Effects of Cannabis Use on Sedation Requirements for Endoscopic Procedures

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Context: Cannabis (or *marijuana*) became legal for recreational use in Colorado in 2012, and this legislation change has created both challenges and opportunities in medicine. More patients are using cannabis, and more patients are now willing to admit cannabis use than in the past, which increases the likelihood that they will be forthcoming about use during medical questioning. Cannabis use may have implications during medical care, including procedural sedation.

Objective: To determine whether regular cannabis use had any effect on the dose of medication needed for sedation during endoscopic procedures.

Methods: A total of 250 medical records were reviewed from 1 endoscopy center and 1 endoscopist to minimize the variability in sedation technique for the study purposes. The cohort was reviewed with regard to age and gender to determine whether differences were present among different groups as to the relative amount of sedation medication required in cannabis users vs nonusers.

Results: Medical records from 250 patients were reviewed, and researchers found that compared with people who did not regularly use cannabis, people who regularly used cannabis required an amount of sedation for endoscopic procedures that was significantly higher (P=.05). The statistical significance persisted when adjusted for age, sex, and use of alcohol, benzodiazepines, and opiates.

Conclusion: Determining cannabis use before procedural sedation can be an important tool for planning patient care and assessing both medication needs and possible risks related to increased dosage requirements during endoscopic procedures.

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Cannabis (or *marijuana*) has been used both recreationally and medicinally for thousands of years. According to a report[1] by the United Nations Office on Drugs and Crime in 2017, global cannabis use in 2015 was estimated to be 183 million people, or 3.8% of the adult population. The largest increase in cannabis use occurred in the United States, where usage increased by 43% between 2007 and 2015. An estimated 13.5% of the adult population used cannabis during this period. The largest increase in use was in people aged 26 years or older. Currently, 10 states (Alaska, California, Colorado, Maine [allowed to possess but not buy], Massachusetts, Michigan, Nevada, Oregon, Vermont, and Washington) and Washington, DC, have legalized cannabis for recreational use, although amounts that are allowed to be carried on a person or

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personally grown vary from state to state. Thirty-three states have legalized medicinal cannabis.[2] These numbers suggest that an ever-increasing population of cannabis users will be seen by medical professionals. It will be important to know how cannabis use may affect medical care and the administration of certain medications, including sedatives and opioids. Current research shows that the half-life of tetrahydrocannabiol, the main component of cannabis, is between 5 and 13 days. Total elimination from the system may take up to 25 days. Hypotheses have been proposed that tetrahydrocannabiol interacts with specific cannabinoid receptors, which could include opioid and benzodiazepine receptors, among other mechanisms of pharmacologic action.[3] Thus, the interaction of opioids or benzodiazepines with these receptors in patients who regularly use cannabis may be altered.

Because cannabis is considered a Schedule I drug by the US Drug Enforcement Agency, research has been almost absent regarding its interaction with medications and its effects on patient response to medications. Gaining information on these issues has been further complicated by the hesitance of patients to report use of an illegal substance. Since the 2012 legalization of cannabis in Colorado, more patients use and disclose their use of cannabis.[4] With new openness about cannabis use, a question specifically addressing this issue was added to our hospital's nursing preprocedure questions in January 2015. A trend seemed to emerge that suggested people who regularly use cannabis may require more sedation to complete endoscopic procedures than people who are non- or infrequent users. The availability of the new specific information allowed for a medical record review to be undertaken to help answer this question.

Before initiating the medical record review, a literature search was conducted to procure research available in this area to date. It was evident that research relating to the effects of cannabis use on the dose requirements for sedation medications was lacking. One Australian study[5] from 2009 reviewed the induction dose of propofol required in patients using cannabis and compared 30 users with 30 nonusers. The research concluded that cannabis use increased the need for propofol during anesthesia when inserting a laryngeal mask.

Two other articles[6,7] were single patient case studies, 1 in Pakistan in 2014 and 1 in Berlin in 2015.[6,7] The Pakistan case study[6] found a possible association with cannabis use and the need for increased anesthesia; the patient was switched from propofol to thiopental for induction of anesthesia when he did not respond to the propofol after a total dose of 300 mg.[6] The Berlin case study[7] also found an increased need for anesthesia, in particular, propofol and morphine.[7] The only US article we found on the topic was not a research article, but an overview of multiple drugs and toxins, including cannabis, that described the effects on the body and potential complications or tolerance to anesthesia in the perioperative setting.[8]

The objective of the current study was to determine whether self-reported regular cannabis use had any relationship to medication needs during procedural sedation. If so, it could affect patient care and add to the limited knowledge base regarding cannabis use and the potential influence on medication interactions, including increased risks and costs associated with the administration of additional doses of medication.

