Ayurvedic management of Presbycusis (project TOPMAC): protocol for an exploratory randomized controlled trial.

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Abstract

Background: Presbycusis is characterized by sensorineural hearing loss in both ears at high frequencies, which affects more than half of older adults by age 75 and is often accompanied by tinnitus and cognitive deterioration. Unfortunately, there are no treatments available to restore hearing loss. Treatment in the majority of cases focuses on improving the quality of life and communication by hearing aids, which have their limitations and drawbacks. Management of tinnitus (ringing in ears) usually associated with Presbycusis is further challenging. Cognitive dysfunction in older adults following hearing loss is another concern that needs to be addressed. Multispecialty approaches involving neurology, audiology, gerontology, and otolaryngology are usually required to manage Presbycusis. Traditional medicine like Ayurveda also explains ailments of similar nature as Bhaadirya and advises using drugs with anti-aging and neuroprotective activity for treatment. In Ayurveda, the condition Baadhirya and Karnanada (senile deafness with tinnitus) is due to vitiation of Vata dosha. Treatments like topical oil pooling (Karnapurana) are usually advised in such conditions to counter Vata, improve hearing capacity, and reduce tinnitus. Kshirabala taila, a medicated oil formulation prepared with Sida cordifolia Linn, is one of the most preferred oils for topical oil pooling in such conditions as it has a definitive indication for sensory dysfunctions. Drugs like Ashwagandha (Withania somnifera L Dunal) are also used as it acts on neurodegeneration and helps to improve cognitive dysfunction. Although found effective in clinical practice, no documented data or clinical trials are found on the effectiveness of these interventions in Presbycusis. The only available data is a case report which reported significant improvement in hearing mechanism with no adverse effects following treatment.

Objective: Hence, an exploratory randomized controlled trial study has been proposed for evaluating the efficacy of Topical Oil Pooling (Karnapurana) with Kshirabala Taila and suppleMentation of Ashwagandha Churna (TOPMAC) on tinnitus suppression hearing and cognitive function protection in patients aged 60-75 years with mild to moderate Presbycusis against Basic Treatment and Health Education (BTHE).

Methods: A parallel, two-group, exploratory RCT conducted in an Indian Ayurvedic research centre at its outpatient service. Participants (n =60) with mild to moderate Presbycusis will be recruited by screening. Participants will be randomised (computer-generated: 1:1) to receive either: Basic Treatment and Health Education (BTHE) for 24 weeks/BTHE +TOPMAC. The Primary objective is to compare the efficacy of TOPMAC weeks on hearing function protection against BTHE. The Secondary objectives are to compare its efficacy on tinnitus suppression and cognitive function protection against BTHE.

Results: Nil

Conclusions: If this exploratory trial is proven effective, it will steer the setting of a definitive RCT to test whether the TOPMAC intervention can be incorporated as a cost-effective integrative approach for managing Presbycusis. The Government of India has already launched a National Programme for Prevention and Control of Deafness (NPPCD) to benefit the deaf population. TOPMAC may later be considered for integration with programmes like NPPCD. Clinical Trial:

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Title page

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Title

Ayurvedic management of Presbycusis (project TOPMAC): protocol for an exploratory randomized controlled trial.

