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Original Article

Speed and trajectory of changes of insomnia symptoms during acute treatment with cognitive–behavioral therapy, singly and combined with medication

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ABSTRACT

Objectives: To examine the speed and trajectory of changes in sleep/wake parameters during short-term treatment of insomnia with cognitive–behavioral therapy (CBT) alone versus CBT combined with medication; and to explore the relationship between early treatment response and post-treatment recovery status.

Methods: Participants were 160 adults with insomnia (mean age, 50.3 years; 97 women, 63 men) who underwent a six-week course of CBT, singly or combined with 10 mg zolpidem nightly. The main dependent variables were sleep onset latency, wake after sleep onset, total sleep time, sleep efficiency, and sleep quality, derived from sleep diaries completed daily by patients throughout the course of treatment.

Results: Participants treated with CBT plus medication exhibited faster sleep improvements as evidenced by the first week of treatment compared to those receiving CBT alone. Optimal sleep improvement was reached on average after only one week for the combined treatment compared to two to three weeks for CBT alone. Early treatment response did not reliably predict post-treatment recovery status.

Conclusions: Adding medication to CBT produces faster sleep improvement than CBT alone. However, the magnitude of early treatment response is not predictive of final response after the six-week therapy. Additional research is needed to examine mechanisms involved in this early treatment augmentation effect and its impact on long-term outcome.

1. Introduction

Insomnia is the most prevalent of all sleep disorders, with 25% of the adult population reporting sleep difficulties and 6–10% fulfilling diagnostic criteria for a chronic insomnia disorder [1–3]. Chronic insomnia can have detrimental consequences in a variety of domains, including mental and cardiovascular health, cognitive functioning, work productivity, and quality of life [4]. Of the different insomnia therapies available, only benzodiazepine-receptor agonists and cognitive–behavioral therapy (CBT) are recognized as having adequate evidence in terms of efficacy and safety [5–8].

Whereas each individual treatment option has its own benefits and limitations, investigators have also combined CBT and medication in order to take advantage of their respective strengths and presumably optimize treatment response [9–12]. Medication is often thought to bring about rapid relief of sleep disturbances, whereas CBT provides more sustained improvements over time. For example, in a study comparing a behavioral intervention against medication and reporting weekly changes [13], medication was effective during the first week of therapy but sleep improvements were not sustained at short-term follow-up, whereas sleep improvements were slightly delayed with behavioral therapy but better sustained over time. Such findings have led investigators to believe that combined therapy would provide the best outcomes by capitalizing on the rapid improvements with medication and sustained benefits of CBT.

Most CBT studies of insomnia focus on sleep changes occurring from baseline to post-treatment (typically 4–8 weeks), whereas

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drug trials often examine the impact of medications on sleep during the first few nights of use and then for a few more nights upon drug discontinuation. However, there are limited data regarding the trajectory of sleep over the course of acute treatment (i.e. first few weeks of therapy). Information on the speed of recovery and trajectory of sleep changes during initial treatment could be informative in studies comparing different combinations or sequences of medication and CBT. Indeed, if hypnotic medications are associated with faster sleep improvements and CBT with more sustained changes over time, it is plausible that adding medication to CBT would result in faster sleep changes without compromising their long-term maintenance. In order to test this assumption, a classic pre-post examination of data is inadequate; rather, sleep has to be monitored on an ongoing basis during the course of treatment.

The first objective of this study was to examine the course of sleep changes over acute treatment for insomnia, and investigate whether adding medication to CBT influences the speed of sleep changes. CBT delivered alone was compared to CBT combined with zolpidem on sleep changes reported by patients on daily sleep diaries kept over a six-week treatment period. A second objective was to determine the number of weeks required to reach an optimal sleep improvement. Third, the study aimed to explore the relationship between the initial sleep change and post-treatment sleep status.

2. Methods

This article reports secondary analyses of a larger randomized clinical trial examining the impact of different treatment sequences using CBT, singly and combined with zolpidem, throughout 6- and 12-month periods. The present report focuses specifically on weekly changes during the first six-week treatment phase. Study participants, procedures, and results pertaining to the main research questions have been described in more details elsewhere [14]. The Institutional Research Board of Ethics from the Institut Universitaire en Santé Mentale de Québec approved the study protocol.

