MARIJUANA EXPOSURE IN PEDIATRIC PATIENTS

Pediatric Care Symposium
April 20, 2017
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Pediatric Emergency Medicine

DISCLOSURES

- I have no financial interests to disclose.
- I will discuss pharmaceutical products used “off-label” or not approved by the FDA.

OBJECTIVES

- Compare the presentations of pediatric cannabinoid exposure
- Review the mechanism of cannabinoid effects and potential uses
- Analyze the effects of recent marijuana legislation on children

THE MOST IMPORTANT MEAL OF THE DAY?

- 8:30 am: Call from EMS bringing in 3-year-old and 20-month-old with altered mental status and concern for carbon monoxide poisoning
- Simultaneous arrival of unresponsive 3 yo and altered 20 mo brothers without their parents
- Father and mother reportedly ill and in the adult ER

WHAT DO YOU DO FIRST?

- Airway
- Breathing
- Circulation
- Disability
- Exposure
INITIAL EVALUATION

- 3 yo boy
- Vital signs: T 36.8, HR 116, BP 76/48, RR 19, 100%
- Pupils: 6 mm and reactive bilaterally
- No evidence of trauma
- Neuro: No spontaneous eye opening, verbalization, or movement, hypotonic, cries out with urinary catheterization, GCS 7

INITIAL EVALUATION

- 20 mo boy
- Vital signs: T 36.2, HR 120, BP 120/76, RR 35, 100%
- Pupils: 5 mm and reactive bilaterally
- No evidence of trauma
- Neuro: Sleepy, ataxic, hypotonic, clinging to nursing staff

DIFFERENTIAL DIAGNOSIS

- Metabolic
- Trauma
- Toxicologic

- Infectious
- Neurologic
- Other
- Cardiac

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DIFFERENTIAL DIAGNOSIS

- Metabolic
  - Hypo/hyperglycemia
  - Hypo/hypomagnesemia
  - Genetic/ Metabolic Disorder

- Infectious
  - Sepsis
  - Meningoencephalitis

- Neurologic
  - Syncope

- Toxicologic
  - Sedative/Hypnotic
  - Opioid
  - Benzodiazepine
  - Alcohol
  - Carbon monoxide
  - Other
  - Intussusception

PARENTS ARRIVE

- What would you like to know?
  - Otherwise healthy children
  - Kids woke up their father, 3 yo later said that he was dizzy
  - Father woke up mother and told her to call 911
  - Father now denies feeling ill, mother believes her nausea is due to pregnancy
  - Family adamant that there are never alcohol or drugs in the house and that the children don't have access to any medications
INITIAL RESULTS

- Point of care glucose normal
- Point of care venous blood gas normal
- No improvement with naloxone
- Pending labs: CBC, CRP, CMP, urine drug screen, carboxyhemoglobin, ethanol, salicylate and acetaminophen levels

WHAT NEXT?

- Intubation?
- Head CT?
- Lumbar puncture?
- Activated charcoal?
- Get breakfast?

...WITH A LITTLE HELP FROM MY FRIENDS...

- 9:20 am: Urine drug screen positive for cannabinoids
- Security present and enters first since the father is carrying a knife
- Father now reports that the parents were at an “adult party” last night and were given banana bread to take home, which he gave to the children for breakfast. He calls the hosts and confirms that the bread contained marijuana.
- Children remained obtunded, but with stable vital signs
- Admitted to the PICU and reported to CPS

CANNABIS

- Cannabis sativa or Cannabis indica
- Flowering tops, seeds, and stems
- Over 200 phytocannabinoid compounds
- Used medicinally since 2737 B.C.
- On U.S. Pharmacopoeia 1851-1937
- No regulations on labeling, storage, or child-proof containers

TETRAHYDROCANNABINOL

- Active at CB1 and CB2 receptors
- 5-20% oral bioavailability
- Slow, irregular peak 1-5 hours after ingestion

POTENTIAL USES

- Two FDA-approved oral medications
- Dronabinol: Schedule III medication for nausea and vomiting in AIDS and cancer
- Nabilone: Schedule II medication for spinal cord injury spasticity
- Approved in Canada and UK
- Sativex: Oral mucosal spray for neuropathic pain
EPILEPSY AND CANNABIDIOL

- Marijuana strains high in CBD and low in THC
- Animal studies showing anticonvulsant properties
- Risk of cognitive dysfunction
- Parental reports of improvement
- Lack of RCT data

