Audiological and vestibular assessment in persons with osteoporosis and osteopenia

by Prawin Kumar P

PROJECT PROPOSAL FORMAT

Part -A

1.0	**Title of the Project**	Audiological and vestibular assessment in persons with osteoporosis and osteopenia
1.1	**Area of Research :**	Auditory and Vestibular systems
1.2	**Principal Investigator**	Dr. Prawin Kumar
1.4	**Principal Co-Investigator(s)**	Dr. Niraj Kumar Singh
1.5	**Collaborating Institution**	Nil
1.6	**Total Grants Required (in figures and in words)**	Rs 5, 28, 000 (Five lakhs twenty eight thousands only)
1.7	**Duration of the Project**	One year
2.0	**Project Summary** (Max. 300 words)	Details enclosed.
3.0	**Introduction** (under the following heads)	More details in the actual proposal

3.1	Definition of the problem	:	Osteoporosis is a medical condition in which the bones become brittle and fragile due to loss of tissue, typically as a result of hormonal changes, deficiency of calcium and/or deficiency of vitamin D. Calcium is vital for the functioning of the hair cells as well as for the neurotransmitter release that triggers the generation of a nerve impulse. A reduction in calcium level could therefore impair the functioning of the auditory and vestibular systems
3.2	Objectives	:	Enclosed
3.3	Review of status of research and development in the subject	:	Enclosed
3.4	International and national status	:	International: Madureira et al (2010) observed that the older adults who experienced falls had impaired balance function. Since old age is found to be associated with reduction in Ca^{2+} concentration, there is a likelihood that the impairment of balance function in these individuals might have been caused by the decreased calcium concentration

(osteopenia/osteoporosis).

National: Preliminary study done by Gargeshwari, Jha, & Singh, 2016 on 12 osteopenic, 11 osteoporotic, and 12 healthy individuals. The results showed evidence for presence of audiological as well as vestibular deficits in individuals with osteopenia and osteoporosis.

3.5	Importance of the proposed project in the context of current status	: The outcome of the study will provide evidence for possible effect of osteopenia and osteoporosis on auditory and vestibular system.

4.0 Work Plan

4.1 Method

Subjects / Participants	: 30 participants in each group (normal individuals, osteopenia and osteoporosis).
Material	: Biologic Navigator pro for recording ABR, C-VEMP and O-VEMP.
Procedure	: Behavioural vestibular test.
Analyses	: Between groups comparison for Normal, Osteopenia and Osteoporosis.

AUDIOLOGICAL AND VESTIBULAR ASSESSMENT IN PERSONS WITH OSTEOPOROSIS AND OSTEOPENIA

Project Summary

Calcium is vital for the functioning of the hair cells as well as for the neurotransmitter release that triggers the generation of a nerve impulse. A reduction in calcium level could therefore impair the functioning of the auditory and vestibular systems. However, the outcome of hearing and balance assessment has rarely been explored in cases with osteopenia and osteoporosis, the medical conditions associated with reduction in calcium levels. Therefore the present study aims at investigating the impact of osteopenia and osteoporosis on the outcomes of behavioural as well as objective auditory and vestibular assessment tests. The study will include 30 healthy individuals as control group and 30 individuals each in the osteopenia and osteoporosis group. The groups will be divided based on the findings of bone mineral density test. All the participants will undergo audiological tests (pure-tone audiometry, immittance evaluation, oto-acoustic emissions, and auditory brainstem response testing) and vestibular evaluation (Fukuda stepping, tandem gait, subjective visual vertical, cervical vestibular evoked myogenic potentials, ocular vestibular evoked myogenic potentials, and video head impulse test). Between groups comparisons will be done to find the differences in auditory and vestibular functioning between the groups. Presently, audiological and vestibular evaluations are not a part of the routine evaluation in individuals with osteopenia and osteoporosis. If the results of the study will show the existence of hearing and vestibular deficits in these individuals, it will provide testimony to the need for the inclusion of auditory and vestibular assessment as part of the routine examinations in these individuals.

Introduction

Osteoporosis is a medical condition in which the bones become brittle and fragile due to loss of tissue, typically as a result of hormonal changes, deficiency of calcium and/or deficiency of vitamin D (WHO, 2004; NIH Consensus Statement, 2000). Osteopenia is also a medical condition in which the protein and mineral content of bone tissue is reduced, but less severely than in osteoporosis (WHO, 2004; NIH Consensus Statement, 2000). These two pathologies thus represent a continuum along the bone mineral density measure.

Loss of bone mineral is a phenomenon that takes place in all human beings. This daily removal of small amounts of bone mineral, a process called resorption, must be balanced by an equal deposition of new mineral if bone strength is to be preserved (International Osteoporosis Foundation, 2015). When this balance tips towards excessive resorption, bones weaken and can become brittle and prone to fracture over time. This continual resorption and redeposition of bone mineral, often termed bone remodelling, is intimately tied to the pathophysiology of osteoporosis (International Osteoporosis Foundation, 2015).

