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**Case report****EFFECT OF CANNABIS ABUSE OVER SPINAL ANAESTHESIA: A CASE SERIES**  
**Spinal anaesthesia in cannabis addicts**

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**Summary**

**Introduction:** *In the modern world, drug abuse is one of the fastest emerging social issues. Cannabinoid receptor agonists are becoming increasingly popular as abused substance due to their ease of cultivation and availability.* **Case report:** *We present a series of three cases who were scheduled for lower limb surgeries planned under spinal anaesthesia. All patients were consuming either cannabis or its products regularly for significant time periods. All subjects were reported with an experience of either failed or delayed effect after the block.* **Conclusion:** *The study concluded that the incidence of failure of the spinal anaesthesia seemed to be higher in the cannabis abusers than among the non-abusers. There was a slower onset and decreased duration of both sensory and motor block in addict patients, with increase requirements of doses of anaesthetic and analgesic agents as compare to non-addict patients.*

**Key words:** *Cannabis abuse; spinal anaesthesia; cannabinoid receptors; failed block; delayed effect.*

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**Introduction**

Drug abuse is one of the most emerging social issue among the modern world problems. Cannabinoids have been used for therapeutic and recreational purposes since long times<sup>1</sup>. Today, synthetic cannabinoid receptor agonists are increasingly being used for abuse purpose due to their ease of cultivation and availability<sup>2</sup>. All these compounds act on cannabinoid receptors, namely CB1 and CB2 which are present at different locations in the body<sup>2,3,4</sup>. Numerous studies suggested the interaction of cannabis and anesthetic drugs like propofol and thiopental affecting the pharmacodynamics in a patient with cannabis abuse under general anaesthesia<sup>5,6</sup>. But, the effect of cannabis abuse over spinal anaesthesia is not well understood till today, as very limited literature is available. Here, we present a series of three cases with regular cannabis abuse, who were scheduled for lower limb surgeries under spinal anaesthesia at our institute.

**Case 1**

A 19-year-old male patient presented with a history of road traffic accident followed by crush injury of right leg. After imaging, vascular injury involving anterior and posterior right tibial artery was diagnosed that could not be repaired and needed urgent amputation of the limb below the level of knee. Immediately, after blood group typing and patient was evaluated for the surgery. The patient was healthy with no significant medical condition. After informed written consent, patient was taken to the operative room. Surgery was planned under spinal anaesthesia.

In the operating room, the patient was continuously monitored by non-invasive blood pressure (NIBP), electrocardiogram (ECG), and pulse oximetry. After documenting the baseline vitals, preloading started with ringer solution. Simultaneously, subarachnoid block was administered at the level of L3-4 intervertebral space using 25G Quinke's spinal needle in right lateral position under all aseptic precautions. A total drug volume

of 2.5 ml containing 0.5% heavy bupivacaine and 25 mcg Fentanyl was administered intrathecally. Immediately, the patient was repositioned in the supine position. The sensory loss was assessed by loss of sensation to cold (using an alcohol swab) and pin prick. Motor block was assessed using Modified Bromage Score (where score 0: no motor loss; score 1: inability to flex the hip; score 2: inability to flex the knee; score 3: inability to flex the ankle or complete motor block)<sup>7</sup>. No sensory and motor loss was observed even after 20 minutes of the injection. The block was considered as failed and was decided to repeat it. A repeat of block was performed with 1.5 ml of 0.5% heavy bupivacaine. Sensory and motor block were assessed as before. A delayed sensory loss was achieved after 12 minutes of injection, up to T10 level. Whereas, there was no motor block observed even after 15 minutes of injection as patient was able to flex the limb at knee joint. The anaesthesia was supplemented with infusion dexmedetomidine 0.3 mcg/kg/hr. Total duration of surgery was 2 hours and was uneventful. Patient started complaining of pain after half an hour of surgery in the recovery room. Paracetamol infusion was given intravenously and patient was shifted to the ward after 2 hours of observation.

After 10 days, patient was rescheduled for revision amputation with infection at the site of previous surgery under subarachnoid block again. After preoperative evaluation, patient was shifted to operation theatre. Under all aseptic precautions, spinal anaesthesia was administered with 3 ml of 0.5% heavy bupivacaine but failed. Spinal block was repeated again and only sensory block could be achieved without motor block at this time. Again, surgery was supported with inj. Dexmedetomidine and completed uneventfully. After repeated episodes of failed and delayed effect of spinal anaesthesia patient was re-enquired about any substance abuse. Now, patient admitted the habit consumption of cannabis for 6 years on regular basis. Surgery completed uneventfully and patient was shifted to recovery room.

### **Case 2**

A 35-year-old male patient posted for reduction and external fixation for fracture of tibia in right leg planned under subarachnoid block. In preoperative evaluation, regular consumption of

cannabis for about 10 years was reported with no significant medical history. Maintaining all aseptic precautions, patient was given spinal anaesthesia with 3 ml of 0.5 % heavy bupivacaine in sitting position. A delayed response to block was observed after 20 minutes of second

block with complete sensory block at T12 level and motor block (Modified Bromage Score 2). Patient started complaining of pain after 1 hour of the surgery, suggestive of decreased duration of block. Further surgery was supplemented with inj. Fentanyl and inj. Dexmedetomidine intravenously and completed in 1.5 hours uneventfully.

### **Case 3**

Another patient 26-year-old posted for fixation of fracture femur (left) at mid shaft level under spinal anaesthesia. In preoperative evaluation, patient admitted the habit of regular cannabis intake for about 8 years was with no significant medical history otherwise. Patient was given spinal anaesthesia with 3 ml of 0.5 % heavy bupivacaine in sitting position. No sensory and motor block was noted even after 20 minutes of block. There was significant pain at the affected limb which led to inadequate position for the spinal block. So, surgery was planned under general anaesthesia. While performing the general anaesthesia, increased requirements of drugs like induction agents and analgesics were noted. However, surgery was completed uneventfully in time duration of 1 hour.