CBD-enriched medical cannabis for intractable pediatric epilepsy
The current Israeli experience

Michal Tzvilev1,2, Shmueli Uziel-Schwartz1, Eran Linden1, Uri Kramer4, Omer Epstein5, Shaya Meza5, Andina Novembre1, Omer Bar-Yam6, Eli Hymans1, Dori Coass5, Michael Dori7, Itzik Getman-Gafni7, Reuven Ben-Zeev8

- 74 patients, ages 1-18 years
- Previously failed 5-7 medications, +/- ketogenic diet, VNS, surgery
- Oil analyzed by chromatography and dosage monitored
- 89% of patients with reduction in seizure frequency
- 46% with adverse effects
  - 18% increased seizures, 22% somnolence, 7% GI symptoms

Cannabidiol in patients with treatment-resistant epilepsy:
an open-label interventional trial

- Prospective, open-label trial of 214 patients ages 1-30 years
- 11 US epilepsy centers
- Oral cannabidiol at 2-5 mg/kg/day to maximum 50 mg/kg/day
- Median reduction in motor seizures of 36.5%
- Adverse events in 79%, serious in 20%

Duration of use of oral cannabis extract in a cohort of pediatric epilepsy patients

- Retrospective review of 119 patients aged 30 days to 18 years
- 49% with some improvement, 24% with 50% improvement
- Adverse events 19%
  - Worsening seizures, somnolence, GI symptoms
- 71% discontinued use of product during study period
CURRENT EVENTS

- Federal Law: Schedule I drug
- Medical use in 29 states and D.C.
- Recreational use
  - California, Massachusetts, Maine, Nevada (2016)

EDIBLE MARIJUANA EXPOSURES

- 433 calls to poison control centers from 2013-2015
- 109 calls for children under age 5
- No deaths
- 2 children required ventilator support
- Colorado and Washington states with highest number of calls

Association of Unintentional Pediatric Exposures With Decriminalization of Marijuana in the United States

State legality status according to presence and year of legislation

- Nonlegal
- Transitional (legalized during 2005-2011)
- Decriminalized (legalized prior to 2005)

Table 2. Symptoms and duration of symptoms of unintentional pediatric exposures (2005 to 2011)

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Nonlegal Status (n = 464)</th>
<th>Transitional Status (n = 89)</th>
<th>Decriminalized Status (n = 236)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous system</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disorientation (%)</td>
<td>97 (21)</td>
<td>38 (42)</td>
<td>147 (62)</td>
</tr>
<tr>
<td>Irritability (%)</td>
<td>29 (9)</td>
<td>3 (3)</td>
<td>11 (5)</td>
</tr>
<tr>
<td>Agitation/anxiety (%)</td>
<td>44 (9)</td>
<td>3 (3)</td>
<td>11 (5)</td>
</tr>
<tr>
<td>Other (%)</td>
<td>44 (9)</td>
<td>3 (3)</td>
<td>11 (5)</td>
</tr>
<tr>
<td>Total</td>
<td>199 (43)</td>
<td>38 (42)</td>
<td>257 (108)</td>
</tr>
<tr>
<td>Electrocardiographic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventricular arrhythmia (%)</td>
<td>9 (2)</td>
<td>2 (2)</td>
<td>9 (4)</td>
</tr>
<tr>
<td>Cardiac and respiratory symptoms</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Respiratory depression (%)</td>
<td>3 (6)</td>
<td>3 (3)</td>
<td>5 (2)</td>
</tr>
<tr>
<td>Mental status (%)</td>
<td>2 (2)</td>
<td>2 (2)</td>
<td>5 (2)</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 h (%)</td>
<td>92 (20)</td>
<td>44 (48)</td>
<td>129 (55)</td>
</tr>
<tr>
<td>&gt;2 h, ≤24 h (%)</td>
<td>95 (21)</td>
<td>32 (35)</td>
<td>129 (55)</td>
</tr>
<tr>
<td>&gt;24 h, ≤72 h (%)</td>
<td>90 (21)</td>
<td>32 (35)</td>
<td>93 (40)</td>
</tr>
<tr>
<td>&gt;72 h, ≤14 days (%)</td>
<td>93 (21)</td>
<td>32 (35)</td>
<td>93 (40)</td>
</tr>
<tr>
<td>&gt;14 days, ≤30 days (%)</td>
<td>53 (12)</td>
<td>5 (5)</td>
<td>5 (2)</td>
</tr>
<tr>
<td>&gt;30 days, &gt;30 days (%)</td>
<td>5 (1)</td>
<td>3 (3)</td>
<td>5 (2)</td>
</tr>
</tbody>
</table>

