Toxic Tetrahydrocannabinol (THC) Dose in Pediatric Cannabis Edible Ingestions

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abstract

OBJECTIVE: The study characterizes cannabis toxicity in relation to tetrahydrocannabinol (THC) dose in pediatric edible cannabis ingestions.

METHODS: This is a retrospective review of children aged <6 years presenting with edible cannabis ingestions of known THC dose within a pediatric hospital network (January 1, 2015–October 25, 2022). Cannabis toxicity was characterized as severe if patients exhibited severe cardiovascular (bradycardia, tachycardia/hypotension requiring vasopressors or intravenous fluids, other dysrhythmias), respiratory (respiratory failure, apnea, requiring oxygen supplementation), or neurologic (seizure, myoclonus, unresponsiveness, responsiveness to painful stimulation only, requiring intubation or sedation) effects. Cannabis toxicity was characterized as prolonged if patients required >6 hours to reach baseline. The relationship between THC dose and severe and prolonged toxicity was explored using multivariable logistic regression and receiver operator characteristic curve analyses.

RESULTS: Eighty patients met inclusion. The median age was 2.9 years. The median THC ingestion was 2.1 mg/kg. Severe and prolonged toxicity was present in 46% and 74%, respectively. THC dose was a significant predictor of severe (adjusted odds ratio 2.9, 95% confidence interval: 1.8–4.7) and prolonged toxicity (adjusted odds ratio 3.2, 95% confidence interval: 1.6–6.5), whereas age and sex were not. Area under the curve was 92.9% for severe and 87.3% for prolonged toxicity. THC ingestions of ≥1.7 mg/kg can predict severe (sensitivity 97.3%) and prolonged toxicity (sensitivity 75.4%).

CONCLUSIONS: The THC dose of edible cannabis correlates to the degree of toxicity in children <6 years old. The threshold of 1.7 mg/kg of THC may guide medical management and preventive regulations.

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WHAT'S KNOWN ON THIS SUBJECT: Previous studies reveal a rise in exposures to edible cannabis in the pediatric population after marijuana legalization. Clinical presentations of cannabis toxicity can be variable and may include serious effects.

WHAT THIS STUDY ADDS: This study determines the ingested dose of tetrahydrocannabinol in cannabis edibles that leads to severe and prolonged signs and symptoms in children <6 years of age. Additionally, it reveals the ability to predict clinical course based on tetrahydrocannabinol dose.

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Unintentional pediatric exposures to cannabis products increased dramatically in the last decade.[1] This is a consequence of the increased legalization of cannabis across North America.[2–4] As of January 2023, all but 4 states in the United States legalized or decriminalized cannabis to some extent.[5] During that time, cannabis products have also been shown to contain increased concentrations of δ-9 tetrahydrocannabinol (THC), the primary psychoactive cannabinoid.[6,7]

Ingestion is the most common route of cannabis exposure among young children.[8,9] Cannabis-infused foods, commonly referred to as edibles, pose a heightened risk in this age group. Edible cannabis products are often sold in forms that may be difficult to distinguish from non-cannabis-containing products. In young children, the rise in overall cannabis exposures between 2017 and 2019 was largely accounted for by edible cannabis ingestions.[10] This trend continued from 2017 through 2021, during which time a higher proportion of children required hospital admission, which suggests an increase in toxicity from these exposures.[11]

Common findings in pediatric marijuana exposures include drowsiness, tachycardia, ataxia, and vomiting. More concerning findings are hypotension, coma, respiratory depression, and seizure, which occur in <3.5% of cases.[2,9,11] Many children are evaluated in a hospital after cannabis ingestion; however, only a small proportion require intensive care admission or invasive supportive measures, such as intubation.[1,11–13] The variability in the degree of illness among these presentations makes risk stratification critical. Edible cannabis toxicity likely depends on THC dose in young children, but what dose predicts a severe clinical course remains largely unknown. Establishing a toxic dose impacts the medical management of these patients and has implications for safety regulations.

