The Effect of Nocturnal Wear of Complete Denture on Sleep and Oral Health Related Quality of Life: Study Protocol for a Cross-Over Randomized Trial

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ABSTRACT

Background: Edentulism and sleep disturbance are chronic conditions that are common in elders and have serious adverse consequences for their functioning and quality of life. Edentulism can disturb sleep through the alteration of the craniofacial structure and surrounding soft tissue. However, the effect of prosthetic rehabilitation of edentulism on sleep quality is still not well understood. The objectives of this study are to test whether nocturnal denture wear affects sleep quality, daytime sleepiness, and the oral-health-related quality of life of edentate elders with moderate to severe sleep apnea and, to identify modifiers of effect of nocturnal denture wear.

Methods/design: We will carry out a single-blind randomized cross-over trial. Seventy edentate elders with moderate to severe obstructive sleep apnea will be enrolled. The study participants will be assigned to wear and not wear their denture in alternate orders for periods of 30 days. The outcome measures will be sleep quality (assessed by portable polysomnography), daytime sleepiness (assessed by the Epworth Sleepiness Scale), and oral health-related quality of life (assessed by validated questionnaire). A number of characteristics (socio-demographic, oropharyngeal morphology, oral and prosthesis characteristics, and perceived general health quality of life) will be assessed by means of clinical examination, 3D imaging of the craniofacial structure, and validated questionnaires at baseline. Linear mixed-effects regression models for repeated measures will be fitted to test the study hypotheses. The main analyses will be based on the intention-to-treat principle. To assess the robustness of the findings to potential incomplete adherence, sensitivity analyses will be conducted while applying the per-protocol principle.
**Discussion:** This practice-relevant evidence could represent a preventive approach to improve sleep characteristics of the older population and improve their well-being and quality of life.

**ClinicalTrials.gov registration number:** NCT01868295.

**KEYWORDS**

Edentulism, complete denture, sleep disorders, sleep quality, obstructive sleeping apnea, and oral health related quality of life.
BACKGROUND

The worldwide population is rapidly aging, with the majority of elders living longer than previous generations [1]. Aging substantially increases the risk of tooth loss and sleep disturbance. In Canada, about one in four seniors aged 65 and older is completely toothless [2], and nearly half of all seniors complain of disturbed sleep [3, 4]. These two chronic conditions have serious adverse consequences for well-being, functioning, and quality of life, and place a significant burden on the health care system [5–8]. The costs associated with sleep disturbance and tooth loss are also substantial [7, 9–12].

The relationship of edentulism with sleep disturbance and sleep-disordered breathing has been well documented [13, 14]. In fact, anatomical changes associated with edentulism and decrease in the vertical dimension of occlusion can negatively influence sleep and lead to obstructive sleep apnea (OSA) [13–18]. Loss of vertical dimension of occlusion leads to a forward and upward mandibular position associated with a backward shift in supine position [16, 19]. This rotational movement of the mandible favors a shift of the tongue and soft palate against the posterior pharyngeal wall. The reduction in the retropharyngeal space associated with impaired function of the upper airway dilatation muscles results in upper airway resistance, and diminished response to negative pressure stimulation [20–22]. Moreover, age-specific compromised pharyngeal anatomy, upper-airway mucosal sensory dysfunction and a decline in pharyngeal sensory discrimination and reflexes have been proposed as being responsible for the vulnerability of edentate elders to airway collapse [23–25]. Furthermore, literature suggests that there is a possible association between sleep disturbance and wearing a complete denture during sleep, which may explain the mechanism underlying the relationship between OSA and edentate individuals [26, 27]. One hypothesized effect was that the use of a denture during sleep may lead
to open bite and mouth breathing with a decrease in the tone of the pharyngeal muscles, thus leading to the development or worsening of OSA [28]; an alternative hypothesis holds that sleep quality and pharyngeal patency is maintained by nocturnal denture use. Moreover, this denture effect appears to be different between healthy edentate elders and those with sleep disturbances [29]. On the other hand, there is a general belief amongst oral health care professionals that edentate individuals should remove their dentures at night. In fact, numerous studies have demonstrated that long-term nocturnal wearing of dentures can reduce the protective effect of saliva and obstruct good oxygenation of the oral mucosa, which makes the it less resistant to mechanical and microbiological aggression, thus increasing the risk of chronic inflammatory changes within the mucosa [30–32]. This leads to an increased risk of traumatic ulcers, denture stomatitis, and alveolar bone resorption in the edentate population [33–37].