Table 3. Medical outcomes and pattern disposition of unintentional pediatric exposures (2005 to 2011)

<table>
<thead>
<tr>
<th>Medical outcomes and pattern disposition of unintentional pediatric exposures (2005 to 2011)</th>
<th>Nonlegal Status (n = 464)</th>
<th>Transitional Status (n = 89)</th>
<th>Decriminalized Status (n = 236)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical outcome of decedent</td>
<td>4 (0.9)</td>
<td>1 (1.1)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Cause of death</td>
<td>4 (0.9)</td>
<td>1 (1.1)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>4 (0.9)</td>
<td>1 (1.1)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Emergency status</td>
<td>4 (0.9)</td>
<td>1 (1.1)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Total hospitalization duration (days)</td>
<td>1 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Medication prescribed</td>
<td>4 (0.9)</td>
<td>1 (1.1)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Follow-up</td>
<td>4 (0.9)</td>
<td>1 (1.1)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Disposition of patient</td>
<td>1 (0.2)</td>
<td>0 (0)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Returned to normal</td>
<td>1 (0.2)</td>
<td>0 (0)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Returned to non-normal or critical care state</td>
<td>2 (0.4)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Figure 2. Distribution of unintentional marijuana exposures reported to poison centers in the United States from 2005 to 2011. Numbers represent calls per state, per 100,000 reasons data for children aged 5 years and younger.
KIDS THESE DAYS

Infant with altered consciousness after cannabis passive inhalation

Yehezka Zarif1,2,3, Eshav Yefet4, Shai Abrav,5 Wael Nasser,7 Tamer Mor,4 Yozan Rakieten6

1 Department of Pediatrics, Barzil-Ashkenazi Medical Center, Zeroka, Israel
2 Department of Pediatrics and Prevent Health, Barzil-Ashkenazi Medical Center, Zeroka, Israel

- 3 mo M with lethargy, temperature 38
- CBC, CMP, EKG, CXR, blood and urine cx, Utox. Ceftriaxone given.
- Sleeping upstairs from 20 cannabis smokers for several hours
- Supportive care with improvement and discharge after 48 hours

A case series of marijuana exposures in pediatric patients less than 5 years of age

George Sam Wang4, Sandeep K. Narang6, Kathryn Wells5, Ryan Chung6

- Retrospective chart review Colorado Children’s Hospital
- 11/09-03/10: Five patients with THC in urine
- 2 admissions (1 ICU), 3 discharged home

Table 1

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Gender</th>
<th>Presenting symptom</th>
<th>Presence of medical marijuana use</th>
<th>Auxillary tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3 yr</td>
<td>Male</td>
<td>Seizures, vomiting</td>
<td>Yes</td>
<td>CBC, CMP, EKG, Utox, Urine Toxic Screen</td>
</tr>
<tr>
<td>2</td>
<td>7 yr</td>
<td>Male</td>
<td>Seizures, vomiting</td>
<td>Yes</td>
<td>CBC, CMP, EKG, Utox, Urine Toxic Screen</td>
</tr>
<tr>
<td>3</td>
<td>10 mo</td>
<td>Female</td>
<td>Seizures, vomiting</td>
<td>Yes</td>
<td>CBC, CMP, EKG, Utox, Urine Toxic Screen</td>
</tr>
<tr>
<td>4</td>
<td>16 mo</td>
<td>Male</td>
<td>Seizures, vomiting</td>
<td>Yes</td>
<td>CBC, CMP, EKG, Utox, Urine Toxic Screen</td>
</tr>
<tr>
<td>5</td>
<td>2 yr</td>
<td>Male</td>
<td>Seizures, vomiting</td>
<td>Yes</td>
<td>CBC, CMP, EKG, Utox, Urine Toxic Screen</td>
</tr>
</tbody>
</table>

PROLONGED COMA IN A CHILD DUE TO HASHISH INGESTION WITH QUANTITATION OF THE METABOLITES IN URINES

Shaun D. Cantin, BSc,1 Michael K. Fulke, BSc,2 Greg E. Keeney, BSc,3 and Beth T. Lip, BSc,4

Department of Emergency Medicine, Division of Emergency Medicine, University of California, San Diego, California, Department of Emergency Medicine, San diego Veterans Affairs Medical Center, San Diego, California, and Department of Pediatrics, University of California, San Diego, San Diego, California

