Lecture

Intratympanic application of gentamicin for treatment of Menière’s disease

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Abstract

Since 1974 we have treated 118 patients suffering from unilateral and bilateral (two patients) Morbus Menière with intratympanic applications of gentamicin-sulfate. In contrast to earlier attempts using this method, we did not try to destroy the vestibular apparatus, but taking into our considerations the recent findings about the pathophysiological mechanism of Morbus Menière, only to damage the secretory epithelium thus preventing the endolymphatic hydrops. Relief from symptoms could be obtained in more than 90% of our patients.

Key words: Menière's disease, gentamicin treatment, intratympanic application

Introduction

The ototoxicity of basic aminoglycoside antibiotics has long been recognized. Schuknecht (1957) was the first who utilized this observation to devise a therapeutic procedure for the treatment of unilateral Morbus Menière with intratympanically applied streptomycin-sulfate. The dread of ensuing deafness, however, did not permit this procedure any routine importance. Later, animal experiments made probable that some substances might be able to selectively protect the sensory cells of the cochlea against the toxic effect of streptomycin-sulfate, leaving the sensory cells of the vestibular apparatus unprotected, thus enabling a selective destruction of the vestibular sensory epithelium, avoiding surgical procedures. One of these substances was Ozothin, an extract of oleum terebinthii.1

Using a combination of streptomycin-sulfate and Ozothin, Lange2 succeeded in treating patients with unilateral Morbus Menière, without severe disturbances of hearing ability in most patients. Although the results obtained were rather satisfying concerning relief from vertiginous attacks, some deafness still occurred and no patient
obtained improved hearing.

In the meantime more details about the pathophysiological mechanisms underlying the genesis of Menière's disease and the action of aminoglycosidic antibiotics upon the various structures of the inner ear became known, and offered new aspects and possibilities for the use of ototoxic antibiotics in the treatment of Morbus Menière.

An abundant number of experiments revealed that the pathophysiological substrate of Menière's disease is a disturbed relation between secretion and absorption of endolymph, thus producing an endolymphatic hydrops (Schuknecht 1974). It became clear that the endolymph is produced by a special system of cells—the so-called dark cells (secretory epithelium) which are located in the stria vascularis of the cochlea and in the planum semilunatum of the crista ampullares of the semicircular canals, whereas the absorption takes place mainly in the endolymphatic sac. Another important finding was that the aminoglycosidic antibiotics damage the secretory epithelium prior to the sensory cells of the inner ear, as was first pointed out by Müsebeck (1963) and later confirmed by Nakai and Hilding and Sparwald et al.

Taking these findings into our therapeutic considerations we no longer strove to destroy the vestibular apparatus, but tried—from 1974 onward—to destroy exclusively the dark cells. We further used gentamicin-sulfate, of which it is known that the gap between cochlea and vestibulotoxicity is even wider than for streptomycin-sulfate.

**Indication**

In about 60 percent of all patients suffering from Morbus Menière, the disease tends to a spontaneous remission; i.e. the attacks get less severe and the intervals between the single attacks become longer until there are no further attacks. That means, before starting the treatment with intratympanally applied gentamicin, we observe the patients over a certain period to see whether there is a tendency for a spontaneous remission. If this was the case, there was in our opinion no reason for using gentamicin. Only in those cases where the attacks became more severe and the intervals shorter did we employ this method. Furthermore, it has to be pointed out that prior to applying gentamicin we tried to manage the disease with one of the proposed medicamental treatments.

In those cases only where neither the course of the disease nor the conventional medical treatment led to a remission, we started the treatment with intratympanally applied gentamicin. That means that only about 30 percent of our patients were treated this way.

**Method**

Prior to the treatment, all patients were submitted to an extensive diagnostic procedure. This included neuro-otological examination with examinations for spontaneous,
positional and positioning nystagmus; optokinetic nystagmus; rotatory and caloric test; audiological examinations, including electric response audiometry (ERA); and radiological examinations. To exclude other severe diseases the patients were submitted to an ophthalmological, neurological, orthopedic and internal investigation. For saving time most of these investigations were performed outclinic. The day after hospitalization the treatment begins.

