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## SPECIAL ARTICLES

# Medical Cannabis and the Treatment of Obstructive Sleep Apnea: An American Academy of Sleep Medicine Position Statement

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The diagnosis and effective treatment of obstructive sleep apnea (OSA) in adults is an urgent health priority. Positive airway pressure (PAP) therapy remains the most effective treatment for OSA, although other treatment options continue to be explored. Limited evidence citing small pilot or proof of concept studies suggest that the synthetic medical cannabis extract dronabinol may improve respiratory stability and provide benefit to treat OSA. However, side effects such as somnolence related to treatment were reported in most patients, and the long-term effects on other sleep quality measures, tolerability, and safety are still unknown. Dronabinol is not approved by the United States Food and Drug Administration (FDA) for treatment of OSA, and medical cannabis and synthetic extracts other than dronabinol have not been studied in patients with OSA. The composition of cannabinoids within medical cannabis varies significantly and is not regulated. Synthetic medical cannabis may have differential effects, with variable efficacy and side effects in the treatment of OSA. Therefore, it is the position of the American Academy of Sleep Medicine (AASM) 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. OSA should be excluded from the list of chronic medical conditions for state medical cannabis programs, and patients with OSA should discuss their treatment options with a licensed medical provider at an accredited sleep facility. Further research is needed to understand the functionality of medical cannabis extracts before recommending them as a treatment for OSA.

**Keywords:** medical cannabis, obstructive sleep apnea, PAP therapy, long-term effects

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## INTRODUCTION

The American Academy of Sleep Medicine (AASM) is the leading professional society dedicated to promotion of sleep health. The AASM promotes sleep health and fosters high-quality, patient-centered care through advocacy, education, strategic research, and practice standards. The AASM endeavors to advance sleep health policy that improves the health and well-being of the general public.

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder that is characterized by repetitive episodes of complete or partial upper airway obstruction during sleep.<sup>1</sup> Untreated, OSA is a potentially lethal disease that increases the risk of numerous health complications including hypertension, congestive heart failure, atrial fibrillation, coronary artery disease, stroke and type 2 diabetes.<sup>2</sup> Data show that untreated OSA is associated with an increased risk of all-cause and cardiovascular mortality, and that this risk can be reduced with effective

treatment.<sup>3,4</sup> Therefore, the diagnosis and effective treatment of OSA in adults is an urgent health priority.

## CANNABIS AND SLEEP

The flower from the cannabis plant has nearly 100 different active compounds called cannabinoids that work on the human endocannabinoid system through two main receptors, the CB1 and CB2 receptors. The two extensively researched cannabinoids are delta-9 tetrahydrocannabinol (THC) and cannabidiol (CBD). THC is the primary psychoactive component of cannabis that results in euphoria, hallucinations, anxiety, and tachycardia by acting on the CB1 receptor, while CBD counteracts the THC effects and has potential medicinal value of analgesia, neuroprotection, and anti-inflammatory action by acting on the CB2 receptor. To maximize the potential therapeutic applicability of medical cannabis, synthetic-based cannabis products

have been developed such as synthetic THC (dronabinol, nabilone), CBD, and nabiximols (1:1 THC/CBD combination). Some of these synthetic cannabis products are approved by the United States Food and Drug Administration (FDA) for certain medical indications.

The effects of medical cannabis on sleep vary depending on acute versus chronic use, withdrawal after chronic use, the type of cannabinoids based on their effects on the CB1 versus CB2 receptors, and the types of synthetic extracts. Early animal studies demonstrated that cannabinoid agonists such as dronabinol improved respiratory stability through peripheral serotonergic antagonism activity, and thereby provide therapeutic benefit to treat OSA.<sup>5</sup> This led to human studies that assessed the effectiveness of dronabinol in pill form of different strengths from 2.5 to 10 mg to treat patients with OSA.<sup>6–8</sup> Prasad et al. reported a significant improvement in apnea-hypopnea index (AHI) of 32% at 3 weeks compared to baseline ( $-14.1 \pm 17.5$ ;  $P = .007$ ). Side effects related to treatment were reported in most patients, and somnolence was reported in 29% to 50% of patients. A recent placebo-controlled randomized trial in people with moderate or severe OSA found a similar response after 6 weeks of treatment using a 10-mg dose of dronabinol that reduced AHI by 33 percent with no change in the Maintenance of Wakefulness Test (MWT) latency scores. Eight percent of patients reported sleepiness and drowsiness.<sup>8</sup>

