improvement was noticed in 60% (9/15) of patients only after white noise 1 month period, but a great amount of improvement in 76.9% (10/13) of patients after 1 month of conventional stimulation demonstrated the degree of tinnitus reduction regarding the stimulation modality. Some patients experienced no improvement or exacerbation of tinnitus, 1 patient was withdrawn from the study, no serious adverse event occurred in this ongoing study.

Conclusion

These preliminary results suggest that CIs have a positive effect on unilateral tinnitus resulting from an SSD. But several hypothesis are pending according to the mechanisms by which the CI reduce tinnitus such as habituation, peripheral electrical nerve stimulation or complex cortical reorganization. This study confirms that CI is an effective approach for tinnitus treatment in selected subjects, but further data still necessary to define the optimal stimulation mode.

PS 695

A Balanced Randomised Placebo Controlled Double-Blind Study to Investigate the Efficacy and Safety of AUT00063 versus Placebo in Subjective Tinnitus: Protocol for a Phase IIa Trial

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Reduced activity at certain sites in the brain (called "voltage-gated potassium channels") has been linked to hearing problems, like age-related loss of hearing or tinnitus (a 'ringing' or buzzing noise in the ears). AUT00063 is an experimental new medicine that has been developed to improve the action of these specific channels and so treat the brain component of these hearing problems. The main purpose of this study is to try to demonstrate an improvement in the severity of tinnitus after 28 days of treatment with the study medicine or the placebo (dummy drug which does not contain the medication). The first participant was recruited in November 2014, and recruitment will continue at 18 UK sites throughout 2015, with a target sample size up to 152. A clinically relevant interpretation of tinnitus severity relates to the functional impact of tinnitus on daily activities and is measured as a primary outcome using the Tinnitus Functional Index. Secondary outcomes consider the effect on tinnitus loudness. Safety and efficacy will be determined by looking at a number of assessments (physical examinations, blood sampling, hearing assessments, questionnaires, etc.) and in case of any serious medical event during the study. A safety follow-up will be conducted after the treatment period.

Here we present the clinical trial design, and discuss some of the design and implementation challenges that we have had to overcome.

ClinicalTrials.gov Identifier: NCT02315508.

Funding

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PS 696

Inhibition of L-type Calcium Channels for Preventing Noise Induced Hearing Loss and Tinnitus

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Background

Increased spontaneous neuronal activity is thought to underlie the pathological changes in tinnitus. Previous studies have demonstrated efficacy of nimodipine, an L-type calcium channel blocker, on reversing these changes in salicylate and quinine induced tinnitus in rat models (Jastreboff, 1991). However, human trials with nimodipine have not consistently demonstrated efficacy as treatment for tinnitus, prompting examination of other calcium channel blockers. In this study, we examined verapamil as a preventative therapy for noise induced tinnitus and hearing loss.

Methods

Male Sprague-Dawley rats (n = 5 - 7/group) were administered verapamil i.p. 15 minutes before a one hour unilateral noise exposure (16 kHz, 106 dB SPL). Hearing thresholds at 12 and 20 kHz were measured using auditory brainstem response (ABR). Gap inhibition of the acoustic startle response (GiASR) was used to assess tinnitus across six frequencies (4, 8, 12, 16, 20 and 24 kHz) at two intensities (45 and 60 dB SPL).

Results

There were no significant differences in hearing thresholds between verapamil and saline groups at any time point or frequency. Within an hour following noise exposure, rats administered verapamil demonstrated enhanced Gap detection at both 45 dB (11.5%, $p < 0.01$) and 60 dB (12.8%, $p < 0.05$, n = 7/group). The effects were more pronounced 24 hours after noise exposure, with rats that received verapamil suppressing their total startle by 18.0% and 20.2% more than controls at 45 dB and 60 dB, respectively ($p < 0.01$, n = 7/group). By five days after noise exposure, rats that received verapamil returned to baseline levels of Gap detection.

Conclusions

Our results demonstrate that verapamil may prevent development of noise induced tinnitus and thus warrants further study. Future studies aim to examine the localization of L-type calcium channels in the central auditory system and explore effects of direct verapamil administration. We also plan to examine whether systemic administration of verapamil prevents synapse loss in the cochlea.

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ABSTRACT BOOK

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