Cannabis and Insomnia

Patients commonly report that use of cannabis reduces the time it takes them to fall asleep —whether or not insomnia was the complaint with which they presented.

By Rolando Tringale, MD and Claudia Jensen, MD

Abstract

Background: Safe and effective medications are needed for treatment of insomnia. In this large retrospective study of cannabis patients, we analyzed clinical data on patient-reported effects on sleep latency before and after the use of cannabis.

Methods We conducted a focused, retrospective analysis of data collected from 166 subjects from two cannabis clinics in Southern California (Ventura and San Clemente). Subjects who reported difficulty with sleeping (n=116) and those who reported no difficulty with sleeping (n=31) were included in this analysis. The primary outcome measures were a comparison of both cohorts and the sleep latency time after the use of cannabis compared with sleep latency time without the use of cannabis. Secondary outcomes were measured by comparing sleep latency between the two cohorts, sleep quality, and effect on dreaming. Analysis was conducted by the Wilcoxon-signed rank test and the Kruskal-Wallis test.

Findings The two cohorts (n=147) did not statistically differ in characteristics except for their ingestion of cannabis orally and in their total cannabis ingested per week. We noted a significant decrease in reported time to sleep after the use of cannabis in both those with and those without reported sleep difficulties. In terms of the secondary outcome, we saw a statistically significant difference (p=0.001) in time it took to fall asleep between both groups.

Conclusions Patients seeking physician approval to use cannabis commonly report benefits on decreasing sleep latency, even if a sleep disorder is not the chief complaint. This previously unreported result is supported by recent findings concerning the endocannabinoid system, as well as voluminous anecdotal evidence. Larger double-blinded studies are indicated to rigorously explore this important clinical effect.

Keywords: cannabis, insomnia, cannabis based medicine, sleep, cannabinoids

ADVERSE EFFECTS OF BENZODIAZEPENES such as Xanax include physical dependence and withdrawal, and irritability. Newer hypnotics such as Ambien and Lunesta can cause complex sleep-related behaviors.

Introduction

Fifty-eight percent of adult Americans have reported symptoms of insomnia a few nights a week or more.[1]

The staggering prevalence of insomnia and the well-known complications of poor sleep quality, such as its effect on productivity, mental health, and cardiac and endocrinologic function, suggest the need for effective treatment of this spectrum of disorders.

Historically, drugs such as morphine, alcohol, and barbiturates were used in various preparations. Cannabis was also used to treat insomnia prior to its prohibition in 1937. Currently, three classes of medications have FDA approval for treating sleep disorders: benzodiazepines, barbiturates and the newest class of non-benzodiazipine hypnotic medications.[2] All have significant adverse side effects, including dependence, serious withdrawal, and complex sleep-related behaviors.

Although its status on Schedule I has made research and procurement of cannabis difficult, several published studies suggest it is effective in the treatment of insomnia. One involved a small but statistically significant double-blind trial in a cohort of insomniacs; others focused on patients with multiple sclerosis and fibromylagia.[3, 4,7,11]

The endogenous cannabinoid anandamide, which acts on the same receptors as THC, has been shown to increase sleep through an adenosine pathway in the rat basal forebrain.[8]

In studies of brain-wave activity, cannabis has been shown to facilitate a relaxed state of alpha-dominated waves. A study supported by the National Institute on Drug Abuse showed increased EEG alpha activity in the early phase of administration of inhaled cannabis (standardized to 2.53% THC).[5]

Studies on humans and animals suggest that THC and CBD have sedative, anxiolytic properties.[6, 14] Side effects are common with the sedative hypnotic class, and some data suggest that cannabis and/or THC have side effects such as grogginess, dry mouth and in some case may lead to a cannabis-withdrawal syndrome similar to most antidepressants.