Abstract

Introduction-Presbycusis is characterized by sensorineural hearing loss in both ears at high frequencies, which affects more than half of older adults by age 75 and is often accompanied by tinnitus and cognitive deterioration. Unfortunately, there are no treatments available to restore hearing loss. Treatment in the majority of cases focuses on improving the quality of life and communication by hearing aids, which have their limitations and drawbacks. Management of tinnitus (ringing in ears) usually associated with Presbycusis is further challenging. Cognitive dysfunction in older adults following hearing loss is another concern that needs to be addressed. Traditional medicine like Ayurveda also explains ailments of a similar nature as *Badhirya* and advises using drugs with anti-aging and neuroprotective activity for treatment. In Ayurveda, *Badhirya* and *Karnanada* (senile deafness with tinnitus) are due to vitiation of *Vata dosha*. Treatments like topical oil pooling (*Karnapurana*) are usually advised in such conditions to counter *Vata*, improve hearing capacity, and reduce tinnitus. *Kshirabalataila*, a medicated oil formulation prepared with *Sida cordifolia* Linn, is one of the most preferred oils for topical oil pooling in such conditions as it has a definitive indication for sensory dysfunctions. Drugs like *Ashwagandha* (*Withania somnifera* L Dunal) are also used as they act on neurodegeneration and help to improve cognitive dysfunction. Although found effective in clinical practice, no documented data or clinical trials have been found on the effectiveness of these interventions in Presbycusis. The only available data is a case report that reported significant improvement in hearing mechanisms with no adverse effects following treatmentHence, an exploratory randomized controlled trial study has been proposed for evaluating the efficacy of Topical Oil Pooling (*Karnapurana*) with *Kshirabala Taila* and suppleMentation of *Ashwagandha Churna* (TOPMAC) on tinnitus suppression, hearing and cognitive function protection in patients aged 60-75 years with mild to moderate Presbycusis.

Methods-A parallel, two-group, exploratory RCT conducted in an Indian Ayurvedic research centre at its outpatient service. Participants (n =60) with mild to moderate Presbycusis will be recruited by screening. Participants will be randomised (computer-generated: 1:1) to receive either

Basic Treatment and Health Education (BTHE) / BTHE +TOPMAC for 24 weeks.. The Primary objective is to compare the efficacy of TOPMAC on hearing function protection against BTHE. The secondary objective is to compare its efficacy in tinnitus suppression and cognitive function protection.

Results-The project was funded in January 2023. The first patient was enrolled in September 2023;eighteen participants were enrolled as of June 2024. The data analysis has yet to start, and the results are expected to be published by January 2025.

Discussion- If this exploratory trial is proven effective, it will steer the setting of a definitive RCT to test whether the TOPMAC intervention can be incorporated as a cost-effective integrative approach for managing Presbycusis. The Government of India has already launched a National Programme for Prevention and Control of Deafness (NPPCD) to benefit the deaf population.TOPMAC may later be considered for integration with programmes like NPPCD.

Trial registration-CTRI/2023/04/051485. Registered 11/04/2023.http://ctri.nic.in

Keywords: ARHL, Presbycusis, *Karnapurana*, *Kshirabala Taila*, Rasayana, *Withania somnifera* L Dunal

Introduction

Presbycusis (Age-related hearing loss) is characterized by sensorineural hearing loss at high frequencies in both ears, delayed central processing of auditory information, and problems understanding speech in loud environments [1]. It is usually associated with an audiogram that reveals the greatest hearing loss at higher frequencies. It affects over half of older adults by age 75 and nearly all over 90 [2]. Hearing loss is often accompanied by tinnitus. Many extensive population-based longitudinal studies have recommended that Presbycusis is independently connected with cognitive deterioration.

Furthermore, the issues and effects of Presbycusis are exacerbated in the elderly due to additional degenerative processes in the central nervous system, which can lead to a loss of neuroplasticity, cognitive ability, and other sensory modes, particularly vision [3]. Age-related hearing loss has an impact on both psychological wellbeing and physical ability. Some recent studies have established independent associations of hearing loss with driving ability, walking difficulty, social isolation, functional decline, and falls [4]. Social isolation causes emotions of incarceration and anxiety, which reduces higher cognitive performance, potentially increasing the economic and societal burden of age-related hearing loss [5]. The risk factors include age, the male sex, diabetes mellitus, hypertension, and hereditary hearing loss [6]. Diabetes or hypertension, if not appropriately

controlled, may also cause hearing problems through chronic arteriosclerosis. They are common chronic diseases inthe aged population, leading to reduced blood flow in the inner ear[6]. Presbycusis is a serious but primarily neglected condition in India. The Indian Government has started the National Programme for Prevention and Control of Deafness (NPPCD) to benefit the deaf population. The aims include medically rehabilitating deaf persons of all age groups and fortifying the existing inter-sectoral linkages to maintain the rehabilitation programme [7].

