Introduction
Meniere’s disease or endolymphatic hydrops of the inner ear is a disease of unknown etiology. Many theories have been proposed for the etiology of Meniere’s. However, the pathophysiology continues to be idiopathic. Most patients have symptoms of vertigo, sensorineural hearing loss, tinnitus, and aural fullness. The course of the disease is progressive. A similar incidence is found in both sexes and it mostly occurs in the fourth to sixth decades of life. However, the most disruptive symptom affecting daily functional life is vertigo that can last hours [1].

The majority of patients respond to medical treatments [2]. However, 10–20% of Meniere’s patients do not respond. Such failure of medical treatment has continued to be a challenge, and surgical destruction of the inner ear has been the definitive method [3].

Chemical ablation is another alternative method standing between the oral medical and destructive surgical treatments. In 1957 Schuknecht [4] reported injecting streptomycin into the tympanum of eight patients; he found that vertigo was controlled in five patients but all had profound hearing loss. This made the method unpopular, until Lange in 1989 reported good control of vertigo by using gentamicin instead of streptomycin injected intratympanically [5].

Gentamicin acts on neurosensory cells, particularly type I hair cells, as it does on the dark cells located in the crista ampullaris of the semicircular canals, the posterior wall of the utricle, and the lateral wall of the crus communes [6]. The action on type I hair cells is thought to reduce vertigo. The damage to the dark cells, which reduces endolymphatic production, decreases episodes of hydrops and consequently causes less damage to the hair cells [7].

One of the disadvantages of intratympanic gentamicin injection observed in some studies is hearing loss in almost half of the patients [8]. Further, although gentamicin is applied in the middle ear, great differences exist in the method of application, the
number of applications, and the amount of gentamicin used [9].

Other studies, however, concluded that a fixed low dose of intratympanic gentamicin treatment was an effective treatment option for patients with disabling or intractable Menière’s disease, with a low incidence of hearing deterioration [10].

Schuknecht et al. [11] showed that the most frequently involved sites by endolymphatic hydrops are the cochlea, followed by the saccule and the utriculus [12]. Therefore, elimination of saccular and utricular function may prevent vertiginous attacks [13].

Unilateral testing of otolith function has become practicable in recent years. Measurement of cervical vestibular-evoked myogenic potential (cVEMP) has become established as a unilateral test of saccular function [14]. Recently, ocular vestibular-evoked myogenic potential (oVEMP) was used to assess the function of the utricule and the utriculo-ocular pathways [15].

In 2002, De Waele et al. showed that 92% of the patients submitted to intratympanic injection (IT) of gentamicin did not respond in cVEMP testing, indicating loss of saccular function in 1 month, which persisted for 1 year after treatment [16].

However, Helling et al. [14] concluded in another study that cVEMP response cannot be considered a reliable indicator of the success of treatment.

The aim of our study was to test the effect of gentamicin on otolithic function, mainly on the utricle and saccule independently, aiming to preserve hearing and improve patients’ outcome.

Patients
This is a prospective study that was carried out on 10 patients of either sex who were referred to Alexandria University Hospital over a period of time starting from 1 March 2013 with the following strict selection criteria:

(1) Presence of unilateral definite Meniere’s disease according to the guidelines of the ‘Committee on Hearing and Equilibrium Guidelines for diagnosis and evaluation of therapy in Meniere’s disease (1995)’ [17].
(2) Age not more than 60 years.
(3) No specific sex.
(4) Have showed no improvement on medical treatment for at least 6 months and those symptoms have significantly affected their normal daily activities.

Patients seen to fulfill the following exclusion criteria were excluded from the study:

(1) Presence of otitis media.
(2) Having a PTA average better than 40 dB.
(3) Allergy to aminoglycoside or having other risks with the use of aminoglycosides for example renal problems.
(4) Affecting ear is the only hearing ear.
(5) Presence of bilateral Meniere’s disease.
(6) Having conductive hearing loss.
(7) Having known disease affecting the cervical vertebrae or spinal cord.

Patients and methods
Written consent was obtained from all patients or first-degree relatives before the study and the study was approved by the local ethics committee. All VEMPs were carried out at the audiology unit of Alexandria Petrol Hospital (Egypt).

All patients in the study group were subjected to full history taking, otoscopic examination, PTA, measurement of cervical and oVEMPs before and 1 month after the IT of gentamicin.

