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[Intervention Review]

Betahistine for tinnitus

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ABSTRACT

Background

Tinnitus is a symptom defined as the perception of sound in the absence of an external source. In England alone there are an estimated ¾ million general practice consultations every year where the primary complaint is tinnitus, equating to a major burden on healthcare services. Clinical management strategies include education and advice, relaxation therapy, tinnitus retraining therapy, cognitive behavioural therapy, sound enrichment using ear-level sound generators or hearing aids, and drug therapies to manage co-morbid symptoms such as sleep difficulties, anxiety or depression. As yet, no drug has been approved for tinnitus by a regulatory body. Nonetheless, over 100,000 prescriptions for betahistine are being filled every month in England, and nearly 10% of general practitioners prescribe betahistine for tinnitus.

Objectives

To assess the effects of betahistine in patients with subjective idiopathic tinnitus.

Search methods

The Cochrane ENT Information Specialist searched the Cochrane ENT Register; Central Register of Controlled Trials (CENTRAL, via the Cochrane Register of Studies); Ovid MEDLINE; Ovid Embase; Web of Science; ClinicalTrials.gov; ICTRP and additional sources for published and unpublished trials. The date of the search was 23 July 2018.

Selection criteria

Randomised controlled trials (RCTs) recruiting patients of any age with acute or chronic subjective idiopathic tinnitus were included. We included studies where the intervention involved betahistine and this was compared to placebo, no intervention or education and information. We included all courses of betahistine, regardless of dose regimens or formulations and for any duration of treatment.

Data collection and analysis

We used the standard methodological procedures expected by Cochrane. Our primary outcomes included tinnitus loudness and significant adverse effects (upper gastrointestinal discomfort). Our secondary outcomes included tinnitus symptom severity as measured by the global score on a multi-item tinnitus questionnaire, depressive symptoms, symptoms of generalised anxiety, health-related quality of life, other adverse effects (e.g. headache, drowsiness, allergic skin reactions (pruritis, rashes) and exacerbation of tinnitus) and tinnitus intrusiveness. We used GRADE to assess the quality of evidence for each outcome; this is indicated in *italics*.

Main results

This review included five studies (with a total of 303 to 305 participants) comparing the effects of betahistine with placebo in adults with subjective idiopathic tinnitus. Four studies were parallel-group RCTs and one had a cross-over design. The risk of bias was unclear in all of the included studies.

Due to heterogeneity in the outcomes measured and measurement methods used, very limited data pooling was possible. When we pooled the data from two studies for the primary outcome tinnitus loudness, the mean difference on a 0- to 10-point visual analogue scale at one-month follow-up was not significant between betahistine and placebo (-0.16, 95% confidence interval (CI) -1.01 to 0.70; 81 participants) (*very low-quality evidence*). There were no reports of upper gastrointestinal discomfort (significant adverse effect) in any study.

As a secondary outcome, one study found no difference in the change in the Tinnitus Severity Index between betahistine and placebo (mean difference at 12 weeks 0.02, 95% CI -1.05 to 1.09; 50 participants) (*moderate-quality evidence*). None of the studies reported the other secondary outcomes of changes in depressive symptoms or depression, anxiety symptoms or generalised anxiety, or health-related quality of life as measured by a validated instrument, nor tinnitus intrusiveness.

Other adverse effects that were reported were not treatment-related.

Authors' conclusions

There is an absence of evidence to suggest that betahistine has an effect on subjective idiopathic tinnitus when compared to placebo. The evidence suggests that betahistine is generally well tolerated with a similar risk of adverse effects to placebo treatments. The quality of evidence for the reported outcomes, using GRADE, ranged from *moderate* to *very low*.

If future research into the effectiveness of betahistine in patients with tinnitus is felt to be warranted, it should use rigorous methodology. Randomisation and blinding should be of the highest quality, given the subjective nature of tinnitus and the strong likelihood of a placebo response. The CONSORT statement should be used in the design and reporting of future studies. We also recommend the development of validated, patient-centred outcome measures for research in the field of tinnitus.

PLAIN LANGUAGE SUMMARY

Betahistine for tinnitus

Background

Tinnitus describes 'ringing', 'whooshing' or 'hissing' sounds that are heard in the absence of any corresponding external sound. Between 5% and 43% of people experience this symptom and for some it has a significant negative impact on their quality of life. Tinnitus can be managed through education and advice, prescription devices that improve hearing, over-the-counter devices that generate background sounds, psychological therapy and relaxation therapy. Drug therapies are used to manage complaints associated with tinnitus such as sleep difficulties, anxiety or depression. No drug therapies exist that manage the tinnitus itself. Nonetheless, betahistine is often prescribed for tinnitus. The purpose of this review is to evaluate the evidence from high-quality clinical trials to work out the effect of betahistine on people's tinnitus. We particularly wanted to look at the effect of betahistine on tinnitus loudness and the side effects of betahistine.

Study characteristics

Our review identified five randomised controlled trials with a total of 303 to 305 participants who suffered from tinnitus. These studies compared participants receiving betahistine to those receiving a placebo. Four study designs allocated participants into parallel groups. In one study, participants consented to take all study medications in a pre-defined sequence. The outcomes that we evaluated included tinnitus loudness and intrusiveness, tinnitus symptoms and side effects.

Key results

The included studies did not show differences in tinnitus loudness, severity of tinnitus symptoms or side effects between participants receiving betahistine and participants receiving a placebo. No significant side effects were reported. We had planned to evaluate changes in tinnitus intrusiveness, depression and anxiety and quality of life, but these were not measured. The evidence suggests that betahistine is generally well tolerated with a similar risk of side effects to placebo.

Quality of the evidence

The quality of the evidence ranged from moderate to very low. The risk of bias in all of the included studies was unclear. The results were drawn from one or two studies only. In some studies, the participants that were included did not fully represent the entire population of people with tinnitus and so we cannot draw general conclusions.