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NIH INSOMNIA ABSTRACT

# Systematic Review of the Efficacy and Safety of Drug Treatments and Combination Treatments in the Management of Chronic Insomnia in Adults

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Management of acute insomnia has traditionally involved pharmacotherapy, hypnotic medications, and complementary and alternative therapy. The use of medications is common practice for both acute and chronic insomnia, despite the fact that the U.S. Food and Drug Administration has approved none of them for long-term use for chronic insomnia. According to a Sleep in America Poll, an estimated 0.5 percent of the population takes sedative medications for insomnia for more than 1 year. In addition, more than 1 in 10 people (11 percent) report using prescription (6 percent) and/or over-the-counter medications (6 percent) at least a few nights a month to help them sleep.[1] Medications commonly used to treat insomnia include antidepressants, antihistamines, anticholinergics, benzodiazepines, and nonbenzodiazepine hypnotics. Many questions and challenges related to medication use for chronic insomnia remain, such as the appropriate treatment for different types of primary and secondary insomnia and the long-term side effects and daytime consequences of using such agents.

The Evidence-based Practice Center's objective was to conduct a systematic review of the efficacy and safety of drug treatments and combination treatments in the management of chronic insomnia in adults. A systematic search of 21 electronic databases was conducted. The following databases were searched: MEDLINE®, EMBASE, CINAHL®, Ovid MEDLINE® in-process and other nonindexed citations, Ovid OLDMEDLINE®, PsycINFO®, EBM Reviews–Cochrane Central Register of Controlled Trials, International Pharmaceutical Abstracts, AMED (Allied and Complementary Medicine Database), HealthSTAR/Ovid HealthSTAR, EBM Reviews–Cochrane Database of Systematic Reviews, ACP Journal Club, Database of Abstracts of Reviews of Effects, Science Citation Index Expanded™, Biological Abstracts, Cochrane Complementary Medicine Field Registry, CAB Abstracts, SIGLE, OCLC Proceedings First, Dissertation Abstracts, Alt HealthWatch, NLM Gateway, and PubMed®.

A study was considered to be relevant to the review if it involved a drug intervention or combined drug and psychological intervention and met the following criteria: (1) the report was written in English; (2) the majority of participants were at least 18 years old; (3) participants suffered from chronic insomnia defined as a sleep disturbance of at least 1 month in duration; (4) participants were randomized to intervention or placebo, except for studies involving a combined drug and psychological intervention in which case a placebo group was not required; (5) participants and assessors were blind to treatment received, except for studies involving combined drug and psychological interventions; and (6) it assessed at least one of the following outcomes: sleep onset latency (SOL), wakefulness after sleep onset, sleep efficiency, total sleep time, sleep quality, or quality of life. SOL was the primary outcome.

If the majority of participants met one of the following criteria, the study population was considered to suffer from chronic insomnia: (1) participants suffered from a sleep disturbance of 4 weeks or more; (2) participants were described as having a chronic sleep disturbance; or (3) participants were selected from a sleep disorders clinic. The Jadad Scale was used to assess study quality. The concealment of treatment allocation was also assessed. Data were analyzed quantitatively using the Random Effects Model.

SOL was significantly decreased by benzodiazepines (mean difference [MD]: -16.5; 95 percent confidence interval [CI]: [-20.5, -12.5]), nonbenzodiazepines (MD: -18.1; 95 percent CI: [-22.5, -13.7]), and antidepressants (MD: -7.4; 95 percent CI: [-10.5, -4.4]). Wakefulness after sleep onset was significantly decreased by benzodiazepines (MD: -23.1; 95 percent CI: [-35.7, -10.5]), nonbenzodiazepines (MD: -12.6; 95 percent CI: [-23.0, -2.3]), and antidepressants (MD: -11.4, 95 percent CI: [-16.2, -6.6]). All of the preceding interventions had a significantly higher risk of harm compared to placebo: benzodiazepines (risk difference [RD]: 0.15; 95 percent CI: [0.10, 0.20]), nonbenzodiazepines (RD: 0.05; 95 percent CI: [0.01, 0.09]), and antidepressants (RD: 0.09; 95 percent CI: [0.01, 0.18]). Only eight studies were identified that analyzed the efficacy of combined treatments for chronic insomnia. A number of comparisons emerged between combined drug and psychological treatments and either single treatment or placebo. Each of these comparisons encompassed a small number of studies and many of them could not be pooled because of important differences in interventions. The results of meta-analyses for individual comparisons and a qualitative description of the studies will be provided.

There is evidence that benzodiazepines and nonbenzodiazepines are effective treatments in the management of chronic insomnia. There is some evidence that antidepressants are effective

**Disclosure:** Dr. Witmans has discussed the unlabeled use(s) of the following FDA-approved products: Benzodiapepines, non-benzodiazepines, and melatonin.

in the management of chronic insomnia; however, more research is required in this area. There is evidence that benzodiazepines, nonbenzodiazepines, and antidepressants pose a risk of harm and that benzodiazepines have a higher risk of harm than nonbenzodiazepines. Additional studies are needed to determine the efficacy of combined treatments for chronic insomnia.

## REFERENCE

1. National Sleep Foundation. Sleep in America Polls. Available at: http://www.sleepfoundation.org/hottopics/index.php?secid=16.