Unfortunately, there are no treatments available to restore lost hearing. Research on restoring hearing is a growing scientific field [8]. Treatment in most persons includes suitable hearing aids, but it is a limited solution withsome drawbacks. Studies have shown that people who would benefit from hearing aids are hesitant to use them due to cost, fit and comfort, maintenance, attitude, device factors, fiscal factors, psycho-social/situational factors, ear problems, and appearance. More precisely, these causes include the hearing aid's ineffectiveness in loud environments, low benefit or low sound quality, and incompatibility with the type of hearing loss. Factors affecting hearing aid fit and comfort include the need for assistance in inserting and removing the hearing aid, feeling uncomfortable, or experiencing adverse effects (e.g., rashes, itching). [9]. The treatment of tinnitus is also challenging [10]. Tinnitus should be managed using neurophysiological methods like tinnitus retraining therapy, a combination of cognitive, directive counseling and sound therapy, hearing aids, and white-noise generators. It also fails in 30-40 % of patients [11]. A recent systematic review recommended that incorporating conventional or complementary and alternative therapies for treating mild cognitive impairment will be beneficial[12]. All functions ofthe nervous system in the human body are represented through *Vata* in Ayurveda. A subtype of *Vata- Prana Vata*, is situated in the head and controls intellectual functions, cardiovascular functions, sense organs, psychological activities, respiration, and reflex activities like sneezing, belching, and deglutition [13]. Since Presbycusis is a sensory dysfunction with cognitive decline, it is evident that the *Prana vata*is impaired here. Ayurveda mentions similar ailments as *Baadhirya* and *Karnanada* (senile deafness with tinnitus) [14]. The diseases Badhirya and Karnanada occur in the ears primarily by*Vatadosha* vitiation. Topical oil pooling (*Karnapurana*) is a commonly employed treatment in such conditions as it does the *Vatashamana*, improves hearing capacity, and reduces tinnitus. No mechanistic studies show the exact mechanism of action of *karnapurana*. However, although histologically, the tympanic membrane is impermeable, a recent study has discovered the possibility of a biological mechanism of active transport through the tympanic membrane to the middle ear. This way, the topical pooled medicine might be absorbed to impart its action to the inner ear [15]. Ayurveda recommends a class of drugs termed *Rasayana*, which possess anti-aging properties to be beneficial in these conditions.

They can exhibit neuroprotective effects in the inner ear and brain tissue. *Kshirabala Taila*, a medicated oil prepared with *Sida cordifolia* Linn, is preferred as the drug of choice as it has definitive indications for sensory dysfunctions [16]. An animal study has also demonstrated that the aqueous root extract of *Sida cordifolia* Linn has a neuroprotective effect due to its anti-oxidative properties and validated the *Rasayana* claim of *Sida cordifolia Linn* in neurodegenerative diseases [17].*Ashwagandha* (*Withania somnifera*(L.) Dunal) is another medicine commonly used as it can regenerate damaged nerve cells and thereby improve nerve function [18]. Recent reviews have shown Ashwagandha as a potent medicine for cognitive function protection [19]. A randomised controlled trial has shown that it effectively enhanced immediate and general memory in subjects with MCI and improved attention, executive function, and information processing speed [20]. The administration of water extract from Ashwagandha (100 mg/kg/d) with drinking water for eight months was safe. It showed no toxicity in rats [21]. It may operate as a GABA mimetic, cholinomimetic, and agonist for α-7 nicotinic receptors for cognitive function protection [22]. Despite being widely used in clinics, no clinical trials or documented data are available on the efficacy of these drugs in Presbycusis. The only available data is a case report recommending an Ayurveda treatment protocol to effectively improve hearing mechanisms in Presbycusis with no side effects [23].

