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Pharmacological Interferences in the Management of the Acute Effects of Cannabis

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Abstract

Cannabis intoxication is associated with number of physical and mental health possibilities with consequent social costs. Nevertheless, little consideration has been given to the examination of likely pharmacological interactions in this situation. Research was done on the PubMed, Lilacs, and Scielo online databases using the terminologies cannabis, intoxication, psychosis, anxiety, and treatment which involved of case reports and controlled clinical trials and are obtainable according to interventions targeting the physiological, psychiatric, and cognitive symptoms provoked by cannabis. The pharmacological interventions reported in these studies included beta-blockers, anti arrhythmic agents, antagonists of CB-1 and GABA-benzodiazepine receptors, antipsychotics, and cannabidiol. Although scarce, the evidence on pharmacological interventions for the management of cannabis intoxication suggests that propanolol and rimonabant are the most effective compounds currently available to treat the physiological and subjective effects of the drug. Additional studies are necessary to establish the real effectiveness of these two medications, as well as the effectiveness of other candidate compounds to counteract the effects of cannabis intoxication, such as cannabidiol and flumazenil.

Keywords: Cannabis; Studies; Acute effects; Psychosis; Anxiety; Pharmacological treatment

Abbreviations: THC: Tetrahydrocannabinol; WHO: World Health Organization; GABA: Gamma Amino Butyric Acid; NSAIDs: Nonsteroidal Antiinflammatory Drugs; LSD: Lysergic Acid Diethylamide; SAMSHA: The Substance Abuse and Mental Health Services Administration; AC: Activated Charcoal.

Introduction

Cannabis sativa has Δ9-tetrahydrocannabinol (Δ9-THC), isolated in the 1960s, as its main psychoactive compound. The concentration of Δ9-THC in the different presentations of cannabis (marijuana, hashish, and skunk) is proportional to the intensity of its toxic effects. In cannabis, considered to be the most consumed illicit substance in the world, increased concentrations of Δ9THC have been reported in recent years [1,2]. At the same time, there has been an increase in the number of patients reporting to specialized services with complaints related to the use of cannabis [3]. A survey in the USA revealed that between 1992 and 1998 the demand for treatment at specialized services has doubled, with the

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percentage of admissions for the treatment of cannabis-related disorders (23%) approaching the admission rates relative to cocaine (27%) and heroine (23%), considering all drug-related hospitalizations.

The use of cannabis has been associated with several psychological, behavioral, and social problems. Besides the chronic effects of the continued use of cannabis, such as dependence, abstinence, varying degree of cognitive impairment, and increased risk of respiratory disorders, its acute effects have also been related to significant physical and mental health problems, and an increasing number of emergency admissions has been linked to cannabis use [4,5].

According to the World Health Organization (WHO), 147 million people, or 2.5 percent of the world population, use cannabis (marijuana), making it the world's most widely cultivated, trafficked, and abused illicit substance [6]. Use is high in the adolescent age group. As an example, among surveyed adolescents in the United States, approximately 7 percent of 8 graders, 15 percent of 10 graders, and 21 percent of 12 graders reported cannabis use in the past month [7]. Several countries, including Canada, Switzerland, and the United States are contemplating or actually liberalizing laws governing cannabis use [8]. At the United States federal level, cannabis products are classified as Schedule 1, i.e., no currently accepted medical use and a high potential for abuse [9,10]. However, over 20 states have decriminalized medical marijuana or are reviewing legislation to allow low-dose delta-9 tetrahydrocannabinol [11].

The intoxication by cannabis is associated with subjective symptoms of euphoria, perceptual distortion, continuous giggling, sedation, lethargy, impaired perception of time, difficulties in the performance of complex mental processes, impaired judgment and social withdrawal. In addition, physical signs of conjunctival hyperemia, increased appetite, dry mouth, and tachycardia can develop in the period of approximately two hours after the use of the substance, corresponding to the plasmatic peak of Δ9-THC. In general, the acute toxicity of cannabinoids is considered to be low. Nevertheless, there are reports of death by brain infarction-especially among teenagers following the acute use of marijuana as well as of cases of patients with severe sequelae resulting from this complication. Similarly, there are reports of coma in children induced by the accidental intake of cannabis, in addition to cases of cardiac arrhythmia, acute myocardial infarction, and transitory ischemic attacks. Factors such as increased heart effort, elevated levels of catecholamine and carboxy hemoglobin in the blood, as well as the occurrence of postural hypotension are among the most commonly reported factors of cardiovascular disease associated with intoxication by cannabis [12].