The objective of this study is to characterize the relation of clinical toxicity to THC dose after edible ingestions in children <6 years old. We hypothesized that both the severity and duration of cannabis toxicity are predictable based on the dose of THC ingested.

METHODS

This was a retrospective study of patient hospital encounters for edible cannabis ingestions from January 1, 2015 to October 25, 2022. This study took place at an urban pediatric hospital network in a state with legal recreational and medicinal cannabis. The network includes 4 inpatient pediatric hospitals with associated emergency departments (ED) and 3 urgent cares. This network provided emergency and urgent care services to an average of 156 880 annual visits during the study, excluding 2022 for which data were not yet published.[14]

The inclusion criteria for this study were patients <6 years old after the ingestion of edible cannabis with a known THC dose. The dose of THC was determined by the documented guardian or caregiver report. In-state regulations during the study period mandated clear and accurate THC dose in milligrams on the labels of recreational products.[15] This allowed for accurate dose estimations based on the number of edibles ingested. When the THC dose was undocumented or reported as unknown, the case was excluded. Patients were also excluded if they had a non-ingestion route of exposure, ingested a nonedible preparation (wax, flower, oil, etc.), or had a prescription for medicinal cannabis. Patients were identified by *International Classification of Diseases, Tenth Revision* codes, positive urine drug screen (UDS) results for THC, or regional poison center documentation of edible cannabis ingestion at a hospital associated with the study. The *International Classification of Diseases, Tenth Revision* codes included were cannabis-related disorder (F12) and poisoning by cannabis (T40.7x). Each encounter was evaluated separately.

Cases were reviewed by 2 investigators (LCP and MWS), and data points were abstracted into a standardized collection spreadsheet (Microsoft Excel 2022, version 16.69). The variables collected were patient demographics, cannabis product, THC dose, ingestion scenario, clinical course (signs, symptoms, effect duration), hospital course (disposition, consultations, length of stay), UDS results, and therapies administered. Symptom resolution was defined as when the patient was documented to be at their baseline or documentation of behaviors normal for the patient's age. We further characterized severe toxicity cases as involving serious cardiovascular (bradycardia, hypotension or sinus tachycardia that required either vasopressor agents or intravenous fluids, or other dysrhythmias), respiratory (respiratory failure, apnea, or required oxygen supplementation), or neurologic (seizure, myoclonus, unresponsiveness, responsiveness only to painful stimulation, required intubation or a sedating medication) findings. Age-appropriate vital signs were determined by using Pediatric Advanced Life Support guidelines.[16] Oxygen saturation <90% by pulse oximeter was classified as hypoxia given local standards. Prolonged toxicity was defined as exceeding 6 hours to return to baseline from the time of ingestion. The 6-hour cutoff was chosen because it is an acceptable ED observation period. Also, most complications associated with fasting from oral intake in this age group evolve after 6 hours.[17–20]

Data were summarized with descriptive statistics. The median value and interquartile range (IQR) were calculated for nonnormally distributed continuous variables and frequencies and proportions for nominal variables. The clinical findings and interventions for edible cannabis ingestions were presented by THC dose (<1 mg/kg, >1–2 mg/kg, >2–4 mg/kg, >4–6 mg/kg, and >6 mg/kg).

Median dose, median duration of signs and symptoms, and admission rate were compared across patients with and without severe toxicity as well as prolonged toxicity. Wilcoxon rank test, χ-square test, and Fisher's exact test were used as appropriate.

Multivariable logistic regression was used to investigate the relationship between the patient's age, sex, and ingested weight-based THC dose and the outcomes of severe toxicity and prolonged toxicity. Age and THC dose were included in the models as continuous variables. The adjusted odds ratios (AOR) and 95% confidence intervals (CI) are reported. For continuous variables, the adjusted unit odds ratios are reported with a 1-unit increase defined as 1 mg/kg of THC and 1 year. Receiver operator characteristic (ROC) curve and area under the curve (AUC) analyses were used to estimate the ingested weight-based THC dose threshold with the highest sensitivity and specificity to independently predict severe toxicity and prolonged toxicity. Statistical significance was defined as $P < .05$. JMP Pro 16.0.0 statistical software was used for analyses.

