FPIN's Clinical Inquiries

Antidepressants for the Treatment of Insomnia in Patients with Depression

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Clinical Inquiries provides answers to questions submitted by practicing family physicians to the Family Physicians Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group (http://www.cebm.net/?o=1025).

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Clinical Question

Which antidepressant medications are most effective for treating insomnia in patients with depression?

Evidence-Based Answer

There is no single antidepressant or class of antidepressants that is most effective for the treatment of insomnia in patients with depression. The use of antidepressant medications can have a positive impact on sleep physiology, but does not seem to improve subjective ratings of sleep quality. (Strength of Recommendation: B, based on one qualitative study and one meta-analysis.)

Evidence Summary

The relationship between depression, insomnia, and treatment is complex. A meta-analysis of sleep and psychiatric disorders found that patients with comorbid sleep disturbances and depression typically have increased sleep latency, increased rapid eye movement (REM) sleep, increased midcycle awakening, decreased slow wave sleep, and shortened REM latency.[1] Therefore, selecting antidepressant agents that increase sleep continuity (i.e., uninterrupted sleep), prolong REM latency, and decrease REM sleep is one strategy for treating insomnia in patients with depression.[2-5] Research on the impact of antidepressants on objective sleep measures is summarized in *Table 1*.[2]

Studies have consistently demonstrated differences between objective and subjective sleep measures in patients taking antidepressants.[6] In a study comparing objective and subjective sleep measures in patients with depression, 18 patients (78 percent) showed at least a 30-minute over- or underestimation of total sleep time. Twelve patients (52 percent) over- or underestimated total sleep time by at least 60 minutes when comparing their subjective sleep ratings with polysomnography.[7]

Research measuring the effect of antidepressants on subjective sleep ratings is sparse. There are no systematic reviews or meta-analyses. Subjective measures of sleep quality are often included as secondary outcomes in clinical trials of antidepressants. Existing studies are further limited by small sample size, short duration, incomplete data reporting, lack of a placebo arm, concurrent hypnotic use, or heterogeneity in rating instruments of perceived sleep quality.

Studies that measured subjective sleep ratings used the three sleep items on the Hamilton Rating Scale for Depression or the Leeds Sleep Evaluation Questionnaire.[2] These studies found that selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) improved subjective sleep measures in patients with depression. In addition, studies have shown that nefazodone, trazodone, or mirtazapine (Remeron) also can improve subjective sleep ratings compared with placebo, SSRIs, or TCAs in patients with depression.[2]

Recommendations from Others

For patients with depression and comorbid insomnia, the American Academy of Sleep Medicine recommends the addition of a low-dose, sedating antidepressant if not contraindicated. Low-dose trazodone, mirtazapine, doxepin, amitriptyline, or trimipramine (Surmontil) may be given in addition to another full-dose antidepressant.[8] Guidelines from the American College of Physicians report conflicting evidence, with some studies indicating

Table 1. Impact of Antidepressants on Objective Sleep Measures

	Short term (five to 10 days)			*Long term (more than 21 days)*			
Drug	*Continuity*	*REM sleep*	*REM sleep latency*	*Continuity*	*REM sleep*	*REM sleep latency*	*Withdrawal REM rebound*
MAOI							
Phenelzine (Nardil)	∞	***	†††	∞	***	†††	†
SSRI							
Citalopram (Celexa), fluvoxamine, paroxetine (Paxil), and sertraline (Zoloft)	↔	**	†††	↔	**	††	†
Fluoxetine (Prozac)	↓	**	†	↓	*	†	∞
TCA							
Amitriptyline	↔	**	††	↑	*	††	†
Imipramine (Tofranil)	↔	**	†††	↔	*	††	∞
Other							
Bupropion (Wellbutrin)	∞	∞	∞	↔	↔/↓	†/↔	∞
Mirtazapine (Remeron)	↑	↔	↔	↑	↔	†/↔	∞
Nefazodone	↑	↔	↔	↑	↔	↔/↓	∞
Trazodone	↔/↑	*	†	↑	↔	†	∞

MAOI = monoamine oxidase inhibitor; REM = rapid eye movement; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant.

*↔ = no change; ∞ = no data; ↑ = increase; ↓ = decrease; * = 10 to 30 percent decrease; ** = 30 to 60 percent decrease; *** = greater than 60 percent decrease; † = 30 to 100 percent increase; †† = 100 to 200 percent increase; ††† = greater than 200 percent increase.*

Adapted with permission from Wilson S, Argyropoulos S. Antidepressants and sleep: a qualitative review of the literature. Drugs. *2005;65(7):932.*

improved sleep ratings with escitalopram (Lexapro) over citalopram (Celexa), nefazodone over fluoxetine (Prozac), and trazodone over fluoxetine. However, the authors caution that in randomized controlled trials and multiple head-to-head trials, there is limited evidence for the comparative effectiveness of antidepressants in treating insomnia in patients with depression.[9]

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Author disclosure: No relevant financial affiliations to disclose.

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