However, tooth loss and not wearing dentures at night have not been recognized as a risk factor for sleep disturbance and OSA. Furthermore, the limited quality of studies on this topic (graded as level ≤ 3 of the Oxford level of grade of evidence) [38] do not permit clinicians to engage in evidence-based clinical decision-making. This lack of knowledge poses legal and ethical problems for clinicians and other dental professionals who are involved in the care of the growing edentate population.

To enable development of clinical-practice guidelines, solid evidence is required. Specifically, a rigorous randomized trial is needed to help determine the effects of denture wearing on patient-relevant outcomes [28, 39–41].

To address this need, we have designed a single-blind randomized cross-over trial. The first objective of the study is to test whether nocturnal denture wear has an effect on sleep quality and daytime sleepiness of edentate elders with moderate to severe sleep apnea. The second objective
is to test whether nocturnal denture wear has an effect on the oral health related quality of life of edentate elders with moderate to severe sleep apnea. The third objective is to identify modifiers of the putative effects of nocturnal denture wear.

**METHODS**

The study protocol was approved by the Research Ethics Board of Health of the Université de Montréal (Project 13-076-CERES-D). The trial is registered in the U.S Clinical Trials Registry NCT01868295.

**Recruitment process**

Participants will be recruited from the area of Metropolitan Montreal. Participants will be recruited through the research, prosthodontics and sleep apnea clinics of the Université de Montréal, associated hospitals, geriatric institute and private sleep clinics.

The research coordinator will contact the patients in person at the clinics with a study information brochure to invite them to participate in the trial. Potential study participants will be asked to contact a research coordinator via dedicated phone number with voicemail. She will describe the study in general terms and assess major inclusion criteria, and the study candidates will be invited to an in-person information/screening session. During this session, the research coordinator will inform these potential participants about the general health risks associated with OSA and will explain all aspects of the study by using a PowerPoint presentation and a study brochure. The interested participants will be screened for eligibility for inclusion in the study. Eligible participants will be asked to read and sign the consent form.
Inclusion/exclusion criteria

Inclusion criteria
To be considered for inclusion in the study, the subject must: 1) be aged 65 years or older; 2) have worn a complete set of removable dentures in the last year and not have worn their dentures during sleep in the last 12 months; 3) have an Apnea-Hypopnea Index (AHI) \( \geq 15 \) at screening; 4) have an adequate understanding of written and spoken English or French; 5) be able to understand and respond to the questionnaires used in the study; 6) agree to follow the research study instructions; 7) agree to adhere to the allocated sequence of interventions; 8) consume no alcohol and 9) not work late at night on the day before polysomnography.

Exclusion criteria
The participants are excluded if: 1) they have an AHI < 15; 2) have any severe cardiologic, neurologic, psychological, or psychiatric condition, respiratory disease, acute airway infection or any other health condition that jeopardizes sleep; 3) have a score of 24 or less on the mini-mental state evaluation (MMSE) [42]; 4) regularly consume more than 2 alcoholic beverages per day for females and 3 for males; 5) are taking medication or any illicit drug that will affect sleep architecture or respiratory muscle activity (i.e., hypnotics, psycho-stimulants, anticonvulsant, or antipsychotics); 6) are on regular continuous positive airway pressure therapy or nocturnal supplemental oxygen; 7) have sleepiness deemed to be unsafe and requiring urgent treatment; 9) or feel that the trial would negatively influence their private life.

Intervention, Randomization, Allocation concealment and Sequence generation
A single-blind randomized cross-over clinical trial will be conducted. The trial will have two sequences and two periods (balanced design).
Eligible study participants will be randomly assigned to wear or not wear their complete denture at night in alternate orders for 2 periods of 30 days (Flow chart, Figure 1). Minimal or no carry-over effect is expected based on the action of the postulated mechanism of intervention [28] (additional analyses of raw data from research team member F.R.A.: Grizzle’s model [43] sequence effect p=0.8, period effect p=0.9, intervention effect p=0.002). Therefore, no wash-out period was deemed necessary.