The Colorado Multiple Institutional Review Board approved the study and granted an exemption as investigators did not have direct contact with patients.

RESULTS

There were 325 hospital encounters for cannabis exposures identified in children <6 years old. Annual encounters for unintentional ingestions of any cannabis product increased from 16 in 2015 to 59 in 2022, whereas edible cannabis ingestions increased from 8 to 27 (Fig 1). We excluded 174 cases for exposure to an unknown cannabis product (105), nonedible cannabis formulation (38), presentation with a medicinal cannabis prescription (20), non-exposure (6), and a non-ingestion route of exposure (5). Non-exposure cases included 5 patients who were documented to have non-THC ingestions by chart review and one asymptomatic patient with negative UDS who was evaluated because a sibling ingested THC. Ultimately, 151 (46%) cases involved ingestion of edible cannabis, and 80 (53%) met the inclusion criteria.

Among the 80 included patients, the median age was 2.9 years (IQR 2.0–3.9; Table 1). THC dose ranged from 0.2 mg/kg to 69.1 mg/kg with a median dose of 2.1 mg/kg (IQR 0.8–5.1). No patients had multiple encounters. Most children presented directly to the pediatric facility; however, 18 (23%) patients were initially managed at an adult hospital before transfer. Seventy (88%) cases involved the child obtaining the cannabis edible from the home. In 6 (8%) cases, the edible was mistaken for a non-cannabis product and given to the child. Fifty-two (65%) cases had a UDS performed, all tested positive for THC. There were 2 cases involving a co-exposure to another medication. The first ingested 0.7 mg/kg of THC and melatonin and the second ingested 8.3 mg/kg of THC and an opiate with morphine and codeine identified on quantitative testing. Patients discharged from the ED had a median length of stay of 6.1 hours (IQR 4.4–9.8). The median length of stay for admitted patients was 24 hours (IQR 18.6–32.3). Length of stay was often impacted by social work evaluation. There were no deaths.

The most common symptom was sedation or lethargy in 68 (85%) patients (Table 2). Twenty-one (26%) patients were described as awake during examination but with some degree of sedation. Eight patients had no signs

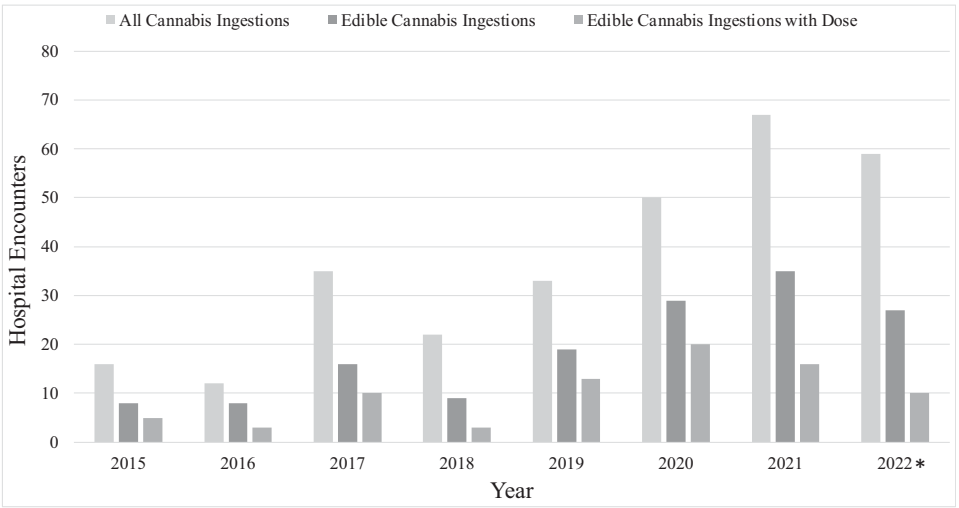

FIGURE 1

Annual patient encounters for suspected pediatric cannabis ingestions of any form (294), edible ingestions (151), and edible ingestions of known THC dose (80) within the children's hospital network from 2015 through 2022.
*Includes through October 25, 2022.

