Medicinal Marijuana : A Promising Potential Treatment for Obstructive Sleep Apnea

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Abstract Obstructive Sleep Apnea (OSA) is a common sleep disorder in mammals characterized by the repeated collapse of the upper airway. It is a known cause of hypertension, cardiovascular disease, and, in some cases, death. OSA is commonly treated by medical devices and surgeries. Although effective, these treatments are associated with unwanted side-effects and further complications. In recent years, the role of medicinal marijuana has grown as a potential treatment for sleep disorders. Further research must be conducted to determine the efficacy and safety of cannabis as a treatment for OSA.

Keywords: Obstructive sleep apnea; Medicinal marijuana; Cannabis; Cannabinoids; CPAP machines

Résumé L'apnée du sommeil obstructive (ASO) est un désordre de sommeil commune dans les mammifères, qui est caractérisé par l'effondrement répétée de la voie respiratoire supérieure. C'est une cause commune de l'hypertension, de la maladie cardiaque et dans quelques cas, la mort. ASO est traitée souvent par les appareils médicaux et les chirurgies. Ces traitements sont associés à l'efficacité modérée, des effets secondaires non-désirés et d'autres complications. Dans les années récentes, le rôle de la marijuana médicale a augmenté comme un traitement potentiel pour les désordres de sommeil. Des recherches supplémentaires sont nécessaires pour déterminer l'efficacité et la sécurité du cannabis en tant que traitement du ASO.

Mots Clés: Apnée du sommeil obstructive; Marijuana médicale; Cannabis; Cannabinoïdes; Machines CPAP

Main Text

In Canada, the prevalence of sleep apnea is an estimated 3% to 7% in males and 2% to 5% in females (*1*). Combined, an estimated 5.4 million adults have been diagnosed with sleep apnea or are at high risk of developing it (*1*). Sleep apnea is characterized by repeated cessation of breathing due to a lack of airflow during sleep (*2*). Of the many types of apneas, obstructive sleep apnea (OSA) is the most common. OSA occurs when an individual's throat muscles intermittently relax, resulting in blockage of the upper airway. In healthy individuals, the airway is kept open by the muscle tone of the genioglossus, palatal, and associated muscles of the throat (*3*). Those affected by OSA suffer from reduced muscle tone due to suppression of upper airway motoneurons (*4*). Sleep naturally suppresses these motoneurons, but neuromodulation also plays a role (*4*). Common symptoms of individuals suffering from OSA include snoring and silent pauses in breathing (*5*). In more severe cases, hypertension, cardiovascular issues, and death are possible (*6*).

The current successful treatments for OSA are medical devices and surgeries. The most common medical devices used are continuous positive airway pressure (CPAP) machines. CPAP machines fit into or over one's nose and allow for the upper airway passage to remain open by projecting a constant and continuous flow of air. Although effective, 46 to 83% of patients with OSA have reported to not adhere to their treatment plans when using CPAP (*7*). Studies have shown that there is no significant association between adherence and the socio-economic level, education or personality of the sufferer (*8*). As such, the negative side effects associated with the devices must be considered when exploring low compliance. Many patients dislike the machine due to its loud noise and lack of comfort. Additionally, claustrophobia and anxiety are prevalent among adults who use CPAP machines (*9*). Some patients opt to undergo surgery to treat OSA, however, the safety and efficacy of these surgeries are unpredictable compared to CPAP (*10*). Surgical interventions are grouped into two phases, where 1 corresponds to soft tissue, while 2 corresponds to bone tissue. Phase

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1 surgeries, such as nasal and palate reduction, act on soft tissue and have a success rate of 50-60% in improving OSA by greater than 50%. Phase 2 surgeries, such as maxillomandibular advancement, act on bone tissue. They have a success rate of approximately 90% but are associated with mental nerve sensory loss and unwanted cosmetic changes (*10, 11*).

For centuries, herbalists have recommended the use of cannabis to treat inflammation, gout, joint pain, and many other conditions (*12*). Most recently, the recreational use of cannabis is becoming more common and the medical benefits of cannabis are being revisited (*13*). With the recent surge in medicinal marijuana support and availability, companies have been quick to market cannabis as a treatment for sleeping disorders (*14*). The use of marijuana as a treatment for OSA, in particular, is highly debated in the scientific community. Cannabis is primarily composed of cannabinoids, a group of compounds which bind to the cannabinoid (CB) receptors in the brain (*14*). An important study by Calik and Carley found decreased apneas when dronabinol, a synthetic version of Δ9-THC, was administered to patients with OSA. The same results were observed in rats chronically instrumented to measure respiration during sleep. Furthermore, they also observed reduced apnea when dronabinol was injected into the nodose ganglia of an established model of vagally mediated reflex apnea. Their study showed that dronabinol's effect in decreasing apnea appears to be due to the activation of both cannabinoid type 1 (CB1) and cannabinoid type 2 (CB2) receptors located on the nodose ganglia of the vagus nerves. These receptors are responsible for regulating breathing rate, tidal volume and constriction of the airways, all of which play a role in healthy breathing during sleep. CB receptors are also abundant among the neurons responsible for respiration and activation of the upper airway (*14*). Dronabinol increases phasic upper airway activity through the activation of CB receptors at the nodose ganglia (*15*). The activation of CB receptors leads to anxiety reduction and inhibition of the arousal system, which incidentally counters the downsides of CPAP machines.

Studies investigating dronabinol as a potential treatment of OSA have shown promising results. OSA is associated with fragmented sleep and decreased slow-wave sleep (SWS) (*16*), and dronabinol treatment has shown strengthened circadian rhythms and an increase in delta waves, which are associated with SWS (*17*). Additionally, dronabinol treatment is associated with fewer nightly instances of apnea and hypopnea (i.e. abnormally shallow breathing) (*18*). Rat physiology is similar to human physiology and current models mimic severe human OSA, therefore, rats are ideal test subjects (*19*). Dronabinol injections into the nodose ganglia of rats lead to stabilization of respiratory patterns and increased activation of the genioglossus allowing for the upper airway to remain open (*20*). In theory, this could allow for the human genioglossus muscle to analogously be activated and prevent it from blocking the upper airway.

Cannabis has the potential to be an effective therapy for OSA. It could potentially be used in conjunction with existing interventions, such as CPAP machines, to counteract their negative side-effects. Further investigation is required to determine the efficacy and safety of medical marijuana as a treatment for obstructive sleep apnea. The most immediate question to address is if marijuana usage can improve adherence to CPAP, as this is currently the most effective treatment. Furthermore, research must be done to examine the effects of different dosages, methods of administration, and strains of marijuana in counteracting OSA itself.

Competing interests
The authors declare that they have no competing interests.

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