Intratympanic gentamicin for Meniere's disease: a meta-analysis

CRD summary
This meta-analysis investigated intratympanic gentamicin treatment for Meniere's disease. The authors concluded that the treatment appeared effective in the relief of vertigo, and that loss of hearing and word recognition were not significant side-effects. Given the weak designs of the included studies, the reliability of the authors' conclusions is unclear.

Authors' objectives
To review the published literature on intratympanic gentamicin treatment of intractable Meniere's disease.

Searching
MEDLINE and EMBASE were searched from 1985 to 2003; the search terms were reported. References from reviews and retrieved articles were also checked. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials, case-control studies, and prospective cohorts or retrospective cohorts reporting on 10 or more patients were eligible for inclusion. Comments, letters, editorials and reviews were excluded.

Specific interventions included in the review
Studies administering gentamicin into the middle ear by transtympanic injection or by using a specially designed catheter were eligible for inclusion. Interventions with concomitant administration of other drugs, such as dexamethasone, by local, oral or parenteral route were excluded.

The majority of the studies applied a titrated protocol, according to the patient's symptoms, rather than a fixed-dose protocol. The number of injections and dose varied in the included studies (e.g. 1 to 24 injections).

Participants included in the review
Studies with patients diagnosed according to the Committee on Hearing and Equilibrium of the American Academy of Otolaryngology Head and Neck Surgery (1985 or 1995) as having definitive Meniere's disease were eligible for inclusion. Patients with related conditions (i.e. post-traumatic, post infectious, syphilis, Cogan syndrome) were not eligible.

Outcomes assessed in the review
Vertigo control, hearing and word recognition, functionality and disability were considered. Most of the included studies reported the frequency of vertigo and hearing reduction (measured in dB). Some studies reported also on word recognition (expressed as a percentage), functional level and the results of caloric tests.

How were decisions on the relevance of primary studies made?
Two independent otolaryngologists reviewed the retrieved articles. Any disagreements were resolved through discussion or by consulting a third reviewer.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Two reviewers extracted the data independently and any discrepancies were resolved by discussion.

The reviewers calculated two success rates for vertigo. One definition was the complete remission of vertigo; the other method was counting complete or substantial control as success. The comparison was between baseline and follow-up at 18 to 24 months.

Methods of synthesis
How were the studies combined?
A classic (Cochran 1954) and a revised (Einarson 1997) random-effects meta-analysis were used to compute the pooled success rates with 95% confidence intervals (CIs). In addition, pooled changes in hearing and word recognition before and after treatment were calculated, along with 95% CIs. Pooled changes in hearing and word recognition were also presented for subgroups. Missing standard deviations for the hearing or word recognition scores were either calculated from the CI, or estimated from the average standard deviation of the included studies.

How were differences between studies investigated?
Statistical heterogeneity was assessed. The studies were analysed separately for prospective and retrospective designs, and the studies were grouped according to the method of drug administration (i.e. fixed or titrated dose).

Results of the review
Sixteen studies (n=627; published in 15 publications) were included in the review. There was one prospective controlled cohort, and 7 prospective and 8 retrospective cohorts.

Vertigo.

The overall success rate for full recovery was 74.7% (95% CI: 67.8, 81.5), based on 15 studies. The removal of 2 studies with values below the expected average effect size explained the heterogeneity, and the subsequent reanalysis raised the success rate to 80%.

The full or substantial recovery rate was 92.7% (95% CI: 89.5, 96.0). The prospective studies showed a greater complete success rate than the retrospective studies, as did studies using a titrated dose rather than a fixed-dose protocol.

Hearing.

The overall reduction in hearing was 1.5 dB (95% CI: -12.0, 9.1; not significant), based on 15 studies. The prospective studies showed a higher reduction than the retrospective studies, as did studies using a fixed dose rather than a titrated-dose protocol. However, none were clinically important (>=10 dB) or statistically significant.

Word recognition.

Word recognition was worsened by 2% after treatment (95% CI: -16.5, 20.4; not significant), based on 12 studies. The prospective studies showed a lower reduction than the retrospective studies, as did studies using a titrated dose rather than a fixed-dose protocol. None were clinically important (>=15%) or statistically significant.

Authors' conclusions
Intratympanic gentamicin treatment for intractable Meniere's disease appeared effective in the relief of vertigo. Furthermore, cochleotoxicity and ototoxicity were not likely to be substantial side-effects of the treatment. However, the designs of the included studies were weak.

CRD commentary
The review was based on a clear research question and explicit inclusion criteria. The search strategy was fairly comprehensive and had no language restrictions. However, the sole focus on published studies meant that publication
bias could not be ruled out. Adequate measures were taken to reduce errors and bias in the final selection of papers and the data extraction process, but it was unclear whether such measures were also applied to the initial screening of papers. Sufficient details of the primary studies were provided, along with some analysis of heterogeneity to support the pooling of data. However, given that there was no apparent assessment of study quality, together with the fact that the included studies employed weak study designs and small samples (all below 100 participants), the reliability of the authors' conclusions is unclear.

**Implications of the review for practice and research**

**Practice:** The authors stated that it is important to select patients carefully for a titrated treatment with low-dose gentamicin. Patients should be informed of all possible therapeutic options and consequences.

**Research:** The authors stated that an adequately powered double-blind, placebo-controlled, randomised trial on the use of gentamicin for Meniere's disease is needed.

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