TABLE 1 Demographics and Characteristics of Pediatric Edible Ingestions, $n = 80$	
Median age, y (IQR)	2.9 (2–3.9)
Sex (%)	
Female	40 (50%)
Male	40 (50%)
Originating hospital (%)	
Pediatric ED	51 (64%)
Adult ED	18 (23%)
Urgent care	11 (14%)
Transfers (%)	22 (28%)
Edible cannabis type (%)	
Gummy	49 (61%)
Chocolate	18 (23%)
Other candy	6 (8%)
Baked good	6 (8%)
Unknown or other edible	1 (1%)
Scenario (%)	
Found in home	70 (88%)
Mistaken as non-THC product	6 (8%)
Found outside of home	4 (5%)
Urine drug screen (%)	
Not performed	28 (35%)
THC positive	52 (65%)
THC negative	0
ED disposition (%)	
Pediatric ICU	10 (13%)
Pediatric inpatient (non-ICU)	30 (38%)
Discharged from ED	40 (50%)
Consultations (%)	
Poison center/toxicology	72 (90%)
Social work	70 (88%)

or symptoms described during their ED observation period, and 6 of these patients' ingestions were witnessed. The timing of signs or symptoms could be estimated in 60 (83%) of the 72 symptomatic patients with a median onset time of 1 hour (IQR 0.8–1.7). Thirty-four (43%) patients did not require medical interventions during the hospitalization period, and 26 (76%) of these patients ingested 2 mg/kg of THC or less. No patients received gastrointestinal decontamination.

Severe toxicity was present in 37 (46%) cases (Table 3). Patients with severe toxicity had a median ingested THC dose of 5.4 mg/kg (IQR 3.2–8.2) with a median duration of symptoms of 20.3 hours (IQR 12.8–29.5). Gummy edibles were responsible for 21 (57%) of these cases. Neurologic effects accounted for 28 (76%) of these presentations. Twenty-four patients (65%) had >1 system that met the severe toxicity definition. The remaining 13 patients had supplemental oxygen requirements (4), hypotension requiring intravenous fluids (2), and severe neurologic effects (7). Onset to severe toxicity could be estimated in 31 (84%) patients with a median onset within 2.3 hours (IQR 1.3–3.8). Fifty-seven patients (74%) demonstrated prolonged toxicity with a median ingested THC dose of 3.7 mg/kg (IQR 1.7–5.7).

In a multivariable logistic regression analysis, THC weight-based dose was a significant predictor of severe toxicity (AOR 2.9, 95% CI: 1.8–4.7). Neither age (AOR 1.2, 95% CI: 0.7–2) nor sex (AOR 0.9, 95% CI: 0.2–3.5) was significant. For prediction of prolonged toxicity, 3 cases were excluded because the time of ingestion was unknown. Using the cases with a known ingestion time, THC weight-based dose was a significant predictor of prolonged toxicity (AOR 3.2, 95% CI: 1.6–6.5) whereas age and sex were not (AOR 1.4, 95% CI: 0.9–2.4 and AOR 0.6, 95% CI: 0.2–2.3, respectively). Excluding the patients with co-exposures did not impact these findings.

Receiver operator characteristic curve analysis to estimate a dose threshold for the prediction of severe toxicity revealed an AUC of 92.9% (Fig 2). Sensitivity and specificity were maximized at a dose of 2.3 mg/kg of THC with a sensitivity of 89.2% and specificity of 86.1%. Four children with severe toxicity fell under this threshold. Two of these patients had temporary hypoxia (2-year-old with a 0.6 mg/kg ingestion and 4-year-old with 1.8 mg/kg ingestion) and 2 patients had severe neurologic effects (3-year-old with a 2 mg/kg ingestion responsive only to painful stimuli and 2-year-old with a 2 mg/kg ingestion seized). For prolonged toxicity, the ROC curve analysis revealed an AUC of 87.3% (Fig 2). Sensitivity and specificity were maximized at a dose of 1.7 mg/kg of THC with a sensitivity of 75.4% and specificity of 90%. The exclusion of the patients with co-exposures did not alter these results.

