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Original Article

Sleepiness and activity in heart failure patients with reduced ejection fraction and central sleep-disordered breathing

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ABSTRACT

Objective: Patients with heart failure (HF) and sleep disordered breathing (SDB) are typically not sleepy, unlike patients without heart failure. Previous work in HF patients with obstructive SDB suggested that sleepiness was associated with a reduction in daytime activity. The consequences of predominately central SDB on sleepiness in HF are less well understood. The aim of this study was to test the hypothesis that subjective sleepiness is associated with reduced daytime activity in HF patients with central SDB, compared to those without SDB.

Methods: The Epworth Sleepiness Scale (ESS), nocturnal polysomnography, and 14 days of wrist watch actigraphy were used to assess subjective daytime sleepiness, nocturnal sleep and breathing, and 24-h activity levels, respectively.

Results: A total of 54 patients with HF were studied, nine had obstructive SDB and were removed from further analysis. Of the patients, 23 had HF with predominantly central SDB (HF-CSA; apnea–hypopnea index (AHI) median 20.6 (IQR 12.9–40.2)/h), and 22 had noSDB (HF-noSDB; AHI 3.7 (2.5–5.9)/h). The median patient age was 68 years (range 59–73 years). There were no significant differences either in ESS score (HF-CSA; 8 [4–10] vs. HF-noSDB; 8 (6–12); $p = 0.49$) or in duration of daytime activity (HF-CSA 14.5 (14.1–15.2) and HF-noSDB 15.1 (14.4–15.3) hours; $p = 0.10$) between the groups.

Conclusion: HF patients with predominately central SDB are not subjectively sleepy compared to those without SDB, despite reduced sleep quality. We speculate that the lack of sleepiness (based on ESS score) may be due to increased sympathetic nerve activity, although further studies are needed due to the small number (n = 5) of sleepy HF-CSA patients. Daytime activity was not different between HF-noSDB and HF-CSA patients.

1. Introduction

Sleep disordered breathing (SDB) disrupts sleep, and is associated with reduced quality of life and with daytime sleepiness [1]. The alleviation of such symptoms is a major therapeutic goal for the treatment of SDB. In heart failure (HF) patients, SDB is known to be associated with increased morbidity [2], and recent randomized trials have tried to establish the most effective treatment [3]. However, although the use of positive pressure devices to treat SDB is often associated with the relief of subjective sleepiness [4], SDB in patients with HF appears not to be associated with sleepiness [5–7]. Indeed, HF patients with predominantly obstructive SDB are less sleepy than those with obstructive SDB but no HF, despite having poorer sleep quality [8].

In clinical practice, the lack of daytime symptoms has implications for the detection of SDB and adherence to treatment [9]. Previous work has suggested that the lack of daytime sleepiness may be due to a reduction in the duration of daytime activity. Hastings et al. [5] studied activity levels in HF patients and found that those with SDB had a shorter duration of daytime activity compared to HF patients without SDB. They also spent more time in

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bed, which may have accounted for the similar symptoms of sleepiness despite a higher arousal index.

An alternative explanation for the lack of sleepiness in HF patients with SDB is that increased sympathetic nerve activity (SNA), related to the HF itself [10], may reduce the propensity to feel sleepy [11]. This may have the greatest impact in individuals with central SDB/central sleep apnea (CSA), in whom HF tends to be more severe [12] and in whom sympathetic nerve activity is higher than in individuals with HF and obstructive SDB and in those with HF without SDB [13]. It is noteworthy that in the study by Hastings et al., approximately half of the HF patients had predominantly obstructive SDB (12 of 22 patients). Thus previous studies have established that patients with obstructive SDB and HF are less sleepy compared to a community cohort with obstructive SDB [8], but the effect of predominantly central SDB in HF on subjective sleepiness and the role of physical activity is less clear.

The aim of the current study was to test the hypothesis that subjective sleepiness is associated with reduced daytime activity in patients with HF and central SDB, compared to HF patients without SDB.

2. Methods

2.1. Subjects

Patients were recruited from the HF clinics at the Royal Brompton and Ealing hospitals in London UK. Those agreeing to participate were classified into four groups on the basis of their sleep study, as follows: (1) HF patients with obstructive SDB (HF-OSA), (2) HF patients with central SDB (HF-CSA), (3) HF patients with no SDB (HF-noSDB), and (4) older healthy participants. Healthy participants were recruited from a list of participants who had volunteered for other studies in our department.

