hs,ht	hs,ht	iw	iw	87%uw
19 (ML)*	61 F	nl	30%uw	2	hs	hs	hs	30%uw	61%uw	70%uw
20 (VG)Φ	49 M	nl	nl	3 + 2	nl	nl	nl	30%uw	31%uw	27%uw
21 (SV)	53 M	hs	nl	1	Sn,hs,ht	hs,ht	nl	48%uw	np	42%uw
22 (FL)	48 M	hs,ht	bw	1	Sn,hs,ht	sn,hs,ht	hs,ht	nr	nr	np
23 (CE)	70 M	nl	nl	1	Sn,hs,ht	hs,ht	hs	27%uw	87%uw	64%uw
24 (SF)	44 M	hs (ipsi)	43%uw	1	Sn,hs,ht	sn,hs,ht	hs	iw	np	iw
25 (AM)	43 F	hs	32%uw	1	hs,ht	hs	hs	37%uw	54%uw	35%uw
26 (VM) Φ	70 F	nl	nl	3 + 1	nl	hs	nl	30%uw	27%uw	nl

sn, spontaneous nystagmus; *ht*, head thrust sign; *nl*, normal; *uw*, unilateral weakness; *hs*, head shaking nystagmus; *bw*, bilateral weakness; *nr*, no response; *iw*, ice water response; *np*, not performed.
*Pts treated with multiple injections to reduce vestibular function.
**Pts treated with multiple injections to control vestibular symptoms Φ Pts treated with multiple injections to reduce vestibular function and to control vestibular symptoms.

The follow-up evaluations performed 3 months, 6 months, and 1 year after the completion of treatment demonstrate the persistence of new bedside vestibular signs in 17 patients. Only spontaneous nystagmus was rarely detectable in the long-term follow-up. In 2 patients (nos. 22 and 24) it was still present after 3 months, and in 1 patient (no. 15) a spontaneous nystagmus was observed with fast phase toward the healthy ear, which was not present after 1 month. After 1 year, although a head thrust sign was still detectable, as a new sign, in 11 patients (50% of the sample), head-shaking-induced nystagmus was the more commonly detectable vestibular sign, still present in 22 patients, in 16 of the latter (72%) as a new sign.

Caloric Testing

A symmetric response was obtained in 9 patients (35%). Unilateral weakness was identified in 16 (72%), with a difference in slow phase velocity between the 2 sides ranging from 28% to 55%. The weaker caloric response was always in the side of hearing loss. In 1 patient a bilateral hypofunction was identified. Posttreatment caloric tests were performed in all 26 patients after 1 month, in 24 after 3 months, and in 23 after 1 year. After 1 month, a reduction of the response in the treated ear was identified in 22 of the 26 (85%). In 12 of them a unilateral weakness was obtained, with a side difference ranging from 27% to 67%. In the remaining 10 patients, there was no response to warm or cold irrigations. An ice water test was performed, and a response was obtained in 4 cases, with no response in the other 6. In 4 patients no evident difference was observed from the pretreatment caloric response. Caloric testing performed in the subsequent follow-up evaluations revealed, with respect to the test performed 1 month after treatment completion, an improvement in caloric response in 7 patients and a further worsening in 9. In patient no. 13, caloric response improved after 3 months, and she had recurrences of the symptoms. She received another injection, and 1 year later an ice water test in the treated ear provoked only a few

Table 2
Pretreatment and posttreatment pure tone average and functional level score

