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Edible Cannabis Toxicity in Young Children; An Emergent Serious Public Health Threat

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Abstract

Introduction

Acute encephalopathy and sometimes, respiratory depression are increasingly reported due to accidental ingestion of cannabis edibles. Six young children presented to a paediatric ED with acute encephalopathy. All had tetrahydrocannabinol positive urine tests. This is the first series of paediatric cannabis poisoning reported in Ireland.

Cases

Case 1: 5 yr. GCS 10, pupils 8mm. Significant hypotension. GCS normal 12 hours after ingestion.

Case 2: 4 yr. GCS 8. Pupils 5mm. Decorticate posturing and tachycardia. GCS 8 for 8 hours more and PICU for poor respiratory effort. Full recovery after 36 hours.

Case 3: 3 yr. GCS 7. Pupils 6mm. Tachycardia, hypoventilation and decorticate posturing. Three generalised seizures, at least 8 hours after ingestion. GCS normalised within 30 hours.

Outcome

Two cases were discharged from ED after 12 hours. 4 cases were admitted to the ward with one requiring PICU. Autonomic instability occurred in 3 cases and resolved early. All cases were referred to TUSLA.

Conclusion

Accidental cannabis poisoning in young children from edibles causes significant morbidity. This is a serious evolving paediatric public health threat with child protection issues. Recognition and notification of all cases presenting to our Emergency Departments is imperative.

Introduction

According to WHO, 147 million people worldwide use cannabis, making it the world's most widely cultivated, trafficked, and abused illicit substance.[1] It is the most abused controlled drug in Ireland.[2] Cannabis intoxication in the paediatric population has been described worldwide as decriminalisation and underenforcement becomes the norm.

Accidental ingestion of cannabis edibles in young children is increasingly reported in ED and PICU settings as acute encephalopathy. Respiratory depression may result depending on the age and dose ingested. A large French multicentre study described PED tertiary admissions between 2004 and 2014 in a paediatric cohort under 6 years. Visits increased 133% and cannabis exposure related calls to toxicology call centres increased 312%. Other toxic exposures increased only 45%.[3] In the USA, severe paediatric intoxications were noted in States where cannabis had been decriminalised.[4,5] From 2014, 50% of calls to poison centres in USA involving e-cigarettes are for accidental swallowing of cannabis liquid in pods, in children less than 5 years.[6] Hashish oil of uncontrolled concentration can be used to make brownies, cookies, gummies, and jellies. Exposure risk is increased for children because of attractive packaging and labelling of edibles to resemble trusted brands. The potency of edible cannabis products varies as false labelling of content from unregulated origins is increasingly a covert method of drug trafficking unlike edibles consumed in licenced “coffee shops” in the Netherlands where small quantities of cannabis are sampled by those over 18 years in a safe environment and government regulated factories in North America. While an average adult inhaled cannabis dose is 5 to 20 mgs of THC, 10 to 50 times this dose can be ingested in edibles with at least a thirty minute time delay for initial effect.[7,8] Adults who order cannabis edibles online for personal consumption are frequently unaware of the danger for young children who often consume several sweets initially.[9]

Our tertiary Paediatric Emergency Department had 6 children under 10 years of age (5 were under 6 years) who presented within an 8-week period from March 17th, 2021 with acute encephalopathy. Each child had a urine sample that tested positive for Tetrahydrocannabinol (THC) on ELISA testing (Eurofins). We describe four serious cases.

Case 1

A 5-year-old presented to the ED after a known ingestion around 8pm. The child was increasingly drowsy over the evening. At 10:30 pm in ED, he was noted to have a GCS of 14/15. He was able to mobilize independently with an ataxic gait. Three hours after ingestion, the GCS dropped to 10/15. Pupils also dilated from 4mm to 8mm and he became hypotensive with a BP of 88/55mmHg. Routine bloods and a urine sample, by catheter, were obtained and a 20ml/kg bolus of normal saline was given. ECG was normal. He needed a second fluid bolus with good effect. After 5 hours, his GCS had improved to 13/15. By 8:00am, he was back to normal and discharged with social work follow up.

Case 2 and Case 3

3-year-old and 4-year-old siblings were disinhibited at 11:00pm following an earlier witnessed ingestion of cannabis jellies (Chuckles Peach Rings) around 8:00pm. The jellies were in a schoolbag in a communal space. Each jelly reportedly had 50mgs of THC and both children became increasingly drowsy and by 5:00am, an ambulance was called.