Patients were eligible for inclusion in the study if they had a known clinical diagnosis of chronic HF, documented left ventricular systolic impairment, and were on medical treatment for HF. Measurement of the left ventricular ejection fraction (LVEF) by echocardiography was used as a marker of left ventricular systolic function, and no patient had an ejection fraction (EF) of >40%. Patients had to be clinically stable with no unplanned hospital admission (for any reason) in the preceding four weeks and no new class of HF medication started in the same time period. Patients using positive airway pressure devices (for any reason) were excluded from the study.

Healthy participants were considered suitable for inclusion if they were free of medical problems. All were asked specifically about hypertension, heart disease, diabetes, or any medical condition requiring regular medication or general practitioner consultation. Those found to have SDB on nocturnal PSG were excluded from the study and an appropriate referral to a sleep clinic made. Individuals with conditions likely to significantly disrupt sleep (ie, chronic pain syndromes) were also excluded from the study. All participants had to be at least 18 years of age and to give informed consent. The study was approved by South West London REC no. 1 (REC no. 09/H0708/35), and all subjects provided written informed consent.

2.2. Protocol

2.2.1. Baseline measurements

After informed consent was provided, a baseline assessment was made, including height, weight, resting oxygen saturations, noninvasive office blood pressure, and neck circumference (measured at the level of the cricoid cartilage). All participants completed the Epworth Sleepiness Scale (ESS) [14] as a measure of subjective sleepiness. In addition, all HF patients also completed the Minnesota Living with Heart Failure Questionnaire (MLHFQ), which measures the effect of the HF syndrome on the physical, social, emotional, and mental aspects of quality of life. A higher score denotes a greater effect on these parameters.

2.2.2. Nocturnal polysomnography

Nocturnal sleep was measured in all participants using standard nocturnal PSG [15]. This included electrencephalography, electromyography, and electrooculography, to enable accurate sleep staging. Respiratory measurements were also undertaken with pulse oximetry, nasal pressure, oronasal thermistor, and respiratory inductance plethysmography (RIP). Sleep position was measured using a sensor integrated into the amplifier box worn by the patient and was classified as prone, supine, or lateral (SOMNOmedics, Randersacker, Germany). All electrodes were attached before participants retired at their usual bed times.

2.2.3. Actigraphy

Activity levels were measured in all participants using actigraphy, which involved the use of a watch-like accelerometer (Actiwatch 4, CamNtech, Cambridge, UK), worn on the nondominant wrist for 14 consecutive days and nights, starting the morning after the sleep study. Subsequent device download provided measures of physical activity (duration, average activity per hour and per 1-min epoch) and some derived data predominantly relating to presumed sleep (sleep efficiency and latency). Participants were also asked to complete a sleep and nap diary for each day that the watch was worn.

2.3. Analyses

2.3.1. Physiological analysis

Analysis of the overnight sleep patterns was undertaken by a single scorer (A.A.) using standard AASM criteria [15] and blinded to the identity of participant (and their diagnoses) at the time of scoring. SDB was defined as an AHI of $\geq$10 events per hour. The type of SDB (obstructive or central) was determined by the predominant event type (>50%). Oxygen desaturation was measured using a $\geq$3% dip criterion. Hypopneas were defined using a $\geq$3% dip criterion or a cortical arousal [15]. Obstructive hypopneas were scored by the presence of inspiratory flow limitation and/or paradoxical movement on thoracic/abdominal effort bands. For the activity measurements, days when the watch was not worn for more than four consecutive hours were excluded from analysis. Daytime activity was measured in arbitrary units and expressed as the average count per day and per 1-min epoch. The mean duration of daytime activity over the 14-day recording was also calculated.

2.3.2. Statistical analysis

The median and interquartile ranges were used to generate descriptive statistics. Groups were compared using the nonparametric Mann–Whitney *U* test with a significance level of 0.05.

In regard to sample size calculation, Hastings et al. (2006) investigated two groups of HF patients (with and without SDB) and found a significant difference in the duration of daytime activity (15.2 $\pm$ 1.2 h in the SDB group vs. 16.3 $\pm$ 1.0 h in the noSDB group, $p \leq 0.01$). The current study was designed to detect a similar difference in daytime activity between HF patients with central SDB and HF patients with no SDB. Assuming a similar magnitude of difference, a sample size of 17 would be required in the two groups (in this case, HF-CSA and HF-noSDB) to achieve 80% power to detect such a difference at $\alpha = 0.05$.