

## Marijuana in Pregnancy

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### Abstract

**Introduction:** The prevalence of recreational drug abuse among young adults, including women, has increased markedly over the last 2 decades. Nearly 90% of these women are of childbearing age. Marijuana remains the drug most commonly used for recreational purposes in pregnancy. However, there appears to be an absence of uniform guidelines for obstetric and anaesthetic management of pregnant patients with a history of marijuana abuse. **Materials and Methods:** A Medline search for articles highlighting drug abuse in pregnancy, with particular emphasis on marijuana abuse in pregnancy, the drug's impact on the fetus and implications for administration of obstetrical anaesthesia was performed. **Results:** Because the pharmacological actions of marijuana are complex and include a unique blend of effects, the clinical picture could be very unpredictable, the diagnosis often difficult, and management at times controversial. **Conclusion:** In the absence of uniform anaesthetic guidelines for pregnant patients with a history of drug abuse, including abuse of marijuana, the decision regarding administration of peripartum analgesia or anaesthesia should be individualised and conducted on a case-by-case basis.

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**Key words:** Anaesthetic implications, Cannabinoids, Drug abuse, Drug addiction

### Introduction

Marijuana has been used for thousands of years for both medical and recreational purposes. Because the pharmacological actions of marijuana are complex and include a unique blend of effects of alcohol, opioids, tranquilisers and hallucinogens, the clinical picture could be very unpredictable and the diagnosis is often difficult.<sup>1</sup> As a result, this form of chemical dependency may continue undetected in pregnancy, significantly affecting pregnancy outcome and peripartum obstetric and anaesthetic management of these patients.

However, there appears to be an absence of uniform guidelines for obstetric and anaesthetic management of pregnant patients with a history of marijuana abuse. A Medline search for articles highlighting drug abuse in pregnancy, with particular emphasis on marijuana abuse in pregnancy, with associated obstetric and anaesthetic implications was performed. This article briefly reviews the anaesthetic implications of recreational marijuana use in pregnancy.

### Definition and Diagnosis of Substance Abuse

By definition, substance abuse is described as “self-

administration of various drugs that deviates from socially or medically accepted use, which if prolonged can lead to the development of psychological and physical dependence”.<sup>2</sup> This disease process, often referred to as chemical dependency, is characterised by periodic or continuous impaired control over drug(s) intake (despite awareness of adverse consequences), preoccupation with the drug(s) acquisition and distortions of mental capacity, most notably denial.<sup>1</sup> Most often, chemical substance use or dependence is first suspected or diagnosed during medical management of another condition, such as hepatitis, human immunodeficiency virus syndrome or pregnancy.<sup>2,3</sup> Psychological and personality characteristics seem to predispose an individual to, rather than result from, substance addiction.<sup>2,4</sup> Regardless of the drug or drugs ingested and the clinical manifestations, it is always difficult to predict the anaesthetic implications in chemically-dependent patients.<sup>1,5,6</sup>

The prevalence of recreational drug abuse among young adults, including women, has increased markedly over the last 2 decades.<sup>1,7-10</sup> Nearly 90% of these women are of childbearing age.<sup>1,5</sup> Consequently, it is not uncommon to find pregnant women who abuse drugs, and numerous

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reports of cases of drug abuse in pregnancy have been published.<sup>7,10-12</sup> Anaesthesia providers become involved in the care of drug-abusing patients either in emergency situations, such as fetal distress, or in more controlled situations, such as request for labour analgesia.

Substances most commonly used in pregnancy include ethanol, tobacco, caffeine, marijuana, cocaine, amphetamines and opioids. Poly-substance abuse is very common.<sup>1,12</sup> The majority of patients with a history of drug abuse or substance addiction deny it when interviewed preoperatively by anaesthesiologists.<sup>4,13</sup> Therefore, a high index of suspicion for drug abuse in pregnancy, combined with non-judgemental questioning of every parturient, is necessary. Risk factors that suggest substance abuse in pregnancy include lack of prenatal care, history of premature labour and cigarette smoking.<sup>14,15</sup> In the United States (US), the American College of Obstetricians and Gynecologists (ACOG) has made multiple recommendations regarding management of patients with drug abuse during pregnancy. Women who acknowledge use of an illicit substance during pregnancy should be counselled and offered the necessary treatment. ACOG also acknowledged that some states consider intrauterine fetal drug exposure as a form of child neglect or abuse under the law.<sup>16</sup>

### Pharmacology and History of Marijuana Abuse

Marijuana is a naturally occurring substance obtained from the plant *Cannabis sativa*. The use of marijuana for both medical and recreational indications dates back to thousands of years ago.<sup>17</sup> More than 61 chemicals known as cannabinoids obtained from the *Cannabis sativa* plant have been identified.<sup>18</sup> Throughout history, no other drug of abuse has aroused more controversy than marijuana. The public debate on marijuana has continued as we enter the 21<sup>st</sup> century; in some countries, it has centred on the possible legalisation of its use, at least for therapeutic purposes.