DISCUSSION

Our findings reveal a correlation between a weight-based ingested THC dose and the development of severe or prolonged cannabis toxicity. This correlation was independent of patient age or sex. We identified dose thresholds that predict who is likely to necessitate hospital evaluation or medical intervention. There are obvious challenges to obtaining data on THC's pharmacokinetic and dynamic effects in the pediatric group, including the federal Schedule I designation. Any ability to risk stratify these ingestions will aid in patient management and help inform policy and regulations.

This study reiterates that cannabis presentations can vary, but classic features do exist. As in other studies, neurologic symptoms predominate.[10,11] Across all dosing thresholds, sedation was the most common clinical finding, followed by tachycardia, mydriasis, ataxia, and hypoxia. A strength of our study is further characterizing central nervous system depression based on patient responsiveness. Although sedation was common, only 26% were described as unresponsive or responsive to only painful stimuli. A

TABLE 2 Clinical Findings of Pediatric Cannabis Toxicity, Interventions, and Disposition Stratified by Tetrahydrocannabinol Dose							
		THC Dosing Range (mg/kg)					
		<1 (*n* = 24)	> 1 to 2 (*n* = 13)	> 2 to 4 (*n* = 17)	> 4 to 6 (*n* = 13)	> 6 (*n* = 13)	All Cases (*n* = 80)
Signs and symptoms	**Mental status**						
	Any sedation or lethargy	14 (58%)	12 (92%)	16 (94%)	13 (100%)	13 (100%)	68 (85%)
	Awake	18 (75%)	6 (46%)	4 (24%)	4 (31%)	0	32 (40%)
	Responsive to voice or tactile stimuli	6 (25%)	6 (46%)	7 (41%)	4 (31%)	4 (31%)	27 (34%)
	Responsive to painful stimuli	0	1 (8%)	6 (35%)	5 (38%)	8 (62%)	20 (25%)
	Unresponsive	0	0	0	0	1 (8%)	1 (1%)
	Other neurologic						
	Mydriasis	1 (4%)	2 (15%)	4 (24%)	7 (54%)	6 (46%)	20 (25%)
	Ataxia	2 (8%)	4 (31%)	8 (47%)	4 (31%)	0	18 (23%)
	Myoclonus	0	0	3 (18%)	6 (46%)	2 (15%)	11 (14%)
	Confusion or disorientation	0	2 (15%)	2 (12%)	5 (38%)	3 (23%)	12 (15%)
	Seizure (any)	0	0	2 (12%)	0	4 (31%)	6 (8%)
	Decreased tone	0	1 (8%)	0	3 (23%)	1 (8%)	5 (6%)
	Speech change	1 (4%)	1 (8%)	3 (18%)	0	0	5 (6%)
	Tremor	0	1 (8%)	1 (6%)	2 (15%)	0	4 (5%)
	Hallucination	0	0	2 (12%)	1 (8%)	0	3 (4%)
	Cardiovascular						
	Tachycardia	2 (8%)	3 (23%)	6 (35%)	6 (46%)	5 (38%)	22 (28%)
	Hypotension	1 (4%)	0	4 (24%)	2 (15%)	5 (38%)	12 (15%)
	Bradycardia	0	0	1 (6%)	0	3 (23%)	4 (5%)
	Respiratory						
	Hypoxia	1 (4%)	1 (8%)	4 (24%)	6 (46%)	6 (46%)	18 (23%)
	Apnea or respiratory failure	0	0	1 (6%)	0	4 (31%)	5 (6%)
	Bradypnea	0	0	2 (12%)	0	2 (15%)	4 (5%)
	Tachypnea	0	0	0	1 (8%)	0	1 (1%)
	Other						
	Nausea or vomiting	4 (17%)	0	5 (29%)	4 (31%)	2 (15%)	15 (19%)
	Conjunctival injection	4 (17%)	3 (23%)	4 (24%)	1 (8%)	1 (8%)	13 (16%)
	Laughter	2 (8%)	3 (23%)	2 (12%)	1 (8%)	1 (8%)	9 (11%)
	Described as “high”, “stoned”, “dazed”	4 (17%)	2 (15%)	1 (6%)	1 (8%)	0	8 (10%)
	Hyperphagia	3 (13%)	0	1 (6%)	0	0	4 (5%)
	Prolonged toxicity (> 6 hours)	9 (38%)	9[a] (75%)	14[b] (88%)	13 (100%)	12[c] (100%)	57[d] (74%)
	Severe toxicity	1 (4%)	2 (15%)	10 (59%)	11 (85%)	13 (100%)	37 (46%)
	Severe neurologic toxicity	0	1 (8%)	6 (35%)	10 (77%)	11 (85%)	28 (35%)
	Severe cardiovascular toxicity	0	0	7 (41%)	5 (38%)	10 (77%)	22 (28%)
	Severe respiratory toxicity	1 (4%)	1 (8%)	5 (29%)	5 (38%)	7 (54%)	19 (24%)
Interventions	No interventions needed	18 (75%)	8 (62%)	4 (24%)	3 (23%)	1 (8%)	34 (43%)
	Intravenous fluids	5 (21%)	4 (31%)	11 (65%)	9 (69%)	12 (92%)	41 (51%)
	Oxygen by nasal cannula	1 (4%)	1 (8%)	5 (29%)	5 (38%)	7 (54%)	19 (24%)
	Sedative medications	0	0	3 (18%)	0	2 (15%)	5 (6%)
	Intubation or noninvasive ventilation	0	0	1 (6%)	0	1 (8%)	2 (3%)
	Vasopressors	0	0	0	0	1 (8%)	1 (1%)
Disposition	Pediatric ICU	0	1 (8%)	3 (18%)	1 (8%)	5 (38%)	10 (13%)
	Pediatric inpatient (Non-ICU)	4 (17%)	4 (31%)	8 (47%)	8 (62%)	6 (46%)	30 (38%)
	Discharged home from ED	20 (83%)	8 (62%)	6 (35%)	4 (31%)	2 (15%)	40 (50%)

