UNIVERSIDADE DA CORUÑA
Grupo de Investigación en Gerontología y Geriatría

Study Protocol and Statistical Analysis Plan

Protocol Official Title: **Bright Light Therapy in Older Adults With Moderate to Very Severe Dementia: Effects on Cognition, Mood, Behavior, and Physiological Parameters**

Brief Title: **Bright Light Therapy in Older Adults With Moderate to Very Severe Dementia (BLT-Dementia)**

ClinicalTrials.gov ID: [Not yet assigned]

Date: 18th June 2021

INTRODUCTION

Dementia is one of the main causes of disability and dependency among older adults worldwide, constituting a public health priority due to its significant human and financial costs to society (WHO, 2017). Aside from cognitive decline, dementia progression leads to the appearance of at least one behavioral or psychological symptom of dementia (BPSD) in the majority of the individuals at some point during their disease (Lyketsos et al., 2000; Steinberg et al., 2008). Pharmacological and non-pharmacological interventions have been proposed for the treatment of both BPSD and cognitive impairment. Numerous guidelines and expert recommendations initially recommend the use of non-pharmacological strategies to manage dementia due to the absence of adverse events (Dyer et al., 2018).

Nonpharmacological interventions in dementia include bright light therapy (BLT). This therapy consists of the controlled application of certain levels of light that can be administered in different ways, such as outdoor sunlight, light boxes, light visors worn on the head, ceiling lights, or the dawn-dusk simulation (Forbes et al., 2014). There is some evidence that effective doses of light would stimulate circadian cycles, thus affecting sleep efficiency, depression or behavioral problems in older adults with dementia (van Maanen et al., 2016; Sloane et al., 2008; Abraha et al., 2017). Of note is the great methodological heterogeneity among the studies with respect to light intensity, frequency, interval, time of day and total duration of the intervention program (Forbes et al., 2014). The lack of consensus on the protocol for BLT application, as well as the existence of little research in person with advanced stages of dementia, calls for further research to explore in depth the immediate, short- and long-term effects of BLT in this population.

OBJECTIVES

To study the short- and long-term effects of bright light therapy on mood, behavior, sleep and cognition in a sample of instituzionalized older adults with moderate to very severe dementia.

To explore the immediate effects of bright light therapy sessions on behavior, mood and physiological parameter in a sample of institutionalized older adults with moderate to very severe dementia.

To compare the effectiveness of bright light therapy sessions with other non-pharmacological interventions in people with dementia.

MATERIAL AND METHODS

Study design

This longitudinal, comparative and prospective study conducted between October 2018 and April 2019, is a 2 x 2 randomized controlled trial using a two-group design (BLT vs. control) and two repeated measures (pre- vs. postintervention). In addition, the behavior, mood and physiological parameters of the BLT group participants were assessed immediatly before, after and during each session.

This study is performed following the CONSORT (CONsolidated Standards of Reporting Trials) 2010 guideline.

Study setting and participants

Participants were recruited between September and October 2018 among residents of the Gerontological Complex La Milagrosa (A Coruña, Spain).

Inclusion criteria: (a) age 65 years or older, (b) diagnosis of dementia, and (c) a score ≥ 4 points on the Global Deterioration Scale (GDS; Reisberg et al., 1982), rangin from moderate to very severe cognitive decline.

Exclusion criteria: (a) high ocular sensitivity to light (photosensitivity), (b) preexisting ocular abnormalities, or (c) having any severe ocular disorder that did not allow them to open their eyes or that implied a very low visual acuity.

39 participants will be recruited, stratified according to their cognitive status and subsequently randomly placed into two groups: the BLT group (=19) and the control group (n=20).

Intervention

Light therapy lamps

For the development of the intervention it was necessary to purchase two light therapy lamps (Beurer TL 100 daylight lamps). These devices (Fig. 1 and Fig. 2) are specially designed for bright light therapy, providing the required uniform illumination with an intesisty of up to 10,000 lux.