- 14 mo F “2 bites” from block of hashish
- Presented comatose 13 hours later
- VS: 36.4, 115, 94/48, 12, 88%
- GCS 7, pupils 5mm sluggish, hypotonic
- ABG: 7.16/66/65, Glic 129
- CBC, CMP, EIOH, APAP, Utox, head CT
- Naloxone, flumazenil
- THC urine 3844 ng/ml (50x level of one cigarette), and decreased to to 203 ng/ml
- Recovery in 48 hours

Ingestion of cannabis: A cause of coma in children

Andrew Macias, MD, Ellen Anderson, RN, Lark Sisak, RN

- 17 mo M with coma, conjunctivitis, lip smacking, Utox +, 6 hrs later with normal mental status and “voracious appetite”
- 2 yr F with drowsiness, euphoria, 1 gm hashish missing from table
- 3 yr F with drowsiness, slurred speech, hypotonia, and ataxia for 3 hrs. Hashish and water in children’s tea set.
- 3 yr M sibling of case 5, responsive only to pain. Admitted for airway obstruction.
CANNABINOID HYPEREMESIS
- First described in 2004
- Intractable vomiting
- Weight loss
- Relieved by hot showers
- Case reports of frequent ED visits, hospitalizations, and extensive work-up
- Treatment: discontinuation of cannabis

SYNTHETIC CANNABINOIDS
- Cannabinimetic chemicals
  - Spice, K2, etc.
  - Sold as "not for consumption"
- 488 calls to Poison Center January-March 2017

SYNTHETIC CANNABINOIDS
- Agitation
- Hallucinations and psychosis
- Tachycardia and hypertension
- Vomiting
- Seizure

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DEDICATED TO THE HEALTH OF ALL CHILDREN™
- 1. Given the data supporting the negative health and brain development effects of marijuana in children and adolescents, ages 0 through 21 years, the AAP is opposed to marijuana use in this population.
- 2. The AAP opposes “medical marijuana” outside the regulatory process of the US Food and Drug Administration. Notwithstanding this opposition to use, the AAP recognizes that marijuana may currently be an option for cannabinoid administration for children with life-limiting or severely debilitating conditions and for whom current therapies are inadequate.
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3. The AAP opposes legalization of marijuana because of the potential harms to children and adolescents. The AAP supports studying the effects of recent laws legalizing the use of marijuana to better understand the impact and define best policies to reduce adolescent marijuana use.

4. In states that have legalized marijuana for recreational purposes, the AAP strongly recommends strict enforcement of rules and regulations that limit access and marketing and advertising to youth.

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5. The AAP strongly supports research and development of pharmaceutical cannabinoids and supports a review of policies promoting research on the medical use of these compounds. The AAP recommends changing marijuana from a Drug Enforcement Administration schedule I to a schedule II drug to facilitate this research.

6. Although the AAP does not condone state laws that allow the sale of marijuana products, in states where recreational marijuana is currently legal, pediatricians should advocate that states regulate the product as closely as possible to tobacco and alcohol, with a minimum age of 21 years for purchase. Revenue from this regulation should be used to support research on the health risks and benefits of marijuana. These regulations should include strict penalties for those who sell marijuana or marijuana products to those younger than 21 years, education and diversion programs for people younger than 21 years who possess marijuana, point-of-sale restrictions, and other marketing restrictions.

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7. In states where marijuana is sold legally, either for medical or recreational purposes, regulations should be enacted to ensure that marijuana in all forms is distributed in childproof packaging, to prevent accidental ingestion.

8. The AAP strongly supports the decriminalization of marijuana use for both minors and young adults and encourages pediatricians to advocate for laws that prevent harsh criminal penalties for possession or use of marijuana. A focus on treatment for adolescents with marijuana use problems should be encouraged, and adolescents with marijuana use problems should be referred to treatment.

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9. The AAP strongly opposes the use of smoked marijuana because smoking is known to cause lung damage, and the effects of secondhand marijuana smoke are unknown.

10. The AAP discourages the use of marijuana by adults in the presence of minors because of the important influence of role modeling by adults on child and adolescent behavior.

TAKE-HOME POINTS

- Cannabis is a source of coma in children
- Pediatric patients often undergo an extensive and invasive work-up before diagnosis, and experience prolonged recovery
- Incidence of exposure is increasing with increasing legality

REFERENCES

REFERENCES


THANK YOU!