Case 2

The 4-year-old was brought to ED resuscitation area at 6 am with a GCS of 9/15. The pupils were 5mm and sluggish. Heart rate (HR) was 170, BP 98/50 mmHg and respiratory rate (RR) was 15/min and shallow. Oxygen was commenced at 6 L/min with adequate saturations. Decorticate posturing was observed on and off over the next 3 hours. Urine was obtained by suprapubic aspiration at 9.30am. By then, pupils were 8mm, BP 85/44. By 10.15 am, right pupil was 6mm and left pupil was 4mm and GCS 8/15. A brain CT was normal. The child was transferred to the ward. By 1.00 pm, the BP was 77/38, HR 94, GCS 7/15 and RR 12/min and shallow. A bolus of 20mls/kg of normal saline was given. Oxygen saturation decreased to 89% on 15L of oxygen. Humidified high flow nasal oxygen (Airvo) was started. The child was transferred to PICU. Respiratory drive improved overnight, and oxygen stopped. By noon, 36 hours after arrival, GCS was 13/15 and was normal by 3:00pm. The child remained in hospital for another 2 days as TUSLA and the Gardai were involved.

Case 3

The 3-year-old sibling of Case 2 arrived at the ED resuscitation area at 6am with pallor and a temperature of 34.1 ^{o} C. The airway was patent, oxygen saturation was 89% in room air and oxygen was started. The vitals were; HR 163, BP 127/78, CRT 2 and a GCS 8/15. Pupils were 6mm and sluggish. Decorticate posturing was observed with stiffening and breath holding with brief mild cyanosis, self-resolving. An intravenous line was sited, and a venous gas showed the following: pH 7.2, PCO2 8.2, lactate 1.4. ECG was normal and urine was obtained by catheter at 10:00am which was positive for THC. The child was transferred to the ward and in the ward, there were 3 episodes of cyanosis associated with tonic-clonic movements of all four limbs. Buccal midazolam was given, and a Code Blue was called. A brain CT was done at 4:00pm which was normal. The GCS improved slowly overnight and was normal by noon the next day. The child remained in hospital for the weekend as TUSLA and Gardai were involved.

Case 4

A 10-year-old ingested his 26-year-old sibling's cannabis sweets (Cannabust) around 17.30pm. By 17.45pm he felt dizzy and ataxic. On arrival to the ED at 6:30pm, he was noted to be very pale, GCS 13/15, RR 18, saturations 100% on room air, BP 110/65. Activated charcoal was attempted orally but then given by nasogastric due a large emesis. He received a saline bolus. GCS normalized within 4 hours. He was observed overnight in ED to be seen by social services.

Discussion

Cannabis, the genus, comes from 2 main species of cannabis plant, *C. indica* and *C. sativa*. The cannabis plant is complex and contains at least 120 compounds called 'Cannabinoids' so far. The *C. sativa* plant yields marijuana (dried crushed flower heads and leaves), hashish (resin) and hash oil (concentrated resin extract) which can be smoked, inhaled or ingested.

Tetrahydrocannabinol (THC) is the main psychoactive cannabinoid in the cannabis plant. The female *C. sativa* plant has the highest concentration of THC, with hybrid plants now producing more concentrated THC than ever before. Recreational marijuana had a THC concentration of 4% in the 1980s but had increased to 12% by 2012.[3,5] The psychotropic effects or potency of any preparation depends on the route and quantity of exposure and the THC content of the preparation.[12,13,14,15]

THC acts by binding to CB1 receptors in the cerebellum, basal ganglia, hippocampus and cerebral cortex. Therefore, toxicity is associated with cognitive and motor impairment. THC receptor binding inhibits neurotransmitters in the autonomic nervous system, acetylcholine, noradrenaline, dopamine, serotonin and GABA. Observed clinical effects are both dose and time dependent and therefore are related to the route of delivery, inhaled or oral. After inhaling cannabis, its effects peak within 30 minutes and last for about 4 hours. Ingested cannabis has lower bioavailability (5 to 20%) compared to the inhaled route due to gastric acid degradation and first pass hepatic metabolism. Onset of psychotropic effects are 30 minutes to 3 hours after oral ingestion and may last up to 12 hours. Although peak concentration usually occurs within 1-2 hours, it can be delayed for a few hours. Elimination half-life ranges from 25 to 36 hours.[6] It is metabolised by hepatic cytochrome oxidase and end products excreted in faeces (65%) and urine (20%). The delayed effects from oral ingestion compared to rapid effects from smoking or vaping is what pose the greatest risk to children and naïve users who consume several edibles initially then overdose.[6,8,10]

