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ORIGINAL ARTICLE

Delta-8-Tetrahydrocannabinol Exposure and Confirmation in Four Pediatric Patients

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Abstract

Introduction Delta-8-tetrahydrocannabinol (THC) is a known isomer of delta-9-THC, both found naturally in the Cannabis sativa plant and thought to have similar potency. Delta-8-THC products are widely accessible in retail shops which may lead to a rise in pediatric exposures with substantial clinical effects.

Case Report This is a case series of four pediatric patients that were seen between June and September 2021. The patients presented with varied clinical symptoms including confusion, somnolence, seizure-like activity, hypotension, and tachycardia after exposure to delta-8-THC products obtained in retail shops. Basic urine drug screen immunoassays revealed positive results for cannabinoids in all patients. Subsequent confirmatory drug analysis of residual biological samples of blood and/or urine was sent to the University of California San Francisco Clinical Toxicology and Environment Biomonitoring Laboratory with the assistance of the Drug Enforcement Administration's Toxicology Testing Program (DEA TOX). Confirmatory testing revealed 11-nor-9-carboxy-delta-8-THC, the metabolite of delta-8-THC. Delta-9-THC and its metabolites were not detected on confirmatory testing in any of the cases.

Discussion Clinical effects of delta-8-THC in children include but are not limited to altered mental status, seizure-like activity, and vital sign abnormalities. Delta-8-THC exposure may lead to a positive urine drug screen for cannabinoids, but confirmatory testing is needed to differentiate from delta-9-THC.

Keywords Tetrahydrocannabinol · THC · Delta-8-THC · Pediatric exposures

Introduction

Delta-8-tetrahydrocannabinol (THC) is an isomer of delta-9-THC, the primary psychoactive cannabinoid found naturally in the *Cannabis sativa* plant that is utilized as marijuana [1]. Cannabinoids primarily exert effects via activation of G-protein-coupled cannabinoid (CB) receptors in brain and peripheral tissues [2]. This results in psychotropic and physiologic effects including relaxation, perceptual alterations, psychosis, paranoia, tachycardia, and decreased vascular resistance. Acute toxicity exerted by delta-9-THC may also result in decreased coordination, lethargy, sedation, and decreased psychomotor activity [3].

THC-containing products have been increasing in commercial availability and concentration [4]. This trend has been associated with increased emergency department (ED) visits and poison control center calls regarding pediatric cannabis exposures [5]. Of the poison control center reported exposures during a 7-month period in 2021, 39% of delta-8-THC exposures were in pediatric patients [6]. One case report of confirmed delta-8-THC consumption in a child showed decreased responsiveness leading to intubation [7]. However, the clinical effects and pharmacokinetics of delta-8-THC, specifically in pediatric populations, are not yet well defined. We present a case series of confirmed delta-8 exposures in pediatric patients and the observed clinical effects.

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Case Series

This is a case series of four individual patients presenting between June and September 2021 to a single urban children's hospital in Texas with a confirmed delta-8-THC metabolite. Consent for publication was obtained. Additionally, compilation and publication of this case series were approved by our academic institution's human subjects' research protection committee. These patients were selected based upon history of exposure to delta-8-THC products. The medical toxicology service was consulted for all four patients and evaluated the patients at bedside.

Time from ingestion to ED arrival was known in 3 cases, and vital signs on arrival and vital sign extremes were collected (Table 1) [8]. Basic urine drug screens performed at the hospital laboratory are qualitative enzyme multiplied immunoassays and detect the presence of cannabinoids via the metabolite 11-nor-9-carboxy-delta-9-THC with a cut-off of 50 ng/ml. In-house comprehensive urine drug panels are liquid chromatography (LC) time-of-flight mass spectrometer tests for a variety of prescription and illicit drugs, including four cannabinoids (limit of detection): delta-9-THC (> 1000 ng/ml), carboxy-delta-9-THC (250 ng/ml), carboxy-delta-9-THC glucuronide (250 ng/ml), and hydroxy-delta-9-THC (5 ng/ml).