Methods

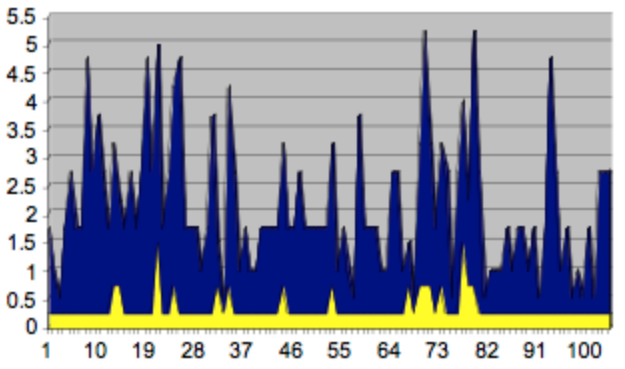
Study Design One of us (Tringale) completed a focused retrospective analysis of data previously collected from a cohort of 166 patients in a cannabis-oriented practice run by the other (Jensen). This group of 166 was blindly selected from a group of charts organized by year of initial presentation, in order to provide a broad sample across three years of patient visits. The demographics of this group can be seen in Table 1, below:

Table 1

Characteristics	Control	Troubled Sleep	P value
Age			
<18 to 30	6	46	
31 to 40	3	17	0.16
41 to 50	13	27	4 deg
51 to 60	6	21	
61 to 70	3	5	
Total	31	166	
Sex			
Male	22	78	
Female	9	38	
Concurrent Symptoms			
Depression	4	12	0.68
Anxiety	8	32	0.84
ADD/adhd	2	15	0.32
Chronic Pain	26	86	0.26
Problem Sleeping	3	31	0.04
Nausea	6	11	0.13
Anorexia	3	15	0.13
Other	5	12	0.37
Unemployed	16	55	0.68
Alcohol Use per Day			
≤12 oz beer*	23	94	
1-2 cans	5	15	
3-6 cans	1	3	0.64
>6 pack	1	1	2 deg
no response	1	3	

**or equivalent wine or hard alcohol consumption*

Demgraphics of study subjects. P value indicates statistical significance.



Improvement after use of cannabis is shown in this graph. Vertical scale shows hours it takes to fall sleep. Horizontal scale shows each patient's response. Lighter color tracks how long it takes to fall asleep with cannabis use. Darker color tracks time to fall sleep without cannabis.

Our focus was on two groups from this population: those with and those without documented difficulty sleeping and those with no reported sleep difficulties. Our primary objective was to measure any associations in the groups between age, sex, alcohol use, amount of cannabis used each week, or other factors found in a review of systems.

Our secondary objective was to evaluate how cannabis use affects sleep latency —the time it takes to fall asleep— in both groups. Other objectives were to examine the effect of cannabis use on sleep quality and dreaming.

The initial exclusion criteria were the absence of an answer to the question on Dr. Jensen's intake form concerning trouble sleeping. The final exclusion criteria were the absence of a full response to the two questions of time to sleep without cannabis use and with cannabis use.

Study Population

Dr. Jensen's clinics were in San Clemente and Ventura, California. Patients had been self-referred and were seeking physician approval to use cannabis to treat a variety of medical conditions.

Data Collection

The data was obtained from January through December 2005 as part of the routine intake form filled out by patients. Each form was read by Dr. Jensen, who did the intake evaluation and elicited additional history. Two HIPAA-trained medical students from USC's Keck School of Medicine (Tringale and Ishimoto) subsequently transposed the data to an Excel worksheet. No patient identifiers were used, and once patients' answers were coded, charts were returned to storage and not opened again.

Statistical Analysis

To compare characteristics of those with and without insomnia we used a chi-squared analysis to detect any statistical difference. To measure sleep latency we evaluated responses in each group using a Wilcoxon-signed rank test. To compare the two groups, we ran a Kruskal-Wallis test because in examining the data set we found the non-insomnia group to be non-parametric in distribution.

Results

The intake data of 166 patients were assessed for eligibility and 147 were included (See tables 1 and 2). The two cohorts were well matched except for their ingestion of cannabis orally (p=0.0494). Those patients who reported sleep difficulties appeared to ingest more cannabis.