It is known that cannabis intoxication leads to impaired motor ability, attention, and short-term memory. In accordance with this, many studies have found a higher prevalence of cannabis use among drivers involved in accidents than in the general population. Currently, there is consistent evidence that people who use cannabis on a regular basis have a higher proportion of acute psychiatric disorders, aggravated by other factors such as personality traits, pre-existing vulnerability, and substance use at an early age. First time use and the dose of cannabis are among the main factors related to this occurrence. Panic and anxiety attacks are among the most commonly reported psychiatric symptoms related to cannabis intoxication and are often responsible for the discontinuation of the use of the substance. Acute psychotic episodes related to cannabis intoxication are described in terms of confusion, disorientation, amnesia, depersonalization, delusions, hallucinations, paranoid ideation, psychomotor agitation, labile affect, and hostility.

These symptoms are usually gone after a maximum of one-week abstinence. In some cases, psychotic episodes secondary to the use of cannabis can persist for a substantial period of time after the acute intoxication and may have some of the features of acute schizophreniform disorders. Further evidence is provided by a systematic review on longitudinal and population-based studies, which showed that cannabis use significantly increases the risk of developing psychotic illnesses in a dose-dependent manner. There is strong evidence that cannabis use can have major detrimental effects on the course of the illness when patients with a pre-existing psychotic condition continue to use the drug. In addition to worsening the outcome and exacerbating the symptoms, cannabis use by people with psychosis can lead to sudden behavioral disturbances such as increased proneness to violence, criminal activity, suspiciousness, and hallucinations. Lately, attempts have been made to better understand the neurobiological mechanisms underlying cannabis related disorders and the functioning of the endogenous cannabinoid system. There is increasing interest for the development of medications capable to reduce the morbidity of these disorders. Because marijuana intoxication is a major public health problem with a growing demand for assistance at emergency departments, the study of possible pharmacological interventions that might help in the management of the acute effects of cannabis use is of great clinical and social relevance [13,14].

The dried flower of the marijuana plant has a large range of THC content, ranging from 1 to 20 percent of the total weight; however, much variability exists among marijuana samples. In general, marijuana potency has increased over the past 20 years. Common slang terms for marijuana include "pot," "grass," "dope," "MJ," "Mary Jane," "doobie," "hooch," "weed," "hash," "reefers," and "ganja". Chemical analogues of THC, called "synthetic cannabinoids" may have been available in Europe as early as 2004, and were first reported in the United States in December 2008. The clinical effects can be similar to natural marijuana intoxication but may also result in more severe life-threatening symptoms [15].

Pharmacology and Toxicity [16,17]

Site of action - The cannabinoid receptor is a G-protein linked receptor, which inhibits adenylylcyclase and stimulates potassium conductance. There are two known cannabinoid receptors: CB1 and CB2.

a. CB1 is found in the central nervous system including the basal ganglia, substantia nigra, cerebellum, hippocampus, and cerebral cortex. It acts presynaptically and inhibits release of several neurotransmitters including acetylcholine, L-glutamate, gamma amino butyric acid (GABA), nor epinephrine, dopamine, and 5hydroxytryptamine.
b. CB2 is found peripherally in the immune system tissues (eg., splenic macrophages and B lymphocytes), peripheral nerve terminals, and vas deferens. It is postulated that it plays a role in regulation of immune responses and inflammatory reactions. Anandamide and palmitoylethanolamide are known endogenous cannabinoid receptor ligands.

Pharmacokinetics

The pharmacokinetics and pharmacodynamics of delta-9 tetrahydrocannabinol (THC) vary by route of exposure as follows [18,19].

Inhaled Marijuana

After inhalation of *marijuana* smoke, onset of psychoactive effects occurs rapidly with peak effects felt at 15 to 30 minutes and lasting up to four hours. These effects mirror plasma delta-9 tetrahydrocannabinol (THC) concentrations. Approximately 2 to 3 mg of inhaled THC is sufficient to produce drug effects in a naïve user. Pulmonary bioavailability varies from 10 to 35 percent of an inhaled dose and is determined by the depth of inhalation along with the duration of puffing and breath holding.