Hence, an exploratory randomized controlled trial has been proposed for evaluating the efficacy of Topical Oil Pooling (*Karnapurana*) with *Kshirabala Taila* and suppleMentation of *Ashwagandha Churna* (TOPMAC) on tinnitus suppression,hearing and cognitive function protection in subjects aged 60-75 years with mild to moderate Presbycusis against Basic Treatment and Health Education (BTHE).BTHE includes treatment for diabetes mellitus, hypertension, and dyslipidemia and counsel related to lifestyle modification and avoiding alcohol and cigarette use. The Primary objective is to compare the efficacy of TOPMAC on hearing function protection against BTHE. The secondary objective is to compare its efficacy in tinnitus suppression and cognitive function protection against BTHE.

Method

Trial design

Multicentre, parallel, two-group, exploratory randomized (1:1) controlled trial. A plan of enrolment, interventions, and assessments is given in Table 1.

Table 1Schedule of enrolment, interventions, and assessments for the TOPMAC study

	Screening	Baseline	Intervention period					End of treatment
TIMEPOINT		Day 1	*Day 29*	*Day 57*	*Day 85*	*Day 113*	*Day 141*	*Day 169*
Potential participant identification and screening	X							
Provision of PIS	X							
Eligibility assessment	X							
Informed consent	X							
INTERVENTIONS:								
Ashwagandha Churna Day-1-168		X	X	X	X	X	X	
Karnapurana Weeks1,5,9,13,17, 21		X	X	X	X	X	X	
BTHE		X	X	X	X	X	X	
ASSESSMENTS:								
Demographics		X						
Tympanometry	X							
Pure tone Average	X				X			X
Speech recognition threshold	X				X			X
Speech discrimination score	X				X			X

Lab investigations	X				X			X
Brainstem-Evoked Response Audiometry		X			X			X
Tinnitus Functional Index		X			X			X
Montreal Cognitive Assessment		X			X			X
Drug Compliance %			X	X	X	X	X	X
Concomitant Medication			X	X	X	X	X	X
Rescue Medication			X	X	X	X	X	X
Adverse reactions			X	X	X	X	X	X

Setting

Likely eligible participants would be identified at the Outpatient department of the National Ayurveda Research Institute for Panchakarma (NARIP). They will be sent for screening at the Institute for Communicative and Cognitive Neuro Sciences (ICCONS). NARIP is an Ayurvedic research hospital, and ICCONS is a medical hospital in rural Kerala, India.

Eligibility criteria

The intended population is adults aged 60-75 diagnosed with mild to moderate Presbycusis. The pure tone audiometry (PTA) will be carried out for the octave frequencies between 0.25 to 8 kHz, and the pure tone average will be calculated for 500 Hz, 1 KHz, and 2 KHz. The patients with a pure tone average of 26-55 dB HL will be included. Other eligibility criteria are shown in Table 2.

Table-2 Eligibility Criteria

Inclusion Criteria:
Patients aged 60-75 years diagnosed with mild to moderate Presbycusis.
Exclusion Criteria:
Conductive hearing loss and abnormal middle ear.
Current hearing aid user(> 3 months)

Patients with features of dementia.
Uncontrolled hypertension (Systolic BP >140mmHg and/or Diastolic BP >90mmHg)
Uncontrolled Diabetes (HbA1c>8%).
Patients with Very high Dyslipidemia (T.Chol> 240 mg / dL, LDL>190mg/dL, HDL>60, Triglycerides > 500 mg/dL) NCEP – ATP III Classification
Patients with Aspartate Amino Transferase (AST) and/ or Alanine Amino Transferase (ALT) > 2 times the upper normal limit, or
Patients with S. Creatinine > the upper limits of the normal.
History of malignancy within five years.
History of cerebrovascular accident within one year
History of use of ototoxic drugs, psychiatric and nervous system drugs.
History of hypersensitivity to the trial drug or any of its ingredients.
Continuing addiction to smoking and usage of tobacco in any form
Individuals simultaneously or previously (within 30 days before the investigation starts) participate in a clinical investigation using experimental drugs or devices.

