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Daytime Sleepiness in elderly people under Hemodialysis: initial data from a randomized placebo-controlled clinical trial

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ABSTRACT

Introduction: Sleep is a complex physiological process that alternates with vigilance periods. Alteration in sleep is associated with chronic pathologies including kidney disorders and results in a deficit in the quality of life. **Objective:** Analyze the effects of Bright Light Therapy (BLT) on the sleep of elderly people with End-Stage Chronic Kidney Disease (ESKD) undergoing hemodialysis. **Methods:** Clinical, randomized, placebo-controlled trial with a quantitative approach where data collection was based on the application of the Epworth Sleepiness Scale in hemodialysis clinics before and after the provision of BLT or placebo lightbox (PLB). It was approved by the Ethics Committee of the Proponent University under nº 4.987.780 and approved too in the Brazilian Registry of Clinical Trials (ReBEC) with the number RBR-8bmjpd4. **Results:** 34 patients formed four groups (17 patients before and the same 17 after BLT and 17 patients before and the same 17 after PLB). Their mean age was 71 years, predominantly (62%-21/34) male. The analysis revealed that daytime sleepiness decreased after using the BLT, ANOVA, and eta-squared 0.05, on the other hand, daytime sleepiness increased significantly after the use of PLB. Performing the Test-t effect size to compare the means of the two groups after PLB and after BLT (6.53 versus 7.88) found a high effect, Cohen's d 4.83 and Hedges'g 4.95. **Conclusion:** There are benefits in the use of BLT in the afternoon for elderly people with ESKD on hemodialysis, in the context of regularization of the sleep-wake cycle.

Keywords: aged; sleep-wake disorders; Renal Insufficiency, Chronic; Renal Dialysis; phototherapy; circadian rhythm.

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INTRODUCTION

Sleep is considered a complex physiological process that alternates with vigilance periods. Accordingly, it is understood that it is an essential biological function for the integrity of all systems of the human body[1,2]. Therefore, any alteration in the quality of sleep will result in a deficit in the quality of life and an association with chronic

pathologies such as hypertension, diabetes, obesity, mental disorders, dementia, and kidney disorders[2].

In this context, due to their influence on maintaining occupational roles, sleep disorders (SD) cause significant changes in occupational and cognitive functions, especially when associated with End-Stage Chronic Kidney Disease (ESKD)3. In this sense, it is noteworthy that the longer the duration of ESKD, the greater the incidence of SD[3], making it possible to perceive the association between the quality of sleep and the morbidity and mortality of these individuals.

Addressing The prevalence of SD in this population ranges from 45 to 80% depending on the study design and sample size[4]. In the analysis of these disorders, the most common are disturbances in the melatonin production cycle due to the intermittent nature of hemodialysis (HD). But there is also insomnia, restless legs syndrome, and hypersomnia in this population group[4].

Corroborating with the Yousef[5] also found a high prevalence of complaints related to sleep or excessive daytime sleepiness, as there is a decrease in melatonin concentration in hemodialysis patients, thus favoring night-time insomnia.

Melatonin supplementation has not yet been approved for this population undergoing hemodialysis. However, there is a 2020 study by Huang and colleagues that obtained positive results for Bright Light Therapy (BLT) in individuals with Chronic Kidney Disease (CKD) undergoing hemodialysis. The explanation for this improvement can be found in the work of Pjerek[6], who suggests that white light is an exogenous modulator of melatonin production, supporting the use of this therapy in these patients.

Furthermore, it is important to understand that there is a significant association between HD and daytime hypersomnia, especially when hemodialysis treatment occurs in the first shift (from 6 am to 10 am)[7]. Therefore, the use of non-pharmacological health promotion strategies aiming to improve sleep quality is essential, especially when there are many associated comorbidities.

In this sense, the use of BLT is indicated. This is recognized as an effective and tolerable treatment for other diseases such as Alzheimer's, Parkinson's, Stroke, and Seasonal Depression because it is effective in regulating the sleep-wake cycle[8-11]. The authors explain that the BLT technology in these pathologies functions through the activation of the suprachiasmatic nucleus (SCN) by nervous signals from specialized photosensitive ganglion cells in the retina. Given that the SCN is the brain's primary circadian pacemaker and is responsible for controlling the sleep-wake cycle, endogenous hormone secretion, and central body temperature, correcting circadian rhythm disturbances through light cycle manipulations may be able to alleviate symptoms associated with mood disorders, Alzheimer's, Parkinson's, and stroke. Since circadian rhythm disruption is a characteristic of these conditions, addressing circadian disorders through light cycle manipulations may be able to alleviate symptoms associated with these pathologies, as sleep is crucial for brain plasticity. Furthermore, patients report that BLT is well tolerated without side effects[12,13].

On how to use BLT, it is noticed in the literature that it varies according to age and purpose. It is recommended to use it in the morning to anticipate the onset of the sleep phase, reduce excessive daytime sleepiness, and advance bedtime at night. However, it is recommended to use it in the afternoon to delay the onset of the nocturnal sleep phase and thus allow awakening only after sunrise[8,14].

