Excessive Daytime Sleepiness is Associated With Poor Medication Adherence in Adults With Heart Failure

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ABSTRACT

Background: A relationship between excessive daytime sleepiness (EDS) and poor treatment adherence has been suspected but not confirmed. We hypothesized that medication adherence would be poorer in adults with heart failure (HF) and EDS and that cognitive status would be the mechanism of effect.

Methods and Results: A sample of 280 adults with chronic HF were enrolled into a prospective cohort comparison study. We identified a cohort with EDS and a control group without EDS and further divided both groups into those with and without mild cognitive decline. Data on medication adherence were obtained at baseline and 3 and 6 months by using the Basel Assessment of Adherence Scale. Regression analysis was used to clarify the contribution of EDS and cognition to medication adherence and to assess relationships over 6 months after adjusting for age, enrollment site, gender, race, functional class, depression, and premorbid intellect. At baseline, 62% of subjects were nonadherent to their medication regime. Nonadherence was significantly more common in those with EDS, regardless of cognitive status ($P = .035$). The odds of nonadherence increased by 11% for each unit increase in EDS (adjusted odds ratio 1.11; 95% confidence interval 1.05−1.19; $P = .001$). In longitudinal models, there was a 10% increase in the odds of nonadherence for each unit increase in EDS ($P = .008$). The only cognition measure significantly associated with medication adherence was attention ($P = .047$).

Conclusions: Adults with HF and EDS are more likely to have problems adhering to their medication regimen than those without EDS, regardless of their cognitive status. Identifying and correcting factors that interfere with sleep may improve medication adherence. (*J Cardiac Fail 2011;17:340−348*)

Key Words: Heart failure, sleep, excessive daytime sleepiness, cognition, vigilance, patient compliance, self-care.

Poor self-care, encompassing treatment adherence, symptom monitoring, and management of symptoms, remains the most common reason for unplanned hospitalization in adults with heart failure (HF).[1−3] Medication adherence, in particular, is integral to controlling volume overload and symptoms, improving functioning and quality of life, and preventing acute decompensation in adults with HF.[4−6] Yet self-care remains poor in HF patients.[7,8] Initiatives to improve HF self-care have had limited success,[9] suggesting that important operative factors have not been identified and considered.

A 2006 Institute of Medicine report called national attention to the devastating effects of daytime sleepiness, including potential problems with treatment adherence.[10] Excessive daytime sleepiness (EDS) is the term used to

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Manuscript received July 26, 2010; revised manuscript received October 30, 2010; revised manuscript accepted November 2, 2010.

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Supported by the National Heart, Lung, and Blood Institute (RO1 HL084394-01A1) and the VISN 4 Mental Illness Research, Education, and Clinical Center, Philadelphia Veterans Affairs Medical Center.

See page 346 for disclosure information.

1071-9164/$ - see front matter

doi:10.1016/j.cardfail.2010.11.002

describe sleep propensity with difficulty maintaining a desired level of wakefulness.[11,12] Sleep propensity reflects the interaction of homeostatic mechanisms that regulate sleep intensity and circadian rhythm, which regulates the timing of sleep.[13,14] The relative strength of the sleep and wake drives reflects chronobiologic and environmental factors, such as physical activity, that stimulate arousal.[15] In adults with HF, contributors to EDS include older age, sleep disordered breathing (SDB), insomnia, depression, and polypharmacy, often with medications that cause somnolence as a primary side effect.[16−19]

The contribution of EDS to poor self-care in HF patients is critical, yet unexplored. We hypothesized that EDS may impair self-care through its effects on cognition.[20,21] Inadequate sleep has been shown to impair information processing, memory, vigilance, judgment, motivation, and decision-making across a wide range of populations.[22−24] Most of these cognitive domains are also susceptible to decline in people with HF,[25,26] 25%−50% of whom have impaired cognition.[27] Therefore, the primary objective of the present study was to determine if medication adherence differs in adults with HF and EDS compared with adults with HF but without EDS and to test cognition as the mechanism of the effect.

Methods

A prospective cohort comparison study was conducted to test the hypothesis that a cohort of adults with HF and EDS would, over time, experience more problems with medication adherence than a cohort with HF but without EDS. A consecutive sample of 280 adults with HF were enrolled from 3 outpatient settings in Philadelphia, Pennsylvania, and Newark, Delaware. Data were collected between 2007 and 2010.