No dysrhythmias other than bradycardia or tachycardia were noted. Prolonged toxicity was only calculated for patients with known time of ingestion. Change from the n designated per column as follows: [a]*n* = 12, [b]*n* = 16, [c]*n* = 12, and [d]*n* = 77.

single patient was unresponsive on arrival and could have been characterized as comatose. She recovered to baseline within 24 hours of ingestion. Seizures, respiratory failure requiring intubation, and hemodynamic compromise requiring vasopressors also occurred. However, these manifestations were rare. The dose range to induce these symptoms was 2 to 69 mg/kg. This wide range suggests other patient characteristics may contribute to the risk of these effects.

TABLE 3A Tetrahydrocannabinol Ingestion Dose, Duration of Symptoms and Admission Needs for Pediatric Edible Ingestions, Stratified by Severity and Duration of Toxicity			
	Severe Toxicity (n = 37)	Absence of Severe Toxicity (n = 43)	P
Median THC dose in mg/kg (IQR)	5.4 (3.2–8.2)	0.9 (0.6–1.9)	<.0001
Median duration of signs and symptoms in h (IQR)	20.3 (12.8–29.5)	6.3 (3–10)	<.0001
Required admission (%)	28 (76%)	12 (28%)	<.0001

Guidance on the anticipated clinical course would influence decisions such as hospital transfer, admission, invasive workups, and other interventions. Broad evaluations can be avoided in most known pediatric cannabis exposures, but expanded workups may be warranted if patients do not meet the typical disease script.[21] A reliable ingestion history could be used to guide resource utilization and management decisions in these cases.

The performance of the ROC curve analyses allows us to propose a weight-based THC dose threshold to identify higher-risk patients. Ingestions exceeding 1.7 mg/kg and 2.3 mg/kg balanced the highest sensitivity and specificity for predicting prolonged and severe toxicity, respectively. Arguably, predicting severe toxicity with high sensitivity is most critical. Changing the THC-dose threshold for severe toxicity from 2.3 mg/kg to the threshold as identified for prolonged toxicity, 1.7 mg/kg, would improve sensitivity to 97.3%. The ROC curve analysis prediction for prolonged toxicity was less accurate than the severe toxicity prediction, with an AUC of <90%. We believe that this is influenced by limitations in retrospectively determining when a patient returned to baseline. Return to baseline documentation was likely impacted by the time of day, frequency of reevaluations, and medical team charting tendencies. We expect that time to return to baseline is likely an overestimation, which would strengthen this prediction.

