



Impact of Cannabis Use on Anti-Anxiety Medication



INTRODUCTION

Anxiety disorders are among the most prevalent mental health conditions, affecting millions worldwide. It is estimated that anxiety disorders affect approximately 18% of the adult population in the United States annually.¹ Individuals with anxiety disorders often rely on medications such as benzodiazepines and selective serotonin reuptake inhibitors to manage their symptoms. However, these medications are often associated with various adverse effects, and there is a need for alternative treatment options that can effectively manage anxiety with fewer side effects.

Cannabis contains over 100 cannabinoids, with tetrahydrocannabinol (THC) and cannabidiol (CBD) being the most studied. THC is known for its psychoactive properties, while CBD is non-psychoactive and has been associated with anxiolytic effects. The endocannabinoid system (ECS), which includes cannabinoid receptors CB1 and CB2, plays a crucial role in regulating anxiety and stress responses. Activation of CB1 receptors in the brain can modulate neurotransmitter release, influencing anxiety levels.² Recent clinical studies have provided mixed results regarding the efficacy of cannabis in treating anxiety disorders. A systematic review and meta-analysis by Bahji et al. found that CBD significantly reduced anxiety in both animal and human studies, with fewer side effects compared to THC.³ Another randomized controlled trial by Shannon et al. demonstrated that CBD treatment reduced anxiety scores in a clinical population with anxiety and sleep disorders.⁴

Observational studies have also provided insights into the real-world use of cannabis for anxiety. A longitudinal study by Turna et al. followed a cohort of medical cannabis users and found that those who used cannabis reported significant reductions in anxiety symptoms over time.⁵ High-THC strains were associated with increased anxiety in some users, indicating the importance of cannabinoid composition in therapeutic outcomes.⁶ Another study by Crippa et al. highlighted that while CBD has a favorable safety profile, THC can exacerbate anxiety symptoms and should be used cautiously.⁷

Benzodiazepines are commonly prescribed for the treatment of anxiety disorders due to their rapid onset of action and effectiveness in acute anxiety episodes. However, they are associated with several drawbacks, including tolerance, dependence, and withdrawal symptoms.⁸ Long-term use of benzodiazepines has been linked to cognitive impairment and an increased risk of falls, particularly in older adults.⁹ Therefore, there is growing interest in alternative treatments, such as cannabis, which may offer anxiolytic benefits without the same level of adverse effects. Emerging therapies focusing on the precise dosing and ratio of cannabinoids are being explored to maximize therapeutic benefits while minimizing adverse effects.^{10,11}

This study aims to investigate the association between cannabis use and the prescription of anti-anxiety medications, providing insights that could support healthcare providers in making informed decisions about integrating cannabis into treatment plans for patients with anxiety, potentially leading to broader changes in prescribing practices.

METHODS

This study focused on a population of 634 adult patients with documented prescriptions anti-anxiety medications including Diazepam, Lorazepam, Hydroxyzine, Buspirone, Alprazolam, and Chlordiazepoxide. Medication names were standardized to generic names. The periods of cannabis use were categorized into 'Before', 'During', and 'After' based on the first and last purchase dates of cannabis products. The Defined Daily Dose (DDD) was calculated based on the standard DDD values established by the World Health Organization (WHO) for each drug prescribed for anxiety. Each patient's daily dose was calculated considering the frequency and strength of the drug to derive the DDD_ratio, which measures the quantity of medication used relative to the standard DDD. A mixed-effects linear regression model was employed to assess the statistical significance of these changes. This approach accounts for individual variability, multiple observations per patient, and handles incomplete data effectively.

RESULTS

The study population comprised 634 adults aged 22 to 88 years, with a mean age of 56 years. Among these participants, 78% were between 18 and 64 years old. The gender distribution included 70% females and 30% males. Regarding racial demographics, 90% of the patients were white, and 1% were Black or African American. Additionally, 90% of the subjects were non-smokers.

Distribution of THC: CBD Ratios

Within this sample, patients purchased cannabis products with 15 different THC ratios while concomitantly using anti-anxiety medications. Notably, 41% of patients used cannabis products with a THC ratio of 19:1, 16% used products with a 1:1 ratio, and 11% used products with a 0:1 ratio (Figure 1).

