Sleep Disturbances in Depression



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KEYWORDS

- Sleep Major depressive disorder Insomnia Hypersomnia Cognitive behavioral therapy
- Hypnotic Antidepressant

KEY POINTS

- Major depressive disorder is frequently accompanied by subjective sleep disturbances and polysomnographic abnormalities.
- Residual sleep disturbance after a major depressive episode is linked to future relapses.
- Sleep problems may be the first sign of the onset of a major depressive episode.
- Obstructive sleep apnea may mimic major depressive disorder and increase risk for depression.
- Pharmacotherapy or behavioral approaches are useful in depressed patients with sleep disturbances.

MAJOR DEPRESSIVE DISORDER Epidemiology and Comorbidity

Major depressive disorder is one of the most common psychiatric illnesses in the United States, with an estimated lifetime prevalence of up to 17%.¹ Affected individuals are at high risk for comorbid medical and psychiatric illness and have worse medical outcomes than the general population.^{2,3} Major depressive disorder is highly correlated with suicidality, and up to 3% of affected individuals ultimately complete suicide.³ The societal cost of major depressive disorder is massive; according to some estimates it may be responsible for up to \$44 billion a year in lost productivity in the United States alone.⁴ Several pharmacologic agents have been developed to treat depression including multiple classes of antidepressant medications (Table 1). These drugs, even when combined with psychotherapy, will ultimately fail in approximately onethird of patients.⁵ Furthermore, treatment for major depressive disorder typically takes at least several weeks to produce noticeable effects.⁵

Diagnosis

Major depressive episodes are defined by a history of a 2 weeks or longer of depressed mood or anhedonia (diminished enjoyment of normally pleasurable activities) with at least 3 of the following: significant weight change or change in appetite, psychomotor agitation or retardation, feelings of worthlessness or guilt, diminished ability to concentrate, recurrent thoughts of death (or suicidal ideation or suicide attempts), and insomnia or hypersomnia.⁶ There are several subtypes and modifiers of depression, each defined by a distinctive set of clinical features and typically responsive to specific types of treatments. Atypical depression, characterized by mood reactivity, hyperphagia, hypersomnia, and hypersensitivity to interpersonal rejection, is described as responding well to monoamine oxidase inhibitors and poorly to tricyclic antidepressants.⁶ Patients with melancholic depression show terminal insomnia, weight loss, and ruminate on negative thoughts and are more likely to respond positively to sleep deprivation

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Table 1 Antidepressant effects on sleep			
Medication Class Examples	Dosage: Depression (Insomniaª)	Pharmacologic Mechanism	Effects on Sleep
Tricyclic antidepressants			
Amitriptyline(Elavil) Nortriptyline (Pamelor)	75–150 mg (25–50 mg) 50–150 mg	Inhibit serotonin and norepinephrine reuptake Anticholinergic and	Sedation REM sleep suppression Increased stage 2 sleep
Doxepin (Sinequan)	(25–50 mg) 75–300 mg (6–50 mg)	antihistaminergic effects	
Clomipramine (Anafranil)	100–250 mg		
MAOis			
Phenelzine(Nardil) Tranylcypromine(Parnate)	45–90 mg 30–60 mg	Inhibit monoamine oxidase, thus increasing norepinephrine, serotonin, and dopamine	Insomnia Potent REM suppression
Serotonin reuptake inhibitor	rs		
Fluoxetine (Prozac) Sertraline (Zoloft) Paroxetine (Paxil) Citalopam (Celexa) Escitalopram (Lexapro)	20–80 mg 50–200 mg 15–60 mg 20–40 mg 10–30 mg	Inhibit serotonin reuptake	Insomnia REM suppression Increased eye movements in NREM sleep
Serotonin-norepinephrine reuptake inhibitors			
Venlafaxine (Effexor) Duloxetine (Cymbalta)	150–450 mg 20–120 mg	Inhibit serotonin and norepinephrine reuptake	Insomnia REM suppression Increased eye movements in NREM sleep
Other antidepressants:			
Trazodone (Desyrel)	150–600 mg (25–75 mg)	Inhibit serotonin reuptake. Blocks alpha1 adrenoreceptors Serotonin- 2 A receptor antagonist	Sedation
Bupropion (Wellbutrin)	100–450 mg	Inhibits norepinephrine and dopamine reuptake	Insomnia/activation
Mirtazapine (Remeron)	15–45 mg (7.5–15 mg)	Alpha2 receptor antagonist. Serotonin-2 and -3 receptor antagonist. Antihistaminergic	Sedation, REM sleep suppression

^a Use of these medications for treatment of insomnia is an off-label usage, not approved by the US Food and Drug Administration.

(see later discussion). In addition, some depressed individuals can develop psychotic symptoms such as delusions and hallucinations and the recommended treatment includes antipsychotics in addition to antidepressant medication.⁶ In major depressive disorder with a seasonal pattern (also known colloquially as seasonal affective disorder), there is a recurrent pattern of depressive episodes that reliably occur during the same time of year (usually winter) for at least 2 consecutive years. Seasonal affective disorder can be treated with light therapy in addition to medications and psychotherapy.⁶

Sleep and Depression

One of the most consistent symptoms associated with major depressive disorder is sleep disturbance.^{7–9} These problems with sleep regulation are not secondary to the illness; rather, they often precede the depressive episodes and can persist during remission. Improving sleep in depressed patients is found to improve outcomes.^{10,11} In addition, imposed sleep deprivation can precipitate depressive episodes in susceptible individuals and alleviate depressive symptoms in

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