The balance between bone resorption and bone deposition is determined by the activities of two principle cell types, osteoclasts and osteoblasts (Huang & Putney, 2011). The alterations in the intracellular calcium ion (Ca^{2+}) concentrations regulate differentiation and functions of osteoclasts (Huang & Putney, 2011). Further, the changes in intracellular Ca^{2+} concentrations are known to function as universal triggers of diverse signalling pathways, including enzyme activation, cell survival and cell differentiation (Huang & Putney, 2011). This would mean that a reduction in the Ca^{2+} concentration is not only likely to affect cell differentiation and survival but also affect the functioning of various neural pathways. All this put together increases the brittleness of various bones of the body.

According to the International Osteoporosis Foundation (IOF), 40% of women in the world have fracture due to osteoporosis during their lifetime. Fractures are associated with increased morbidity/mortality and diminished quality of life in a variety of ways, including decline in physical and emotional functioning (Randell et al., 2000). Falls are responsible for 90% of the hip fractures (Suzuki, Kim, Yoshida & Ishizaki, 2004) and are the sixth leading cause of death among patients aged 65 years and older (Baraff, Della, Williams & Sanders, 1999). In addition to the high mortality, there are other deleterious consequences of falls including restriction of mobility, disability, social isolation, insecurity and fear, inducing a cascade of events that are harmful to health and quality of life in the elderly (Lachman et al., 1998; Legters, 2002). Research suggests that altered balance is the greatest contributor towards falls in the elderly, with a high correlation between balance deficit and incidence of falls (Silsupadol, Siu, Shumway-Cook & Woollacott, 2006). Furthermore, the programs targeting mainly balance training have been demonstrated to be effective in prevention of falls among the elderly (Rogers, Fernanadez & Bohlken, 2001), many of whom might be affected with low bone mineral density.

Need for the study

It is well documented that intercellular calcium helps in the regulation of nerve impulses and is also vital for the functioning of the hair cells as well as for the neurotransmitter release from the hair cells that triggers the generation of a nerve impulse (Chan & Hudspeth, 2005; Huang & Putney, 2011). Thus, reduced calcium could lead to improper release of neurotransmitter even at the auditory and vestibular periphery, leading to hearing, balance and postural deficits. Further, Madureira et al (2010) observed that the older adults who experienced falls had impaired balance function. Since old age is found to be associated with reduction in Ca^{2+} concentration, there is a likelihood that the impairment of

balance function in these individuals might have been caused by the decreased calcium concentration (osteopenia/osteoporosis). Therefore it appears that there could be a relationship between the reduced levels of calcium and balance sustenance ability in an individual. However, this aspect has been sparingly investigated.

The altered bone composition results in structural changes of the bones such as kyphosis (Sinaki, Brey, Hughes, Larson & Kaufman, 2005), which can also lead to balance issues. In a study by Abreu et al (2010), it was found that women with osteoporosis had worst balance and maximum oscillation in evaluation of balance using the Polhemus system in four upright postural situations when compared to non-osteoporotic women. In the group with osteoporosis, Lynn et al (1997) observed larger sway amplitudes and inappropriate use of balance maintenance strategies than the controls when evaluated using the computerised dynamic posturography (CDP). Recent evidences suggest that the density of otoconia is reduced in adult female osteoporotic rats (Vibert et al, 2008). Since otoconia are present in the utricle and saccule which are vital for generating the vestibular evoked myogenic potentials (Colebatch & Halmagyi, 1992; Curthoys et al, 2010), impairment of VEMP could be expected in these patients. However, this has not been investigated, to the best of our knowledge.

Decrease in the bone mineral density is also known to cause absorption of bones in the middle ear, further causing thinning of them, and changing the middle ear characteristics (Kanzaki, Ito, Takada, Ogawa & Matsuo, 2006). Changes can also occur due to altered stiffness in the soft tissue elements of the middle ear (Nager, 1977), epitympanic spurs and proliferation of fibrous tissue adjacent to the ossicles (Davies, 1968). The process of bone demineralisation, which causes osteopenia and osteoporosis, can also affect the temporal bone in which the cochlea is housed (Monsel, 2004). It can result in mechanisms which can