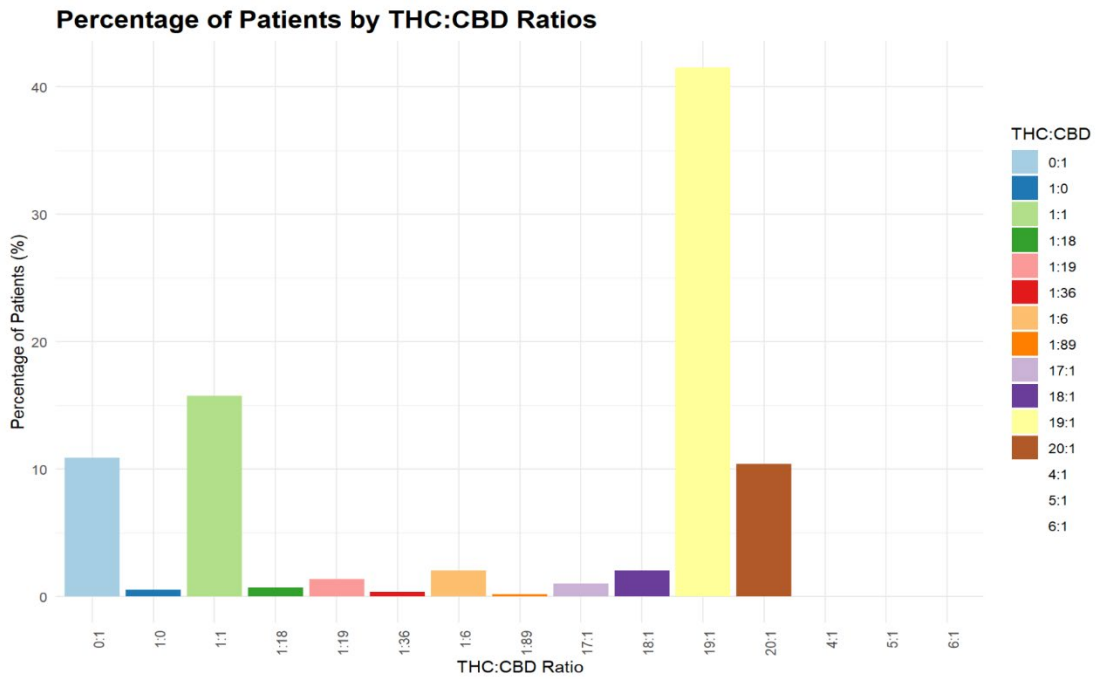


Figure 1. Distribution of THC:CBD ratios in cannabis products purchased by patients using anti-anxiety drugs.

Differences in dosage of anti-anxiety drugs between periods of cannabis use

The analysis revealed changes in the mean Defined Daily Dose (DDD) ratios across different periods of cannabis consumption. Prior to cannabis use, the mean DDD ratio was recorded at 0.727. During the period of cannabis consumption, there was a slight increase in the mean DDD ratio to 0.762. However, following the cessation of cannabis use, the mean DDD ratio decreased to 0.659.