Additional testing for delta-8-THC and metabolites in blood and/or urine specimens were sent to the University of California San Francisco (UCSF) Clinical Toxicology and Environment Biomonitoring Laboratory with the assistance of the Drug Enforcement Administration's Toxicology Testing Program (DEA TOX) to undergo qualitative and quantitative testing by LC quadrupole time-of-flight mass spectrometry [7, 9]. The testing panel utilized has more than 1200 analytes and can distinguish between delta-8-THC, delta-9-THC, and their metabolites. The level of detection for 11-nor-9-carboxy-delta-8-THC in urine is 8 ng/ml and in plasma/serum is 31 ng/ml. Testing results for each patient are outlined in Table 2.

Patient 1

An 18-month-old female with an unremarkable past medical history presented to the ED with reported seizure-like activity. The patient's mother noted that she had delta-8-THC gummies in a jewelry box in her bedroom. The patient's sister opened the jewelry box and gave the gummies to the patient. The ingestion time was unknown as it was not witnessed by the parent. On initial evaluation, the patient was not arousable. Blood pressure was at the high end of normal for age (109/62), and heart rate was at the low end of normal for age (104). On hospital day 1, the patient's respiratory rate lowered to 13, and their lowest SpO2 was 95%, but the patient did not require supplemental oxygen. A non-contrast computed tomography (CT) of the head was performed and revealed no intracranial abnormality. The patient had a normal electroencephalogram (EEG) result. The patient was discharged on hospital day 2 with return to neurological baseline. Basic urine drug screen showed positive cannabinoids, and an in-house comprehensive urine drug panel was positive for carboxy-delta-9-THC glucuronide. Two urine samples collected within 4.5 h of each other were sent to UCSF and revealed different levels of 11-nor-9-carboxy-delta-8-THC in each sample, 109 ng/ml (collected earlier) and 292 ng/ml, in the absence of delta-9-THC or its metabolite.

Patient 2

A 3-year-old male with an unremarkable past medical history presented to the ED approximately 50 min following an ingestion of 2–3 gummies allegedly containing delta-8-THC (Fig. 1). His father noted that a co-worker bought these and left them in the back of the car. That evening, the patient entered the car from daycare and was placed in his car seat. He saw the candy and ate 2–3 gummies. Almost an hour later, he became "lethargic" and was brought to the children's hospital. In the ED, he was found to have tachycardia with a heart rate of 157 and hypotension with a blood pressure of 50/30 which was treated with three boluses of IV fluids. On hospital day 1, the patient was found to be sedated but easily arousable. His mentation continued to improve, and he was discharged on hospital day 2. His basic urine drug screen was positive for cannabinoids. An in-house comprehensive urine drug panel was only positive for carboxy-delta-9-THC glucuronide. His urine was sent to UCSF and revealed 11-nor-9 carboxy-delta-8-THC 1390 ng/ml. Delta-9-THC and its metabolites were not found.

Patient 3

A 6-year-old female with an unremarkable past medical history presented to the ED with approximately 4 h of nausea, vomiting, and sedation. The patient was treated with an over-the-counter cold medication for an upper respiratory virus for the past few days and improved. Upon return from school on the day of presentation, she became nauseated, lightheaded, and lethargic. On arrival to the ED, she was hypoxic with an oxygen saturation of 87% which improved with two liters of oxygen via nasal canula. Her respiratory rate was normal. She was also tachycardic with a heart rate of 141 and hypertensive with a blood pressure of 140/97. A non-contrast CT of the head revealed no intracranial abnormality. Basic