Methods

After approval from the hospital risk manager, a retrospective medical record review was undertaken to collect data on age, sex, and use of alcohol, opiates, benzodiazepines, and cannabis as related to the amount of sedation required to complete endoscopic procedures. This research was eligible for exception under 45 CFR 46.101 (B) (4). To maintain consistency, a single endoscopist (M.A.T.) evaluated all patients. The endoscopy center is located in the surgical services department at a Level III trauma hospital in a small city in Colorado. The data were collected on cases performed from January 1, 2016, to December 31, 2017, after the legalization of recreational cannabis use in Colorado.

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Data about cannabis use at this facility had been collected by registered nurses during admission assessment under the query of illicit drug use. Starting in 2014, 2 years after the legalization of recreational cannabis in Colorado, the admission assessment was revised to separate the use of cannabis products from illicit drugs, such as methamphetamine, cocaine, and heroin. It was not regular practice during this time to inform endoscopists of drug use; therefore, the endoscopist was not typically aware of a patient's cannabis use when performing procedures.

We aimed to obtain a cohort of at least 25 people who regularly used cannabis to compare them with a population of people who did not regularly use cannabis. Patients who self-reported using cannabis on a daily or weekly basis (by smoking or ingesting edibles) were categorized as regular cannabis users. Patients who reported sporadic use or topical use (usually consisting of cannabidiol oils or ointments) were considered nonusers. Patients who reported that they did not use cannabis were also included in the nonuser group.

Patients included in this study were aged 18 years or older and had an endoscopic procedure performed by the endoscopist during the study period. The cohort was reviewed with regard to age, sex, and gender to determine whether variations were present among different groups as to the relative amount of sedation required in cannabis users vs nonusers. The status of alcohol, benzodiazepine, and opiate use was also reviewed. Other drugs or toxins were not considered.

Statistical analysis was performed using the *t* test and Mann-Whitney *U* test. The data analyzed were the average doses of fentanyl, midazolam, and propofol required for the procedures for patients in each group. $P<.05$ was considered statistically significant.

Results

The trial population (N=250) was randomly chosen from 1158 cases performed by the endoscopist during a 2-year period (2015-2017). The cannabis group (n=25) received 19 colonoscopies, 2 esophagogastroduodenoscopies (EGDs), and 4 colonoscopy/EGDs. The nonuser group (n=225) received 180 colonoscopies, 27 EGDs, and 18 colonoscopy/EGDs. The greater amount of sedation needed for regular cannabis users compared with nonusers was statistically significant (**Table**). The statistical significance persisted when adjusted for age, sex, and use of alcohol, benzodiazepines, and opiates.

The primary outcome analyzed was the dose of sedative medications needed to complete endoscopic procedures in cannabis users vs nonusers. A statistically significant difference existed in the amounts of the 3 types of sedation (fentanyl, midazolam, and propofol) used in procedures for cannabis users in comparison with nonusers. Using the *t* test, we found that the 3 drugs did not have equality of variance and that the difference was statistically significant (fentanyl, $P=.029$; midazolam, $P<.001$; propofol, $P=.026$; **Table**). Because the data were not normally distributed, the Mann-Whitney *U* test was performed as a follow-up

Table.
Amount of Required Sedation in Regular Cannabis Users Compared With Nonusers

	Amount of Sedation Required			*P* Value	
Sedative	Cannabis Nonusers (n=225)	Cannabis Users (n=25)	Greater Requirement, %	*t* Test	Mann-Whitney *U* Test
Fentanyl, μg	109.91	125.93	14	.029	.003
Midazolam, mg	7.61	9.15	19.6	<.001	<.001
Propofol, mg	13.83	44.81	220.5	.026	.001

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nonparametric test. Statistical significance was upheld (fentanyl, P=.003; midazolam, P<.001; and propofol, P=.001; **Table**). The results of the Mann-Whitney U test showed that even when the assumption of normality was dropped, the results were still statistically significant.

Cannabis users required a mean of 125.93 µg of fentanyl, 9.15 mg of midazolam, and 44.81 mg of propofol compared with nonusers of (109.91 µg of fentanyl, 7.61 mg of midazolam, and 13.83 mg of propofol, respectively) (**Figure**). Compared with nonusers, cannabis users required 14% more fentanyl, 19.6% more midazolam, and 220.5% more propofol for the duration of the endoscopic procedure.