Patient no. (initials)	Age and sex	Pre PTA	Post PTA (1 month)	Post PTA (12 months)	Pre SDS	Post SDS (1 month)	Post SDS (12 months)	Injections (no.)	Pre FS	Post FS
1 (CP)	75 F	75	80	70	10	15	25	1	3	1
2 (DR)	50 M	40	40	45	90	90	85	1	4	1
3 (MI)	63 F	70	75	75	20	25	20	1	4	2
4 (SD)	70 F	85	85	90	13	15	10	1	5	1
5 (ME)	80 M	60	60	60	65	60	55	1	3	1
6 (CA)	39 M	45	40	50	85	90	80	1	4	1
7 (PT)	45 M	65	75	60	60	45	55	1	5	2
8 (LM)	58 M	80	85	85	15	10	10	1	4	2
9 (BN)	47 M	65	65	60	50	50	60	1 + 1	4	2
10 (FP)	50 F	70	80	85	35	25	15	1	5	1
11 (CG)	56 M	35	35	40	95	95	85	1	4	2
12 (TE)	38 M	50	45	35	70	75	90	2	4	1
13 (AC)	72 F	50	60	45	75	65	80	1 + 1	4	3
14 (FD)	77 F	70	70	70	40	45	45	1	5	2
15 (VG)	66 F	55	55	70	65	60	45	1 + 1	5	2
16 (BI)	71 F	50	55	50	80	80	75	1 + 1	4	1
17 (CE)	57 F	60	70	90	50	40	15	1	4	2
18 (FM)	55 F	25	25	40	100	100	90	1	5	1
19 (ML)	61 F	NR	NR	NR	NR	NR	NR	2	3	1
20 (VG)	49 M	45	55	60	75	70	55	3 + 2	4	3
21 (SV)	53 M	65	60	40	50	55	85	1	5	2
22 (FL)	48 M	80	80	80	25	20	20	1	4	2
23 (CE)	70 M	35	35	20	95	95	100	1	4	1
24 (SF)	44 M	50	50	45	75	80	85	1	3	1
25 (AM)	43 F	55	50	35	60	70	85	1	4	1
26 (VM)	70 F	45	80	85	85	35	25	3 + 1	4	4

Pre PTA, pretreatment pure tone average; *Post PTA*, posttreatment pure tone average; *Pre SDS*, pretreatment speech discrimination score; *Post SDS*, posttreatment speech discrimination score; *Pre FS*, pretreatment functional score; *Post FS*, posttreatment functional score.

beats of nystagmus. To summarize, after 1 year the caloric test was consistent with a severe hypofunction (response to ice water) of the treated ear in 7 patients (30%), and with a complete ablation of caloric vestibular function in 4 patients (17%).

Hearing Outcome

All patients were evaluated before treatment and after 1 year. Results are shown in Table 2. Pure tone average (PTA) and speech discrimination score (SDS) before treatment were taken from the worst audiogram within 6 months before the beginning of protocol.) None of the patients who received only 1 injection presented hearing loss in direct temporal relationship to the treatment. Only 1 patient (n° 26) developed a considerable sensorineural hearing loss that may be considered a consequence of the treatment because it was observed about 15 days after the third injection. After 1 year, according to the 1995 AAO-HNS criteria (change in PTA of $>$ 10 dB or change in SDS $>$ 15%), hearing was better in 15% of patients, unchanged in 62%, and worse in 23%. If SDS is used as the evaluation tool, improved hearing was observed in 15% of the patients and worsened hearing in 19%. The remaining 66% of the patients presented no change in hearing threshold.

Functional Outcome

Patients were compared, pretreatment and posttreatment, with the functional level scale recommended in the 1995 AAO-HNS. Results are summarized in Table 2.

In the most recent 6-month evaluation period, all but 3 of the patients showed an improvement in functional level score.

Patient no. 13 developed, 4 months after the first injection, a recurrence of the disease, so she was re-treated. At the 1 year assessment, she had been free from vertigo spells for 6 months, but she complained of 2 crises of Tumarkin (sudden loss of balance).

Patient no. 20 received 3 gentamicin-FTA injections before developing a unilateral vestibular weakness without any bedside vestibular sign. After 2 months he complained of recurrent vertigo spells and received 2 more injections. At the 1-year assessment, he had been symptom free for 2 months.

DISCUSSION

We believe that transtympanic gentamicin can be considered the treatment of choice in patients with intractable

unilateral MD disease; other solutions, such as vestibular nerve section or other kinds of ablative surgery are to be reserved for those patients for whom transtympanic gentamicin has failed.