IT of gentamicin was performed under local anesthesia induced by applying EMLA cream to the EAC and TM of the lesion ear and waiting for 30 min. Direct perfusion of a single dose of 12 mg (0.3 ml of 40 mg/ml) was carried out using a 14-G spinal needle [14]. The injected ear was kept in the uppermost position for 30 min. This position would facilitate gentamicin diffusion to the inner ear through oval and round windows.

Protocol for cervical VEMP: the patient is made to sit with tonic contraction of ipsilateral sternocleidomastoid (SCM) muscle to the stimulated ear by looking or moving the head against resistance. Electrode montage: the ground is on the forehead, the positive electrode is placed on the middle third of the ipsilateral (SCM), and the negative electrode is placed on the ipsilateral sternoclavicular joint. The stimulus given is tone burst of 500 Hz in Blackman shape (2-1-2), intensity of 95 dB in HL delivered by AC (insert phone), 5/s, at 150 tone bursts. The filter used is of 10–1000 Hz. This is analyzed for P13 and N23, latency and amplitude.

Protocol for oVEMP: the patient is made to sit with tonic contraction of the contralateral inferior oblique muscle by looking upward in midline. Electrode
montage: The ground is placed on the forehead, the positive electrode is placed 1 cm below the lower eyelid of the contralateral eye to the stimulated ear, and the negative electrode is placed 1 cm below the positive one. The rest of the parameters are the same as those for cVEMPs except that the analysis is for N10, latency and amplitude.

Results
This study was performed on 10 patients with intractable Meniere’s disease. Sixty percent of the patients were male. The mean age was 36.50 years with a SD of 9.48. Fifty percent of the patients were injected in the right ear and 50% were injected in the left ear (Table 1).

The morphology of VEMPs categorically rated as present, absent, or distorted showed that there was a significant change in morphology before and after injection. Before the injection 10 and 0% of patients had absent waves in the oVEMP and cVEMP tests, respectively; after injection this percentage increased significantly to 70 and 100%, respectively. The level of significance was remarkable with an oVEMP $P$ value of 0.002. The significance for cVEMPs was $P$ less than 0.001, with our level of significance set at $P \leq 0.05$ (Table 2).

For those with preserved reflexes, further comparison was carried out on the preinjection and postinjection latencies and interpeak amplitudes. With regard to VEMPs before injection, the mean N1 latency was $12.0 \pm 0.35$ ms, whereas the mean P1 latency was $15.68 \pm 1.17$ ms. The mean N1P1 amplitude was $3.05 \pm 1.92$ micro Volts (μV). For the three patients with preserved reflexes after injection, the mean N1 latency was $12.26 \pm 0.29$ ms, whereas the mean P1 latency was $15.10 \pm 1.14$ ms. The mean N1P1 amplitude was $1.41 \pm 0.53$ μV. The $P$ value for N1 latency was 0.204, that for P1 latency was 0.662, and that for N1P1 amplitude was 0.226. Consequently, no significant effect of IT injection of gentamicin was found in these patients, as $P$ level was set at $P \leq 0.05$.

With regard to cVEMPs before injection, the mean P13 latency was $15.96 \pm 1.13$ ms, whereas the mean N23 latency was $23.52 \pm 0.36$ ms. The mean P13N23 amplitude was $23.85 \pm 10.40$ μV. Postinjection correlation was not possible as all patients had lost their cVEMPs (Table 3).

The effect of injection of gentamicin on hearing in our patients was also analyzed. The mean threshold for hearing at each of the tested frequencies for all patients was analyzed and compared before and after injection. Overall analysis showed no significant difference in hearing levels before and after injection in all six tested frequencies of PTA. $P$ values were 1 for 250 Hz, 0.882 for 500 Hz, 0.221 for 1000 Hz, 0.081 for 2000 Hz, 0.158 for 4000 Hz, and 0.907 for 8000 Hz. Level of significance was set at $P \leq 0.05$ (Table 4).