Inclusion criteria specified enrollment of adults with chronic stage C HF confirmed by echocardiographic and clinical evidence. Potential subjects were screened to discern their ability to participate in the study (eg, visual acuity sufficient to read study materials, hearing sufficient to engage in a dialogue, and English literacy sufficient to enable accurate cognition testing).[28] We included subjects with mild cognitive decline[29] as measured by the Telephone Interview of Cognitive Status (TICS).[30] The TICS is composed of 11 items, with a maximum score of 41; higher scores indicate less impairment. A score in the range of 21−25 suggests mild cognitive decline. We sought to enroll individuals with only mild cognitive decline, so anyone with a TICS score ≥24 was included.

Otherwise eligible individuals were excluded if they lived in a long-term care setting where self-care was not a reasonable expectation, worked nights or rotating shifts, or had renal failure requiring dialysis, an imminently terminal illness, plans to move out of the area, a history of serious drug or alcohol abuse within the preceding year, or major depression (Fig. 1). Major depression was identified in 2 ways: Patients described in the medical record as having major depressive illness were not contacted; and everyone was screened with the 9-item Patient Health Questionnaire (PHQ-9).[31] We excluded anyone reporting ≥5 of the 9 symptoms more than half of the days in the past 2 weeks; 1 of the symptoms had to be depressed mood or anhedonia. For those who passed screening, we continued to use a subset of data from the PHQ-9 (ie, the PHQ-2) at each testing interval as an indicator of mild depressive symptoms, as described subsequently. Most of the data were collected during home visits by trained research assistants. Clinical information was abstracted from the medical record by registered nurses. SDB was not an exclusion criterion, because our focus was on identifying the effect of EDS on self-care, regardless of the cause.

A total of 2,469 adults with HF were considered for enrollment, and 333 were eligible to participate. Major reasons for ineligibility were distance, illness severity, renal dialysis, dementia, prior stroke, or living in an institutional setting. Some of these issues reflect the university referral center where most patients were recruited. Furthermore, because this was a cohort study, as cohorts were saturated, patient eligibility focused on criteria related to EDS and cognitive status, which eliminated 323 otherwise eligible individuals. A total of 280 individuals were enrolled and followed for 6 months. Attrition was only 13.6% (n = 38) over the 6 months of follow-up with data on EDS, cognition, and medication adherence collected in person at baseline and 3 and 6 months.

Using data collected at baseline, we identified a cohort with EDS and a control group without EDS using the Epworth Sleepiness Scale (ESS). Both groups were further divided into those with and without mild cognitive decline, as described below.

Measurement

Daytime Sleepiness. EDS was measured with the ESS, a validated research tool considered to be a valid measure of daytime sleepiness.[32] The ESS is an 8-item self-report scale on which respondents rate the likelihood of falling asleep in boring situations such as riding as a passenger in a car. Test-retest reliability (r = 0.82) and internal consistency (α = 0.88) have been established.[33] In the present study, the alpha coefficient was 0.78. Responses on a 4-point Likert scale are summed, with higher scores indicating greater sleepiness. Others have shown that even HF patients with SDB report relatively low levels of EDS.[34] Therefore, we used a cut point of >6 for the determination of EDS on the advice of the instrument author (Johns, personal communication, 2007).

Cognitive Decline. Sleep loss is known to affect simple and complex attention, processing speed, working memory, short-term memory, reasoning, and crystallized cognitive ability, with simple attention being the most sensitive to sleep deprivation.[23] A neuropsychologic test battery measuring these major cognitive domains was administered to all participants. The battery included the Psychomotor Vigilance Task (PVT)[35] (simple attention), the Trail-Making Test B[36] (complex attention), the Digit Symbol-Substitution Test[37] (processing speed), the Probed-Recall Memory Task[38] (working memory), the Letter Number Sequencing test[37] (short-term memory), and crystallized cognitive ability or premorbid intellect (American National Adult Reading Test (ANART)[39] (Table 1). The number of tests on which subjects scored below their age-based norm was used as the measure of cognitive status.[37] Specifically, anyone scoring <1.5 standard deviations on ≥2 of the paper-and-pencil cognition tests was judged to have a mild cognitive decline. The PVT is not influenced by practice, aptitude, or education, although it is influenced by age and gender.[40] Therefore, age and gender were used as covariates in the analysis, as discussed subsequently. The ANART also was used as a covariate in analysis.[39]

Medication Adherence. Medication adherence was assessed with the Basel Assessment of Adherence Scale, a structured