Figure 1. Lamp Beurer TL 100

Figure 2. Light therapy lamps in the intervention room

Intervention

BLT sessions were carried out in a quiet room of the Gerontological Complex especially enabled for their proper development and were implemented by a research psychologit specialized in Gerontology. The devices used for the intervention were bright white light lamps providing an intensity of 10,000 lux. Four users participated in each session, placing two users per lamp, seated in a comfortable chair with armrests 70 cm from the lamp. The sessions were 30 minutes/day in the time slot between 10:30 and 12:00 in the morning, 5 days a week (Monday to Friday) for 4 weeks (total 20 sessions). Two groups of participants per day were established, the first shift being from 10:30 to 11:00, and the second from 11:15 to 11:45 a.m., which means the stimulation of 8 people per day (month). During the sessions, while exposed to light, participants were watching documentaries on neutral topics (nature, Spanish and Galician culture, etc.). Each session lasted 30 minutes, unless the participant expressed the desire to

leave the room and could not be convinced to remain in it without generating agitation. Participants who responded negatively to light exposure were immediately withdrawn from the intervention. Only those sessions in which the person remained at least 80% of the expected time (≥ 22.5 minutes) were considered as sessions performed. Additionally it is established as a final criterion to consider the participant to complete at least 80% of the scheduled sessions (16 out of 20 sessions).

In every session, the researchers supervised the users to ensure full compliance with the treatment and recorded the physiological parameters (heart rate and blood oxygen saturation) as well as the mood and behavior of the participants.

Measures

Pre- and post-intervention assessments were performed on all subjects in the sample (control and experimental group). Pre-intervention data were collected during the week before the start of the intervention, and post-intervention data were recorded during the week after the end of the intervention. Additionally, data on physiological parameters, mood and behavior were recorded in each session for the participants of the experimental group.

Socio-demographic variables

Age (years), gender, and educational level.

Mini-Mental State Examination (MMSE)

Cognitive evaluation: brief screening test for cognitive impairment.

Severe Mini-Mental State Examintation (SMMSE)

Cognitive evaluation: brief assessment of severe cognitive impairment in advanced stages of dementia. This test was applied only to individuals who obtained a score of 10 points or less in the MMSE.

Cambridge Cognitive Examination (CAMCOG)

Cognitive evaluation: more comprehensive cognitive assessment of participants with moderate cognitive impairment (GDS = 4). This scale includes the evaluation of the following domains: orientation, language, memory, attention and calculation, praxis, abstraction, perception and executive function.

Severe Cognitive Impariment Profile (SCIP)

Cognitive evaluation: a more comprehensive cognitive assessment of participants with moderate-severe to very severe cognitive impairment (GDS = 5, 6 and 7). This scale allows obtaining a performance profile in each of the cognitive domains evaluated (comportment, attention, language, memory, motor, conceptualization, arithmetic, and visuospatial) and calculating a total score indicative of the degree of cognitive impairment: moderately severe, severe, very severe and profound.

Cornell Scale for Depression in Dementia

Mood evaluation: assessmet of signs and symptoms of major depression in patients with dementia focusing on the week preceding the interview. The Cornell Scale utilizes two semi-structured comprehensive interviews that elicits information from the patient and the informant. In those cases in which the patient is not able to respond due to the level of cognitive impairment, information is obtained only from the interview with the informant.

Neuropsyquiatric Inventory Questionnarie (NPI-Q)

Mood and behavior evaluation: a brief restrospective (1 month) caregiver self-administered questionnarie for the assessmet of 12 neuropsychiatric symptoms: delusions, hallucinations, agistation/aggression, dysphoria/depression, anxiety, euphoria/elation, apathy/indifference, disinhibition, irritability/lability, aberrant motor behaviors, nighttime behavioral disturbances, and appetite/eating disturbances.

Cohen-Mansfield Agitation Inventory (CMAI)

Mood and behavior evaluation: a caregiver rating questionnaire for the assessment of the frequency of manifestations of agitated behaviors. Ratings refer to the two weeks prior to its administration.

Rating for Anxiety in Dementia (RAID)

Mood and behavior evaluation: a clinical rating scale to evaluate severity of anxiety including somatic symptoms and specific fears. Scoring should be based on the two weeks prior to the caregiver interview.

Sleep Disorders Inventory (SDI)

Sleep evaluation: this inventory is an expanded version of one item of the Neuropsychiatric Inventory (NPI). It recorded the frequency, severity, and caregiver burden of sleep-disturbed behaviors for the two weeks prior to its administration.