To achieve a balanced allocation of participants in each sequence, a permuted block randomization with varying block sizes using SAS® PROC PLAN will be used [44–51]. Randomization and administration of opaque sequential envelopes will be carried out off-site. The study participants will receive these envelopes at their home via the sleep technologist. Each participant will receive a sequentially numbered, sealed, opaque and tamper-proof envelope indicating the sequence of intervention, and intervention will start on the same day (one week after baseline assessment). All the investigators, the research coordinator and the scoring service providers will be blinded to the intervention assignment. Data will be gathered, measured, recorded, and entered in a blinded fashion. Blinding will be lifted once data analysis is complete. Although it is not possible for the participants to be “blind” to the intervention, they will be asked not to discuss their interventions with any research staff. Any question from participants during the intervention period will be answered by two independent prosthodontists and, if necessary, a sleep clinician, as these individuals will not be involved in data collection or data analyses.

**Data collection**

Persons who consent to participate in the study will be invited to visit the clinical research laboratories of the Faculty of Dental Medicine at the Université de Montréal at their
convenience. During this visit, one trained and calibrated research trainee will conduct baseline data collection including a clinical examination, administration of study questionnaires and Cone-Beam Computed Tomography (CBCT) scan (NewTom 5G CBCT, QR S.r.l.-Verona, Italy), as described. Then, in the same week, they will conduct one baseline portable overnight recording (level II polysomnography) [52]. Follow-up data will be collected at the end of each period by the sleep technologist at home by means of one portable overnight recording and the outcome questionnaires. The sleep technologist will install the device at the participants’ homes on the evening of recording, verifying electrode impedance and signal quality. This approach will allow us to maximize the participation of seniors and will increase their adherence to the study procedures [53].

**Primary outcome measures**

The selection of the outcomes was based on a literature review and on consultation with experts in sleep and oral health disease [54, 55].

The primary outcome is sleep quality, as measured by the AHI index. This index is a marker of sleep quality that represents the number of apneas and hypopneas per hour of sleep [56]. The AHI index will be measured with diagnostic portable polysomnography units for overnight home use [57]. Standard polysomnography measurements will include total sleep duration, sleep efficiency, sleep onset latency, electro-encephalogram (EEG) arousal index, spontaneous arousals, and sleep-stage distribution. Upon return of the device, polysomnographic data will be downloaded and scored using REMLogic software (Embla Inc., Canada) to assess AHI, snoring index, respiratory disturbance index, flow limitation, respiratory efforts related arousals, and average and minimal oxygen saturation. These respiratory events will be scored by Sleep Strategies Inc. (Canada), according to American Academy of Sleep Medicine guidelines [58].
Secondary outcome measures

Secondary outcomes will be daytime sleepiness and oral health-related quality of life.

The Epworth Sleepiness Scale (ESS) will be used to assess perceived daytime sleepiness. The ESS is an eight-item, 4-point scale (0-3) with strong internal consistency (Cronbach’s alpha=0.81) and half-split reliability (r=0.82) [59]. Participants will be asked to rate their chance of dozing in eight different sedentary situations. Scores ≥10 suggest excessive daytime sleepiness.

Oral health-related quality of life (OHRQoL) will be measured by means of the Oral Health Impact Profile (OHIP-20) [60]. This instrument is a disease-specific measure of people’s perceptions of the impact of denture wear on their physical, psychological and social impacts on their quality of life. This validated and highly reliable (alpha=0.88) oral health disease-specific instrument has been widely used in geriatric dental research [61–63] and has been tested and validated in English- and French-speaking Canadians for cross-cultural validity [50]. The range of the scale is 20-120 points, with lower scores indicating better OHRQoL [60, 64].

The primary and secondary outcome measures will be collected at baseline and at the end of each 30-day period.