Participant identification

Screening

Individuals attending the OPD of NARIP identified as likely eligible to participate in the study will be given a Participant Information Sheet (PIS). A trial team member will check initial eligibility if interested in participating. If the person is likely eligible, the researcher will send them to ICCONS for further screening.

Eligibility confirmation

Eligibility confirmation will be done at ICCONS by an experienced audiologist and neurologist. This assessment will include tympanometry, pure tone audiometry, and Montreal Cognitive Assessment (MoCA). The patients with a pure tone average of 26-55 dB HL will only be included.

Consent

Written informed consent would be obtained before starting trial-related procedures or data collection. A suitably qualified and experienced person delegated by the Principal Investigator will get the consent. We have pilot-tested the readability and comprehension level of the consent materials. For the participants with literacy challenges and visual impairment, the bystander of the subject will help in the informed consent process.

Randomisation, blinding, and allocation concealment

After getting consent, participants would be randomly chosen to receive either Basic Treatment and Health Education (BTHE) for 24 weeks or BTHE +TOPMAC in a 1:1 ratio using the serially numbered opaque sealed envelope provided by the CCRAS headquarters. It is impossible to blind participants or the investigators due to the trial design. The principal investigator enrolled the participants and assigned the intervention. However, the Investigator conducting the audiometric evaluation is blinded. The statistician analyzing the collected data will also not be blinded to allocation.

Interventions

Comparator:

In BTHE, participants will receive treatment for diabetes mellitus, hypertension, and dyslipidemia and counsel related to lifestyle modification and avoiding alcohol and cigarette use. Advice on optimizing individual acoustic environments is provided-includes reducing background noise and engaging in face-to-face conversations to maximize exposure to nonverbal communication cues. Lip reading classes will also be offered. This ancillary care is provided within the scope of this trial.

TOPMAC intervention:

The Topical oil pooling will be done on weeks 1, 5, 9, 13, 17, and 21. The preparatory procedure includes temporal region massage with processed gingelly oil (*murchita tila taila*) followed bysudation therapy. The main therapeutic procedure is to instill 5 ml of *Kshirabala Taila* in each auditory canal for 15-20 min in the morning. The therapy procedure includes massaging the ear base, and after 15-20 min, the oil will be wiped with dry cotton. *Ashwagandha Churna* will be supplemented with a dose of six gm at bedtime with 10 ml of cow's ghee for 24 weeks. Participants in both groups are covered under clinical trial insurance.

Study training

A trained Panchakarma therapist will perform The Topical oil pooling per the institute's Standard Operating Procedure (SOP). Trained technicians from ICCONS would do all audiometry evaluations. The Investigator’s Brochure and SOPs developed for the project are communicated to all investigators. Further intermittent meetings of the Investigators are planned. The re-orientation/interaction with the study staff is repeated periodically during the Investigator's

meeting.

Concurrent healthcare for all participants

All subjects would be instructed to access routine healthcare, including medicines and consultations with other health professionals. Details of co-interventions would be noted at the assessments on day 29, day 57, day 85, day 113, and day 141.

Primary outcomes

Include differences in the average 500 Hz, 1 KHz, and 2 KHz in PTA from baseline and after the 24th week of intervention. PTA is the gold standard for measuring sensitivity and identifying the presence and degree of hearing loss. Pure-tone (isolated frequency) audiometry evaluation over the range of frequencies critical for everyday listening can determine the degree, configuration, and type of hearing loss in a manner detailed enough to assist the healthcare team in determining the etiology and prognosis for the hearing loss as well as the optimal treatment strategy [24]. Pure-tone evaluation is typically performed in a sound-treated booth to reduce the impact of external sounds, with the booth environment and electro acoustic equipment calibrated to American National Standards Institute (ANSI) standards to optimize inter-test and intra-test reliability. Primary outcomes also include Brainstem Evoked Response Audiometry (BERA) changes and differences in Speech recognition threshold and Speech discrimination score.

