

# Cannabis consumption before surgery may be associated with increased tolerance of anesthetic drugs: A case report

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## ABSTRACT

**Introduction:** Cannabis is the most commonly used illicit drug worldwide in adults. Several studies suggest an interaction of cannabis intake

and anesthetic drugs like propofol and thiopental, but the pharmacodynamic interaction between cannabis and commonly used anesthetic drugs is still not well understood. **Case Report:** A 37-year old male patient with a history of regular cannabis consumption and cannabis intake the day before surgery was admitted for an arthroscopic shoulder stabilization. Induction of anesthesia required large doses of propofol, thiopental and sevoflurane. Maintenance was achieved with the additional application of nitrous oxide to provide clinical tolerance of the surgical procedure. Return of consciousness and the postoperative course were uneventful. **Conclusion:** History of cannabis intake should be taken into routine preoperative assessment and patients should be closely monitored by experienced anesthesia staff for adequate anesthetic depth and analgesia.

**Keywords:** Anesthesia, Cannabis, Interaction, Pharmacodynamics

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## INTRODUCTION

Cannabis is the most consumed illegal drug worldwide and there is a growing number of ongoing programs to offer a legal source of cannabis to chronically sick patients [1].

Several studies suggest an interaction of cannabis intake and anesthetic drugs like propofol and thiopental

[2]. However, this interaction and its implications for anesthetic practice in patients with chronic cannabis intake is not well understood.

Herein, we describe a case of a patient scheduled for a routine surgical procedure with a history of regular cannabis and tobacco consumption, who needed large amounts of different anesthetic agents to provide sufficient condition for intubation.

## CASE REPORT

A 37-year-old male patient, 93 kg bodyweight, 206 cm tall, was scheduled for an arthroscopic stabilization of his right shoulder due to a traumatic glenoid fracture. His medical history revealed an appendectomy at the age of nine with no anesthetic problems. The patient was healthy and in good medical conditions. He reported a daily nicotine usage of 10-15 cigarettes, a cannabis intake of 1g per week and an occasional use of alcohol. He admitted smoking one cannabis cigarette the day before surgery.

In the operating room non invasive cardiorespiratory monitoring measured a blood pressure of 120/70 mmHg, a heart rate 80 bpm and an oxygen saturation (SpO<sub>2</sub>) of 98%. Prior to induction the patient was oxygenated with a FiO<sub>2</sub> of 1.0 and a flow of 12L/min for 5 minutes. A regional anesthetic technique like an interscalene block had been declined by the patient.

Over an iv-line on his left backhand (BD Venflon™ Pro Safety 18G, Becton Dickinson, Heidelberg, Germany) 0.2 mg of fentanyl (Fentanyl®-Janssen, Janssen-Cilag, Neuss, Germany) were injected and the patient reported of a dizzy feeling after four minutes. 200 mg of propofol (Braun Propofol®-Lipuro, B. Braun, Melsungen, Germany) were administered without any anesthetic effect as the patient was still speaking with the anesthesia staff. Another two doses of propofol of 100 mg each were injected, but the patient did not show any reduction of his conscious state. The iv cannula was checked for correct position and no signs of extravasation of the anesthetic agents were detected.

The anesthetic regime was changed. We decided to administer 500 mg of thiopental (Thiopental Inresa® 0,5g, Inresa Arzneimittel, Freiburg, Germany), that finally induced anesthesia. However, the patient was still breathing spontaneously with a tidal volume of 100-150ml and a respiratory rate of 20/min requiring assisted ventilation using a face mask that was not tolerated by the patient. 4 vol% of isoflurane (Forane®, Abbott, Ludwigshafen, Germany) was added to achieve tolerance of the assisted ventilation.

After 3 minutes of isoflurane-supplemented assisted ventilation a size 5 laryngeal mask (LMA/Unique™ Single Use, Teleflex Medical, Kernen, Germany) was inserted to further improve ventilation. The tidal volume was increased to 200 ml requiring a peak inspiratory pressure of 30 cm H<sub>2</sub>O. A further dose of 200 mg of propofol

was administered to deepen the anesthesia so that the patient was finally sufficiently ventilated. Due to the need to position the patient on the left side, neuromuscular blockade was achieved with 100 mg succinylcholine and endotracheal intubation was performed without any complications (Cormack II, tube size 8 mm, Covidien Mallinckrodt™ Hi-Contour, Covidien Germany, Neustadt/Donau, Germany).

After intubation sufficient ventilation was achieved by a tidal volume of 650 ml, a respiratory rate of 16 and an etCO<sub>2</sub> of 40 to 45 mmHg. In the operating room anesthesia was maintained with an end-tidal volume concentration (etVol%) of 2.4% sevoflurane (Sevorane®, Abbott, Ludwigshafen, Germany). Nitrous oxide was added with a concentration of 50% and a flow of 1L/min.

