Cannabis and its effect on anesthesia

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The author presents a timely discussion of the effects of cannabis on anesthesia. He explores the pharmacology of cannabis and alerts the anesthetist to possible interactions between anesthetic agents and marijuana.

Anesthetists are aware of the growing popularity of marijuana (cannabis). They see more of their patients admitting to its use. However, many anesthetists are not aware of the potential adverse effects which may occur if marijuana is taken prior to the administration of an anesthetic. By itself, marijuana may cause cardiac arrhythmias, cardiac and respiratory depression, or even pulmonary edema. In conjunction with an anesthetic, marijuana can cause severe complications.

Marijuana defined

Marijuana, or cannabis, is obtained from the hemp plant. The plant is commonly cut up, dried, incorporated into cigarettes, and smoked. Cannabis is by no means a simple compound; it contains more than 286 different chemicals.[1]

The chemical composition is made up of several isomers of tetrahydrocannabinol, and several cannabinoids. The compounds which have the most impact on anesthesia are two of the cannabinoids; *cannabinol* and *cannabidiol.* Other compounds which impact on anesthesia are: delta 9 tetrahydrocannabinol and delta 8 tetrahydrocannabinol, as well as its metabolite II hydroxy tetrahydrocannabinol. (For the sake of brevity tetrahydrocannabinol will be referred to as THC, with the appropriate prefix.)

Recently published research on the potential effects of cannabis shows that it is: ". . . more potent than the synthetic tranquilizer chlorpromazine, the sedative and hypotensive alkaloid reserpine, the powerful short acting barbiturate thiopentone, the hallucinogen lysergide or morphine."[2]

As with any other drug the systemic level would be determined upon the amount ingested and the potency of the drug, the half life, and the concomitant use of other drugs which may affect the metabolism of the ingested drug. With a prescribed medication, the anesthetist generally knows exactly what he is working with or against. With cannabis, however, the amount of the drug absorbed is probably impossible for the anesthetist to determine by himself.

The social and legal implications of cannabis use may cause the patient to be reluctant in discussing the extent of his involvement with the drug, especially with a person unfamiliar to him. In addition, the form in which cannabis is obtained (primarily in bulk or in pre-rolled cigarettes) precludes the possibility that the average consumer may know the true drug content of the amount absorbed.

THC content varies depending upon the type of plant used and the form in which it is ingested.

"Hashish oil is a more concentrated cannabis product which has a THC content of 60-90%, while a typical marijuana cigarette contains less than 3%."[3]

Cannabis is sometimes mixed with hashish oil to increase the subjective high, thus increasing the total THC content. Highly lipid soluble, THC has a tendency to accumulate in the fatty tissues of the body such as the brain and gonads. The half life of THC is 72 hours, and THC metabolites are recoverable in the urine for more than a week.[3] The tricyclic antidepressive drugs inhibit the metabolic transformation of THC in the liver by 20-30%.[2]

Determining the degree of drug interaction

When confronted with a patient who smokes cannabis, the anesthetist should consider the frequency of cannabis use as well as the time elapsed since the last usage. This would allow for an estimation of the relative activity of the drug, in much the same manner as determination is made of the relative activity of any other drug.

A drug taken on an as circumstances may require (PRN) basis with low frequency may not interact with an anesthetic to the same degree as the same drug taken on a chronic basis. This information along with the knowledge of the half life, the pharmacological action, and interactions of the drug better prepare the anesthetist to adapt his anesthetic to the situation at hand.

Pharmacological activity of the cannabinoids

The majority of the effects of cannabis on the body are accomplished by two of the cannabinoids and THC and its metabolites. The two cannabinoids, cannabidiol and cannabinol, have been found to possess various pharmacological properties which are:

"Cannabidiol potentiates barbiturate sleeping time, has anti-epileptic properties, and decreases the rate of serotonin uptake. . . . cannabinol decreases intestinal motility and is a potent prostaglandin synthetase inhibitor.[3]

The degree to which cannabidiol potentiates barbiturate sleeping time depends upon several factors, including the amount of the barbiturate used, the amount of cannabis ingested, and any factor which may alter the metabolism or redistribution of either the barbiturate or cannabidiol, such as the use of tricyclic antidepressants, chronic heavy alcohol ingestion, and so on. The anticonvulsant effect of cannabis is not clinically useful, as tolerance to this effect rapidly develops with chronic use.