Secondary outcomes

Consist of differences in the tinnitus functional index from baseline and after the 24th week of intervention. The secondary outcome also includes the Montreal Cognitive Assessment (MoCA) score difference.TFI is considered the gold standard in measuring tinnitus severity. It is a 25-item questionnaire that will identify the tinnitus severity of the patient by calculating the overall TFI Score. The eight subscales address eight critical domains of negative tinnitus impact I: intrusive (unpleasantness, intrusiveness, persistence), SC: sense of control (reduced sense of control), C: cognitive (cognitive interference), SL: sleep (sleep disturbance), A: auditory (auditory difficulties attributed to tinnitus), R: relaxation (interference with relaxation), Q: quality of life (qol) (quality of life reduced), E: emotional (emotional distress). In this way, the TFI score and sub-score will measure the improvement in subjective wellbeing and quality of life related to tinnitus.

Adverse events

Any adverse event or Adverse Drug Reaction (ADE/R), if seen during the trial period, will be documented- suitable and timely management would be done, and the same would be reported to the

Ethics committee and the sponsor(s) at the earliest. Considering the subject's age and the character of the intervention, predictable AEs include gastrointestinal side effects (nausea, vomiting, and diarrhea), dizziness, fatigue, ear pain, itching in the ears, and fullness in the ears. Safety reporting would begin from the point of randomization and finish when the subject has finished their 169th-dayassessment.

Sample size determination

A previously published report on the administration of topical oil pooling in patients of Presbycusis showed that the average hearing level for the frequency of 500 Hz, 1 KHz, and 2KHz after treatment was 53 decibels (For air conduction defect of the right and left ear both) [11]. We based our sample size calculation on the assumption that the average hearing level at these three frequencies will be 50 dB in the TOPMAC + BTHE group, while it will be 60 dB in the BTHE group. A difference of 10 db after treatment between both groups has been considered clinically meaningful. With a standard deviation of 12 dB, 80% power, and a confidence interval of 95%, the calculated sample size for each arm is 23. The sample size becomes 28.75, rounded to 30 per arm, adding an attrition rate of 25%. Therefore, 60 participants must be enrolled in the trial (30 in each arm). The attrition rate was based on the clinical experience in treatment compliance. Moreover, in previous studies on Ayurveda interventions among elderly participants, such attrition had occurred. An interim analysis will be performed after 25% of participants complete the study duration, and then the reassessment of the attrition rate will be considered along with the original sample size.

Data collection

Baseline assessment

Include demographic data and Ayurveda parameters. It also includes assessing BERA, Tinnitus functional index, and MoCA score (Table 1).

Treatment logs

For BTHE and TOPMAC intervention sessions, the drug compliance reports will record the date, clinician details, day of the intervention, mode of delivery, and drugs issued.

Follow up assessment

All participants will attend on day 29, day 57, day 85, day 113, day 141, and day 169 for follow-up. Drug Compliance %, Concomitant Medication, and Rescue Medication will be assessed on all visits. In addition to that, PTA, BERA, lab investigations, Tinnitus Functional Index, and MoCA Score will be repeated on day 85 and day 169 (Table 1).

Early discontinuation/withdrawal of participants

During the study, subjects can withdraw at any time. Also, the Investigator may discontinue a subject from the study if they judge it indispensable for any reason- the patient is not ready to continue or is non-compliant with the study procedure (At least 80% compliance is crucial to continue in the study), the patient develops a life-threatening crisis or any other severe sickness due to other pathology which requires emergency treatment or making it necessary to introduce new treatment during the study period, (ADE/R) requiring hospitalization. The decision to withdraw a subject from the study will be made only by the Investigator, who will give a thorough justification and indicate further management if needed. The Sponsor and the Ethics Committee will be informed within two working days.