Ingested Marijuana

When compared to inhalation, cannabis ingestion has a delayed onset of psychoactive effects that ranges from 30 minutes to three hours. Clinical effects may last up to 12 hours. Orally administered cannabis has low bioavailability (5 to 20 percent) because of chemical degradation in gastric acid and substantial first-pass metabolism in the liver. In naïve users, psychotropic effects occur with 5 to 20 mg of ingested THC. THC is lipid soluble, highly protein-bound (95 to 99 percent), and has a volume of distribution of 2.5 to 3.5 L/kg.

THC metabolism occurs via hepatic cytochromes oxidases, CYP2C9 and 3A4. The primary active metabolite is 11hydroxy THC, and the inactivated metabolite is THC-carboxylase. THC crosses the placenta with fetal plasma concentrations 10 to 30 percent of maternal concentrations. It also accumulates in breast milk at a concentration as high as eight times maternal plasma concentrations. After metabolism, THC is mostly excreted as hydroxylated and carboxylated metabolites via feces (65 percent) and urine (20 percent). Although difficult to measure, the elimination half-life of THC is slow, ranging from 25 to 36 hours. This lengthy half-life is likely due to slow release from lipid storage compartments and enters hepatic circulation. Elimination half-life is longer in regular cannabis users.

Recreational use

Recreational marijuana use often consists of smoking the dried flower in the form of rolled cigarettes (joints) and water bongs. THC is also extracted using various solvents (butane, ethanol, hexane, isopropanol) to create highly concentrated products (60 to 99 percent of weight) including oils and tinctures called "wax," "dabs," "budder," and "shatters". In addition to being smoked, these highly concentrated products are also vaporized (eg, using electronic cigarettes) or mixed in food products (such as brownies, cakes, candies, and beverages) and ingested.

In regions where marijuana use is legal, ingested forms are popular and may pose a risk of unintentional ingestion by children or excessive ingestion by adults. As an example, in Colorado, some companies have produced packaging for marijuana products that mimic popular candy. Furthermore, many of these products contain up to four times the suggested dose of 10mg [20,21].

Medicinal use

Medicinal marijuana is supplied as dried flowers of the Cannabis sativa plant that are smoked as described for recreational cannabis use. Derivatives of cannabinoids are

also available as pharmaceuticals in some countries including oral preparations (dronabinol and nabilone) and a spray for buccal use (nabiximols). Marijuana and its components have been proposed for various medicinal purposes, such as chronic severe pain (eg, due to cancer), refractory nausea and vomiting, anorexia and cachexia, glaucoma, and seizures. However, none have been proven to have greater efficacy than other currently available medications. Of these indications, medical marijuana is most frequently prescribed for severe or chronic pain. An oromucosal spray containing THC and cannabidiol (Sativex), also called nabiximols, has been shown to have some efficacy as a multipurpose analgesic in combination with traditional therapy and is approved for use in Canada and elsewhere but not in the United States. No controlled studies demonstrate the efficacy of inhaled marijuana as an adjunct to traditional pain medications for patients with cancer-related pain. Trials in patients with multiple sclerosis have failed to show consistent pain reduction.

Although inhaled, buccal, or ingested marijuana has shown some efficacy for refractory nausea and vomiting or glaucoma, consensus expert guidelines do not support its use. Cannabinoids demonstrate anticonvulsant properties in animal models, but no randomized controlled human trials have proven efficacy [22,23].

Adverse toxic effects

Recreational cannabis intake to achieve psychoactive effects can often result in adverse effects because there is no clear demarcation between doses that achieve symptoms desired by a marijuana user and noxious effects. In adolescents and adults, inhaled doses of 2 to 3 mg of delta-9 tetrahydrocannabinol (THC) and ingested doses of 5 to 20 mg THC impair attention, concentration, short-term memory and executive functioning. More severe adverse effects may occur at doses >7.5 mg/m THC, including nausea, postural hypotension, delirium, panic attacks, anxiety, and myoclonic jerking. Psychosis has also been associated with use of higher potency/concentrated marijuana products [24,25].