2.1. Participants and study design

Participants were recruited through newspaper advertisements and referrals from health care practitioners in the Québec City area. Inclusion criteria were: aged $\geqslant$30 years and diagnosis of chronic insomnia based on a combination of criteria from the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) [15] and the International Classification of Sleep Disorders [16]. These criteria were further operationalized as (1) difficulties initiating and/or maintaining sleep, defined as a sleep onset latency and/or wake after sleep onset >30 min, with a corresponding sleep time of <6.5 h at least three nights per week (as measured by daily sleep diaries); (2) insomnia duration longer than six months; and (3) significant distress or impairment of daytime functioning (rating of $\geqslant$2 on item 5 of the Insomnia Severity Index).

Exclusion criteria were: (1) presence of a progressive medical illness (e.g. cancer, dementia) directly related to the onset and course of insomnia; (2) use of medications known to alter sleep (e.g. steroids); (3) lifetime diagnosis of any psychotic or bipolar disorder; (4) current diagnosis of major depression, unless treated and in remission; (5) more than two past episodes of major depression; (6) history of suicide attempt; (7) alcohol or drug abuse within the past year; (8) sleep apnea (apnea/hypopnea index >15), restless legs, or periodic limb movements during sleep (movement index with arousal >15/h); or (9) night-shift work or irregular bedtime and arising time. Patients with stable medical (e.g. hypertension) or psychiatric disorders (e.g. dysthymia, anxiety) were included in the study provided that these conditions were not the primary cause of insomnia. Patients using sleep medications no more than twice weekly were enrolled after they withdrew from the medications for at least two weeks. Individuals using alcohol as a sleep aid were also required to discontinue this practice at least two weeks prior to baseline assessment.

Of the 486 individuals who completed telephone screening for eligibility assessment, 242 completed second-stage screening, and 160 of those were included in the study. Participants were randomized to CBT alone (n = 80) or combined CBT plus zolpidem (n = 80). After completing this six-week initial treatment, they were randomized a second time to an extended treatment for the next six months. The current report focuses solely on the first treatment phase.

2.2. Measures

2.2.1. Sleep diary

Participants kept daily sleep diaries during a two-week baseline period and the six-week acute treatment phase (weeks 1–6). The primary dependent variables derived from the diaries were sleep onset latency (SOL), wake time after sleep onset (WASO; excluding the last awakening prior to rising for the day), total sleep time (TST), time spent in bed (TIB), sleep efficiency (SE; ratio of sleep time to the time spent in bed), and sleep quality (SQ). The sleep diary is a standard assessment instrument in insomnia research [17], which allows for prospectively monitoring sleep patterns over extended periods in the patient's home.

2.2.2. Insomnia Severity Index (ISI)

The ISI [18,19] is a seven-item instrument assessing the nature, severity and impact of sleep disturbances in the past month. Total score ranges from 0 to 28 (0–7: absence of insomnia; 8–14: subthreshold insomnia symptoms; 15–21: moderate insomnia; 22–28: severe insomnia).

2.3. Treatment components

Participants in both conditions (CBT alone and CBT plus zolpidem) received six weekly consultation sessions of CBT, a multicomponent intervention that features behavioral, cognitive, and educational components [18,20]. CBT sessions were facilitated by master's level clinical psychologists using a treatment manual [20]. The following procedures were introduced sequentially during treatment (see Box 1).

2.3.1. Cognitive-behavior therapy

Restriction of time in bed was introduced at session 1 and consisted of limiting time spent in bed to the actual sleep time and gradually increasing it back to an optimal sleep time [21]. Each participant was prescribed an individualized sleep window, which was adjusted weekly. It was increased by 15–20 min when sleep efficiency was >90%, decreased by the same amount when sleep efficiency was <80%, and kept stable when sleep efficiency was 80–90%. The recommended sleep window was always $\geqslant$5 h per night in CBT and always $\geqslant$5.5 h in the combined condition.

Stimulus control was introduced at session 2 and included the following instructions: (1) go to bed only when sleepy at night; (2) use the bed and bedroom only for sleep and sex (i.e. no reading, TV watching, or worrying); (3) get out of bed and go into another room whenever unable to fall asleep or return to sleep within 20 min and return to bed only when sleepy again; (4) arise at the same time every morning; and (5) avoid daytime napping [22].

Cognitive therapy (sessions 3–4) aimed to alter faulty beliefs and misconceptions about sleep [20]. Examples of faulty beliefs that were targeted included unrealistic sleep expectations