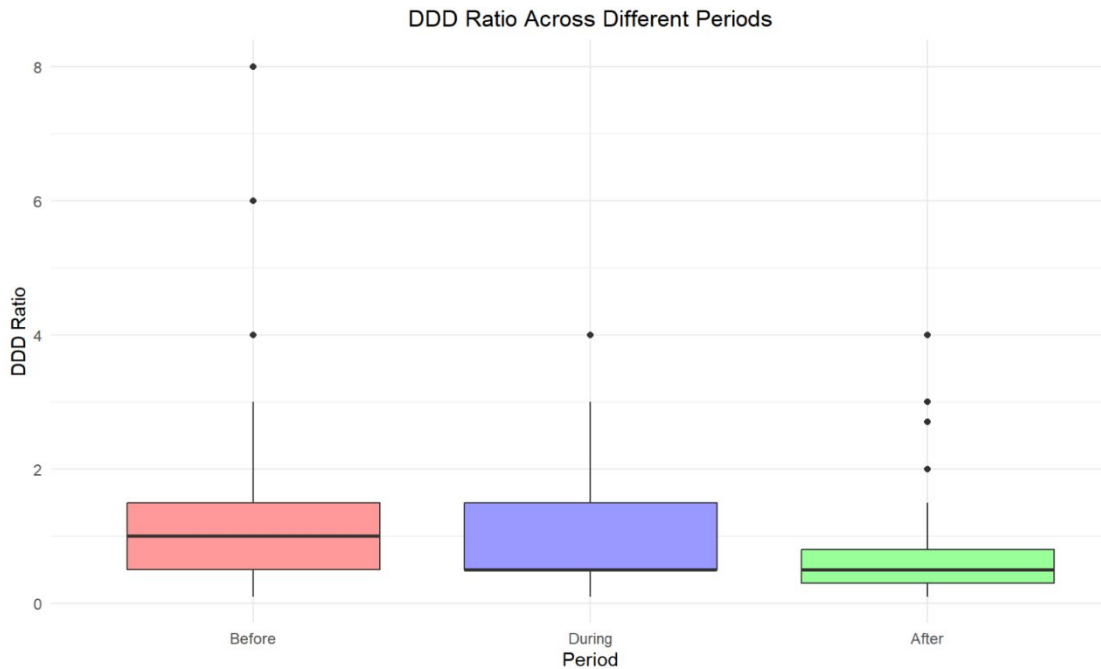


Figure 2. Mean DDD ratio of anti-anxiety drugs across periods of cannabis use.

A mixed effects linear regression model was used to account for the repeated measures within patients and adjust for other covariates in the model. The results of the model are described below:

During cannabis use, there is a significant increase in the DDD ratio of about 25.18% compared to the Before period. The increase is statistically significant, indicating that DDD ratio increases while patients are actively using cannabis, the effect persisted after controlling for age, gender, race, ethnicity, type of drug, milligrams of THC, THC:CBD ratio, and smoking status ($b= 0.25$, $p <0.001$).

After cannabis use, there is a significant decrease in the DDD ratio of approximately 9.89%, compared to the Before period. The mixed effects model shows a significant reduction in the prescription of these drugs in the period after cannabis consumption even after adjusting for covariates ($b= -0.098$, $p <0.001$).

Anti-anxiety drug type

Among patients using cannabis and benzodiazepines, there is a significant reduction in the DDD ratio of approximately 20.48% compared to other anti-anxiety medications in the adjusted model ($b = -0.20$, $p <0.001$). This finding underscores the negative association between cannabis and the use of benzodiazepines specifically (Figure 3).