Data management

Data would be collected using paper CRFs and Electronic CRFs and maintained by the Principal Investigator. Regularly monitoring data entry and data collection processes will be executed during the project. The electronic CRF for data entry will also used to check the data accuracy and validity of the data. The modeling imputation technique will impute any outlier or missing data.The parameters having follow-ups will be imputed through the time series modeling, and those with single-point observation will be imputed with the population's average or median, depending on the variable's distribution. The data will be collected and entered in the CRFs identified by the enrollment IDs only. The Consent document and the Screening and Baseline information containing the participant's names or identities will be secured more cautiously. The electronic format will be locked by password, and access to this dataset will be restricted to authorized persons only. The shared data file will be locked with a separate code that can be accessed after the code is disclosed on request. The statistician at the CCRAS Headquarters will analyze the data. After completion of the study, the data will be stored for at least five years.

Statistical methods

Data shall be managed through SPSS29 .0 version. The data would be individually analyzed for central tendencies (mean, median), range, standard error, standard deviation, and 95% confidence intervals for each intervention arm in each of the groups in the study. Data will be tabulated and graphically shown using a standard format, MS Excel, and other software programs. For non-parametric values, the Wilcoxon signed rank test and Mann Whitney U test will be performed, and for parametric values, a paired t-test and student's t-test will be done. Further, multivariable

regression and Cox regression analysis will be used if any confounding factor or censored data is found during the analysis. Bayesian analysis may also be performed if any necessity arises after the initial phase of data analysis.This study will assess mild to moderate presbycusis patients based on impairment. Clinically, it is established that the moderate impairment participants have a lesser chance of cure, and mild impaired persons have a higher chance of cure, which is the available information before the study starts. So, we use this information as prior distribution to calculate the posterior response of the participants. Further, Bayesian analysis gives another angle to explore the outcome and reduce the researcher's dependency on p values.

Regression analysis will control diversity during analysis and stratify results by demographic factors such as sex, socioeconomic status, and comorbidities. The analysis will be done by stratifying these factors to estimate the effect of intervention as accurately as possible. The regression analysis will consider these factors to determine the intervention's adjusted effect. In the case of the dichotomous or multinomial type of data, a separate analysis will be performed for each stratum, or logistic regression analysis will be used.

Data monitoring

This study will be monitored by the Data and Safety Monitoring Board (DSMB) of the TOPMAC project at NARIP, Cheruthuruthy. A particular quality control program would be initiated to secure an agreement with the present approved protocol, GCP, related regulations, and Standard Operating Procedures (SOPs) of NARIP. The Principal Investigator will develop data management and monitoring plans and manage the trial's daily activities. The DSMB team will do quality assurance checks to ensure the integrity of randomisation, study entry procedures, and data collection. The DSMB team will conduct at least one e-Clinical Research Form inspection once a year. Additionally, the sponsor may monitor or audit the study per the present approved protocol, GCP, relevant regulations, and SOPs.

Ethics and dissemination

The institutional Ethics Committee at NARIP (F.No.3/1/2020/NARIP/Tech./2036 dated 31-01-2023) and ICCONS (IEC No.IEC006 dated 21-03-2023) approved this study (Protocol-1 dated 03-02-2023). This protocol is reported according to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statement [25] (Completed SPIRIT checklist: Additional file 1). Results would be published in a peer-reviewed journal with authorship eligibility according to the criteria of the International Committee of Medical Journal Editors.

Results

The project was funded in January 2023, the first patient was enrolled in September 2023, and as ofJune 2024, eighteen participants were enrolled. The data analysis has yet to start, and the results are expected to be published by January 2025.

Discussion

This randomized exploratory trial is proposed to assess the efficacy of TOPMAC intervention in improving hearing status in adults aged 60-75 years with mild to moderate Presbycusis.

Strength

The TOPMAC intervention was methodically developed, amalgamating existing best and anecdotal shreds of evidence, and is the first trial to evaluate the effectiveness of Ayurveda intervention in Presbycusis as an add-on to BTHE. The quantitative outcome measures included in the trial will give valid data about the possibility of doing a definitive RCT of the TOPMAC intervention.