Indeed, there seems to be a number of well-documented therapeutic actions of marijuana, including its antiemetic, analgesic and anticonvulsant properties.<sup>19</sup> More recently, the use of marijuana as an appetite stimulant has been indicated in terminally ill patients.<sup>19</sup> However, the existence of psychoactive properties, development of tolerance and potential for abuse have discouraged the therapeutic use of marijuana.

### Epidemiology of Marijuana Abuse

A survey of students in Asia showed that, at some time in their lives, 3% to 6% of female students have used marijuana.<sup>20</sup> The same survey showed that 5% to 10% of female students have used other drugs. Asuni and Pela<sup>21</sup> reported that drug abuse is escalating in Africa, where the

most common and easily available drug of abuse is still marijuana. The lack of funds and trained personnel makes it difficult to implement preventive programmes against drug abuse. It is very likely that drug abuse will worsen in Africa unless more effective measures are implemented to control the current situation.

The lifetime prevalence of marijuana use among female college students in Brazil was reported to be 26%.<sup>22</sup> Marijuana users were classified as having a stable, descending and once pattern of consumption frequency. These patterns were related to socioeconomic status and peer group. Richardson et al<sup>23</sup> conducted a study of substance-abusing mothers and their neonates in Australia and concluded that the incidence of substance abuse reached 7 per 1000 total births. In France, a study of cannabis use in French adolescent females reported a 41.2% occasional or regular marijuana use.<sup>24</sup> In the US, it is estimated that marijuana is used by 9.5% to 27% of pregnant women.<sup>25</sup> In New Zealand, 5% of mothers reported smoking cannabis during pregnancy; demographically, they were younger, of lower parity, better educated and more likely to use alcohol, cigarettes, coffee and other hard drugs.<sup>26</sup>

### Pathophysiology and Clinical Presentation of Marijuana

Marijuana is smoked for its hallucinogenic properties. Of the 61 known cannabinoids, delta 9-tetrahydrocannabinol (THC) is the most potent psychoactive agent and is extremely important in the recreational use of cannabis. It is believed that approximately 50% of THC and other cannabinoids present in a cannabis cigarette are inhaled and entered into the bloodstream.<sup>18,27</sup> High fat solubility of cannabinoids leads to rapid accumulation in adipose tissue, from which they are slowly released into the brain. The plasma elimination half-life of cannabinoids in occasional users is approximately 56 hours; in chronic users, it is only 28 hours.<sup>27</sup> However, adipose tissue sequestration may extend the tissue half-life to approximately 7 days. It has been reported that complete elimination of a single dose may require up to 30 days.<sup>18</sup> Cannabinoids undergo metabolism in the liver and form >20 metabolites, most of which have psychoactive properties.

The effects of acute marijuana use include euphoria, tachycardia, conjunctival congestion and anxiety. Every body system is affected, although acute toxicity of cannabis is very rare.<sup>28</sup> The pharmacological actions of marijuana are complex and include a unique blend of effects of alcohol, opioids, tranquilisers and hallucinogens. Therefore, the clinical picture could be very unpredictable and the diagnosis is often difficult. A high level of suspicion is necessary. Marijuana and alcohol are frequently used together, yet there has been little study of how the presence of one drug

might affect the consumption of the other.

A distinct withdrawal syndrome may be observed following a relatively short period of recreational marijuana use. Johnston et al<sup>29</sup> reported that dependence might, in fact, be a significant consequence of repeated, daily intake of cannabinoids. Abstinence following exposure to 4 or 5 marijuana cigarettes a day (1.8% to 3.1% of THC), for even a short period of time (3 days), was associated with a substantially increased latency to fall asleep and rapid eye movement.<sup>30</sup> Given the negative mood and behavioural symptoms associated with marijuana abstinence following recreational drug intake on a daily basis, it appears likely that the onset of the withdrawal syndrome may partially maintain chronic marijuana use.<sup>30</sup> A similar pattern has been reported with other drugs, such as nicotine and caffeine.