cause sensorineural hearing loss. It can also result in compression of the auditory nerve (Applebaum & Clemis, 1977), obstruction of vascular shunts (Nager, 1975) and narrowing of the auditory canal (Applebaum & Clemis, 1977). It has been seen that as the bone fragility increases, the hearing loss (degree & prevalence) increases (Monsel, 2004). In cases with osteopenia and osteoporosis, changes in bone density, mass, and dampening of the finely tuned motion mechanics of the middle ear can cause conductive hearing loss whereas changes occurring in the otic capsule and the temporal bone affects the inner ear causing sensorineural hearing loss (Nager, 1975). Furthermore, calcium ions are important for the efficient release of the neurotransmitters during the transduction process in the cochlea (Khetarpal & Schuknecht, 1990; Vergara, Latorre, Marrion & Adelman, 1998, Hacohen, Assad, Smith & Corey, 1989). They (calcium ions) also play a vital role in the recycling of potassium ions, especially removal of K^+ ions from the hair cells (Chan & Hudspeth, 2005; Eatock, Corey & Hudspeth, 1987). A deficiency in calcium, which is seen in osteopenia and osteoporosis, could therefore hinder the recycling of K^+ ions and cause dysfunction in the neurotransmitter release and thereby sensorineural hearing loss. However there are very few studies that have explored the audiological test findings in osteoporosis and osteopenia, especially a complete audiological profile.

In studies done by a group of researchers on 12 osteopenic, 11 osteoporotic, and 12 healthy individuals, the results showed evidence for presence of audiological as well as vestibular deficits in individuals with osteopenia and osteoporosis, with more severely impaired results in the later (Gargeshwari, Jha, & Singh, 2016; Jha, Gargeshwari, & Singh, 2016). However, the generalization of these results to the population could be questionable due to a small sample size. Nonetheless, the results are encouraging enough to warrant the need for further study on larger sample sizes.

Aim and objectives

The present study aims to investigate the impact of osteopenia and osteoporosis on the outcomes of various behavioural and objective audiological and vestibular assessment tests. The specific objectives are as follows:

1. To investigate the effect of osteopenia and osteoporosis on the outcomes of behavioural audiological assessment (pure-tone and speech audiometry).

2. To investigate the effect of osteopenia and osteoporosis on the outcomes of physiological tests (immittance evaluations, oto-acoustic emissions and auditory brainstem responses).

3. To examine the impact of osteopenia and osteoporosis on behavioural balance assessment (Fukuda stepping test, sharpened Romberg and subjective visual vertical test).

4. To study the effect of osteopenia and osteoporosis on physiological vestibular evaluation (cervical VEMP, ocular VEMP and video head impulse test).

Method

Participants

Individuals who have undergone bone mineral density (BMD) testing under the supervision of a medical professional will be included in the study. According to the WHO (2007) recommendation the participants will be classified as having osteopenia if their T-score (outcome of bone mineral density test) is between -1.1 to -2.5 and osteoporosis if their T-score is $\geq$-2.6 (in the negativity). Those having T-scores better than -1.1 (towards positivity) will be considered to have normal bone mineral density. Thirty participants will be

included each of the three groups (normal, osteopenia and osteoporosis), making a total of 90 participants.

Instrumentation and Environment

A calibrated two channel clinical audiometer Inventis Piano with TDH-39 headphones housed in MX-41/AR ear cushions will be used for finding air-conduction and doing speech audiometry. Radio ear B-71 bone vibrator along with the same audiometer will be used for measuring bone-conduction thresholds. A calibrated middle ear analyzer Grason-Stadler Incorporated (GSI) Tympstar will be used for obtaining tympanogram type, static compliance, ear canal volume, acoustic reflex threshold and middle ear resonance frequency. The Otodynamics ILO V6 will be used for recording transient and distortion product OAEs. Biologic navigator pro with SINSER insert earphones will be used to for auditory brainstem response (ABR) and cervical and ocular vestibular evoked myogenic potentials (cVEMP & oVEMP). An ICS Impulse video head impulse test system with monocular camera will be used for evaluating the three sets of semicircular canals. All the tests will be carried out in acoustically treated air-conditioned rooms with permissible noise level as per the guidelines recommended by the American National Standards Institute (ANSI, 1999).

Procedure

A detailed structured case history will be obtained from each participant. This will involve questions pertaining to auditory and vestibular systems and also other sensory systems. This will be done before the participants are evaluated using the audiological and vestibular test battery.

Air-conduction and bone-conduction thresholds will be tracked using modified ascending-descending technique (Hughson & Westlake, 1944) to assess the hearing

sensitivity of the subject. Pure-tone average will be calculated as the average of air-conduction thresholds obtained for 0.5 kHz, 1 kHz, 2 kHz and 4 kHz pure-tones. Speech audiometry will include calculation of speech recognition threshold, speech identification scores and uncomfortable level using appropriate word lists in the participant's native language. Tympanometry will be done using 226 Hz probe-tone to obtain the tympanogram type. Ipsilateral as well as contralateral reflex thresholds will be obtained at 0.5 kHz, 1 kHz, 2 kHz and 4 kHz.

