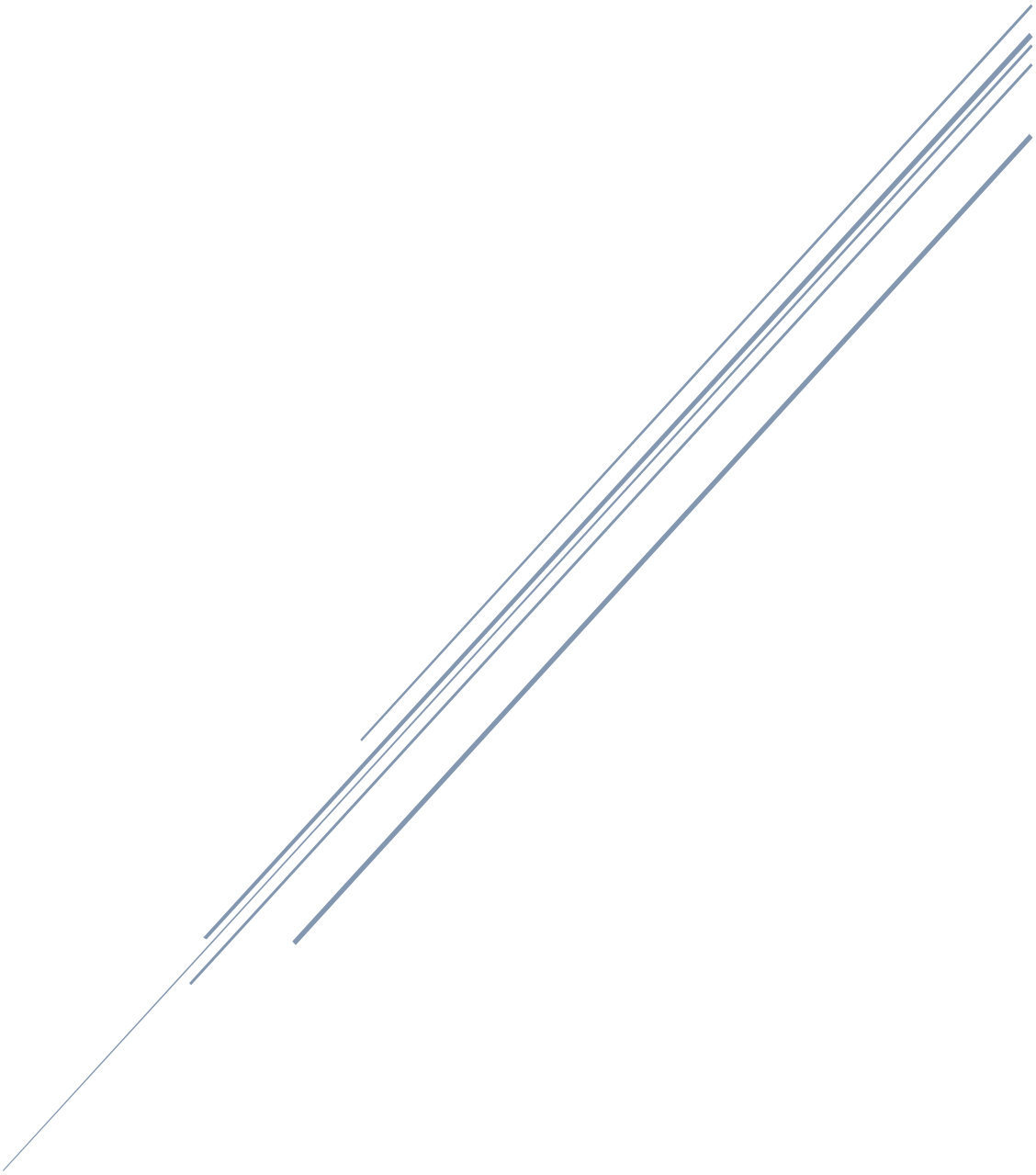
EFFECT OF TOPICAL INTRA-AURICULAR LIDOCAINE ON TINNITUS: A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED STUDY.

NCT05711641



AUGUST 04, 2022

STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN:

Tinnitus is a prevalent symptom, which can drastically impact the quality of life of the individual and for which there is still no proven effective treatment. Lidocaine has been widely investigated with high rates of tinnitus suppression, but its systemic use has not been shown to be viable due to the fleeting response and the risk of potentially serious side effects. The clinical observation of the improvement of chronic tinnitus in some individuals after the use of otological drops indicated for the treatment of otitis externa aroused our interest in the action of topical intraauricular lidocaine in reducing the intensity of tinnitus, motivating the realization of this study.

The objective of this study is to evaluate the action of 10% topical intraauricular lidocaine on the perception of tinnitus intensity compared to placebo.

This project was designed as a randomized, crossover, placebo-controlled, double-blind, randomized clinical trial. It was approved by the Research Ethics Committee (REC) of the host institution under opinions number 4.188.11 and 5.562.868, and was registered at ClinicalTrial.gov under identification number NCT05711641. The participants were properly informed and signed a informed consent form.