Toxicity in children is most often reported after ingestion of a highly concentrated food product or hashish resin. Estimated oral doses from 5 to 300 mg in pediatrics have caused a range of symptoms such as mild sleepiness, ataxia, behavior changes, excessive and purposeless motor activity of the extremities (hyperkinesis), coma, and respiratory depression with more severe intoxication correlated with higher estimated doses. For example, in a small cohort of 38 children presenting to an emergency department for acute marijuana intoxication after ingestion, degree of symptoms corresponded to an estimated dose as follows: 3.2 mg/kg of THC led to observation and minimal medical intervention, 7.2 mg/kg of THC led to admission to an inpatient floor and moderate medical intervention, and 13 mg/kg of THC led to admission to an intensive care unit and major medical interventions. Patients without prior THC exposure more commonly had lethargy or somnolence and had a longer duration of clinical symptoms. Similarly, as concentrated hashish resin has become more available in France, a corresponding increase in the number and severity of annual admissions has occurred among infants and young children.

Clinical Manifestations

The clinical manifestations of acute cannabis (marijuana) intoxication vary according to age. Neurologic abnormalities are more prominent in children and include ataxia, excessive and purposeless motor activity of the extremities (hyperkinesis), lethargy, and prolonged coma, which may be life-threatening. Acute marijuana intoxication is an unusual primary complaint in adolescents and adults. Patients who come to medical attention are more likely to have hyper emesis or behavioral problems (eg, dysphoria or agitation) caused by adverse cannabis effects or medical emergencies (eg, bronchospasm or pneumothorax) associated with the method of inhalation. Chest pain with myocardial infarction in young adults without any prior history of coronary artery abnormalities has also been rarely described. The issue of causation is unclear, however, in light of the frequency of cannabis use in the general population and the presence of unsuspected atherosclerosis or other cardiac condition in some of these patients [24,26].

Children

In children, acute marijuana intoxication typically occurs after exploratory ingestion of marijuana intended for adult use. Less commonly, intentional exposure of children by caretakers, including encouragement of cannabis inhalation to promote sleepiness and to decrease activity, has been reported. Pediatric ingestions of marijuana products happen more frequently in regions with decriminalization or legalization of cannabis use. After limited exposures, children may display sleepiness, euphoria, irritability, and other changes in behavior. Vital signs may show sympathomimetic effects (eg, tachycardia and hypertension) or, in patients with depressed mental status, bradycardia. Nausea, vomiting, conjunctival injection, nystagmus, ataxia, and, in verbal children, slurred speech may also be present.

Dilated pupils have frequently been reported, although miosis has also been described. In large overdoses (eg, ingestion of edible products, concentrated oils, or hashish), coma with apnea or depressed respirations can occur. Although not typical of pediatric cannabis intoxication, seizures have also been reported. In one instance, cocaine was also found on urine screening [27]. In one retrospective series of 29 children under age 3 admitted with documented cannabis exposure, seizures occurred in four patients, all of whom had ingested hashish resin.

Adolescents and adults

The physiologic signs of cannabis intoxication in adolescents and adults include:

a. Tachycardia
b. Increased blood pressure or, especially in the elderly, orthostatic hypotension
c. Increased respiratory rate
d. Conjunctival injection (red eye)
e. Dry mouth
f. Increased appetite
g. Nystagmus
h. Ataxia
i. Slurred speech
j. Acute exacerbations and poor symptom control in patients with asthma.
k. Pneumomediastinum and pneumothorax suggested by tachypnea, chest pain, and subcutaneous emphysemas caused by deep inhalation with breath holding.
l. Rarely, angina and myocardial infarction.
m. The risk for myocardial infarction among regular cannabis users has been found to be as high as 4.8 times baseline.

Drug testing for cannabinoids

Hospital testing for cannabis typically consists of urine drug screen. Standard urine drug screens that are available in most healthcare facilities consist of immunoassays that detect delta-9 tetrahydrocannabinol (THC) metabolites, primarily THC carboxylase. The lower limits of detection range from 20 to 100ng/mL, depending upon the specific assay [28]. The Substance Abuse and Mental Health Services Administration (SAMSHA) standard is 50ng/mL, with confirmatory testing using 15ng/mL, as the lower limits of detection [29]. In situations where a positive screen for cannabis has legal implications or may impact school attendance or sports participation, individuals may claim that the test results from passive inhalation of marijuana smoked by others. In adolescents and adults, it is difficult to achieve sufficient concentrations from secondhand smoke from typical cannabis cigarettes to detect metabolite concentrations above most urine drug screen limits [25,30]. However, studies using products with higher THC content (typical of what is more commonly used since 2005).

