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EDITORIAL

Addictive Substances and Sleep: More Research is Needed

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Since a long time, addictive substances have been found to affect sleep quantity, quality, and sleep architecture. In addition, certain substances have been found to induce other physiological processes during sleep, thereby affecting the quality or quantity of sleep. However, we have limited data to suggest that addictive substances may influence sleep quality and quantity either by inducing or relieving other sleep disorders.

Restless legs syndrome (RLS) also known as Willis–Ekbom disease (WED), named after the doctor who first described it in 1945 [1] is a less understood, but a commonly treatable chronic sleep disorder that is characterized by severe sensory-motor dysfunction. The affected individuals often report an urge to move legs, especially at night with worsening of symptoms at rest and an improvement by movement [2]. This disorder has been linked to the dopamine abnormalities in the brain, which in turn has been found to be regulated by opioid receptors [3, 4]. Furthermore, opioid has found a place in the management of RLS in selected cases [5].

Opioid withdrawal presents with muscle aches and pains, often along with the restlessness [6]. These features often overlap with the symptoms of RLS and considering the neurobiological underpinnings, it may be possible that some of the patients develop RLS during opioid withdrawal. Case reports and case series suggested that RLS is seen in the patients during opioid withdrawal, including dextropropoxyphene and tramadol [7, 8]. However, large studies in this area are limited and to the best of our knowledge, only one study is available that suggested the prevalence of RLS as 13% among patients with opiate withdrawal [9]. Recognition of RLS and its distinction from myalgia that occurs during opioid/opiate withdrawal are important for a number of reasons. First, RLS may induce sleep disturbance in these patients, which is completely amenable to treatment [7, 8]. Addressing the RLS may thus facilitate the detoxification process. Second, in contrast to myalgia, which generally lasts for only initial 3–5 days after opiate/opioid withdrawal, symptoms of RLS may persist for a longer duration, thus, requiring treatment to be continued during the post-detoxification process [7, 8].

A recent study suggested that RLS is seen in around 50% subjects during opioid withdrawal [10]. Moreover, there is evidence that concurrent cannabis use or cannabis itself may either prevent or ameliorate symptoms of RLS [10, 11].

Similarly, tobacco, in particular, smoking is considered a risk factor for the development of RLS [12]. However, contradictory data are also available suggesting improvement in RLS following tobacco chewing and the absence of effect of smoking over RLS [13–16].

The antinociceptive and psychoaffective effects of cannabis are well known. The potential benefits and the efficacy of cannabis use in the treatment of RLS was first reported in a case study [11]. In a subjective evaluation, all six patients reported an improvement in sleep quality and symptomatic relief of RLS with minimal side effects.

The effect of medical cannabis in the sleep field is gaining much attention. Cannabinoids work on the endocannabinoid system (ECS). Among the various cannabinoids, delta-9 tetrahydrocannabinol (THC) and cannabidiol (CBD) are extensively studied. Cannabinoids that work on the human ECS act through two main receptors, namely the CB1 and CB2 receptors. One such synthetic cannabinoid is dronabinol, which has undergone preclinical and clinical studies [17–19]. However, with the limited safety profile of medical cannabis in the field of sleep medicine, the American Academy of Sleep Medicine (AASM) has released a position statement, which clearly pointed out the lack of evidence on the use of medical cannabis and further cautioned that "medical cannabis and/or its synthetic extracts should not be used for the treatment of OSA due to unreliable delivery methods and insufficient evidence of effectiveness, tolerability, and safety" [20]. However, it has been argued that further

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longitudinal and controlled trials are needed to fully explore the potential use of cannabinoids in the sleep field [21].

In conclusion, this is an important area that requires attention. There is a need to conduct two kinds of studies for a better understanding—experimental as well as epidemiological. Robust data generated from both kinds of trials simultaneously will help us to understand sleep physiology in a better manner.

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