Discussion
Controversies remain, despite the fact that the identification of Meniere’s disease goes back to more
function. of vestibular ablation of gentamicin on saccular
that cVEMP can be used to assess the adequacy
conclude in agreement with this study’s suggestion
100% of patients lost their cVEMPs. Thus, we can
et al. [14] in whose study also
reported by Helling
cVEMP after IT gentamicin, similar to that
In our study 100% of our patients lost their
the saccule.
will disappear in case of delay of treatment of the disease.
35% of patients [19], we suggest that the 30%
reported the absence of
present cVEMP , which means that none of the cases
had absent cVEMP before injection. Even though a
study by Welgampola et al. showed improvement; this is mostly because of our
the case in our study, in which only one patient (10%)
doctors concluded that incomplete cell death or due to uncr ossed fibers of
vestibulo-ocular reflex pathway [19]. In our study, the
effect of gentamicin was similar; 70% of our patients
lost their oVEMPs after injection. The remaining 30%
had distorted waves. None of our patients preserved
their reflexes completely after injection.

With regard to the effect of Meniere’s disease on
cVEMP, only 30% of our patients had distorted
cVEMPs before injection and the remaining 70% had
present cVEMP, which means that none of the cases
had absent cVEMP before injection. Even though a
study by Welgampola et al. reported the absence of
waves in 35% of patients [19], we suggest that the 30%
of the distorted figures in the present study would later
disappear in case of delay of treatment of the disease.
We think it represents early affection of the disease of
the saccule.

In our study 100% of our patients lost their
cVEMP after IT gentamicin, similar to that
reported by Hell ing et al. [14] in whose study also
100% of patients lost their cVEMPs. Thus, we can
conclude in agreement with this study’s suggestion
that cVEMP can be used to assess the adequacy of vestibular ablation of gentamicin on saccular function.

than 150 years. IT injection of aminoglycosides
introduced by Schuknecht is considered a breakthrough,
even though the exact effect of gentamicin on the inner
ear is still not 100% clear.

Our patients showed no statistically significant
effect of IT gentamicin on hearing considering the
overall results, which is in accordance with those of
Kasemsuwan et al. [1] This suggests that IT gentamicin
will have better results in patients with intractable
Meniere’s disease who have better hearing.

Some studies showed hearing improvement after IT
gentamicin; for example, 16% of patients showed
improvement in a study by Sala et al. [18] This is mostly because these patients were in the early stage of
the disease at which decrease in hydrops gives a chance
for cells in earlier stage of damage to heal. This was not
the case in our study, in which only one patient (10%)
showed improvement; this is mostly because of our
strict selection of patients who already had a hearing
loss of at least 40 dB.

With regard to the effect of Meniere’s disease on
oVEMP and Meniere’s disease is scarce. In our study, oVEMPs were found to be absent in 10%
of patients and distorted in another 10%, which
is in accordance with the study in which Schuknecht
concluded that utricle was less affected by Meniere’s
disease than was saccule [11].

Studies on the effect of gentamicin on oVEMP are
deficient in the literature. Only guinea pig studies could
be found where ‘70%’ of animals lost their reflexes
after being injected with 2 mg of IT gentamicin. These
authors concluded that incomplete abolition was either
due to incomplete cell death or due to uncrossed fibers of
the vestibulo-ocular reflex pathway [19]. In our study, the
effect of gentamicin was similar; 70% of our patients
lost their oVEMPs after injection. The remaining 30%
had distorted waves. None of our patients preserved
their reflexes completely after injection.

Latencies were almost similar in the remaining three
patients in relation to their own preoperative results.
Amplitudes when compared with preoperative preserved
reflexes were diminished but this was statistically
insignificant. Our results were in accordance with those
of other authors such as Helling et al. [14] where the
utricle was also less affected by IT gentamicin than was
the saccule. They suggested that it was due to different
patterns of absorption by different parts of the inner ear.

**Conclusion**

We can thus conclude that our single low-dose injection
can have significant effect on the otolithic function,
predominantly on the saccule, with no significant
effect on hearing.

**Acknowledgements**

**Conflicts of interest**

None declared.

**References**

1. Kasemsuwan L, Jariengprasert C, Chaturapatanont S. Transtympanic
Assoc Thai 2006; 89:979–985.
2. Klockhoff I, Lindblom U, Stahle J. Diuretic treatment of Meniere
100:262–265.
3. Brown JS. A ten year statistical follow-up of 245 consecutive cases of
endolympathic shunt and decompression with 328 consecutive cases of
4. Schuknecht HF. Ablation therapy in the management of Meniere’s
5. Lange G. Gentamicin and other ototoxic antibiotics for the transtympanic
246:269–270.
6. Kimura RS. Distribution, structure, and function of dark cells in the


