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LETTERS TO THE EDITOR

Real effect vs placebo effect

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I read with interest the article by Vgontzas et al, entitled "Effects of trazodone versus cognitive behavioral therapy in the insomnia with short sleep duration phenotype: a preliminary study".[1] However, suggesting that "trazodone, but not CBT-I (Cognitive Behavior Therapy-Internet), significantly improves objective sleep duration and reduces hypothalamic-pituitary-adrenal axis activation" based on the small sample size of 7 patients on trazadone may not be appropriate.

It is surprising that the authors state that they wanted to study trazodone despite American Academy of Sleep Medicine recommendations not to use trazodone in the guidelines for treatment of insomnia disorder. Despite the popularity of trazodone, American Academy of Sleep Medicine guidelines state that "We suggest that clinicians not use trazodone as a treatment for sleep onset or sleep maintenance insomnia (versus no treatment) in adults." This is based on the investigations on efficacy of trazodone 50 mg vs zolpidem 10 mg and placebo. The final sample for the trazodone and placebo groups included 187 adults with sleep-onset insomnia. Participants were administered either trazodone or placebo in a double-blind fashion for 14 consecutive nights. In their study, the trazodone group experienced significantly more side effects than the placebo group. Chief among these were headache (trazodone, 30%; placebo, 19%) and somnolence (trazodone, 23%; placebo, 8%). In all, 75% of trazodone participants reported adverse events.[2] Although trazodone was more effective at improving self-reported sleep quality, there were no differences in sleep-onset latency, total sleep time, or wake after sleep onset and was the reason the US Department of Veterans Affairs and the US Department of Defense Clinical Practice Guidelines also do not recommend "use of trazodone for treatment of chronic insomnia disorder."[3]

The authors have used "short sleep" based on the closest clinically meaningful cutoff (total sleep time < 7 hours) to the median value (total sleep time < 6.8 hours) measured with actigraphy at pretreatment (mean value for 2 consecutive weeks). This seems to be too liberal in terms of enrollment criteria. The authors had used the short sleep duration definition of less than 5 hours in their earlier studies, as this was associated with risk of hypertension and type 2 diabetes. Mortality risk was significantly increased only in people with insomnia who slept fewer than 6 hours (odds ratio = 4.33; 95% confidence interval: 1.25–15.04) in their earlier study.[4] The stricter definition of total sleep time of less than 5 hours might be more meaningful to evaluate the differential effect of an intervention.

CITATION

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DISCLOSURE STATEMENT

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