Immaturity of brain synapses may be important in toxicity in young children as well as the dose ingested per kilogram body weight. Effects can be stimulant, hallucinogenic or sedative. Unlike older children, those under 6 years present with altered sensorium from encephalopathy with dilated sluggish pupils, injected conjunctiva, euphoria, stupor or coma. Autonomic instability, either high or low blood pressure, often with tachycardia is described.[3,7] Respiratory depression and/or gastrointestinal symptoms (nausea, vomiting, hyperphagia, dry mouth and thirst) may also occur in some children.[6]

In a small cohort of 38 children presenting to an ED for acute cannabis intoxication after ingestion, degree of symptoms corresponded to an estimated dose. A dose of 3.2 mg/kg of THC led to observation and minimal medical intervention while 7.2 mg/kg of THC led to admission and moderate medical intervention. Doses of 13 mg/kg of THC led to admission to PICU and major medical interventions. [8]

Our younger cases exhibited dilated pupils and altered sensorium with a GCS that varied from 5 to 10. Two cases had significant autonomic instability which required fluid boluses and additionally hypertonia with clonus. The ten years old had milder symptoms but charcoal had been given within an hour of ingestion.

This is consistent with published literature that shows that younger children tend to present with CNS depression. A systematic review by John Richards et al (2019) found that lethargy was the common presenting feature of cannabis toxicity in children with mean length of stay being 27.1 hours, while 18% needed ICU care.[4]

A study in Colorado by Heizer et al (2018) found a dose relationship in the severity of symptoms in young children with accidental exposure. They also reported that children presented mostly with lethargy or somnolence (84%). [8]

We noted that one of our cases had generalised seizures. Seizures are rare and maybe due to adulterants, although a French study reported seizures in 4 out of 29 children admitted to ED with cannabis toxicity over a 10-year period. Peak effect may depend on the time of last meal, dose and rate of consumption and other health confounders e.g. prematurity.[8,13,15,17] We noted urinary retention in most of the patients and urine was obtained invasively. Perhaps an imbalance in GABA inhibition alongside dopamine and serotonin receptor imbalance are responsible for observed autonomic instability with urinary retention. The time course for peak clinical deterioration was 2 to 3 hours and subsequent improvement was 6 to 8 hours in 4 cases, but two cases remained symptomatic until 36 hours. These outliers may have ingested a larger ingested dose per kilogram of body weight and psychotropic effects persisted due to the lipophilic binding in the brain especially of young children. Packet THC content must be interpreted as hypothetical as production is uncontrolled.

Our case series points to an emerging problem that has been described in other jurisdictions, where cannabis use has been decriminalised or under-enforced. In Ireland, the Adult Cautioning Scheme introduced from December 14th 2020 promotes decriminalisation and follows similar trends worldwide.[5,10,11] Increased access to higher potency cannabis in edibles and ingestion of cannabis in liquid form is a major emergent serious threat for young children [4, 6, 11, 13, 14] Such edible cannabis products are attractive in presentation and are not in childproof packaging. Although no deaths have yet been reported internationally, indirect fatality from trauma with blood levels of cannabis(49ng/ml) nine times the legal limit for driving(5ng/ml) in Colorado is described. Wang et al (2016) describe the death of an 11-month-old who presented with metabolic acidosis, tachycardia and a positive urine drug screen. Long term health effects on children are yet to be discovered. [15,16,17] However, PED and PICU admissions and calls to poison centres have increased. These products have uncontrolled concentrations of THC as they are largely made illegally and often supplied through the internet.[6]

Food Safety Authority of Ireland (FSAI) has issued a warning for the public on April 26th, 2021 with photographs of how these recent cannabis jellies are packaged with names resembling known safe products (Trrlli, Skittles, Stoney Patch, [see below]).[15]

Some examples of the cannabis sweets

Point of care urine toxicology should be done routinely when an afebrile, previously well young children present with altered sensorium without focal findings.[6] Treatment is mainly supportive and activated charcoal is useful, if used within 1 hour of ingestion, when GCS level permits. It is possible to avoid a brain CT if urine toxicology is positive. All the cases were referred to child protection services. Two cases involved the Gardai.

Cannabis is increasingly perceived as harmless and the use of edibles amongst adults is becoming socially acceptable. Young children are at risk through accidental ingestion. The new Adult Cautioning Scheme will accentuate evolving child protection issues of this emergent serious public health threat. Recognition and notification of all cases presenting to hospitals is imperative and education of our staff and parents.

Declaration of Conflicts of Interest:
The authors declare no current conflict of interest.

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