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Somnambulism During Monotherapy with Mixed Amphetamine Salts

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Attention-deficit hyperactivity disorder (ADHD) is a common childhood neurocognitive and behavioral disorder, with reported worldwide prevalence of 5–10% in school-aged children¹. The preferred first-line Food and Drug Administration (FDA)-approved medications for ADHD are stimulant medications, which include immediate-release (IR) and delayed-release formulations of methylphenidate (MPH) and amphetamines². Sleep disturbances, including reduced total sleep time, increased sleep-onset latency, and reduced sleep efficiency have been reported as side effects of stimulant treatment³. However, somnambulism or sleepwalking is rarely considered as a side effect of stimulant medication. We report two pediatric cases of somnambulism associated with the use of extended-release dextroamphetamine/amphetamine (mixed amphetamine salts or MAS).

Case Report

The first patient was a thirteen year old female with a normal developmental history and intellectual capacity who has been followed with a diagnosis of ADHD since she was 6 years old. Her past medical history revealed that she had two previous sleepwalking episodes, when she was 5 years old, but had been asymptomatic since then. The patient did not have any other history of medical or neurological illness. She was on no medications other than extended-release MPH. Her father also had a history of sleepwalking and the rest

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of her family history was negative for sleepwalking or significant psychiatric illness (e.g., mood disorders or psychosis).

Our patient had been on several immediate-release and delayed-release formulations of MPH either as monotherapy or in various combinations over the past 7 years. Her symptoms of ADHD showed moderate improvement with high-dose MPH treatment. Due to continued difficulties paying attention in school, her medication was switched to MAS extended release, 10 mg daily.

One week after beginning MAS, two episodes of sleep walking were reported. Once, she was found walking around her home at 3 AM, after her parents noticed her empty bed. She was unresponsive at that time, and had no memory of the incident in the morning. The second instance was not observed, but her mother found the kitchen to be in disarray one morning, and the patient was found to have crumbs in her bed. She denied any memory of walking or eating during the night. The same dosage was continued with close follow up because of apparent benefit from the medication and uncertainty whether her recent sleepwalking episodes were related to the medication or simply a re-emergence of previous somnambulism. There were no further episodes of somnambulism reported.

The second patient was an eight year old boy referred to our outpatient clinic with complaints of difficulty in paying attention to lessons at school, getting bored easily, and hyperactivity (swinging legs, fidgeting). His developmental history and intellectual capacity were within the normal range. He had no history of depressive, manic, or psychotic symptoms. The patient had no prior personal history or family history of somnambulism. His 14 year old brother had a history of ADHD and oppositional defiant disorder, and was on extended-release MAS.

The boy was in good physical health with normal neurological findings. Following clinical assessment, he was diagnosed with ADHD-combined type, and extended-release MAS 5mg daily was initiated and gradually titrated to 10mg daily.

After the first month, there was significant improvement in his attention and concentration while fidgety behavior at school was reduced, as reported by his teacher. However, on several occasions his mother observed him walking around the kitchen in the middle of the night. She reported that he was unaware and unarousable at that time, and later had no recollection of these incidents. His medication was then switched to the delayed release formulation of MPH because the somnambulism was recurrent and disturbing for the patient and his family. After changing his medication regimen, the somnambulism resolved and no further episodes of sleepwalking were noted.

Discussion

Somnambulism includes a series of complex behaviors that are usually initiated during partial arousals from slow wave sleep (stages 3 and 4) and culminate in walking around with an altered state of consciousness and impaired judgment (AASM ICSD-III 2014). It is more common and typically benign in children.

Sleepwalking is frequently related to fatigue, prior sleep loss, or anxiety in children. It can also occur as a reaction to drugs, medications, and alcohol, as well as medical conditions such as seizures. Medications that have been reported to cause sleepwalking include neuroleptics, hypnotics, lithium, amitriptyline, topiramate and β -blockers⁴. The greatest risk for drug-induced somnambulism has been found to occur two to fourteen days after the initiation of treatment with a new medication, and somnambulism can be very transient or may last until the medication is discontinued⁵.

Our review of the literature revealed no cases of somnambulism associated with MAS and to our knowledge there are only two documented cases of somnambulism: one associated with MPH abuse⁶ and another with MPH use⁷. As somnambulism is a disorder of slow-wave sleep and has most frequently been shown to occur in conjunction with medications that increase slow-wave sleep, it is counterintuitive that somnambulism would be induced by stimulants, which are known to decrease slow-wave sleep.

The exact mechanism of amphetamine-induced somnambulism is not known. Amphetamines act on the monoamine system, primarily dopamine, and to a lesser extent norepinephrine and serotonin, to increase transmitter function by facilitating release, blocking reuptake, and reducing degradation; these neurotransmitters are known to play a role in the regulation of arousal⁸.

A causal relationship between MAS and somnambulism cannot be determined in our first case because the patient had previous personal and family history of somnambulism and because MAS treatment was continued without further episodes. However, that patient had been asymptomatic for 8 years and the sleepwalking occurred within a week after starting MAS treatment. In second case, the causal relationship appears to be more likely, because that patient had never previously experienced somnambulism and these episodes ceased after switching medications. These cases suggest a possible etiological link between MAS and somnambulism that is neither simple nor absolute.

Hughes JR in his review article suggest that stimulants, neuroleptics and central nervous system (CNS) depressants such as hypnotics, along with other conditions (e.g., sleep deprivation and stress), can lead to somnambulism and concluded that any condition changing the excitation-inhibition balance in the CNS may precipitate sleepwalking⁹.

The use of stimulants has substantially increased over the last decade¹⁰ and now these medications are prescribed to patients in a wider age range, with increased use in preschoolers¹¹ and adults¹². Given the large number of patients currently prescribed stimulants, the risk of somnambulism may be significant, even if only a small proportion of patients are affected. Hence, clinicians should be aware of the possibility of somnambulism as an adverse effect potentially related to stimulant medication. Clinicians should inquire about somnambulism when prescribing stimulant medications and counsel patients and families accordingly.

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