### **Discussion**

We reported a series of cases with regular cannabis abuse who had repeated episodes of either failed or delayed effect of spinal anaesthesia. Multiple studies are already available favoring the interaction between cannabis abuse and anesthetic drugs used during general anaesthesia<sup>5,6</sup>. But, literature suggesting the effect of cannabis abuse over spinal anaesthesia is very sparse and limited. In the last few years, numerous studies have reported that the incidence of failed spinal anaesthesia was more common among substance abusers like opioids, tramadol, marijuana and others<sup>7,8</sup>. Maha M.I. Youssef et al studied the effect over spinal anaesthesia among the patients with addiction histo-

ry to Marijuana, Cannabis, Tramadol, and Clonazepam. They observed the incidence of failure of the intrathecal anesthesia to be higher in the addict than in non-addict patients.

In general, a number of factors might be responsible for this failed, delayed or inadequate effect of spinal anesthesia. Factors like problem in technique while performing the block or any anatomical variation in the subarachnoid space were ruled out by itself, as no case appeared to have a patchy or unilateral block. Another factor responsible for the above result after spinal block could be the quality and handling of drug used, however this was also excluded by proper drug manufacturer specifications and storage facilities. By excluding out most of these factors, patient had no other apparent cause affecting the success rate of the procedure but chronic substance abuse.

After repeated exposure to high doses of any drug for longer duration, some receptors may develop a state of tolerance to overcome the chronic exposure to drugs. Although, tolerance develops within weeks of regular use due to downregulation of both CB1 receptors and endocannabinoid levels<sup>9</sup>. This could lead to decrease in response to the similar dose and concentration of the drug. Numerous theories are suggested for explaining the development of tolerance due to cannabis abuse. Cannabinoids act primarily via adenylyl cyclase G-protein-coupled receptors, namely CB1, CB2 receptors. Down regulation of these receptors decreases the response to the drug, the receptor function and the affinity for agonists. Cannabis tolerance might also result from uncoupling between the receptor and intracellular second messengers by increasing adenylyl cyclase activity<sup>3,4</sup>.

The excessive exposure to exogenous cannabinoid compounds could also affect mu, kappa, and delta receptors. This might lead to variability in the release and function of the endogenous peptides which are responsible for pain relief. Also, chronic use of cannabis and related compounds can influence many receptors centrally and peripherally in the nervous system including receptors involved in local anesthesia. The antinociceptive effect produced by cannabis is proposed to be mediated by a decreased calcium and increase potassium transmembrane conductance via inactivation of the voltage-activated channels<sup>6,8</sup>. Thus, leading to minimization of pain threshold along with escala-

tion of the response towards pain stimuli as compare to non-abusers<sup>7</sup>.

Undoubtedly, cannabis and its related products have been used for medicinal and recreational purposes since ancient times. It is widely used for the management of variety of condition like pain, spasticity, seizure disorders and anorexia as supported by the enormous literature availability<sup>9</sup>. But, during these trails the amount and duration for which cannabis is used for was very limited and did not lead to any cross tolerance and down-regulation of receptors. A study conducted by King et al, found that there was no statistically significant difference observed in the doses of propofol, fentanyl or ketamine in the cannabis group compared with the control group among patients who self-report cannabis use before esophagogastroduodenoscopy<sup>8</sup>. This study was conducted on a small sample size and due to the self-reported nature of cannabis use dose, route (oral vs inhaled) or frequency of drug could not be not specifically differentiated. Also, number of studies available for supporting this fact are very limited.

CB1 receptors are widely distributed in the central and peripheral nervous systems, especially the hippocampus, cortex, olfactory areas, basal ganglia, cerebellum, and dorsal horn of the spinal cord. Activation of these receptors inhibits the production of cyclooxygenase, lowering the inflammatory component of acute pain and the central sensitization at the dorsal horn of the spinal cord<sup>10</sup>. The receptors involved in spinal anesthesia are comparable in distribution, constitution and function to cannabinoid receptors in certain parts of the body such as the spinal cord, making them affected by the prolonged exposure to cannabinoid compounds<sup>11</sup>. So, based on the above theories, there would be an expected decrease in the duration of spinal anesthesia among abusers as compare to non-abusers. Therefore, increase the dose of anaesthetic and analgesic drugs should be considered in order to achieve the desired effect<sup>8</sup>.

After correlating the findings of our study with the present literature, we could suggest that the interaction between local anaesthetic and cannabinoid receptors especially at the level of spinal cord can lead to tolerance and resistance to local anesthetic drugs. This is translated to the body as delay in the onset, decrease in the duration of spinal anesthesia or even complete failure of response of the

usual dose of the local anesthetic, thus demanding to increase the dose of local anesthetic to overcome this state of tolerance<sup>7,11</sup>. Indubitably, multiple well-structured clinical trials must be conducted for better understanding of pathophysiologic consequences of cannabis abuse and its further implications over the spinal anaesthesia.

### **Conclusion**

This case series adds to our knowledge about the effect of cannabis abuse over spinal anaesthesia by concluding that the incidence of failure of the spinal anaesthesia could be higher in the cannabis abusers than in non-abuser patients. Also, cannabis abuse could lead to slower onset and decreased duration of both sensory and motor block among abusers, with increase requirements of doses of anaesthetic and analgesic agents than non-abusers. However, the above findings to be supported with the research trials in future for better correlation between cannabis abuse and its effects over spinal anaesthesia.

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