It is interesting to note that cannabidiol's effect on serotonin places it in a class of drugs related to lysergic acid diethylamide (LSD), mescaline, the tricyclic compounds, amphetamines, morphine, and others. Crombie and his associates showed that the level of serotonin in the brain increased four-fold "two hours after the administration of cannabis resin."[2] The mode of action of cannabidiol on serotonin appears similar to that of the tricyclic antidepressant imipramine. Because of the diversity of serotonin, its total interaction with the cannabinoids is difficult to fully assess.

Cannabidiol is not alone in its ability to affect the autacoids. Cannabinol decreases prostaglandin synthetase. The spectrum of action of the prostaglandins are as numerous as they are diverse, with different prostaglandins exhibiting different effects on the body. The action of the cannabinoids on serotonin and prostaglandin takes cannabis well beyond the limits of any simple drug and increases the difficulty in ascertaining its total systemic impact, especially when used in conjunction with a general anesthetic.

THC and its metabolites

After absorbtion, THC is carried in the lipid-containing constituents of the plasma, where it is eventually distributed to and absorbed by the various fatty tissues, an action comparable to that of thiopentone. Delta 9 THC is the isomer believed responsible for most of the psychological effects seen with cannabis use. However, delta 8 THC, an isomer which occurs in small amounts, has similar action. Delta 9 THC is rapidly converted to II hydroxy delta 8 THC by the microsomal enzyme system. This metabolite, when given alone in clinical experiments, produced a much more profound psychological high than did the parent compound.

Of primary importance to the anesthetist are the effects of THC upon the cardiovascular and respiratory systems, the heat regulating system, and acetylcholine. THC causes cardiac depression by depressing ". . . the calcium dependent ATPase activity of the cardiac muscle sarcoplasma."[2] On the electrocardiogram, this depression may appear as premature ventricular contractions (PVCs), arrhythmias with flattening of the T-wave, T-wave inversion, or a decrease in voltage of the P-wave. Tachycardia, which is believed to be caused by increased levels of epinephrine, may be seen. However, bradycardia is also a recognized effect of THC. THC's much heralded effect of bronchodilation may be overshadowed by the fact, that in

toxic doses, pulmonary depression or pulmonary edema may occur.[2]

THC depresses the body's temperature regulatory mechanism. A drop in body temperature could result if the subject is exposed to a cold environment after smoking. THC depletes the stores of acetylcholine in synaptosome preparations by as much as 50%, thus THC can be considered to have an anticholinergic effect.

Anesthetic considerations

In its relation to anesthetic agents, cannabis has some synergistic as well as antagonistic effects. The synergistic effects include the following:

1. An increase in the sleeping time of barbiturates by cannabidiol.
2. Potentiation of the nondepolarizing muscle relaxants created by the anticholinergic effects of THC.
3. ". . . injected noradrenalin [norepinephrine] is potentiated by both the cannabinoids and THC."[2]
4. As a good substrate, THC competitively inhibits any drug dependent upon the nonspecific enzyme system for metabolism.
5. Any drug which causes respiratory or cardiac depression may have its effect augmented by cannabis.
6. The inhalational anesthetics which sensitize the myocardium to the catecholamines may have a more profound response due to the increased level of epinephrine. However, THC, which increases the level of 5Ht (serotonin) in the brain, is antagonistic to reserpine, which normally lowers the 5Ht level.

In considering the far-reaching effects of cannabis, anesthesia should probably be avoided *if at all possible* for those individuals who have used cannabis within the preceeding 72 hours. If anesthesia is unavoidable, then regional anesthesia is the preferred technique with special emphasis placed on maintaining the integrity of the respiratory and circulatory systems.

Conclusion

Cannabis is a drug with far-reaching social, legal, and medical implications. Further research needs to be done regarding the interactions of cannabis in conjunction with anesthetic drugs on serotonin and prostaglandin. Today, the cannabis user poses a very real challenge for the anesthetist. It is imperative that the anesthetist understand the actions of anesthetic agents, the actions of cannabis and the possible interactions of both.

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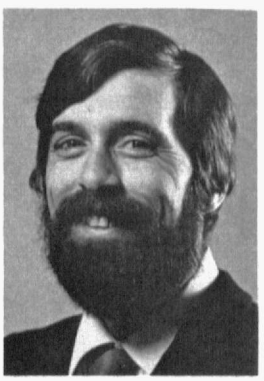

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