As for the secondary-outcome measure of self-reported sleep latency time, 104 of 116 patients reporting difficulty with sleep, and 21 of 31 reporting no difficulty with sleep were included. We noted a significant decrease in reported time to sleep after the use of cannabis in both those groups. with (median -1.25 hours, p=0.000) and those without,

continued on next page

Insomnia *from previous page*

median -0.5 hours, (p=0.000) reported sleep difficulties. *(See graph on previous page)*. Both groups of patients reported it took them less time to sleep if they used cannabis. In terms of between-cohort effect of cannabis ingestion on sleep, we observed a statistically significant difference (p=0.001). Even though both groups' sleep improved with cannabis, the group reporting trouble sleeping experienced a much greater effect. In order to account for the observed difference in the baseline characteristic of oral use of cannabis, we excluded those patients and the difference persisted (p=0.001).

Among those who had reported trouble sleeping, 79% reported increased sleep quality after using cannabis. We saw less consistent responses with respect to dreaming, with 21% reporting a decrease in dreaming, 28% reporting no change, and 44% leaving the question blank. (Table 3)

Table 2

Cannabis Characteristics	Control n=31	Trouble sleeping n=116	P-value
Route of administration			
oral	2	28	0.049
pipe	14	56	0.66
bong	10	54	0.33
vaporizer	6	24	0.89
joints	12	57	0.60
other	1	8	0.53
no response	5	6	
Medication time of day			
morning	10	43	0.90
midday	11	30	0.14
afternoon	14	51	0.53
evening	21	76	0.26
nighttime	13	66	
no response	6	12	
How much per week			
0-1 gram	1	11	
1.1-3 grams	2	11	
3.1-5 grams	2	21	
5.1-10 grams	12	26	.1524
10.1-20 grams	2	22	2 deg
20.1-30 grams	0	15	
30.1-60 grams	0	1	
>60 grams	0	1	

CANNABIS USE PATTERNS OF STUDY SUBJECTS

Table 3

Sleep Quality: n=116	
Increase	79%
decrease	1%
no response	16%
no change	3%
dreams	
increase	8%
decrease	21%
no response	44%
no change	28%

REPORTED CHANGE IN SLEEP QUALITY AND DREAMING

Comment

This is the largest retrospective study on the clinical effect on sleep through patient-reported data. The results seem to support the growing body of research that has demonstrated a sleep-inducing effect of cannabis. Both those with sleep difficulties and those without reported a significant decrease in time to sleep after the use of cannabis. This suggests cannabis may be an effective treatment for insomnia.

The significant difference between those patients reporting insomnia and those who did not indicates that there are various levels of insomnia severity. As a median, it took 30 minutes less time for patients to fall alseep, even if they didn't report sleep toubles. Those with sleep troubles, as a median spent 15 minutes less time falling asleep. By validating patients' historic reporting of better sleep with a quanitifable difference, this data supports the use of cannabis-based medicine for the treatment of insomnia, especially insomnia with resistant or contraindications to traditional methods of treatment.

Traditionally the use of cannabis to induce sleep has been based on anecdotal evidence. Some small studies conducted in the 1970s showed cannabis to have hypnotic properties. Recent research points to a role for the endocannabindoid system in regulating the sleep cycle. By affecting the rhythm of the adenosine pathway, the endocannabinoid system likely plays a role in helping the system reach a threshhold level that allows the sleep cycle to begin.[5]

Exogenous cannabindoids such as THC and CBD may override disregulation of this system by resetting the threshhold level of adenosine. Furthermore, CBD appears to have a modulating effect on the endocannabinoid system through inhibition of anandamide hydrolysis and may allow for a wider clinical window with less of the side effects associated with THC.[10]

There are significant barriers to using cannabis based medicine (CBM) in the United States and other countries Access to standardized pharmaceutical-grade CBM is limited, as is physician's ability to write a clear prescription with dosing recommendations. Still, many patients appear to be able to standardize their dose of CBM through trial and error. Most patients have chosen to dose through smoking, which as a route of delivery has been extensively studied by Tashkin and systematically reviewed in publications by Mehra and Tetrault.[3,14] Even though inhaled CBM appears safe, most cannabis clinicians would likely agree that the oral sublingual sprays, such as oral sprays of glycerin and an alcohol-based extract of CBM or Sativex (GW Pharmaceuticals), are the best routes of administration available.