Table 1 Time from ingestion to ED and vital signs

Patient	Age/sex	Time from ingestion to ED arrival	Normal vital signs for age			Initial vital signs on ED arrival					Vital sign extremes during hospitalization					
			BP	HR	RR	BP	HR	T	RR	SpO2	Lowest BP	Highest HR	Lowest T	Highest T	Lowest RR	Lowest SpO2
1	18-month-old female	Unknown	85–105/40–57	98–135	25–40	109/62	104	36.4 °C	23	95%	81/54	145	35.9	36.4C	13	95%
2	3-year-old male	50 min	88–109/45–64	86–123	21–29	92/45	119	36.4 °C	22	94%	50/30	157	36.2	36.4C	13	93%
3	6-year-old female	220 min	93–114/54–73	74–111	18–24	140/97	141	36.4 °C	23	93%	91/76	141	36.4	36.4C	23	87%
4	16-year-old female	110 min	111–137/63–86	58–92	13–19	136/73	113	36.9 °C	23	97%	121/63	113	36.9	36.9C	23	96%

ED, emergency department

BP, blood pressure (systolic blood pressure/diastolic blood pressure)

HR, heart rate

T, temperature (in degrees Celsius)

RR, respiratory rate

SpO2, oxygen saturation

Note: vital signs obtained from UptoDate [8]

Table 2 Qualitative and quantitative laboratory testing

Patient	Age/sex	Basic urine drug screen	Comprehensive urine drug panel	DEA TOX quantitative testing	Other substances on DEA TOX testing
1	18-month-old female	Cannabinoids	Carboxy-delta-9-THC glucuronide	11-nor-9-carboxy-delta-8-THC 109 ng/ml and 292 ng/ml (urine)	None
2	3-year-old male	Cannabinoids	Carboxy-delta-9-THC glucuronide	11-nor-9-carboxy-delta-8-THC 1390 ng/ml (urine)	None
3	6-year-old female	Cannabinoids	Dextromethorphan and levorphanol	11-nor-9-carboxy-delta-8-THC 929 ng/ml (plasma)	Dextromethorphan, dextrorphan, and lidocaine
4	16-year-old female	Cannabinoids and benzodiazepines	Fluoxetine	11-nor-9-carboxy-delta-8-THC 31.6 ng/ml (serum)	Fluoxetine and midazolam

Basic urine drug screen and comprehensive urine drug panel were performed at the primary hospital's laboratory
Subsequent qualitative and quantitative testing was performed at UCSF in conjunction with their DEA TOX program
All samples tested negative for delta-9-THC or its metabolites on DEA TOX qualitative and quantitative testing

Fig. 1 Delta-8-infused candy packaging

urine drug screen was positive for cannabinoids. The in-house comprehensive urine drug panel was positive for dextromethorphan and levorphanol. On hospital day 2, the patient reported eating cookies at school during snack time and taking vitamin gummies at home. A plasma sample was sent to UCSF and revealed delta-8-THC, 11-nor-9-carboxy-delta-8-THC 929 ng/ml, dextromethorphan, dextrorphan, and lidocaine. Delta-9-THC and its metabolites were not found on this subsequent testing.

Patient 4

A 16-year-old female with a past medical history of depression treated with fluoxetine presented to the ED after being found unresponsive. The patient reported obtaining and using a vaping pen at school from a classmate. She went back to class and almost 2 h later became lightheaded, dizzy, and fell from her chair. Afterwards, she became unresponsive with episodes of jerking. Paramedics noted she was maintaining her airway and had normal vital signs. She was given midazolam for suspected seizure activity. She was brought to ED where she became alert and oriented within 4 h of when she reported vaping. A basic urine drug screen showed positive cannabinoids and benzodiazepines. The in-house comprehensive urine drug panel was positive for fluoxetine. A serum sample was sent to UCSF and revealed 11-nor-9-carboxy-delta-8-THC 31.6 ng/ml, fluoxetine, and midazolam. Delta-9-THC and its metabolites were not found on this testing.

Discussion

Delta-8-THC is a structural isomer of delta-9-THC with lower psychotropic potency [1]. Comparatively, it is less expensive to produce and more stable because it does not easily oxidize to cannabinol as delta-9-THC does, which lends itself to a longer shelf life [10]. As a result, it has previously been investigated in animal studies as a low-dose therapy for eating disorders to increase food intake [11]. It has also been studied as an oral antiemetic in pediatric oncology patients and has been shown to effectively prevent vomiting in children receiving chemotherapy with minimal side effects [10]. In this study, the side effects noted in three of eight total subjects were irritability and euphoria. Recently, delta-8-THC has risen in popularity among recreational users and has become more widely distributed in commercial settings [12, 13]. Additionally, a query for delta-8-THC Google searches showed that the legal status of delta-9-THC by state was inversely associated with delta-8-THC interest [14].