Limitations

The study also has limitations as only effectiveness outcomes are included, not feasibility outcomes. The following limitation is that the trial design has no follow-up period. The lasting effects of the treatment on Presbycusis and associated symptoms may need to be assessed. Nevertheless, a case study has been reported wherein the treatment effect of Ayurvedic medicines in Presbycusis was sustained for a follow-up period of six months when no treatment was administered [23].The study will apply only to Asian countries where Ayurveda is practiced. Nonetheless, the applicability of this protocol is limited in other continents. However, they could also replicate this model if there is accessibility of trained panchakarma therapists to perform the *Karnapurana* procedure and have regulatory permission to use *Ashwagandha*.

Another limitation is the absence of subjective Ayurvedic diagnostics in the research design, which might influence the broader integration of Ayurvedic treatments into conventional medical practice. However, *Badhirya and Karnanada* are described in Ayurveda and can correlate with various symptoms of Presbycusis. Though the standardized or validated assessment criteria for severity are not available in Ayurveda terminology, the outcome measures/tools for assessment of Presbycusis are conceptually applicable to inferring the results in *Badhirya*. Also, this protocol evaluates the patient's Prakriti (psychosomatic constitution) using the Standardized Ayur Prakriti web portal developed by CCRAS [26].*Prakriti* is considered an essential part of Ayurvedic Diagnostics [27].

While the Tinnitus Functional Index is a robust tool for assessing tinnitus impact, the absence of a broader quality of life measure for other dimensions possibly affected by the treatment is yet another limitation of this protocol. These limitations will be considered in the future definitive RCT.

Conclusion

If this exploratory trial is proven effective, it will steer the setting of a definitive RCT which will incorporate the limitations as decribed above, to test whether the TOPMAC intervention can be incorporated as a cost-effective integrative approach for managing Presbycusis.

Abbreviations

ADE	Any adverse event
ADR	Adverse Drug Reaction
BERA	Brainstem Evoked Response Audiometry
BTHE	Basic Treatment and Health Education
CCRAS	Central Council for Research in Ayurvedic Sciences
CRF	Case Record Form
DSMB	Data and Safety Monitoring Board
GCP	Good Clinical Practice
ICCONS	Institute for Communicative and Cognitive Neuro Sciences
MoCA	Montreal Cognitive Assessment
NARIP	National Ayurveda Research Institute for Panchakarma
NPPCD	National Programme for Prevention and Control of Deafness
PIS	Participant Information Sheet
PTA	PureTone Audiometry
RCT	Randomised Controlled Trial
SOP	Standard Operating Procedure
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
TOPMAC	Topical Oil Pooling (Karnapurana) with KsirabalaTaila and suppleMentation of Ashwagandha Churna

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Authors' contributions

KKV, the Principal Investigator, conceived and designed the study and drafted the manuscript. SVT, PGN, NML, PM, BY, BCS, SD, and NS contributed to the study design, provided specific content, and edited the trial protocol and manuscript AT provided statistical oversight. KKV acts as a guarantor. All authors have reviewed and approved the final manuscript.

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Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

The institutional Ethics Committee at NARIP (F.No.3/1/2020/NARIP/Tech./2036 dated 31-01-2023) and ICCONS (IEC No.IEC006 dated 21-03-2023) approved this study.

Consent for publication

Not applicable.

Competing interests

Some authors work in the Sponsor organization. However, the trial medicines are not proprietary drugs manufactured or marketed by the sponsor. They are *Ayurveda* medicines mentioned in the classical texts.

Declaration of Generative AI and AI-assisted technologies in the writing process

The authors declare that no generative AI or AI-assisted technologies have been used in the writing process.

Multimedia appendices

Multimedia appendix 1: SPIRIT Checklist

Multimedia Appendix 2: CONSORT-EHEALTH V1.6.

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Supplementary Files

Untitled.
URL: http://asset.jmir.pub/assets/bc3da666a4405df564826943333a80ad.pdf

Multimedia Appendixes

SPIRIT Checklist.
URL: http://asset.jmir.pub/assets/262e58114cfaa2e354b28d1dd572c590.pdf

CONSORT- E Health (V 1.6.1).
URL: http://asset.jmir.pub/assets/0b4af27d7777eb1f152c2540dba7a4b0.pdf