Actiwatch AW4 - Actigraphy

Figure 3. Actiwatch AW4

Sleep evaluation: actigraphy is a non-invasive method of monitoring circadian rhythm. Actiwachs are worn on the non-dominant wrist of the participants and record movements that are used to estimate sleep parameters with specialized algorithms in computer software programs. Both experimental and control group participants wore the actiwach for 5 days before and 5 days after the intervention.

Among the parameters obtained from actigraphy records, the following were chosen for analysis in the present study: sleep latency, sleep efficiency and total sleep

Bedford Alzheimer Nursing Severity Scale (BANS-S)

Functional evaluation: a nursing-staff administered questionnaire for the assessment of disease severity in advanced stages of dementia. The questionnarie comprises 7 items: dressing, sleep-wake cycle disturbances, speech, eating, ambulating, muscle rigidity and eye contact.

Interact scale

Mood and behavior evaluation: the Interact Scale, and its shortened version, named Interact short, were used for the evaluation of inmediate effects in the experimental group. Both allows the assessment of changes on mood and behavior, the Interact scale during the sessions, and the Interact short scale in the 10 minutes immediately preceding and in the 10 minutes immediately following the session.

Pulse oximeter

Physiological parameters evaluation: the heart rate and blood oxygen saturation of the participants in the experimental group were recorded at the beginning and end of each session using a mobile finger pulse oximeter

Ethics

The participants and their legal guardians were informed about the study and they signed the corresponding informed consent. All the information was transmitted adapted to the level of comprehension of the participants in order to facilitate their understanding and comfort throughout the study. The present research protocol (code 2017/408) had the favorable authorization from the Galician Research Ethics Committee of Xunta de Galicia (Spain) and was developed in accordance with the Declaration of Helsinki.

Data management and statistical analysis

The data of the participants are coded/pseudo-anonymized to ensure confidentiality and users' privacy for research use. Identifiable information is coded with artificial identifiers. The documentation to re-identify the participants will be only available to a medical doctor that collaborates with the research group, ensuring privacy during all data exploitation and dissemination (conferences, Ph.D. thesis, and scientific articles).

The general description of the population studied is performed by univariate analysis. The distribution in the study groups of sociodemographic factors (gender, age, level of education) was evaluated with Student's t test (or Mann-Whitney U test if the assumption of normality is not met or if the sample size is not large enough) for continuous variables and Pearson's Chi-square test for categorical variables. The normal distribution of the variables is tested using the Saphiro-Wilk test. For subsequent analyzes, parametric or non-parametric tests were applied depending on whether the assumption of normality was met or not for each measured variable. Two-way analysis of variance (ANOVA) is used to determine the existence of differences in agitation, behavior, anxiety, cognitive status or severity of dementia at two points in time (pre- vs. post-). Intrasubject variables were considered as intrasubject variables, these measures over time, and intersubject variables were the study group (control or experimental). The differences between the groups are tested by means of the group-tempo interaction. Sphericity assumptions are determined by Mauchly's sphericity test. In case of sphericity transgression, the Pillai trace test or the univariate F-test adjusted to epsilon (Greenhouse-Geisser) (Geisser and Greenhouse, 1958) is performed.

The Wilcoxon signed-rank test or the Paired t test are employed to measure significant changes between the Interact short scores from before to after the intervention sessions for each of the assessed mood and behavior items. Likewise, these same tests are used to analyze the evolution of the Interact during scores, comparing the average scores of the first week with those of the fourth week. In addition, the evolution of mood and behavior scores throughout the four weeks of treatment is analyzed with the Friedman test for related samples. The Paired t test is also used to determine the existence of any differences from before to after the sessions in physiological parameters. In the variables in which statistically significant differences are found, Cohen's d or r values are used to report the effect size (ES) of these changes. The interpretation of the importance of the ES is made according to the benchmarks defined by Cohen, as follows: small ES (d = 0.2 or r = 0.1), medium ES (d = 0.5 or r = 0.3), and large ES (d = 0.8 or r = 0.5).

The significance threshold is set at a p-value of less than 0.05. All data analysis are performed with the statistical programs SPSS (version 25.0), RStudio software package (Version 1.3.1093) and JAMOVI (The jamovi project, 2020, Version 1.2).

Duration of the project

	2018												2019												2020											
	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
Project preparation and methodolgy																																				
Recruitment																																				
Evaluation and intervention phase																																				
Data analysis																																				
Dissemination																																				

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