Unintentional Cannabis Ingestion in Children: A Systematic Review

John R. Richards, MD, Nishelle E. Smith, MS, and Aimee K. Moulin, MD

Objective To analyze published reports of unintentional cannabis ingestions in children to determine presenting signs and symptoms, route of exposure, treatment, and outcome.

Study design PubMed, OpenGrey, and Google Scholar were systematically searched. Articles were selected, reviewed, and graded using Oxford Center for Evidence-Based Medicine guidelines.

Results Of 3316 articles, 44 were included (3582 children age ≤12 years). We found no high quality (Oxford Center for Evidence-Based Medicine level I or II) studies and 10 level III studies documenting lethargy as the most common presenting sign and confirming increasing incidence of unintentional ingestion in states having decriminalized medical and recreational cannabis. We identified 16 level IV case series, and 28 level V case reports with 114 children, mean age 25.2 ± 18.7 months, range 8 months to 12 years, and 50 female children (44%). The most common ingestion (n = 43, 38%) was cannabis resin, followed by cookies and joints (both n = 15, 13%). Other exposures included passive smoke, medical cannabis, candies, beverages, and hemp oil. Lethargy was the most common presenting sign (n = 81, 71%) followed by ataxia (n = 16, 14%). Tachycardia, mydriasis, and hypotonia were also commonly observed. All cases were cared for in the emergency department or admitted, and mean length of stay was 27.1 ± 27.0 hours. Twenty (18%) were admitted to the pediatric intensive care unit, and 7 (6%) were intubated.

Conclusions Unintentional cannabis ingestion by children is a serious public health concern and is well-documented in numerous studies and case reports. Clinicians should consider cannabis toxicity in any child with sudden onset of lethargy or ataxia. *(J Pediatr 2017;■■:■■-■■).*

See editorial, p •••

Cannabis is the most commonly used illicit drug throughout the world, with over 180 million users.[1] In the US, there are an estimated 22.2 million people (8.3%) aged 12 years or older who are current users of cannabis based on the 2015 National Survey on Drug Use and Health.[2] Adult cannabis use and prevalence of cannabis use disorder has more than doubled over the past decade.[2] In 2011, there were 456 000 emergency department visits related to cannabis use, a 21% increase from 2009.[3] As of 2017, over one-half of all 50 states had passed legislation to allow medical cannabis and 8 had legalized recreational cannabis (**Table I**).[4] Cannabis has become a major industry in states in which its recreational use is legal. In Colorado, legal cannabis generated $2.39 billion in sales in 2015 and represented the second largest excise tax revenue source, at $121 million.[5] At the federal level, cannabis remains a schedule I drug since 1970 "with no currently accepted medical use and a high potential for abuse" by the Drug Enforcement Administration. Food and Drug Administration regulations on manufacturing, packaging, labeling, and marketing do not apply to state-decriminalized recreational cannabis. An unfortunate consequence of this increasing legalization, availability, and marketing of cannabis has been a parallel increase in unintentional pediatric exposures from passive smoke, edible products such as cookies, and unsecured or unfinished hashish or joints.[6] Such ingestions have led to serious and prolonged cannabis intoxication resulting in extensive diagnostic testing and hospitalization for monitoring. The objective of this study was to review the published literature regarding the unintentional ingestion of cannabis by children to characterize presenting signs and symptoms, route of exposure, treatment, and outcome. To date, this has not been previously investigated and published.

Methods

All published studies, case series, or case reports of unintentional ingestion of cannabis in young children (age 12 years or less) were considered in the literature search. This age cut-off was chosen because the transition between unintentional and intentional ingestion appeared to be most distinct at this stage of maturity,

PICU	Pediatric intensive care unit
THC	Δ9-tetrahydrocannabinol
TW	Text words

From the Department of Emergency Medicine, University of California Davis Medical Center, Sacramento, CA

A.K.M. is supported by a postdoctoral training grant in health services research from the Agency for Healthcare Research and Quality (T32 HS022236). The other authors declare no conflicts of interest.

http://dx.doi.org10.1016/j.jpeds.2017.07.005

Table I. List of states, territories, and years for which medical and recreational cannabis were legalized