Ultimately, we propose that exposures exceeding 1.7 mg/kg of THC would benefit from being managed where pediatric services and prolonged observation or admission capabilities are available. Transfer to a tertiary facility could be avoided in children with smaller ingestions who do not require interventions beyond observation. Home observation through poison center guidance may require a larger safety margin and likely widespread improvement in cannabis regulations.

The single patient with severe toxicity below the 1.7 mg/kg threshold was a 2-year-old with a 0.6 mg/kg THC exposure. He had days of viral symptoms preceding his ingestion and increased fatigue prompted presentation. He required a nasal cannula temporarily during ED observation. It is possible that an infectious illness drove hypoxia, or the THC dose reported was inaccurate; however, this case may also reveal vulnerability to THC effects in children with other illnesses.

We recognize that using THC dose to risk stratify cases has its limitations. In our sample, this strategy could only be applied to 53% of suspected edible ingestions. In addition, the thresholds may not universally apply to all settings such as unregulated cannabis markets in which reported THC content is unreliable.

In these circumstances, toxicity features and the timing of initial symptoms could also guide management. Most patients in the study developed THC effects within 2 hours of ingestion and severe effects within 4 hours. Although edible cannabis absorption can be erratic, this timing is consistent with previous pharmacokinetic and pharmacodynamic investigations.[22–24] Thus, asymptomatic children post-ingestion could likely be monitored for 2 hours for evolving clinical effects. Additionally, all patients with severe toxicity required >6 hours to return to baseline (median 20.3 hours). Therefore, patients who will have a prolonged clinical course could be identified by the presence of severe effects, with most declaring themselves within 4 hours of their ingestion.

The increase in pediatric cannabis exposures has been associated with increased marijuana legalization.[3,10,25] The threshold predictive of severe and prolonged toxicity should influence cannabis regulations. A commonly enforced serving size for recreational edibles is 10 mg of THC. However, packages may contain up to 10 servings.[15] Based on our findings, a 10 mg THC ingestion would be unlikely to cause severe toxicity in most young children. With each additional 1 mg/kg of THC, the odds of severe or prolonged symptoms triple. Limiting the total THC content per package or individually packaging each serving could make a significant impact. Using the 25th percentile weight for a 3-year-old female (12.8 kg), access to >2 10 mg serving sizes would exceed 1.7 mg/kg, placing the child at risk for

TABLE 3B Tetrahydrocannabinol Ingestion Dose, Duration of Symptoms and Admission Needs for Pediatric Edible Ingestions, Stratified by Severity and Duration of Toxicity			
	Prolonged Toxicity >6 h (n = 57)	Toxicity Duration <6 h (n = 20)	P
Median THC dose in mg/kg (IQR)	3.7 (1.7–5.7)	0.7 (0.5–1.4)	<.0001
Median duration of signs and symptoms in h (IQR)	14.5 (9.1–24.4)	2.8 (0.5–4.6)	<.0001
Required admission (%)	37 (65%)	0	<.0001