The use of nighttime cannabis for PTSD patients with significant nighttime sleep disturbances may be a future direction of research. Clinicians can utilize THC/CBD reduction of the duration of REM sleep, a time which appears to be a source of trauma and disrupted sleep for patients with frequent nightmares or disturbing dreams, for therapeutic effect.[12]

Several limitations of our study warrant discussion. A larger percentage of the patients in this study reported difficulty sleeping compared to the national average of 58%. Our subset of patients' increased rate of insomnia is likely secondary to co-morbid mood disorders, pain, and other sleep-disturbing medical conditions. Cannabis, by enhancing endocannabinoid tone and adjusting neurotransmission rates, promotes homeostatis within the body. Further research on a strict selection of patients without co-morbid pain, nausea, anxiety and depression conditions may help us isolate the clinical effects of cannabis on primary insomnia.

The patients studied may have over-reported their symptomology to establish the need for a medical cannabis recommendation. This may increase their baseline reporting of difficulty sleeping and even skew their recall on the extent of cannabis' effect on sleep.

In comparing those experiencing sleep difficulties and those who didn't, the group reporting sleep difficulties appeared to ingest more cannabis orally. This pattern suggests that as a group, achieving steady levels through the night was preferred to maintain sleep and prevent mid-sleep awakenings.

Can we now generalize the positive sleeping effects for all patients? Studies on fibromyalgia noted orally-ingested THC to have practical application for the treatment of insomnia, although some dropped out because of adverse side-effects.[11] In this study we were able to observe a large, diverse population base regularly using inhaled cannabis with acceptable side effects.

Many medications are known to be changed by oral versus inhaled administration (such as albuterol, atrovent, inhaled steroids).

Additionally the patients are likely reporting sleep latency in terms of timing their self-administration to the desired time to sleep. In utilizing an edible agent, other studies have delayed the onset of pharmacologic activity by 30 minutes to one hour compared to the rapid effect of inhalation methods reported primarily here. The next step in research should be to perform a larger randomized controlled trial using CBM in an oral and inhaled route.

Edible cannabis has been shown to take 30 minutes to an hour to begin exerting its effects, which then may last three or four hours. Inhaled cannabis exerts effects within seconds, but the effects only last for about 20 minutes. The next steps in research should include clinical trials comparing the efficacy of oral and inhaled cannabis on insomniacs without co-morbid sleep-affecting conditions.

Anecdotally, we see a persistent characterization of cannabis as either sativa or indica. Understanding why Cannabis indica is consistently reported to be more effective for sleep will shed light on which compounds in cannabis are sedating. It has been suggested that non-cannabinoids such as "certain sesquiterpene alcohols, including guaiol and isomers of eudesmol," are enhancing the hypnotic effect of cannabis indica.[9]

Another factor may be concentration of THC, whereby lower levels induce sleep and higher levels cause increased dopaminergic activity. THC:CBD ratio may be equally significant.

We infer that any compound that actively modulates the endocannabinoid system in vivo may have a clinical effect on sleep. Future studies might seek to determine which components of cannabis are sedating.

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CANNABIS-BASED SLEEP AIDS include (from left) buds of "Grand Daddy x Hindu Kush" and "Purple Kush," two strains considered "pure Indica" by Harborside Health Center's Rick Pfrommer; "On the Rise Super Gingerbread" (4-to-8 doses, made with 3.75 grams of Cannabis) and "Eat Me" capsules (1 strong dose made with 622 mg of High Grade Cannabis trim. Flower photos by Rachael Szmajda, edibles photos by Yolanda Felix.