The drug is applied by the use of a polyethylene tube (10 to 12 cm in length, 1.6 to 1.8 mm in diameter) placed either transmeatal or after an endaural incision and folding forward of the eardrum placed into the middle ear. After the eardrum has been folded back, the tube is secured by a packing and a skin suture in front of the external ear (Fig. 1). It is also possible to insert a ventilation tube. Getamicin is instilled into the external ear canal and pressed into the middle ear by a Politzer balloon. Twice daily 0.4 ml (16 mg) of gentamicin sulfate are instilled. The period between the instillations should be 6 to 8 hours. After the instillation the patient should lie on the side opposite the treated ear for about an hour. Depending on the progress the dosage can be increased to 0.6 mg (24 mg). The bone conduction is checked every morning. Using Frenzel’s glasses, the occurrence of any spontaneous nystagmus is
checked. The patients are questioned about sensations of unsteadiness or dizziness. This treatment is continued until the patient experiences either subjective dizziness (which is always described as being different from that during an attack) or a spontaneous nystagmus occurs to the healthy ear or the bone conduction is reduced, all of which indicate that there is damage to the inner ear. The tube can then be removed and after 1 or 2 more days of observation, the patient can be discharged. The average length of stay in our clinic was 12 days. We do not undertake any further medical treatment. Occasionally the spells of dizziness or unsteadiness can be so severe that we prescribe an antivertigo drug for one or two weeks.

From January 1974 to December 1984, 118 patients were treated in this way. The oldest patient was 72, the youngest 12 years old. The latter had a rare case of juvenile Menière's disease. Two of the patients had bilateral disease. In these cases first one ear was treated and then, after an observation period of six months, the other ear was treated. No contraindications to this treatment were found.

Results

In practically all the patients the spells of dizziness could be eliminated. The caloric excitability of the treated ear remained constant. In three cases there was loss of vestibular function, in the other patients there was a more or less noticeable caloric hypoexcitability. In 24% of the patients the hearing ability improved, in 17% there was a decrease in hearing (an improvement or worsening of the auditory performance was measured as a change in the threshold curve in the pure-tone audiogram of more than ±10 dB). It should be pointed out that among the 27 patients whose hearing

| Number of patients    | 118 | —   | Tinnitus
| Content with treatment| 112 | 95  | Disappeared
| Vertigo               |     |     | Improved
| Disappeared           | 107 | 91  | Unchanged
| Improved              | 11  | 9   | Deteriorated
| Unchanged             | —   | —   | Pressure feeling
| Hearing               |     |     | Disappeared
| Unchanged             | 67  | 57  | Improved
| Improved              | 29  | 24  | Unchanged
| Deteriorated          | 20  | 17  |
| Deafness              | 2   | 2   |
improved, there were six who had had constant moderate impaired hearing for more than one year and after treatment their hearing could be considered normal. In the two cases in which deafness resulted there was a bacterial infection of the middle ear. Tinnitus could only be improved in a number of patients. Some symptoms, such as a pressure in the ears, tinnitus, and occasional unsteadiness, occurred in some of our patients years after the treatment in times of psychologic or physical stress, change in weather or other factors (Table 1).

It is the aim of the treatment, as we have already mentioned, to damage the secretory epithelium but at the same time to maintain the function of the vestibular apparatus and the cochlea. The treatment is discontinued as soon as there is an indication that the sensory cells have been damaged. There are, however, no objective criteria for the onset of damage to the dark cells, so that in some cases the treatment was discontinued too soon and the attacks began again. After a repeated gentamicin application there was no recurrence of the attacks.

Conclusions

There is practically no indication against this kind of treatment. Even bilateral diseases can be treated this way, provided both ears are not treated simultaneously but successively, with an observation time of at least six months between the treatment of each ear.

The method should not be employed in patients older than 70 years, as beyond this age an unilateral loss of vestibular function will hardly be centrally compensated and persistent vertigo or disequilibrium may result.

It is to be assumed that when there are slightest signs of loss of function of inner ear performance such as vertigo, nystagmus or a lowering of the bone-conduction in the audiogram, these functional losses are completely reversible, whereas, the secretory epithelium is, at least in part, irreversibly destroyed.

Practically all methods of medical treatment of Menière's disease show an improvement of the symptoms, which is most temporary, and when the treatment is discontinued the attacks return. The intratympanic application of gentamicin results in a long-term improvement and in some cases in complete remission of the disease.

References

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Intratympanic gentamicin in Menière's disease


