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The potential for there to be a drug treatment for troublesome tinnitus has been a topic of substantial and long standing interest, and questions about this arise very often in the clinic. Many compounds of interest have been trialled, and of 219 recruiting or completed tinnitus studies described on clinicaltrials.gov, 68 (31%) involve drug treatments or dietary supplements. One of the reasons for the sparse progress to date has been the lack of effort: this has not been an area where financial nor time resources have been deployed until relatively recently. In this section we review what was reported regarding tinnitus and pharmacology in 2016, including tinnitus caused by drug treatments, how that might be prevented, and tinnitus treatment by drugs.

The literature search that underpinned this section was conducted on PubMed, used the key words tinnitus and drug, considered human studies only, and papers published in English between 1.1.16 and 31.12.16.

Ototoxicity and its prevention

Platinum-based chemotherapy is highly effective in treating cancer, and has contributed to modern survival rates which approximate 66% five years after diagnosis [1]. These treatments are ototoxic however, leading to permanent hearing loss and tinnitus in many cancer survivors, which can potentially lead to reduced quality of life in survivorhood. The extent of ototoxicity appears to depend on several factors, including genetic susceptibility and cumulative dose among others [1]. Van As et al published a Cochrane Review in 2016 [2] of different infusion durations of cisplatin in children, and how this might potentially prevent ototoxicity: only one randomised controlled trial was identified. This had only immediate post treatment follow-up, and no consideration of tinnitus. In a context where post-treatment development or progression of hearing loss can occur with cisplatin treatment
in adults, and where tinnitus can develop in 40% of patients, this is inadequate, as van As and colleagues discuss.

Some cancer patients receive both platinum-based chemotherapy and radiotherapy, and ototoxicity is a major concern when the tumour is in the head and neck, such that the cochlea is doubly vulnerable. Niemensivu et al [3] noted that patients undergoing high dose cisplatin and radiotherapy treatment “will suffer from hearing deficits” but sought to investigate the ototoxicity effects of low dose cisplatin, and radiotherapy. Whilst the report of reduced hearing loss and tinnitus compared with higher doses of cisplatin are encouraging, this study did not involve high frequency audiometry (10-16kHz), and the patient numbers (n=9) were too low for any definitive conclusions.

Other drugs that can cause ototoxic tinnitus include quinine and salicylate, and their modes of action were studied by Alvan et al [4]. Whilst there is a consensus that both drugs affect the cochlear Outer Hair Cells (OHC), which are involved in the fine-tuning of the mammal cochlea, rather than the Inner Hair Cells (IHC), which convert the vibrational energy of sound into neural impulses, Alvan and colleagues propose that the OHC impact of quinine and salicylate is accomplished by quite different molecular mechanisms, and this may have important implications for prevention, and deeper understandings of cochlear dysfunction.

Treatment: reviews

Literature reviews can be of major value, allowing assessment of the quality of published evidence, and the synthesis of data across studies to increase the strength of a particular finding. Several reviews in the area of drug treatments for tinnitus were published in 2016 from quite different perspectives. Nguyen et al undertook a fascinating and innovative review [5] of patents taken out between 2011 and 2015 regarding drug delivery for inner ear disorders. The 34 patents they identified ranged from new therapeutic agents, to systems of sustained release, to new technologies for drug delivery. Whilst tinnitus was not the only topic of this paper, clearly this is an area of great interest regarding treating tinnitus, and this paper makes a significant contribution to the literature.

One particular option for drug treatment of inner ear disorders is the intra-tympanic administration of steroids, and Lavigne et al reviewed the evidence [6]. Their conclusion was that they identified some but not unequivocal evidence that intra-tympanic steroid injection may be beneficial for some inner ear disorders that include tinnitus in their symptom profile, such as Ménière’s disease and idiopathic sudden sensorineural hearing loss, and that there might be some improvement in the associated tinnitus for some patients. There was no evidence of benefit for tinnitus alone however.

An exploratory review of an interesting idea was...
undertaken by Smith and Zheng [7]. They proposed that tinnitus may be considered as a form of ‘sensory epilepsy’, based in part on the finding that some anti-epileptic drugs may improve tinnitus in some cases. They then explore the possibility that cannabis and related compounds may have an anti-epileptic effect, and thus may improve tinnitus. Whilst this is essentially speculative, the fact that some in the tinnitus community are prepared to envisage innovative hypotheses and proposals is encouraging.

Treatment: clinical trials
Two papers each reporting the results of a clinical trial were published in 2016. Singh et al investigated the potential benefits of vitamin B12 in a pilot study[8]. This was a placebo controlled double blind trial and whilst the results of the pilot indicated some benefits for tinnitus severity, there are some caveats. The outcome measures used were not validated and robust instruments, and the treatment and placebo groups both contained a mixture of vitamin B12 deficient and sufficient individuals, who might be expected to have quite different reactions to the six weekly intramuscular B12 injections that comprised the treatment under investigation.

Polanski et al investigated the potential benefits of antioxidant therapy [9] for tinnitus in older patients, the treatments under study comprising Gingko biloba, vitamins C and E, and papaverine hydrochloride versus an inert placebo. No benefits for tinnitus with these therapies was found using the Tinnitus Handicap Inventory [10] as an outcome measure.

Whilst not a trial, some other data regarding dietary supplements for tinnitus was published in 2016. Coelho and colleagues [11] undertook a large survey (n=1788) across 53 countries, and 23.1% of the respondents self-reported taking dietary supplements for tinnitus. There were reported benefits for sleep, emotional state, concentration, and for hearing, with some adverse effects including headaches. The authors reflected on the potential biases in a survey of this kind, and concluded that whilst supplements are not generally beneficial for tinnitus, in some patients there might be an effect.

Discussion
Although there were some publications of interest regarding potential drug treatments for tinnitus in 2016, they were not replete, and this is an area that might benefit from sustained and comprehensive efforts.
References


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