The most recent literature data confirm the tendency to deliver a low dose of gentamicin and to reduce the number of administrations. It is recognized that cochlear damage is dose related,[6,11,13,17] and it is also evident that complete ablation of the vestibular function is not necessary to obtain total control of vertigo and that this policy could result in a greater incidence of hearing loss.[1,7,13]

One of the problems related to transtympanic gentamicin therapy is the impossibility of estimating the amount of drug reaching the inner ear.[10] A part of the injected solution is lost through the eustachian tube or may not have direct contact with the round window. This could justify some unsuccessful cases, in which it has been necessary to administer numerous injections. Also for this reason many authors perform a myringotomy to expose the round window niche.[13] We mixed gentamicin with a glue so as to permit drug permanency in the middle ear for a longer period of time. In this way we obtained a more prolonged release to the inner ear, in the manner of a "retard" preparation.

The pharmacokinetics of a gentamicin-FTA mixture in the middle ear was studied in animals. Gentamicin levels in the inner ear liquids have been detected 8 hours after administration, persisting for almost 24 hours, rapidly reducing after 72 hours, and still present, in more reduced levels, even a week after administration.[19] Gentamicin was found neither in the contralateral ear nor in the blood, hence showing an absolute absence of systemic effects.[19] The association between gentamicin and FTA reduces concentration variability. In this way we obtain a more prolonged release of the drug to the inner ear. Other reports confirm this statement.[20] Moreover, it has been demonstrated that drug level and spatial distribution are markedly influenced by the time the applied substance remains in the middle ear and that the total amount of drug varies with delivery method.[20] In fact, a single drug application with volume stabilization in the middle ear has been demonstrated to allow greater absolute drug levels in the inner ear compared with a single brief application without volume stabilization.[20]

To establish the end point of gentamicin treatment, we adopted the protocol suggested by Minor to identify vestibular hypofunction onset[13]: the treatment was considered complete when any of the bedside vestibular signs resulted positive or there was a considerable worsening in the caloric response. In 85% of the patients, 1 injection was sufficient to obtain a vestibular hypofunction. However, 4 patients needed further treatment to control their symptoms.

Total ablation of vestibular function is not necessary to obtain satisfactory symptom control; total ablation could indeed be highly undesirable, especially in older people, because it may provoke a persistent and irreversible imbalance due to lack of vestibular compensation. At the 1-year follow-up, vestibular function was reduced in 20 patients; only in 3 patients did we form a complete ablation of vestibular function.

In very few patients, we observed prolonged vertigo after the injection, probably due to rapid vestibular damage. Most patients complained of moderate and transitory unsteadiness.

Only 1 patient, during the follow-up, needed to repeat vestibular rehabilitation.

The clinical vestibular signs caused by treatment with gentamicin, due to unilateral vestibular hypofunction, could, in some patients, disappear; this may be due to the recovery of activity in the peripheral vestibular system or may be caused by long-term adaptation in response to a reduced vestibular signal. Cochlear toxicity was observed in only 1 patient—after he was given 3 injections. Our results, in terms of audiometric and vestibular functions, are similar to other reports.

After 1 year, even if the follow-up is too short to draw conclusions, the remaining patients' audiometric data aligned with other reports; the hearing auditory variations are probably attributable to the natural course of MD and not linked to the employed treatment.

Pretreatment and posttreatment functional scale data, assessed by the 6-point scale recommended in the 1995 AAO-HNS, show that in most of the patients the treatment was effective. After 1 year, a substantial improvement in functional status was detectable in 23 of the 26 patients (88%). In 18 of these (69%), only 1 gentamicin-FTA injection was administered.

CONCLUSIONS

In our experience, the combination of gentamicin and fibrin glue permits a reduction of the number of administrations in patients with intractable unilateral MD. This protocol permits the administration of an ototoxic drug with a simple injection through the tympanic membrane, hence avoiding a myringotomy or application of a tympanostomy tube.

Spontaneous nystagmus, post head shaking nystagmus, and head thrust sign are the clinical signs that indicate onset or progression of unilateral vestibular hypofunction. These signs were obtained with only 1 injection in 81% of the patients.

With this schedule, we have not noticed a hearing loss incidence increase, and functional results seem to overlap those in the literature. A larger number of patients and a longer follow-up are needed to confirm the effectiveness of our protocol.

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