Impairment of cognition, coordination, and judgment lasts much longer than the subjective mood change of feeling "high". Psychomotor impairment lasts for 12 to 24 hours due to accumulation of marijuana in adipose tissue, slow release of THC from fatty tissue stores, and enterohepatic recirculation. However, a marijuana user may think that he or she is no longer impaired several hours after the acute mood-altering effects have resolved. As an example, a placebo-controlled trial with licensed pilots found that smoking marijuana impaired performance on a flight simulator for up to 24 hours, although only one of the nine subjects possessed self-awareness of this.

False positives for cannabinoids are rare, because the chemical structure is unique, and immunoassays are targeted toward metabolites of THC. Reported false positives for THC include: dronabinol, efavirenz, proton pump inhibitors, hemp seed oil, nonsteroidal antiinflammatory drugs (NSAIDs), and baby wash products in infants. However, most package inserts for commercially available immunoassays will list possible false positives for their cannabinoid assay. If required for clinical or social indications, confirmatory testing of urine, blood or serum can be sent to reference labs by gas chromatography and mass spectrophotometry. However, results of confirmatory testing do not return quickly enough to affect clinical care.

Other ancillary studies -Most adolescents and adults do not warrant any testing for the diagnosis or treatment of acute cannabis (marijuana) intoxication. Patients with chest pain suggestive of myocardial ischemia or infarction warrant a 12-lead electrocardiogram and possibly cardiac biomarkers (eg, troponin T or I). Chest radiograph may assist in the diagnosis of stable patients with chest pain indicative of a spontaneous pneumothorax. However, patients with signs of a tension pneumothorax should undergo decompression prior to chest radiography. Bedside ultrasound may assist with rapid diagnosis of pneumothorax in these unstable patients.

Children may warrant testing for other potential causes of altered mental status depending upon whether the exposure is known and based upon specific physical findings including rapid blood glucose, electrolytes, blood gas analysis, and neuro imaging (eg, computed tomography of the head). Neuro imaging should be avoided in known cannabis exposures unless focal

neurologic findings are also present or concerns for other etiologies such as head trauma exist.

Diagnosis

Regardless of age, acute cannabis intoxication is a clinical diagnosis. However, diagnosis in the pediatric population can be difficult because a history of exposure is often lacking and the symptoms of marijuana exposure are non specific. Thus, urine drug screens can be helpful in confirming the diagnosis because any positive result in children identifies acute exposure. Urine drug screens are less helpful in adolescents and adults for the diagnosis of acute intoxication. Although testing is usually positive several hours after acute exposure it can also be positive well after symptoms have resolved. As an example, positive results for delta-9 tetrahydrocannabinol metabolites have been reported up to 10 days after weekly use and up to 25 days for after daily use [31]. Thus, cannabis testing does not provide any specific information on the timeline of exposure or correlate with severity of intoxication.

Management

The management of cannabis (marijuana) intoxication consists of supportive care. Because of the differences in toxic manifestations the management differs significantly by age.

Children

Children with cannabis (marijuana) exposure are much more likely to demonstrate severe or life threatening toxicity consisting of excessive and purposeless motor activity (hyperkinesis) or deep coma. Consultation with a regional poison control center and a medical toxicologist is encouraged for all symptomatic exposures.

