



## MEDICATION EFFECTS ON SLEEP

by Frank Roman MD JD

The consumption of medications, for preventive or curative purposes, is a way of life in our society. Superimposed on our daily medical regimen is the ingestion of supplements, vitamins, caffeinated products, nicotine, alcohol, and recreational drugs. The spectrum of potential side effects of these substances are well documented in various sources, most famously in the Physician's Desk Reference (PDR). However, the medication effects on sleep or more specifically sleep architecture are not as well documented. Like in many aspects of sleep medicine, the knowledge obtained has been through the collective experience of the practitioners in the field in the last few decades. It is up to these same practitioners to continue to build on our databases. Therefore it is extremely important to document both in the clinical history and the diagnostic workup including polysomnographic records, the medications, and supplements the patient is presently taking.

**A urine drug screen (UDS) is an underutilized test in sleep centers one which would be most helpful in identifying chemicals that may affect sleep**

The following is a small sample of some of the changes in sleep architecture or sleep in general that some medications may cause. By no means is this a comprehensive list of drug categories or specific medications. Benzodiazepines, non-benzodiazepines, and melatonin agonist receptors were purposely excluded due to space constraints and previous discussions in past articles.

Selective serotonin reuptake inhibitors have been reported to cause insomnia in 5-35% of depressed patients. Insomnia emerges fairly early in treatment and tends to persist. The granddaddy of the SSRIs, Prozac (fluoxetine), decreases total sleep time and increases wake time and Stage I sleep in depressed patients for up to one year. In addition, it has been associated with prominent slow eye movements in non-REM (Prozac eyes). SSRIs are also associated with increased frequency of PLMS as well as REM sleep without atonia.

The selective serotonin and norepinephrine reuptake inhibitors, specifically Effexor (venlafaxine) has been reported to cause insomnia in 4-18% in different studies. However somnolence can also occur in approximately 30% of patients in a dose dependent fashion. Polysomnographic data suggests an increase in Stage Wake and Stage I plus frequent periodic limb movements during sleep.

The serotonin antagonist and reuptake inhibitors specifically Desyrel (trazodone) is commonly used as a hypnotic despite limited polysomnographic data. It is suggested that it may increase total sleep time and decrease Stage REM. The other medication in this class, Serzone (nefazodone), increases REM with subjective reports of vivid dreams or even nightmares.

The norepinephrine and specific serotonin antagonist, Remeron (mirtazapine), is reported to be subjectively sedating. In a small polysomnographic study in depressed patients there was an increase in sleep efficiency and total sleep time with no significant effect on REM or slow wave sleep. There is also some limited reports of this medication being effective in mild obstructive sleep apnea. Unfortunately, it is also associated with increased appetite and significant weight gain.

Despite the advent of newer drugs, tricyclic antidepressants are still in common use. The half-lives of these medications range from 15-30 hours leading to high concentration during sleep with bedtime dosing but unfortunately high risk of daytime sedation. The most common one in practice is Elavil (amitriptyline), which is known to increase sleep continuity, decrease Stage REM, but increase phasic eye movements or REM density.

Anti-Parkinson's drugs are somewhat more difficult to pigeon hole since patients with Parkinson's disease have multiple sleep complaints including insomnia, hypersomnia, fatigue, vivid dreams or nightmares. Moreover, the first manifestation of Parkinson's disease may be REM behavior disorder. The most common drugs in this category used for sleep, specifically movement disorders, include Sinemet (levodopa/carbidopa), dopamine agonists such as Requip (ropinirole), and Mirapex (pramipexole) both FDA approved for restless legs in recent years. Levodopa/carbidopa has been shown to improve sleep at lower doses, however at higher doses may disrupt sleep with nightmares, hallucinations, vocalizations, and excessive daytime sleepiness. Polysomnographic data is mixed with possible increase in Stage REM or decreased Stage REM, increased REM density, and possible decreased

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slow wave sleep. The dopamine agonist in general tend to increase total sleep time in restless legs syndrome. At higher doses it may cause a decrease in sleep latency on the multiple sleep latency test. Also, one must be aware of recent reports of compulsive gambling or shopping and hypersexuality on these medications.

Despite the wide spread use of hypolipidemic drugs, there is very little polysomnographic data regarding their effects on sleep architecture. Subjective data suggests some medications in this class, Lipitor (atorvastatin), Mevacor (lovastatin), Zocor (simvastatin) may lead to insomnia in a small percentage of patients. On the other hand, Lopid (gemfibrozil) and Atromid (clofibrate) are reported to cause sleepiness.


In general, cortical steroids have been associated with insomnia in up to 70% of patients in a dose dependent fashion. Insomnia has been reported more frequently in asthmatic patients receiving moderate to high doses of steroids. There have also been reports of hypomania as I can personally attest to after seeing my son John Christian on steroids for his bronchial asthma. Inhaled cortical steroids do not seem to have the same severity or incidence of side effects but there have been case reports of insomnia, hyperactivity, and even psychosis. Polysomnographic data reveals a marked decrease in Stage REM as the most consistent effect of steroids.

Antiarrhythmics most commonly are associated with fatigue with a prevalence as high as 10% in some studies. Cordarone (Amiodarone) has also been associated with nightmares and insomnia. Cardizem (Diltiazem) may cause abnormal dreams and sleepiness. Sedation is a common side effect of opioid medication. The degree of sedation depends on the type of opioid, half-life, dose, and the frequency of dosing. Polysomnographic data demonstrates opioids decrease slow wave sleep and REM sleep. Interestingly, subjective reports include better sleep quality thought to be secondary to better pain control. On somewhat of a tangent, recent direct to consumer ads tout the superiority of Advil PM to Tylenol PM based on pain control and not necessarily on improving sleep architecture.

In the author's opinion, a urine drug screen (UDS) is an underutilized test in sleep centers which would be most helpful in identifying chemicals that may affect sleep. In general, there are two types of UDS that are typically used, immunoassay and gas chromatography -mass spectrometry (GC-MS). Immunoassay is the most common method used since it allows for large scale screening through automation and rapid detection. The main disadvantage of immunoassays is obtaining false positive results when detection of a drug in the same class requires a second test for confirmation. GC-MS, on the other hand, is able to detect small amounts of a specific drug. It is more accurate and sensitive than immunoassays but unfortunately more expensive and time consuming. Particularly interesting is the length of time some drugs can be detected in urine. For example: alcohol 7-12 hours, amphetamines 48 hours, barbiturates up to three weeks for long acting compounds, benzodiazepines up to 30 days for long acting compounds, cocaine metabolites 2-4 days, opiates up to 4 days depending on the type, and finally marijuana which can be detected up to 3 days for single use and over 30 days in the long term heavy smoker. A positive finding of a UDS should always be confidential, be taken in the context of the clinical history and polysomnographic findings and not to make a citizen's arrest.


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