A two-channel ABR for standard clicks will be recorded using Biologic Navigator Pro auditory evoked potential system. Before recording the evoked potentials, the electrode placement sites will be scrubbed using a commercially available abrasive gel. The disc type surface electrodes will be placed using commercially available conduction paste and secured in place using surgical plaster. The absolute and inter-electrode impedance will be maintained below 5 kΩ and 2 kΩ respectively. The other stimulus and acquisition parameters for recording of ABR are shown in Table 1.

Table 1.

Stimulus and acquisition parameters for recording auditory brainstem responses

Stimulus parameters		Acquisition Parameters	
Stimulus	Click	Amplifier Gain	100000 times
Onset phase	Rarefaction	Filter setting	100-3000 Hz
Intensity	90 dB nHL	Time window	10 ms
Rate	11.1/s & 90.1/s	Number of sweeps	1500
		Electrode placement	Non-inverting (+): Vertex (Cz)
			Inverting (-): Mastoids of both ears (M1 & M2)
			Ground: Forehead (Fz)

For the FST, the participants will be instructed to stretch both their arms in front of them and march with their eyes closed at the same place for 50 steps at a rate of about 1 step/s. The angle of deviation >45° in either direction and/or distance of deviation >1m will be considered abnormal, as reported previously (Harit & Singh, 2012). For the sharpened Romberg test, the participant will be asked to stand on a foamed surface of minimum 4 cm thickness with arms outstretched in front and feet positioned heel-to-toe for 30 seconds. The duration of balance sustenance in this position (maximum up to 30 seconds) will measured using a stop watch. An average of 5 trails will be considered as the final value.

The subjective visual vertical test will be done using the bucket test. The participant will be instructed to place his/her head as inside the bucket as comfortable and align the position of the strip present along the diameter of the base of the bucket in their perceived vertical position. The angle of deviation from the actual vertical will be noted by a pointer indicating the angles on a 360° protractor attached to the back of the base of the bucket. The bucket will be handed at different angles during every trial and an average of 10 trials will be considered as the final value of vertical deviation. A >3° deviation of the perceived vertical from the true vertical will be deemed to be abnormal result (Karlberg, Aw, Halmagyi & Black, 2002; Hafstrom, Fransson, Karlberg & Magnusson, 2004).

For the cVEMP recordings, the electrodes will be placed at the sternoclavicular junction (inverting), superior 1/3rd of the sternocleidomastoid muscle (non- inverting) and forehead (ground). For the activation of the sternocleidomastoid muscle, the participants will be asked to turn their head away from the ear of stimulation. The recording will be done for tone-bursts of 500Hz, 750Hz and 1000Hz. The tone-bursts will be presented to the ear at an intensity of 125 dB peSPL using a stimulation rate of 5.1Hz. The band-pass filter used will be 1–1500 Hz and the responses will be averaged for 200 sweeps. The pre-stimulus rectification

will be used to control for the effects of variations in the electromyographic activity between the cVEMP recordings.

The oVEMP will be obtained by placing the non-inverting electrode on skin surface 1 cm below the centre of the lower eye-lid, inverting electrode 2 cm below the non-inverting and ground on the forehead, as used previously (Rosengren, Todd & Colebatch, 2005; Singh & Barman, 2013, 2014, 2015, 2016). The participants will be instructed to maintain a 30° upward centre gaze by staring at a strip placed at the appropriate elevation. The recording will be done using tone bursts of 500Hz, 750Hz and 1000Hz. The tone-bursts will be delivered to the ear canal at an intensity of 125 dB peSPL using a repetition rate of 5.1Hz. The band-pass filter of 1–1000 Hz will be used and the responses will be averaged for 200 sweeps.

Video head impulse test will be administered using ICS impulse system with monocular camera for recording the eye movement. A target will be placed at the distance of 1 metre and the subject will be asked to gaze at the target. A head thrust will be given 20 times in pitch, roll and yaw planes and VOR gain will be calculated as ratio of eye velocity to head velocity in all the planes. Saccades at the time of head thrust (covert saccades) and after the head thrust (overt saccades) will be considered an abnormal finding.

Statistical analysis

The data obtained for various tests across the groups will be subjected to the Shapiro-Wilk's test of normality. Depending upon the results of this test, the parametric or non-parametric statistical analysis will be used for between groups comparison of results.

Implications of the study

1. The study will help us to have a comprehensive idea about the status of audiological and vestibular health in individuals with reduced bone mineral density.

2. The findings of the study will help us to understand one of the probable cause of falls, fractures and eventually deterioration in the quality of life in elderly individuals.

3. It will give us the idea whether individuals with reduced bone mineral density should undergo audiological and vestibular evaluation as a routine test which would prevent falls if assessed and intervened early.

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