States or territories	Recreational	Medical
Alaska	2015	1999
Arizona		2010
Arkansas		2016
California	2016	1996
Colorado	2013	2000
Connecticut		2012
Delaware		2011
District of Columbia	2014	1998
Florida		2016
Guam		2014
Hawaii		2000
Illinois		2013
Maine	2016	1999
Maryland		2003
Massachusetts	2016	2012
Michigan		2008
Minnesota		2014
Montana		2004
Nevada	2016	2000
New Hampshire		2013
New Jersey		2009
New Mexico		2007
New York		2014
North Dakota		2016
Ohio		2016
Oregon	2014	1998
Pennsylvania		2016
Puerto Rico		2016
Rhode Island		2007
Vermont		2004
Washington	2012	1998

with intentional ingestion representing prior knowledge and assent to cannabis use. Data were abstracted systematically from a query of PubMed, OpenGrey, and Google Scholar from inception to April 2017. Non-English language publications were included and translated. To maximize results, our search strategy included only free-text words (TW) as filters: ("cannabis"[TW] or "cannabinoid"[TW] or "marijuana"[TW] or "cannabinoids"[TW] or "hash"[TW] or "hashish"[TW]) and ("children"[TW] or "pediatric"[TW] or "child"[TW] or "toddler"[TW] or "infant"[TW] or "baby"[TW] or "girl"[TW] or "boy"[TW]).

References in each selected publication were also carefully hand screened for any additional relevant reports. A gray literature search was also performed using OpenGrey, Google, and Google Scholar. All authors reviewed the articles independently, and articles without mention of specific route of exposure were excluded. The PRISMA guidelines were followed.[7] Articles were excluded if intentional ingestion was noted. Articles were graded using the Oxford Center for Evidence-Based Medicine levels of evidence.[8] These levels are defined as I = properly powered and conducted randomized clinical trial, systematic review, or meta-analysis; II = well-designed controlled trial without randomization; prospective comparative cohort; III = case-control studies, retrospective cohort studies; IV = case series with or without intervention, cross-sectional studies; and V = opinion of authorities, case reports. Reviews of poison center data were considered level III. Demographics, sex, route of exposure, vital signs, symptoms, toxicology results, disposition, treatments, length of stay, and outcomes were extracted from the articles and summarized (**Table II**).

Results

The search resulted in 3316 articles with 44 eligible for inclusion and involving 3582 children age 12 years or less (**Figure 1**). There were no high quality (Oxford Center for Evidence-Based Medicine level I or II) prospective studies. Examples of clinical studies and cases excluded were trials of medical cannabis for treatment of epilepsy, adolescent use, and socioeconomic and psychiatric investigations regarding children with cannabis-using parents.

There were 10 level III studies identified. In 2009, Spadari et al[33] reported the first retrospective study of unintentional cannabis ingestion in children, with 93 cases over 7 years reported to the Marseille Poison Center in France. The age range was 8 months to 8 years old, with the majority (86%) under age 3 years. Most cases were oral ingestions (98%) with cannabis resin (ie, hashish [80%]). The most common symptoms were somnolence (n = 45), hypotonia (n = 10), mydriasis (n = 8), and agitation (n = 8). The most serious presentations included respiratory depression (n = 5) and seizure (n = 2). This was followed by Le Garrec et al[53] in their 2014 retrospective review over a 3.5-year period of unintentional cannabis ingestions admitted to the Robert Debré University Hospital pediatric intensive care unit (PICU) in Paris, France. There were 7 cases, with an average age of 16 months (range 12-33 months). Five patients presented with Glasgow Coma Scale <8, and 3 were intubated. The average length of stay was 19 hours.

Lovecchio and Heise[54] reviewed call data from a regional poison center in Arizona before and after decriminalization of cannabis in late 2010. There were no calls concerning unintentional cannabis ingestion in 2010, 6 in 2011, 27 in 2012, and 16 in 2013. However, no details were given regarding the specific exposures except for 2 children who presented with hypoventilation requiring supplemental oxygen therapy after ingesting cannabis-infused chocolate chip cookies. Claudet et al[55] reviewed patients with unintentional cannabis ingestion treated at a children's hospital in Toulouse, France from 2004 to 2014. Twenty-nine children under 3 years old were admitted, of whom 10 (34%) had a decreased level of consciousness and were admitted to the PICU. Four experienced seizures prior to admission, and 3 were intubated. Resin was the main form of ingested cannabis (69%).

Cao et al[56] analyzed exposure calls coded to cannabis-infused brownies, candies, cookies, beverages, or other foods reported to the National Poison Data System from 2013 to 2015. There were 190 calls for children less than 6 years old, with 59 calls specifically for brownies, cookies, and candies alone. Over 90% of calls occurred in decriminalized states. More than one-half were treated at a hospital, and 2 children were intubated. Onders et al[57] reviewed unintentional cannabis exposures among children less than 6 years old in the US National Poison Data System from 2000 through 2013. There were 1969

FLA 5.5.0 DTD ■ YMPD9323_proof ■ September 6, 2017