### Marijuana in Pregnancy

The active ingredient in marijuana, THC, freely crosses the placental barrier and directly affects the fetus. Since most marijuana-addicted parturients also abuse other substances, such as tobacco, cocaine and alcohol, it is difficult to identify the specific effects of cannabis on the fetus.<sup>31</sup> It appears that the chronic use of marijuana results in decreased uteroplacental perfusion and intrauterine fetal growth restriction (IUGR).<sup>31</sup> It may alter the pituitary-adrenal axis and hormone production, adversely affecting fertility and pregnancy.<sup>32</sup> Suppression of ovulation has been reported in chronic cannabis smoking.<sup>18</sup> The production of both oestrogen and progesterone by the human placenta may also be altered. There is some evidence that chronic cannabis use may be associated with functional brain changes and subtle impairment in cognitive function.<sup>33</sup>

The effects of chronic cannabis exposure result in significant changes in the respiratory system, including bronchitis, squamous metaplasia and emphysema.<sup>34</sup> Smoke from cannabis cigarettes is known to suppress both the hormonal and cell-mediated immune responses.<sup>18</sup> Although marijuana is not an established human teratogen, recent well-conducted studies suggest that it might have subtle negative effects on neurobehavioural outcomes, including sleep disturbances, impaired visual problem-solving, hyperactivity, impassivity, inattention and increased delinquency.<sup>35</sup> Low neonatal birth weight, increased risk of complications during labour and delayed cognitive development in infants of cannabis-addicted mothers have been reported.<sup>36</sup> Hatch and Bracken,<sup>37</sup> in a prospective study of 4000 pregnancies in marijuana-abusing mothers, reported an increase in the incidence of low birth weight (<2500 g) infants and small for gestational age infants. In the same study, marijuana was also related to preterm delivery. Scragg et al<sup>38</sup> concluded that frequent maternal

cannabis use may be a risk factor for sudden infant death syndrome. However, this finding requires further research. Therefore, one would be prudent to avoid marijuana use during pregnancy, just as one would do with most other drugs, which might affect the fetal well-being.

### Anaesthetic Implications

Cannabis has a biphasic effect on the autonomic nervous system.<sup>39</sup> At low or moderate doses, the drug leads to an increase in sympathetic activity and a reduction in parasympathetic activity, resulting in tachycardia and an increase in cardiac output. At high doses, sympathetic activity is inhibited and parasympathetic activity is increased, leading to bradycardia and hypotension.<sup>40</sup> An increase in supraventricular and ventricular ectopic activity may occur; however, life-threatening tachycardia or bradyarrhythmias have not been reported. Reversible ST segment (plateau phase of ventricular repolarisation) and T wave (rapid phase of ventricular repolarisation) abnormalities have been reported following marijuana intake. However, it is not clear whether these changes are related to drug ingestion independently of effects on the heart rate.<sup>40</sup> The anaesthesiologist should entertain the possibility of drug abuse when conducting the differential diagnosis of unexplained intraoperative cardiovascular or autonomic nervous system abnormalities.

The cardiovascular effects of marijuana (myocardial depression and tachycardia) may potentiate the effects of anaesthetic drugs affecting the heart rate and arterial pressure. Adverse interactions of marijuana with propranolol and physostigmine have been reported.<sup>41</sup> Cannabis may enhance the sedative-hypnotic effects of other drugs that depress the central nervous system. Studies have shown cross-tolerance of cannabis with alcohol, barbiturates, opioids, benzodiazepines and phenothiazines.<sup>42</sup> During general anaesthesia, the additive effects of marijuana and potent inhaled anaesthetic agents can result in pronounced myocardial depression.<sup>43</sup> In patients with a history of acute marijuana abuse, agents that increase the heart rate, such as ketamine, pancuronium, atropine and epinephrine, should be avoided.

Cannabis inhalation leads to impairment of the lung function similar to tobacco smoking. It has been reported that regular marijuana use appears to be at least as damaging to the airway epithelium as smoking tobacco, despite the smaller daily number of marijuana joints smoked. Marijuana and tobacco appear to have an additive effect on the bronchial epithelial function. Oropharyngitis and uvular oedema causing airway obstruction under general anaesthesia have been reported.<sup>44</sup> In addition, adverse psychiatric and autonomic reactions to cannabis may interfere with the safe induction of anaesthesia and

postoperative recovery.

It is a common consensus that vaginal delivery and regional anaesthesia, are, respectively, the preferred obstetric and anaesthetic management choices for marijuana-abusing parturients. However, after it has been determined that a parturient is using marijuana in pregnancy, the obstetrician and the obstetric anaesthesiologist must decide on individual (case-to-case) basis whether the patient is a candidate for vaginal delivery and regional anaesthesia.

**Conclusion**

Maternal marijuana abuse in pregnancy continues to increase around the world. The diverse clinical manifestations of cannabinoids, combined with the physiologic changes of pregnancy, and pathophysiology of coexisting pregnancy-related disease might lead to serious complications and significantly impact anaesthetic management. An understanding of the physiology of pregnancy, pathophysiology of pregnancy-specific disorders and anaesthetic implications of marijuana, as well as other drugs' abuse in pregnancy, is needed to tailor a safe anaesthetic plan for these high-risk patients. In the absence of uniform guidelines on the management of pregnant patients with a history of drug abuse, including marijuana, the decision regarding peripartum analgesia or anaesthesia should be individualised.

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