Discussion

The findings of this study suggest that regular cannabis use has a significant effect on the amount of sedation required to perform an endoscopic procedure. To our knowledge, this is a previously unreported effect of cannabis, and the exact mechanism of the interaction is unknown. Our observation that the effect of regular cannabis use was consistent across different drug classes was of particular interest. The standard practice of the endoscopist was to use no more than 10 mg of midazolam, which provides one possible explanation for the lower SD from nonusers to users. We found that cannabis users tended to require closer to the maximum amount of the medication that is typically used, so they may have been more likely to need a higher dose for sedation and, therefore, were switched to propofol earlier than the standard patient. Nonusers required, on average, less midazolam for sedation.

With little research currently done in this area and the continued increase in legalization and use of cannabis, the field of anesthesia and sedation needs further studies with greater depth.

One limitation of this study was that it was a retrospective medical record review that consisted of data collection and analysis. Another limitation was the small sample size, which consisted of a subsample of 25 cannabis users; however, the comparison sample of nonusers was much larger. The legalization of cannabis in Colorado has increased the likelihood that patients will report use; however, the stigma of use may continue to lead patients to underreport cannabis use.

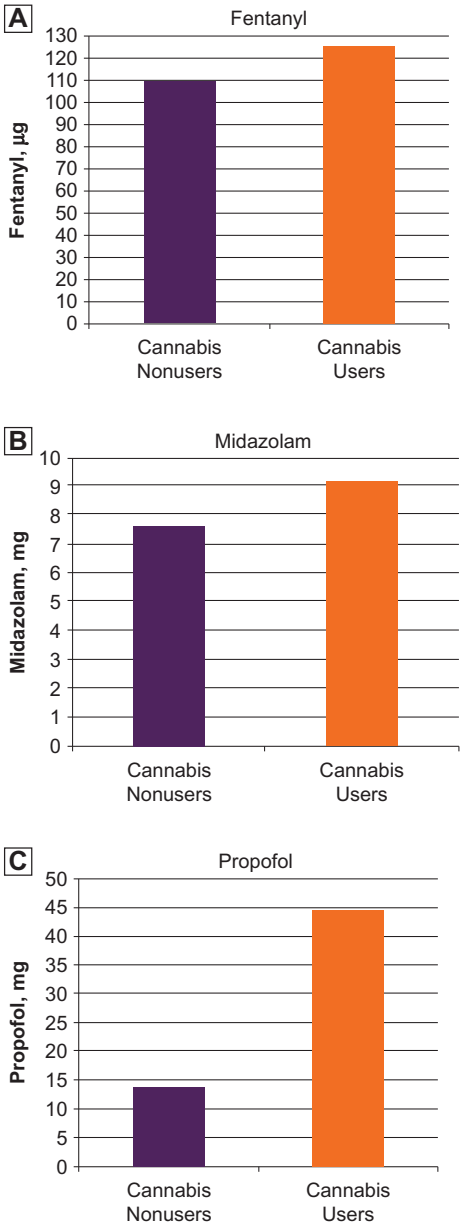


Figure.
Relative amounts of sedation used for endoscopic procedures in cannabis users vs nonusers. Sedation medications used included (A) fentanyl, (B) midazolam, and (C) propofol.

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Additionally, some factors were not considered, including variations that might occur in women who had a total hysterectomy—because of the increased challenge of a more mobile and tortuous colon. Endoscopies in these patients typically take longer to perform.[9] Other variables, such as pain tolerance, race, and duration of procedure, also known to affect medication doses, were not factored into this study.[10]

Further research should include not only patients who receive moderate sedation, but also patients undergoing general anesthesia. In addition to noting an increased need for sedation, the incidence of adverse events, side effects, and increased need for reversal agents is an issue that needs to be evaluated. Although this study did not address any incidence of adverse events or side effects, it is well known that hemodynamic and respiratory function may be compromised in patients who take opioids, benzodiazepines, or propofol for sedation, especially in combination. These effects are dose dependent; the higher the dose given, the greater the chances for adverse events or compromise.[11] The complex pharmacology and drug interactions will also need further evaluation.

Using higher doses of medication could also lead to increased costs, both for the provider and the patient. Not only does each medication get charged to the patient, but the added use of propofol could incur a large cost if another practitioner, such as an anesthesiologist, is needed, depending on state standards, comorbidities, and practice location (freestanding clinic vs hospital).

Conclusion

A strong correlation appears to exist between the regular use of cannabis and the need for increased doses of the sedative medications fentanyl, midazolam, and propofol required in the performance of endoscopic procedures. The correlation could prove to be important in making medical decisions related to the sedation of cannabis users. Knowledge of a patient's use of cannabis prior to sedation can help prepare endoscopists, nurses, and anesthesia providers for the potential need for more medication, increased costs, and possible risks associated with dose-dependent adverse events.

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Author Contributions

All authors provided substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; all authors drafted the article or revised it critically for important intellectual content; all authors gave final approval of the version of the article to be published; and all authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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