Opinion Article

CLINICAL INVESTIGATION

Antidepressants and sleep: What you should know

Submitted: 06 October 2021; Accepted: 20 October 2021; Published online: 27 October 2021

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Introduction

It is well known that several antidepressant medicines can impair sleep quality, owing to increased noradrenergic and dopaminergic neurotransmission and activation of serotonergic5-HT2receptors.SerotoninandNorepinephrine Reuptake Inhibitors (SNRI), Norepinephrine Reuptake Inhibitors (NRI), Monoamine Oxidase Inhibitors (MAOI), Selective Serotonin Reuptake Inhibitors (SSRI), and activating Tricyclic Antidepressants (TCA) are the most well-known among them. Antidepressants with anti-histaminergic effect, such as sedating TCA, mirtazapine, and mianserine, or antidepressants with strong antagonistic action at serotonergic 5-HT2 receptors, such as trazodone and nefazodone, on the other hand, enhance sleep swiftly.

Some patients report improved sleep quality after just one dose of mirtazapine, which has been linked to a faster onset of antidepressant activity in mirtazapine.

According to data from the US Food and Drug Administration (FDA) study register, the average prevalence of treatment emergent sleeplessness in SSRI clinical trials was 17%, compared to 9% in the placebo group. The average rate of treatment-emergent somnolence in SSRI patients was 16%, compared to 8% in placebo patients. The study with citalopram had the lowest rate of treatment-emergent insomnia complaints (less than 2%). Patients with Obsessive Compulsive Disorder (OCD) who were treated with high-dose fluvoxamine had the greatest rates of treatment emergent insomnia and somnolence, at 31% and 27%, respectively. Treatment emergent insomnia was recorded in 13% of SNRI-treated patients in clinical trials, compared to 7% in the placebo arm, and treatment emergent somnolence in 10% of SNRI treated patients, compared to 5% in the placebo arm. In individuals with generalised anxiety disorders treated with venlafaxine, treatment emergent insomnia and somnolence was the most common (both 24%). Levomilnacipran had the lowest rates of treatment-emergent insomnia and somnolence (both less than 2%). In clinical investigations with sedating antidepressants, such as mirtazapine and trazodone, the reported prevalence of treatment-emergent insomnia complaints in patients with Major Depressive Disorder (MDD) was relatively low, in contrast to SSRI and SNRI treatment (below 2%). However, the rate of treatment-emergent somnolence was extremely high, with 54% of patients treated with mirtazapine experiencing it, compared to 18% of patients in the placebo arm, and 46% of patients treated with trazodone experiencing it, compared to 19% of patients in the placebo arm. It's worth noting that antidepressant's acute effects on sleep are evident not only in patients' subjective complaints, but also in PSG studies. While SSRIs, SNRIs, and activating TCAs increase REM latency, suppress REM sleep, and may affect sleep continuity, sedating antidepressants reduce sleep latency, enhance sleep efficiency, increase SWS, and have little to no effect on REM sleep. Although the antidepressants sleep-disrupting and sleep-promoting effects are strongest in the first few weeks of treatment, they may linger in some patients, exacerbating insomnia complaints or producing daytime somnolence. As a result, sedative antidepressants are usually more suggested for depressed patients with clinically significant sleeplessness. It has recently been demonstrated that such treatment lessens the demand for benzodiazepines in MDD patients. Combining benzodiazepines and SSRI/SNRI medications is frequently required to alleviate anxiety and insomnia as early as the first week of treatment. However, there is a possibility that a patient suffering from depression or sleeplessness will be unable to discontinue medication after 14 day to 28 days and could develop dependency. However, because sleep complaints normally improve after a few weeks of good depression treatment with an SSRI/SNRI, it's worth considering whether hypnotics are a better short-term therapeutic option for a patient than risking over sedation while on a sedative antidepressant. In long-term maintenance treatment, the sedating effect of such antidepressants is usually a growing problem,

necessitating the need to reduce the drug dose. It has the potential to significantly reduce the efficacy of the maintenance treatment. Weight gain is a side effect of sedative antidepressants, which has been demonstrated for mirtazapine but not for trazodone. Vortioxetine has recently been reported to have sleep-related effects, with clinical action mediated mostly by selective serotonin reuptake inhibition and direct modulation of serotonergic receptor activation (such as 5-HT3, 5-HT7, 5-HT1D, and 5-HT1B). In a study that compared the effects of vortioxetine and paroxetine to a placebo in a group of 24 healthy male volunteers, it was discovered that vortioxetine doses of 20 and 40 mg suppress REM sleep by increasing REM sleep latency and decreasing REM sleep duration, similar to paroxetine doses of 20 mg. Both medicines also reduce overall sleep time while increasing sleep stage N1 duration. The deleterious effects of vortioxetine on sleep quality are only noticeable at high doses. When compared to SSRI and SNRI medicines, the rate of treatment-emergent insomnia complaints or somnolence during therapy with vortioxetine is lower, according to the FDA clinical trial registry.

Antidepressants, including those with sedative characteristics, might disrupt sleep by causing or exacerbating sleep problems. In as many as 28% of patients, minaserin and mirtazapine can cause restless legs syndrome. SSRI and venlafaxine have both been linked to treatment-emergent RLS. SSRI, SNRI, and TCA have been shown to cause or worsen sleep bruxism and disrupt muscular tone modulation during REM sleep, resulting in REM sleep without atonia, which can lead to REM sleep behaviour disorder. Antidepressants, despite being indicated for the treatment of post-traumatic sleep disturbance, can cause nightmares. This side effect occurs most frequently after mirtazapine treatment, as it has been recently observed. Finally, antidepressants that cause weight gain are contraindicated in patients with sleep apnoea, a common but underdiagnosed sleep problem among adults with mental illnesses.