Importantly, the long-term use of these products on other sleep quality measures, their tolerability, and safety are still unknown. Dronabinol is not FDA approved for treatment of OSA. Medical cannabis and synthetic extracts other than dronabinol have not been studied in patients with OSA. Additionally, the safety and efficacy of other delivery methods (eg, vaping, liquid formulation, oral capsule) have not been studied. Medical cannabis and other synthetic extracts may not only have differential effects on the CB1 and CB2 receptors; their delivery methods might also create differential effects. Therefore, further research is needed to understand their functionality before recommending them as a treatment for OSA.

## POSITION

It is the position of the AASM:

- 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 treatment effectiveness, tolerability, and safety, and OSA should be excluded from the list of chronic medical conditions for state medical cannabis programs.
- That patients with OSA should be advised to discuss their treatment options with a licensed medical provider at an accredited sleep facility.

## DISCUSSION

Most states in the United States do not have laws legalizing the use of cannabis. However, certain states have laws that legalize

it for medical and recreational use. At least one state has announced that OSA will be added to the list of medical indications for the use of medical cannabis.<sup>9</sup> This is concerning as the announcement was based on limited evidence citing pilot or proof of concept studies with small sample sizes. Additionally, the duration of these studies was only 3–6 weeks, and therefore the long-term effects of use of these medical cannabis products and the effect on OSA is unknown at this time. Also, treatment with the use of medical cannabis has shown adverse effects such as daytime sleepiness and may lead to unintended consequences such as motor vehicle accidents. Most studies only evaluated a specific synthetic cannabis extract (ie, dronabinol). The effects of other medical cannabis products for treatment of OSA are unknown currently.

PAP therapy remains the most effective treatment option for OSA.<sup>10</sup> Adherence with PAP therapy is optimized by a patient-centered approach that includes pretreatment education and ongoing follow-up.<sup>11</sup>

Dronabinol is one of the many synthetic medical cannabis extracts. The composition of cannabinoids within medical cannabis varies significantly and is not regulated. Therefore, synthetic medical cannabis may have differential CB1 and CB2 receptor effects, with variable efficacy and side effects in the treatment of OSA.

There is a need for increased funding and further research on the use of synthetic medical cannabis extracts to treat OSA. We need a better understanding of the pathophysiologic mechanisms on how synthetic medical cannabis extracts work differentially on the CB1 and CB2 receptors peripherally to help patients with OSA. This may also identify other potential synthetic extracts with higher efficacy and lesser side effects to treat OSA. Because of the potential for misuse and increased costs, the lack of evidence on beneficial effects, and risk of side effects including increased daytime sleepiness, which might lead to more harm than benefit, the AASM takes the position that medical cannabis should not be used for the treatment of OSA at this time.

## CONCLUSIONS

Based on the available evidence, it is the position of the AASM that medical cannabis should not be used for the treatment of OSA. The AASM also advises state legislators, regulators and health departments that OSA should not be included as an indication for their medical cannabis programs. Further research is needed to better understand the mechanistic actions of medical cannabis and its synthetic extracts, the long-term role of these synthetic extracts on OSA treatment, and the harms and benefits.

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## DISCLOSURE STATEMENT

This position statement was developed by the board of directors of the AASM to help physicians and other health care providers make decisions about the appropriate treatment of patients with OSA. It is published by the AASM as an advisory that is to be used for educational and informational purposes only.