In this context, it is understood that this research is original and unprecedented as it aimed to analyze the effects of BLT on the sleep of elderly people with ESKD on hemodialysis.

METHODS

This is a clinical randomized controlled study with a quantitative approach[15]. BLT is beneficial for regulating sleep disturbances in elderly patients with ESKD on maintenance hemodialysis. The research was developed in three hemodialysis clinics located in Fortaleza, Ceara, Brazil. The sample was calculated according to the hemodialysis census of the city where the research was done. However our findings are from preliminary results of an ongoing study, the objective is to read a sample of 60 patients.

The study population consisted of elderly people with a minimum age of 60 years and a maximum age of 94. To determine which patient would be in each group, a raffle was held to choose which lightbox to deliver. The inclusion criteria were as follows: elderly aged between 60 and 94, being admitted to a hemodialysis clinic. The exclusion criteria were blindness, inability to understand, use of photosensitizing medications, or refusal to participate in any of the phases of the study after signing the Informed Consent Form.

The information consisted of a total of nine open- and closed-end questions about the introductory characteristics of the elderly and their pathology history.

ESS (Epworth Sleepiness Scale)

The ESS is a self-administered questionnaire with eight questions, but in this study, it was applied by the person responsible for the research (only by the principal researcher), because of the limitations of the patients. Respondents were asked to rate, on a 4-point scale (0-3), their usual chances of dozing off or falling asleep while engaged in eight different activities (reading, watching TV, sitting doing nothing in a public place, passenger in a car or bus for one hour, lying down in the afternoon, sitting and talking, sitting right after lunch and not using alcohol or in the car stopped for a few minutes in traffic). ESS scores vary from zero to 24, the bigger the result the worse the daytime sleepiness.

Placebo light versus Bright light therapy intervention

The procedure was explained to the elderly and took place in three hemodialysis clinics located in the capital of northeastern Brazil. About the consent, verbal and written consent was obtained from the elderly or their guardian when necessary. The Information Form was completed by the researchers.

According to the randomization, the participants entered the research gradually and the groups were being formed. After the application of the tests, the elderly used the bright lightbox, or placebo light box, in his/her home for four weeks, for 30 minutes every afternoon. The therapeutic lamp was a portable light box 6×6.5×1 inches in size with an array of 72 eye-optimized light-emitting diode (LED) lights. Ac- According to the manufacturer, it delivers 10,000 lux of wide-spectrum non-flickering white light to simulate natural sunlight. The placebo one delivers only 500 lux. The follow-up took place over the phone to check for possible adverse effects. After this intervention, the tests were reapplied.

Statistical analysis

Firstly, descriptive statistics was used to describe ESS scores[16]. The Kolmogorov-Smirnov test was utilized to assess the normality of the sample data. To evaluate the differences between the groups, the test-t effect size varies in four levels: 0-0.2 (No effect), 0.2–0.5 (Little effect), 0.5–0.8 (Meddle effect), and >0.8 (High effect).

Furthermore, the one-way analysis of variance (ANOVA) for independent groups and ANOVA effect size[16]. The statistical significance level cording to Fritz et al.[17], is as follows: eta-squared, epsilon-squared, and omega-squared vary from zero to one and is divided into four levels: <0.01 (No effect), 0.01 – 0.04 (Little effect), 0.04 – 0.11 (Middle effect) and >0.11 (High effect).

Ethical considerations

The researchers refer to the preliminary results of a project approved by the Ethics Committee of the Proponent University under no 4.987.780 and Certificate of Presentation for Ethical Appreciation no 50545621.5.0000.5052. Thus, the participants agreed and signed the Informed Consent Form, by the precepts of Brazilian Laws nº 466/12[18] and 510/2016[19], preserving anonymity and the ethical principles of scientific research with human beings. The study was approved too in the Brazilian Registry of Clinical Trials (ReBEC) with the number RBR-8bmjpd4.

RESULTS

In data collection, so far 54 patients were contacted to be arbitrarily randomized into two groups. However, 18 were excluded for several reasons: blindness (2/18=12.5%) inability to understand (2/18=12.5%), or refusal to participate in any of the phases of the study after signing the Informed Consent Form (12/18=75%).

To aid in the analysis, the database was developed with the following division into codes: CODE 1.0 (group before using the placebo light), CODE 1.1 (group after using the placebo light), CODE 2.0 (group before using bright light therapy), and CODE 2.1 (group after using bright light therapy).

Starting with the characterization of the sample, all of them have been undergoing hemodialysis, about the time: less than one year 38,2% (13/34), from two to three years 64,7% (22/34), from four or more 79,4% (27/34). 62,5% (20/34) were male and the mean age was 71.7 years (standard deviation- SD=9.7). The mean of the time was 3.0 in CODE 1.0, and 3.3 in CODE 2.0 The descriptive analysis is in Table 1.