Treatment is supportive and consists of the following measures:
The duration of coma is typically one to two days Full recovery is expected.

a. Lysergic acid diethylamide (LSD) and other hallucinogens (eg, phencyclidine [PCP], dextromethorphan, or psilocybin).
b. MDMA (ecstasy) (see "MDMA (ecstasy) intoxication", section on 'Clinical features').
c. Synthetic cannabinoids (see "Synthetic cannabinoids: Acute intoxication", section on 'Clinical manifestations').
d. Maintain airway, breathing, and circulation. Patients with lethargy and coma should receive supplemental oxygen, assessment and support of airway and breathing, and vascular access. Patients with apnea or at risk for aspiration should undergo rapid sequence endo tracheal intubation and receive assisted ventilation.
e. Measure rapid blood glucose to exclude hypoglycemia.
f. Administer naloxone to patients presenting with features of opioid intoxication. Naloxone will not reverse coma due to cannabis toxicity.
g. Seizures - Seizures have rarely been described after cannabis intoxication in children and may be associated with coingestants (eg, cocaine). Initial treatment of toxin-associated seizures consists of benzodiazepines (eg, lorazepam or midazolam). If seizures persist despite multiple doses of benzodiazepines, then treatment for status epilepticus caused by toxins. Dysphoria - Dysphoria is not a common presentation in pediatric marijuana exposure. However, if symptoms of marked anxiety or agitation develop, benzodiazepines (eg, lorazepam) are frequently effective and have a low adverse effect profile.

Adolescents and adults

Mild intoxication - Mild intoxication with Dysphoria can be a common presentation in either naïve or chronic marijuana users after ingestion or inhalation of a high-potency product such as an edible or concentrate. Most patients can be managed with a dimly lit room, reassurance, and decreased stimulation. Short-acting benzodiazepines (eg, lorazepam) can be helpful in controlling symptoms of anxiety and have a low side effect profile.

Severe intoxication

Severe physiologic effects are rare after cannabis use and their presence should prompt the clinician to consider co ingestion of other recreational drugs including cocaine, amphetamines, and phencyclidine or coexisting mental illness. (See 'Adolescents and adults' above). Marked agitation or combativeness not responsive to reassurance and benzodiazepines may necessitate the use of other medications, depending upon the cause, and is rarely encountered with intoxication from cannabis alone. The approach to sedation of the acutely agitated or violent adult is discussed in detail separately.

Chest pain

Chest pain in association with cannabis use should be managed according to etiology as follows:
Acute coronary syndrome – Substernal squeezing chest pain suggestive of myocardial ischemia or infarction may occur rarely in association with cannabis use. Patients

complaining of chest pain suggestive of coronary insufficiency should be evaluated for acute coronary syndrome and treated accordingly.

Pneumothorax or pneumo mediastinum

Inhalation and breath holding during cannabis use may cause a pneumothorax or pneumo mediastinum with sharp, pleuritic chest pain and subcutaneous crepitus. Management of a pneumothorax depends upon its size and includes oxygen administration and, if necessary, evacuation with needle decompression or chest tube insertion. No specific treatment is necessary for uncomplicated pneumo mediastinum.

Asthma exacerbation

Cannabis use may cause chest tightness with bronchospasm and wheezing. Standard therapy for status asthmaticus should be provided.

Gastrointestinal decontamination

We suggest that patients who ingest cannabis (marijuana) not undergo gastrointestinal decontamination with activated charcoal (AC). After ingestion, most symptoms are delayed up to three hours, which limits the efficacy of AC. Also, the clinical effects of cannabis ingestion are often limited and good outcomes occur with supportive care alone. In addition, in children, clinical toxicity may include rapid onset of altered mental status or vomiting, which may raise the risk of aspiration if AC is administered. There is no role for gastrointestinal decontamination after toxicity caused by inhaled cannabis.

Cannabis hyper emesis syndrome

Cannabis hyper emesis syndrome is typically seen with chronic marijuana use but can be seen with acute or acute chronic use. Patients may complain of abdominal pain, vomiting, or nausea that is typically relieved by hot showers. Acute treatment consists of symptomatic care including intravenous fluid hydration, antiemetic (eg, ondansetron and benzodiazepines). Cessation of marijuana use is also recommended. Limited observational evidence (case reports and case series) also suggests that topical capsaicin cream (supplied in concentrations of 0.025 to 0.1 percent) applied once in a thin film over the abdomen may improve acute severe abdominal pain and emesis in patients not responsive to ondansetron or benzodiazepines. Evidence is lacking to determine if capsaicin cream has a role for the treatment of chronic symptoms.

