Sleep, Hypertension, and Nocturia: Multicomponent Approach for Comorbid Illnesses

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INTRODUCTION

Elevated nighttime blood pressure (BP), poor sleep, and nocturia are comorbid, mutually exacerbating conditions. Both elevated nighttime systolic blood pressure (SBP), and poor sleep disrupt the diurnal pattern of urine excretion by increasing nighttime sodium (natriuresis) and water (diuresis) excretion leading to increased nighttime urine production causing nocturia. This increased frequency nighttime awakenings with nocturia, in turn, contributes to poor sleep and elevated nighttime SBP. We postulate that treatments targeted towards these etiologies will help break this vicious cycle.

Traditionally, antihypertensive medications are dosed in the morning targeting daytime BP. However, some research suggests that nighttime BP best predicts risk for major cardiovascular events. Several clinical trials of bedtime dosing of BP medication–chronotherapy– show better nighttime BP control. However, no clinical studies have considered or tested chronotherapy as a treatment for nocturia. With respect to poor sleep, we have shown that brief behavioral treatment of insomnia (BBTI) significantly improves not only sleep but also self-reported nocturia among the elderly. Therefore, we envision a multicomponent approach with chronotherapy (bedtime dosing of certain antihypertensives) and behavioral sleep intervention (BBTI) to concurrently address the prevalent and chronic, mutually exacerbating conditions: nocturia, poor sleep, and hypertension.

STUDY OVERVIEW

This pilot study will provide critical preliminary data regarding the relation between sleep and nighttime BP in seniors In the proposed pilot study 30 community-dwelling older adults (aged >65) who take at ≥1 daily non-diuretic antihypertensive medication, have a mean SBP >135 mm Hg, and awaken ≥2 times nightly to void will be randomly assigned to one of the 3 groups of 10 participants each to 1) morning (am) HTN medication dosing, 2) BBTI with am HTN medication dosing, 3) nighttime non-diuretic HTN medication dosing (chronotherapy) for 6 weeks. At baseline and 6 weeks, participants will undergo 48-hour ambulatory BP monitoring, in-home sleep study, complete a 3-day bladder diary. Data from this study will provide feasibility and pilot data for a subsequent, larger, and more definitive trial.

Outcome measures:
1) Change in mean sleep time systolic BP dip pre- vs post-intervention- measured by 24-hour ambulatory BP monitor (ABPM)
2) Change in nocturia frequency as determined by 3-day bladder diary
3) Change in nocturnal polyuria measured by NPi- nocturnal polyuria index=(nocturnal urine volume/24-hour volume)*100
4) Change in global Pittsburgh Sleep Quality Index (PSQI) scores pre- vs post-intervention

Data Analysis:
In this pilot investigation, we will perform descriptive and graphical analyses as well as inferential analyses. As appropriate for a pilot study, we will focus on the magnitude of effects rather than on the *p*-values.

First, we will compare baseline characteristics between the 3 groups using analysis of variance (ANOVA), Kruskal-Wallis, chi-square and Fisher's exact tests, as appropriate. Any significant differences will be used as additional covariates in sensitivity analyses. Second, we will fit a series of analysis of covariance (ANCOVA) models using the SAS® GLM procedure with pre- to post-intervention change in each continuous outcome as the dependent variable: BBTI (yes/no), chronotherapy (yes/no) and baseline value of outcome as independent variables. Third, we will construct means contrasts appropriate for testing the hypotheses. Magnitude of the estimate and/or its statistical significance of: BBTI vs usual care and chronotherapy vs usual care contrasts will be interpreted as a test of hypothesis 1.1. Finally, we will add changes in measures of sleep (decrease in WASO) and % of deep sleep to the above model as an additional independent variable and notice the reduction in magnitude of the above means contrasts.