The entire induction period took 15 minutes from the application of fentanyl to the maintenance state with sevoflurane and nitrous oxide at the end. Only after the application of sevoflurane and nitrous oxide the patient had a significant drop in his blood pressure and heart rate. After fractional (4x2ml) application of akrinor (cafedrine hydrochlorid 200 mg and theodrenalinhydrochlorid 10 mg, Akrinor®, CT Arzneimittel, Berlin, Germany) the patient showed a stable blood pressure of around 110/60 mmHg through the whole procedure. For intraoperative analgesia a total amount of 0.5 mg of fentanyl was administered. 20 minutes before the end of procedure 2 g metamizole (Novaminsulfon-ratiopharm®, Ratiopharm, Ulm, Germany) were applied. Since the patient had a constantly high blood pressure (150/80mmHg) after extubation and no pain, he also received 60 µg clonidine (Catapresan®, Boehringer Ingelheim Pharma, Ingelheim, Germany). After 30 minutes of observation in the post-anesthesia care unit, the patient was fully awake, showed no signs of persisting anesthetic drug effect and was discharged to the surgical ward. Post-surgical pain was controlled with 500 mg metamizole every eight hours. The patient was discharged 2 days after surgery.

## DISCUSSION

Here we report the case of a 37 years old male with a regular cannabis abuse who required excessive doses of different anesthetic drugs for induction of anesthesia. We postulate that this might be related to a pharmacological interaction of cannabis and anesthetic drugs resulting in tolerance of higher anesthetic dosages.

In the literature the effect of cannabis on anesthetic drugs are discussed controversially.

Flisberg et al. [2] could show, that patients with a history of cannabis consumption needed significant more propofol to successfully achieve the insertion of a laryngeal mask, than the control group. They concluded that regular cannabis users show a more variable response to induction of anesthesia with higher doses of propofol needed [2]. These human data are supported by Brand et al. [3] who reported a dose-dependent antagonistic

interaction between tetrahydrocannabinol (THC) and propofol in mice.

In contrast, several experimental studies have also shown an enhancement of the sedative effect of intravenous [4] and inhalational [5] anesthetic drugs by THC, so that an individual dose titration and continuous monitoring of the anesthetic depth is recommended.

In our case the use of thiopental and propofol did not seem to have the expected effect on the patient's consciousness. Furthermore the induction and maintenance of anesthesia with high concentrations of isoflurane and sevoflurane did not achieve adequate anesthetic depth. Only when nitrous oxide had been added to sevoflurane, sufficient tolerance of the surgical procedure could be provided. In connection with pharmacokinetics, similar findings have been reported by Symons [6] describing a patient with a history of cannabis smoking, who required repetitive doses of propofol (3x50mg), midazolam (2x1mg) and ketolorac (10 mg), besides high concentrations of isoflurane and nitrous oxide to maintain anesthesia for a tooth extraction.

A possible pharmacodynamic explanation could be that propofol and thiopental mediate their effects over the gamma-aminobutyric acid type a (GABA (A)-receptor), like the volatile anesthetics, sevoflurane and isoflurane, which may have been influenced by THC and other cannabinoid compounds.

Liu et al. [7] observed that GABA (A)-receptors could form a complex with G-Protein-Coupled-Receptors (Dopamine-5-Receptor) resulting in a reduced efficacy of the GABA transmission.

So a possible explanation for the pharmacodynamic interactions in our case could be the ability of the CB1-Receptor and the GABA (A)-Receptor to form such a receptor complex resulting in a lower GABA neurotransmission. A hint for these theory, could be the fact that in our case no anesthetic - which mediated its effect through the GABA (A)-receptor - could provide optimal conditions for intubation. Only when nitrous oxide, which blocks the NMDA-receptor, was provided to our patient, sufficient anesthesia could be achieved and maintained.

It also needs to be mentioned, that plasma and blood concentrations of THC in frequent cannabis users (four times per week a cannabis cigarette with 54mg THC content) are detectable up to more than 30 hours after consumption.[8] Moreover it has to be considered, that the amount of THC depends on the type of plant species, cultivation, climate and soil and ranges from one to 20% in herbal cannabis.[9, 10] Therefore, we would recommend, that surgical patients refrain from consuming cannabis as long as possible prior to surgery, since the way of interaction with anesthetic drugs is not safely predictable. The interaction of THC with anesthetic drugs is complex, possibly resulting in increased sensitivity [4] or greater tolerance to anesthetic drugs, the latter with a higher need of anesthetic agents to induce anesthesia. In patients with greater tolerance of anesthetic drugs nitrous oxide, could

be one possible solution to avoid possible interactions between GABA (A)-receptor signaling and THC. Since the mode and the effect of interaction is not predictable history of cannabis intake should be taken into routine preoperative assessment.

Limitations of our reported case are, that we did not have any monitoring of depth of anesthesia applied, a relatively low fentanyl induction dose (200µg, 2µg/kg), no THC blood level measurements and no knowledge of any genetic mutation of the patients GABAA-receptor.

## CONCLUSION

Patients with regular cannabis consumption are recommended to closely monitored for adequate anesthetic depth and analgesia, treated by experienced staff only and regional anesthetic techniques should be favored. Patients are recommended not to consume cannabis as long as possible before the surgical procedure.

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## Author Contributions

Georg Richtig – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Götz Bosse – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Friederike Arlt – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Final approval of the version to be published

Christian von Heymann – Substantial contributions to conception and design, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

## Guarantor

The corresponding author is the guarantor of submission.

## Conflict of Interest

Authors declare no conflict of interest.

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