Morin CM, Vallieres A, et al. Cognitive Behavioral Therapy [CBT], Singly and Combined With Medication, for Persistent Insomnia. JAMA 2009;301(19):2005-2015.

Reviewed, no change to conclusions, December 2016

Design: Randomized clinical trial

Population/sample size/setting:

- 160 patients (97 women, 63 men, mean age 50) treated for insomnia in a university setting in Quebec
- Inclusion criteria were age over 30 with a diagnosis of chronic insomnia based on (1) daily sleep diaries showing sleep onset latency or wake after sleep onset of at least 30 minutes, with less than 6.5 hours of sleep 3 nights per week, (2) duration of insomnia longer than 6 months, (3) significant impairment of daytime functioning on the insomnia severity index (ISI), a 7 item scale (0=no disturbance of function, 28=maximum disturbance of function)
- Exclusion criteria were (1) progressive medical illness, (2) use of medication known to alter sleep, (3) lifetime diagnosis of psychotic or bipolar disorder, (4) current diagnosis of major depression, unless adequately treated, (5) more than 2 past episodes of major depression, (6) history of suicide attempt, (7) alcohol or drug abuse in past year, (8) sleep apnea, restless legs, or periodic limb movements with arousal, or (9) night-shift work or irregular sleep pattern

Main outcome measures:

- After eligibility was determined, participants were initially randomized to one of two intervention groups: CBT alone for 6 weeks (n=80) or CBT plus 10 mg/d zolpidem for 6 weeks (n=80)
- A second randomization was done with those who completed the 6 week period; the 75 participants who completed CBT were randomized to extended CBT for 6 months (n=38) or to no treatment for 6 months (n=37); the 74 who completed CBT plus zolpidem were randomized to extended CBT alone for 6 months (n=37) or to CBT plus zolpidem as needed for 6 months (n=37)
- Numerous analyses were reported, but the salient ones were sleep onset latency, time awake after sleep onset, total sleep time, and response to treatment as assessed by ISI (a 7 point reduction in ISI was defined as a treatment response; reduction of the ISI score to 7 or less was defined as a treatment remission)
- For most analyses, CBT was equal to CBT plus zolpidem, both at the end of 6 weeks and for those who continued to receive CBT up to 6 months
    - CBT plus zolpidem yielded a small increase in total sleep time (about 20 minutes) over CBT alone at the end of 6 weeks
    - Treatment response (a 7 point decrease in ISI) was observed at 6 weeks for 45/75 CBT alone and 45/74 CBT plus zolpidem patients

    - Insomnia remission (an ISI score of 7 or less) was observed at 6 weeks for 29/75 CBT patients and for 33/74 CBT plus zolpidem patients
- In addition to data from sleep diaries, polysomnography (PSG) was done: 3 nights at baseline, 2 nights at 6 weeks, and 2 nights at 6 months
    - Baseline PSG scores were better than for sleep diaries: sleep latency was shorter, time awake after sleep onset was shorter, total sleep time was greater, and sleep efficiency was greater (e.g., baseline efficiency by PSG was about 83%, but by sleep diary was about 68%)
    - Improvements in sleep parameters for PSG were smaller than were recorded by sleep diaries, and again the improvements were equal in CBT alone and in CBT plus zolpidem
- During the 6 month extended treatment period, patients who had been in the CBT plus nightly zolpidem group and then were randomized to CBT alone slept just as well as those who were randomized to CBT plus zolpidem prn
    - There was a small advantage for those who had only CBT for both treatment responders and treatment remitters at the follow-up which was done 6 months after the end of the 6 month extended treatment period

Authors' conclusions:

- CBT, used alone or with zolpidem, was effective for treating persistent insomnia
- The addition of zolpidem produced only modest benefits in the 6 week treatment phase
- Because all participants were white and less than 10% were over 65, generalization of these findings should be done with caution
- CBT restricts time in bed, and may produce an initial reduction in total sleep time
- Extended, individualized CBT did not add significant benefits beyond those which were observed with the initial, 6 week group therapy intervention
- If patients are receiving CBT plus medication, it makes good clinical practice to discontinue medication while they are still receiving CBT, in order do minimize drug exposure and risk of dependence

Comments:

- A large number of analyses are done, but some phenomena were not discussed or explained
    - The sleep diaries in Table 2 and the sleep lab in Table 3 gave different estimates of sleep parameters, especially at baseline; the sleep lab showed shorter sleep latencies, less time awake after sleep onset, and greater sleep efficiency than was reported in the sleep diaries
    - Sleep efficiency by sleep diaries was 69% at baseline, and in the sleep lab was 83% at baseline; the latter was just as good as the sleep efficiency after both the acute and extended CBT treatment interventions

    - Sleep efficiency in Table 2 (sleep diaries) increases considerably during the 6 week acute phase, while total sleep time changes by only a small amount; this must be attributable to decreases in time in bed with CBT, but these times were not reported and have to be calculated by the reader
    - The bed times with CBT do appear to decrease with CBT; the calculated bed time at baseline was 498 minutes in the CBT only group, and was 397 minutes after 6 weeks, a decrease of 100 minutes
- There was no placebo for zolpidem; however, this probably is not a limitation of the study; if zolpidem had had a measureable added effect to that of CBT, it would not have been clear whether that added benefit were due to a placebo response, but because zolpidem had such a small effect, a placebo comparison is not necessary

Assessment: Adequate for evidence that group CBT reduces the severity of insomnia and the daytime consequences of insomnia, and that these effects persist for at least 6 months
Adequate for evidence that zolpidem does not appreciably enhance the effectiveness of CBT
Adequate for evidence that a 6 week group CBT is effective for the treatment of insomnia, and that additional individualized CBT may not be required for benefits to be achieved and maintained