Regarding the clinical differences between the patients, there was no statistical significance, as in both groups all of them had systemic arterial hypertension and diabetes. The group was divided into 21 men and 13 women, and this did not generate a statistical difference. Therefore, the groups were equal from the statistical point of view. In this context, it was used the eta-square test for the ESS which was found to be 0.05 with IC 95 0.000-0.162.

For the analytic statistics, the total score of the ESS was used before and after the intervention with both kinds of lights, as shown in Table 2.

About the variation of the sleepiness scale in the groups (CODE) we found in CODE 2.0 a result bigger than in CODE 1.0. This occurred because the groups were randomized in an aleatory fashion, the group treatment is represented in Figure 1. This difference was not statistically significant.

DISCUSSION

Sleep is a complex and fundamental physiological process for maintaining the integrity of body systems such as memory, binocular vision, thermoregulation, energy conservation, and restoration[2]. Thus, it is understood that poor sleep quality is associated with risk factors for various pathologies[20].

Associated with ESKD, it is noticed that there is a higher prevalence of sleep disorders in patients with ESKD compared to healthy individuals, such as restless leg syndrome, insomnia, and obstructive sleep apnea[21].

Some factors are related to sleep disorders in these patients, such as hemodialysis time, joint pain, urea, parathyroid hormone, phosphorus, potassium, hemoglobin levels, and advanced age[2].

Table 1: Descriptive statistics of Epworth Sleepiness Scale- ESS

CODE	N	Mean	Std. Deviation	Std. Error
1.0	17	7.47	5.125	1.281
1.1	17	6.41	5.046	1.262
2.0	17	9.53	5.416	1.354
2.1	17	7.88	4.775	1.194
Total	68	7.82	5.090	1.273

Table 2: Analysis of effect size of Epworth Sleepiness Scale- ESS

ANOVA	SSa	df	MSb	F
Between Groups	91.926	3	30.642	1.348
Within Groups	1455.29	64	29.006	
Total	1547.22	67		
Test-t effect size between CODE 1.1 versus CODE 2.1				
	CODE 1.1	CODE 2.1	Effect size	
Mean	6.53	7.88	Cohen's d	Hedges'g
SD	5.149	4.498	4.835	4.952
n	17	17		

aSum of Squares. bMean Square. cANOVA Eta varies from zero to one and is divided into four levels: < 0.01 (No effect), 0.01 – 0.04 (Little effect), 0.04 – 0.11 (Middle effect), and >0.11 (High effect). dCI: Confidence Interval 95%13. eTest-t effect size varies in four levels: 0-0.2 (No effect), 0.2 – 0.5 (Little effect), 0.5 – 0.8 (Meddle effect), and > 0.8 (High effect)

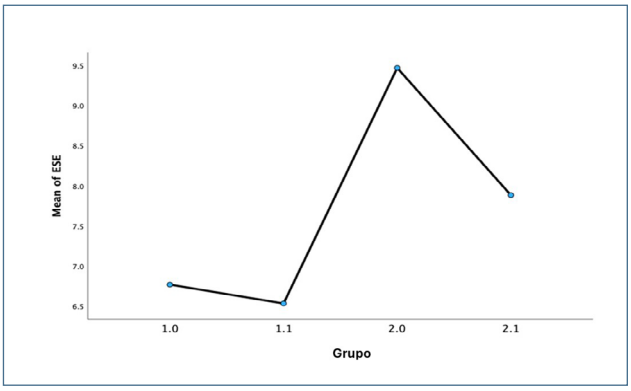

Figure 1: Variation of the Epworth Sleepiness Scale-ESS in the groups (CODE).

Hemodialysis has sleep-inducing effects, such as the production of interleukin-1, increased body temperature, and cerebral osmotic imbalance that leads to lowered consciousness[21].

However, it can influence the quality of sleep, either due to the environment or the high emotional burden that these patients carry caused by the disease itself and the therapeutic approach[22]. Thus, sleep disorders are related to worse quality of life, morbidity, and increased mortality[23].

In this scenario, a pilot randomized controlled study of light therapy in renal transplant recipients for sleep-wake disturbances showed significant improvement in sleep efficiency and sleep latency[24].

Now, about our findings, we found an increase in ESS means after placebo light from 7.31 to 7.62 or a worsening in daytime sleepiness. On the other hand, the study revealed a decrease in ESS means from 8,85 to 8.31 demonstrating the benefit of BLT in daytime sleepiness (Figure 1 and Table 2). The ANOVA effect size, including the four groups, by eta-squared was .013, a little, but significant effect.

Performing the Test-t effect size to compare the means of the two groups after placebo light and after bright light (7.62 versus 8.31) found a high effect, Cohen's d 5.560 and Hedges'g 5.741.

To finish, regarding the limitations of the study, the sample size is a limiting factor, and the scarcity of literature made it difficult to understand the findings. But our findings are preliminary to an ongoing study.

Bright light therapy in the afternoon is beneficial for elderly patients with ESKD on hemodialysis, mainly as it regulates the sleep-wake cycle impaired by daytime sleepiness of the hemodialysis. It is suggested that the researcher continue the study to increase the sample size.

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