Exposure to delta-8-THC occurs primarily via ingestion or inhalation as it is available in the form of edibles and vaping cartridges. Children are at increased risk for ingestion of delta-8-THC given this recent increase in commercial availability, especially in the form of edibles, such as gummies, which are indistinguishable from their non-cannabis containing counterparts [5, 7, 12, 15, 16].

Similar to delta-9-THC, delta-8-THC has demonstrated functional activity as a partial agonist at CB receptors 1 and 2 [17]. Activity at the CB1 receptors, mostly distributed in the brain, is thought to drive the clinical effects of cannabinoids, including regulation of cognition, memory, motor function, nausea, and vomiting [3, 17]. The pharmacokinetics of THC vary depending on route of administration. Oral ingestion has a delay of 30–90 min with maximum effects seen after 2–3 h, while inhaled THC shows effects within minutes, reaching a maximum effect after 15–30 min [2].

Research regarding relative potency is limited. The change in position of the double bond in the alicyclic ring from Δ^9 to Δ^8 does not alter qualitative effects of THC but reduces its psychotropic potency [18]. One study found similar reported subjective effects following oral ingestion of delta-8-THC compared to delta-9-THC with an estimated relative potency of 2:3 in children, respectively, thought to possibly be due to lower CB1 receptor density in children [2, 10]. Upon oral ingestion, subjects reported early somatic symptoms such as dizziness, fatigue, and incoordination.

In our population, all patients had subsequent DEA TOX testing at UCSF confirming exposure to delta-8-THC products. Three had oral ingestion of delta-8-THC gummies, and one had vaped delta-8-THC. Three of the patients experienced central nervous system depression, and two developed seizure-like activity. Case reports of seizures resulting from acute ingestion in pediatric patients have been documented [14, 15]. Additionally, one of our patients developed hypotension and tachycardia. Another patient developed oxygen desaturation requiring supplemental oxygenation via nasal canula. Similarly, one prior case report of confirmed delta-8-THC consumption in a child showed decreased responsiveness leading to endotracheal intubation [7]. The basic urine drug screen was positive for cannabinoid for all four patients. The in-house confirmatory urine drug panel was only positive in two patients for carboxy-delta-9-THC glucuronide, and at time of testing, there was no availability to test in-house for delta-8-THC in the biological specimens. However, the samples sent to UCSF revealed that all four patients were positive for 11-nor-9-carboxy-delta-8-THC. Despite the in-house confirmatory testing being positive carboxy-delta-9-THC, the UCSF testing did not reveal any delta-9-THC or its metabolites in any of the cases. Our results show that delta-8-THC can show up positive on an immunoassay urine drug test for cannabinoids and cross-react as a false positive for carboxy-delta-9-THC glucuronide on confirmatory testing. Though not routinely performed and unlikely to be clinically useful, further send-out testing for delta-8-THC would be needed to accurately identify these exposures if a clinical history for suspected delta-8-THC exposure is not elicited.

Conclusion

Pediatric patients have a higher risk of being exposed to delta-8-THC given the increased availability of delta-8-THC products. Clinical symptoms following exposure can include confusion, somnolence, seizure-like activity, hypotension, and tachycardia. Delta-8-THC may cross-react with

currently available drug screening and confirmatory testing and lead to positive results for cannabinoids and false-positive results for the presence of carboxy-delta-9-THC glucuronide. Eliciting clinical history on delta-8-THC exposure, such as specific questioning of edibles purchased at local retail shops or the Internet, should be implemented in any pediatric patient with an undifferentiated exposure. Ongoing efforts to educate the public regarding the potential danger of these products in young children and to improve the labeling and safe storage of these products are warranted.

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Declarations

Conflict of Interest None.

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