In addition, case reports have documented the successful use of haloperidol to abort severe episodes of hyper emesis not responsive to fluid hydration and administration of anti emetics, and benzodiazepines. In one instance, hospital admission was avoided after administration of 5 mg of haloperidol intravenously. However, more evidence is needed to evaluate the safety and efficacy of this therapy including the indications, dose, and route of administration.

Disposition

Disposition is determined by several factors including patient age, social circumstances, duration of toxicity, and type of symptoms as follows:

Children

The duration of symptoms after acute marijuana exposure in children can vary from four to 48 hours depending upon the dose ingested. Patients with persistent vomiting altered mental status or excessive, purposeless motor activity (hyperkinesis) warrant hospital admission. Patients who remain asymptomatic or become asymptomatic following exploratory ingestion of legally acquired cannabis products may be discharged after a brief observation period (eg, four to six hours after ingestion). Ingestion of illicit marijuana or intentional exposure of a child warrants involvement of a child abuse team, when possible, and should be reported to child protection services. (See "Child abuse: Social and medico legal issues", section on 'Reporting suspected abuse').

Adolescents and adults

Most symptoms after acute marijuana use in adults and adolescents resolve within a few hours and will not require hospital admission. Hospital admission may rarely be needed for prolonged delirium or agitation requiring repeated doses of benzodiazepines or antipsychotics. These patients should also be screened for substance use disorder, mood disorders, and, if needed, undergo psychiatric consultation and appropriate referrals to substance-use treatment programs. (See "Treatment of cannabis use disorder"). The disposition for patients with complications of marijuana use depends upon the degree of illness and response to therapy. Patients with proven myocardial infarction or pneumothorax requiring chest tube thoracostomy warrant hospital admission to an appropriate level of care [32,33].

Summary and Recommendations

Serious cannabis intoxication is rare in adolescents and adults. Exploratory ingestions of marijuana products have been described in young children and are more frequent in regions with decriminalization or legalization of cannabis use. Less commonly, intentional exposure of

children by caretakers, including encouragement of cannabis inhalation to promote sleepiness and to decrease activity, has been reported.

a. In young children, ingestion of cannabis (marijuana) may cause life-threatening coma with apnea or depressed respirations. Seizures have also been reported. Other features following limited pediatric exposures include behavioral changes, lethargy, and physiologic effects of intoxication as seen in adolescents and adults.
b. Children may warrant testing for other potential causes of altered mental status depending upon whether the exposure is known and based upon specific physical findings.
c. The findings of cannabis intoxication in adolescents and adults include tachycardia, blood pressure changes (hypertension, or in the elderly, orthostatic hypotension), conjunctival injection, dry mouth, increased appetite, nystagmus, ataxia, slurred speech, euphoria, perceptual changes, and psychomotor impairment.
d. Chest pain in adolescents and adults who use cannabis recreationally may arise from a pneumothorax, exacerbation of underlying pulmonary disease such as asthma, or, rarely, myocardial ischemia or infarction.
e. In adolescents and adults, no specific testing is necessary. Investigation for other intoxicants may be indicated if symptoms are prolonged, or if other marked physiologic abnormalities exist such as hyperthermia, acidosis, significant rhabdomyolysis, or end-organ toxicity.
f. Regardless of age, acute cannabis intoxication is a clinical diagnosis. Urine drug screens can be helpful in confirming the diagnosis in young children because any positive result identifies acute exposure. Urine drug screens are less helpful in adolescents and adults and are not routinely needed for diagnosis or management. (See 'Diagnosis' above and 'Drug testing for cannabinoids' above.) Management of young children with ingestion of cannabis (marijuana) consists of exclusion of hypoglycemia in patients with altered mental status and supportive care of coma. Excessive muscle activity (hyperkinesis) should be initially treated with benzodiazepines (eg, diazepam or lorazepam).
g. Most adolescents and adults presenting for treatment of acute cannabis intoxication have mild intoxication with Dysphoria that can be managed with a dimly lit room, reassurance, decreased stimulation, and, in some patients, benzodiazepines (eg, oral lorazepam).
h. Chest pain in association with cannabis use should be managed according to the underlying etiology (eg, acute coronary syndrome, pneumothorax, or asthma exacerbation).
i. We suggest that patients who ingest cannabis (marijuana), either unintentionally or for recreational use not undergo gastrointestinal decontamination with activated charcoal (AC) (Grade 2C).

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