Covariates

We will also collect data on socio-demographic, medical, and anthropometric (weight, height) characteristics, oropharyngeal morphology (measured by a 3-dimensional imaging system, CBCT), as well as edentulism-associated characteristics (vertical dimension of occlusion according to prosthodontic standard criteria, the history of tooth loss, history of denture use, and nocturnal denture wear) [65] and general health. Perceived general health will be assessed by the use of the Short Form-36 (SF-36) [66]. The SF-36 is a generic self-administered questionnaire.
consisting of 8 multi-item subscales: physical functioning, social functioning, role limitations due to physical health problems and role limitations due to emotional problems, mental health, vitality, pain, and general health perceptions. The SF-36 has excellent internal consistency and discriminates between individuals with and without chronic disease [66–68]. The computerized scoring system will be used according to the user’s manual, in which higher scores represent a better condition [69].

**Sample size justification**

Assuming that (i) the minimal clinically important difference in the AHI score between the two interventions is 5 events/hour (based on the opinion of the expert clinicians, Delphi method) [70], (ii) the SD of the distribution of the difference in AHI score between interventions is 10.6 events/hour (based on estimates from our pilot data) [28], and (iii) the drop-out rate is 10% (based on our pilot data), a sample size of 70 study participants will ensure a 0.90 power to reject the null hypothesis if it is indeed false, at a two-sided Bonferroni-adjusted alpha level of 0.0167 (to account for the three study outcomes).

The sample size of 70 would ensure a power of more than 0.90 to detect a difference of 2.5 units in the mean ESS score (assuming that the SD is 3.5 units) [71], and a difference of 17 units (minimal clinically important difference) [72] in the mean OHIP score (assuming that the SD is 23.8 units) [73], at a two-sided Bonferroni-adjusted alpha level of 0.0167 [74, 75].

**Statistical analysis**

Descriptive analyses for all variables will be performed. In case of apparent material deviations from normality, the distributions of the dependent variables will be normalized by appropriate transformations.
Mixed linear models will be fitted in SAS Proc Mixed (SAS version 9.3, SAS Institute Inc., USA) to test the associations between the intervention and each of the study outcomes [76]. The model will include variables for intervention, randomization sequence, period and baseline value of the study outcome as fixed effects and subject as a random effect. Hypotheses concerning model parameters will be tested by Wald tests with an approximate F null distribution.

To test for potential modification of the impact of the intervention by presence of sleep disturbance at baseline, and the degree of sleep disturbance at baseline, we will introduce a series of interaction terms between the intervention status and each of these characteristics (one at a time) into the above-described linear models.

All of the analyses will be carried out in accordance with the intention-to-treat principle, and various strategies will be contemplated to account for post-randomization missing data in case of non-balanced missing data and/or attrition of more than 10% of participants. However, in the sensitivity analyses, we will also carry out per-protocol analyses to assess the robustness of our findings to potential incomplete adherence: specially, patients with major protocol violations and/or poor adhere will be excluded.

**DISCUSSION**

This research could inform planning for a preventive approach to improving sleep characteristics of the older population and, thereby, improve well-being and quality of life. The evidence produced by this trial will assist in producing truly evidence-based practice guidelines used by primary care providers, dentists, and sleep medicine specialists, who provide care for the millions of edentate seniors all around the world [56].
TRIALS STATUS

The project is currently in the recruitment phase.

ABBREVIATIONS

AHI: Apnea-Hypopnea Index; CBCT: Cone-Beam Computed Tomography; EEG: electroencephalogram; ESS: The Epworth Sleepiness Scale questionnaire; MMSE: The mini-mental state examination; OHIP-20: The Oral Health Impact Profile questionnaire; OHRQoL: oral health related quality of life; OSA: Obstructive sleep apnea; SF-36: The Short Form-36 Health Survey questionnaire.

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS’ CONTRIBUTIONS

EE, NH, and HN drafted the manuscript. EE, NH, and GL participated in the conception, design and coordination of the study. FA, JF, and IK helped revised the manuscript and participated in the conception, design of the study. All the authors revised and approved the final manuscript for publication.

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FIGURE LEGENDS

Figure 1. Trial Design
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Figure 1. Trial Design