The selected subjects were patients of an otolaryngology center who sought care for tinnitus complaints between April 7, 2021, to April 6, 2022. Of them, 113 patients met the inclusion criteria, and none of the exclusion criteria, and were invited to participate in the study through WhatsApp contact. Thirty-three patients responded and attended the initial appointment, one was excluded for having only pulsatile tinnitus on the day of the appointment. Thirty two patients were enrolled and 28 completed both assessments.

The inclusion criteria were age over 18 years, continuous tinnitus for at least six months, and a visual analog scale (VAS) tinnitus intensity score of at least three points on the days the substances were administered. The exclusion criteria were otologic infection, tympanic membrane perforation, anatomic external ear changes, pulsatile tinnitus, objective tinnitus, known allergy to lidocaine or other topical anesthetics, pregnancy, cardiac arrhythmia, epilepsy, previous history of seizure, or use of anticonvulsants.

The website www.randomization.com was used to define the order of substance administration, defining whether the patient would start the study as a case or a control. The subjects were randomized by the “Heads or Tails” method in cases of bilateral and symmetrical tinnitus, with one Real coin (official currency of the country) being tossed by the patient himself. “Heads” was previously defined as the right ear, and “tails” as the left ear. In the case of bilateral and asymmetrical tinnitus, the study ear was the ear where the tinnitus was perceived with greater intensity.

The subjects were evaluated regarding the action of intra-auricular topical lidocaine on tinnitus intensity compared to a placebo. The study ear was defined in the first evaluation, the order of substance administration was randomized, and the patients had their medical history researched and underwent physical examination with somatosensory tinnitus analysis and audiological evaluation.

Tinnitus intensity in each ear was measured by the VAS, which ranged from 0–10 points, immediately before each administration and immediately after the substances were removed. The VAS was also used to evaluate somatic maneuvers to determine tinnitus modulation, considered positive in the case of a VAS score variation in at least one of the maneuvers.

An audiological evaluation was carried out in an acoustically treated booth, with TDH 39 and HD 200 headphones, using the MADSEN Itera II audiometer. The tonal threshold between 250–16 kHz was researched by an ascending and descending technique. A tonal threshold up to 8 kHz was classified according to the criteria by Lloyd and Kaplan. The audiometric threshold of high frequencies (9–6 kHz) was measured to determine the tinnitus pitch in these frequency ranges.

The psychoacoustic measures used for analysis in this study were the tinnitus loudness and the minimum masking level (MML), measured in decibel sensation level (dBSL) and performed before and after the application of each of the substances. The pitch was assessed by pure tone sound stimuli or narrow band (NB) noise, being measured in Hz.

Tinnitus loudness was analyzed by presenting the sound most similar to the patient's tinnitus, determined by the pitch, in the ipsilateral ear in cases of unilateral tinnitus or the ear with better hearing in cases of bilateral tinnitus, increasing the intensity by 1 dB until finding the volume closest to the patient's tinnitus.

The MML was assessed by an NB sound presented to the ipsilateral ear. Starting from the patient's threshold detected for this type of sound, the volume was increased by 1 dB every four seconds until the presented sound masked the tinnitus.

The substances used were 10% lidocaine (active substance) or distilled water (placebo). They were produced in the same compounding pharmacy, being replaced by new ones every 90 days and being stored in identical bottles identified as: "Substance 1" and "Substance 2."

The patient was positioned in a lateral decubitus position, with the tested ear facing up, and 20 drops of the randomized substance were administered and remained in the external acoustic meatus (EAM) for five minutes at each treatment session. For medication removal, the patient was instructed to sit with their head tilted to the side of the study ear, the substance was removed by gravity, and the ear was dried with gauze.

Each ear was its own control and crossover administration was two weeks apart.

Data analysis:

The mean VAS, tinnitus loudness, and MML were compared between lidocaine and the placebo before and after the administration of each substance to evaluate the effect of lidocaine on tinnitus.

To investigate whether any characteristics of the sample correlated with tinnitus variation after the administration of the substances, we compared the VAS, tinnitus loudness, and MML variations related to the variables sex, bruxism/ temporomandibular disorder (TMD), cervical changes, somatosensory tinnitus, modulation, and hearing loss.

Statistical analysis:

Qualitative characteristics of patients and tinnitus were described using absolute and relative frequencies, and quantitative characteristics were described using summary measures (mean, standard deviation, median, minimum, and maximum value). VAS, tinnitus loudness, MML, and variations for each administration were described using summary measures, and the variations between substances were compared using Generalized Estimating Equations (GEE) with marginal normal distribution and identity link function, assuming an interchangeable correlation matrix between substances.

The analyses were performed using the IBM-SPSS for Windows version 22.0 software and tabulated using the Microsoft Excel 2010 software. Statistical significance was set at 5%.