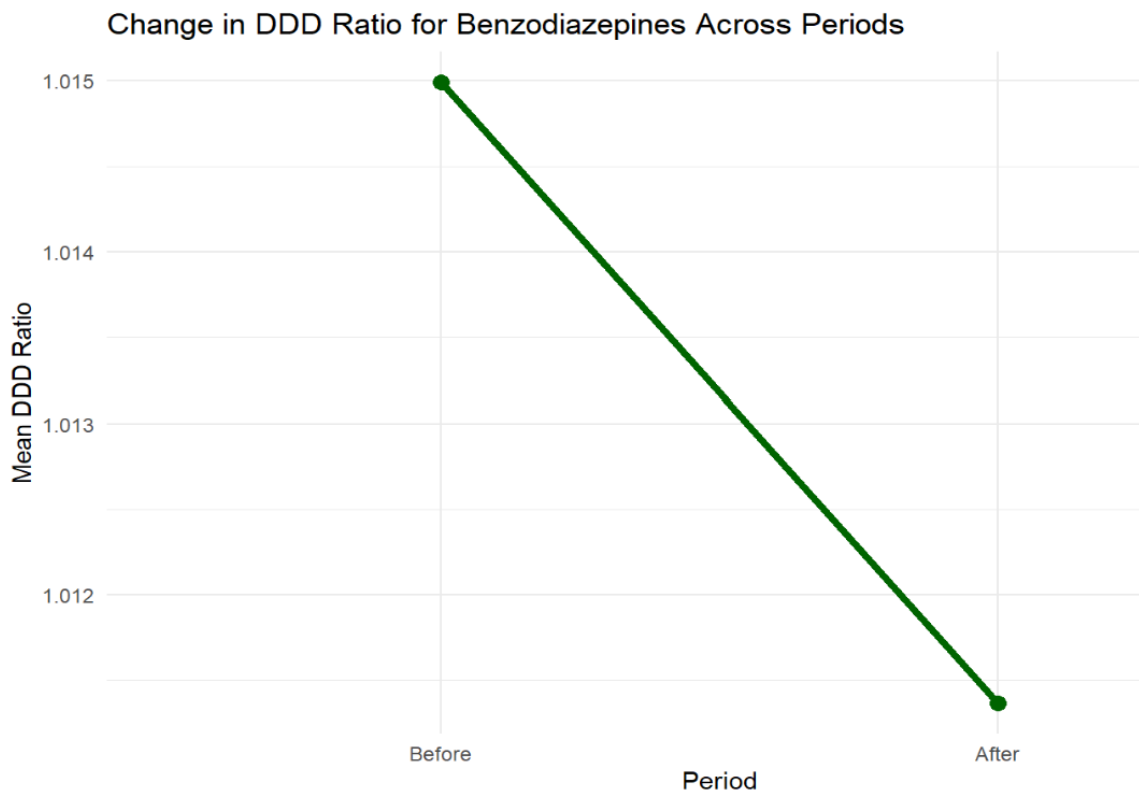


Figure 3. Prescribed daily dose of Benzodiazepines before and after starting cannabis use.

Demographics

The results indicate that gender, age, race, ethnicity, and smoking status do not significantly affect the DDD ratio.

Cannabis product type

Cannabis aqueous solution shows the least anti-anxiety medication DDD_ratio. However, no statistical significant difference in the DDD_ratio was found between consuming aqueous solution cannabis products and other products.

THC:CBD ratio

Among the different cannabinoid concentration ratios, a 1:36 THC:CBD ratio shows a lower DDD_ratio on these patients. However, this association was not statistically significant.

Milligrams of THC and DDD_ratio

No significant association between mg of THC and DDD ratio was found, which suggests a higher dose of THC does not have an impact on the use of anti-anxiety agents.

CONCLUSIONS

Our study highlights significant variations in the use of anti-anxiety medications in relation to cannabis consumption periods. Specifically, we observed an increase in the dose of anti-anxiety drugs prescribed during cannabis use and a subsequent decrease following cessation. These findings suggest that while cannabis consumption might initially elevate the use of anti-anxiety medications, it is associated with a long-term reduction.

Notably, patients using both cannabis and benzodiazepines demonstrated a significant reduction in benzodiazepine usage compared to other anti-anxiety medications.

Demographic factors, cannabis product types, and the THC:CBD ratio did not significantly influence these outcomes, indicating a consistent effect across various patient profiles.

The observed decrease in DDD ratio following cannabis use could indicate potential therapeutic benefits of cannabis in managing anxiety, which might help in reducing the overall burden of medication use.

DISCUSSION

The observed results of this study align with previous research indicating that cannabis can alter medication usage patterns among patients with anxiety disorders. For instance, Bahji et al. 3 reported that while CBD has anxiolytic properties, the psychoactive effects of THC might contribute to an initial increase in anxiety symptoms, potentially explaining the increased DDD ratio during active cannabis consumption. The significant decrease in the DDD ratio post-cannabis use supports findings by Turna et al. 5, who observed long-term reductions in anxiety symptoms among medical cannabis users. It is important to note that in this sample of patients with anxiety, there was a high percentage of patients using cannabis products with a high THC:CBD ratio, and our findings might be driven by the high content of THC. This could imply that the psychoactive effects of THC play a significant role in the initial increase in DDD ratio observed during cannabis use. Furthermore, while mixed effects models account for incomplete data during the follow-up period, there might have been fewer observations for patients in the during and after periods. These potential limitations underscore the need for cautious interpretation of the findings and highlights the importance of further research with larger and more balanced sample sizes.

Our study contributes to the understanding of cannabis and anxiety management by highlighting a substantial reduction in benzodiazepine use, which aligns with growing evidence suggesting that cannabis, particularly CBD, may offer an alternative to benzodiazepines with a lower risk profile. The lack of significant associations with demographic factors and specific cannabinoid ratios suggests that the anxiolytic benefits of cannabis are broadly applicable, yet further research is needed to optimize dosing and cannabinoid composition. These considerations are essential for healthcare providers considering the integration of cannabis into anxiety treatment regimens, potentially guiding more personalized and effective therapeutic strategies.

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