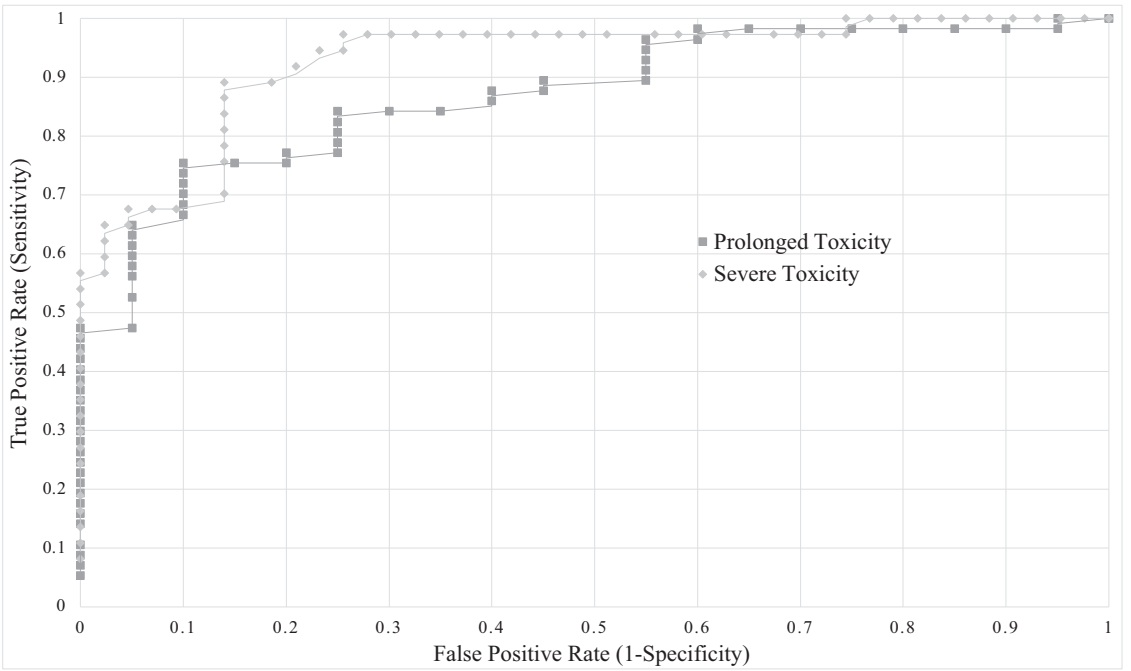

FIGURE 2
ROC curves for severe toxicity (AUC 92.9%) and prolonged toxicity (AUC 87.3%) for pediatric edible cannabis ingestions.

serious toxicity.[26] Historically, dose limitations via blister packaging and other child-resistant methods decreased unintentional pediatric poisonings.[27–29] In Canada, strict regulations are in place, including a THC limit of 10 mg per package; yet cannabis-related pediatric hospitalizations still rose after edible legalization, and edible exposures were an independent predictor of admission to the ICU.[3,4,30] Other factors may also play a role in hospitalizations, such as the unfamiliarity and novelty of the cannabis toxidrome in children. Nonetheless, the Canadian experience highlights the need for additional measures to improve cannabis safety. These strategies could include further consumer education and minimizing the attractiveness of cannabis to children.

There are limitations to this study. This study reflects the most common pediatric age group that unintentionally ingests edibles; however, it excludes other age groups.[10,11,31] In this state, cannabis products are tested for potency and packaging labels must display accurate THC dose information. This state also passed rules requiring serving sizes to be obvious to the consumer, such as 1 gummy or a score of chocolate. Thus, estimates of ingestion dose were intuitive to determine by caregivers.[15] However, there may have been errors in parent/guardian reporting, and reporting bias may have also influenced the accuracy of caregiver history. Although quality mandates are in place for THC dose accuracy, the Food and Drug Administration has not approved federal testing requirements or standards. In this study, not all patients had confirmatory testing to prove cannabis exposure. However, the history and symptoms of toxicity would support edible ingestion in cases in which a UDS was not performed. Finally, the retrospective study design is limited by the completeness of medical chart documentation.

CONCLUSIONS

Ingestion of edible cannabis in children <6 years old can lead to clinically significant toxicity. The THC dose ingested can be used to risk stratify patients in this age group, with ingestions exceeding 1.7 mg/kg being more likely to develop severe and prolonged toxicity. This threshold should be considered in both medical management decisions and development of marijuana regulations.

ABBREVIATIONS

AOR: adjusted odds ratio
AUC: area under the curve
CI: confidence interval
ED: emergency department
IQR: interquartile range
ROC: receiver operator characteristic
THC: tetrahydrocannabinol
UDS: urine drug screen

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