Articles You Might Have Missed

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Kang AM, Brooks DE. US Poison Control Center Calls for Infants 6 Months of Age and Younger. *Pediatrics*. 2016;137(2):e20151865.

Background Research on pediatric unintentional exposures rarely focuses on children less than 6-months of age because their developmental abilities are expected to limit possible exposures. The majority of exposures in this age group are thought to be due to therapeutic or dosing error.

Research Question What are the circumstances and drugs implicated in unintentional exposures among children ≤6 months of age?

Methods Retrospective cohort analysis of all calls reported to the National Poison Data System [NPDS; representing all US poison control centers (PCCs)] between January 2004 and December 2013 involving exposures to patients age 0 days to 6 months. Reasons for exposures were coded as intentional, unintentional, adverse reaction, or miscellaneous. Therapeutic errors were coded under “unintentional” and were further

characterized as quantitative (wrong dose) or non-quantitative (given twice, too soon, wrong medication, or wrong route).

Results There were 271,513 reported exposures among children ≤6 months of age, representing 1.1% of the total number of reported human exposures over the study period. The vast majority (97.6%) of exposures involved a single substance. Interestingly, 97.5% of exposures occurred in a residence, while only 85.2% of calls originated from a residence, indicating that caregivers are not always calling a PCC before going to a health care facility (HCF). Not surprisingly, 96.7% of exposures were coded as unintentional, with 50.7% being general unintentional and 36.7% being therapeutic error. Quantitative and non-quantitative therapeutic errors were roughly equal (19.7% v. 18.6%).

Diaper cream and rash products were responsible for the most ($n = 7495$) general unintentional exposures while acetaminophen ($n = 22,208$) was the most common cause of therapeutic error. Cough & cold products and ibuprofen, neither of which is recommended in this age group, were also common causes of therapeutic error. Ethanol and combination cough & cold preparations were responsible for the most major clinical effects for general unintentional exposures and therapeutic errors, respectively. Most (88.0%) exposures were managed outside of a HCF, and 0.9% of calls resulted in a moderate or severe effect. There was a total of 12 deaths.

Conclusion Exposures involving patients ≤6 months of age are almost exclusively unintentional in nature, with therapeutic errors being the reason for a third of all exposures. There was a sizeable discrepancy between the site of exposure and the origin of the PCC call.

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Critique As mentioned in the text, misclassification occurred as some calls were classified as intentional (both misuse and abuse). While this only represented 0.2% of all reported exposures, it underscores the limitations of using NPDS data. In addition, the definition of terms was scattered throughout the manuscript, with some definitions being found in the introduction, others in the methods, and other in the supplemental information. Similarly, limitations of the study were dispersed throughout the discussion; localizing them to the end of the manuscript would aide in reading and interpreting the study.

Implication for Toxicologists While most poison prevention programs focus on preventing exposures to the exploratory toddler, this study highlights the need for early educational interventions. These interventions should focus on PCC utilization (given the large number of self-referrals) and medication administration (given the frequency of therapeutic errors). This study also draws attention to the inappropriate use of certain medications (cough and cold preparations, ibuprofen) in this age group. Toxicologists need to keep a broad differential when examining and evaluating a newborn.

Gaither JR, Leventhal JM, Ryan SA, Camenga DR. National Trends in Hospitalizations for Opioid Poisonings Among Children and Adolescents, 1997 to 2012. *JAMA Pediatr.* 2016;170(12):1195–1201.

Background Morbidity and mortality due to opioid poisoning is increasing. Research in the adult population has shown a parallel relationship between opioid prescribing practices and hospitalizations for opioid poisoning. To date, no such data exists for the pediatric population.

Research Question How have hospitalization rates for pediatric opioid poisonings changed during the current prescription opioid epidemic?

Methods Retrospective analysis of serial cross-sectional data utilizing the Kids' Inpatient Database (KID) evaluating the rates of children and adolescents, 1–19 years of age, admitted to US hospitals for opioid poisoning. Data was collected every three years between 1997 and 2012. Among those 15–19 years of age, admissions for heroin and methadone poisoning were also analyzed. Poisonings were further classified as intentional, unintentional, and undetermined. Results were then weighted to provide national estimates.

Results In total, 13,052 hospitalizations for opioid poisoning were identified during the study period. The annual incidence of hospitalizations per 100,000 children increased from 1.40 to 3.71 (165% increase) over the 16-year study period. The proportion of male patient hospitalizations increased from

34.7% in 1997 to 47.4% in 2012. The largest increase was in the group aged 1–4 years of age (0.86 to 2.62; 205%) while adolescents (15–19 years old) saw an increase of 176% (3.69 to 10.17). Adolescents also had an increase of 140% in poisonings attributed to suicide or self-inflicted injury. Prescription opioids accounted for the most hospitalization across all years in the adolescent group, but hospitalizations for heroin increased 161% (0.96 to 2.21) while poisonings involving methadone increased 950%, from 0.10 to 1.05 per 100,000 children. A total of 176 children died over the course of the study period.

Conclusion The current opioid epidemic has led to a significant increase in hospitalizations for opioid poisonings across all pediatric age groups. Admissions for heroin, methadone, and poisonings attributed to suicide or self-inflicted injury continue to rise.

Critique In addition to examining hospitalizations for prescription opioids, the study separates hospitalizations for heroin and methadone, allowing for more data concerning trends in prescription and illicit opioid abuse. The use of the KID allows for a more complete description of the problem of pediatric opioid poisonings.

There were several limitations, including the inability to track readmissions for individual subjects. As *ICD-9-CM* codes were used by the KID to identify patients, further delineation of which specific prescription opioids were responsible for the hospitalizations was not possible. This data would be useful in targeting preventative interventions. There was also limited data concerning the clinical scenario and laboratory confirmation of these poisonings. Lastly, this study presents data from 1997 to 2012 and as such, the results are already out of date.

Implication for Toxicologists This study adds further evidence to the negative effects the current opioid epidemic is having on the pediatric population. Additional efforts need to be made in combating prescription drug abuse as well as unintentional exposures.

Wang GS, Le Lait MC, Deakyne SJ, Bronstein AC, Bajaj L, Roosevelt G. Unintentional Pediatric Exposures to Marijuana in Colorado, 2009–2015. *JAMA Pediatr.* 2016;170(9):E1–E6.

Background More states are legalizing medicinal and recreational marijuana. Detailed information regarding the incidence of exposure and clinical effects on the pediatric population is lacking.

Research Question What is the incidence of pediatric marijuana exposure before and after recreational marijuana legalization in Colorado compared to the rest of the United States?

Methods Retrospective cohort study of patients, 0 to 9 years of age, who presented to Children’s Hospital Colorado (CHC) or were reported to the Colorado regional poison center (RPC) following single-agent exposure to marijuana between January 1, 2009 and December 31, 2015.

Results A total of 62 CHC patients were identified and analyzed. The average rate of pre-legalization exposure (2012–2013) was 1.2 per 100,000 population compared to 2.3 post-legalization (2014–2015). During the post-legalization period, the median patient age was 2.4 years (IQR, 1.4–3.4) and 60% were male. Roughly half of the exposures were due to recreational products, and half (48%) were due to edible products. The majority (65%) of patients were observed and discharged from the ED or Urgent Care, 21% were admitted to an inpatient ward and 15% were admitted to an intensive care unit (1 patient was intubated, 1 required continuous positive pressure). The median length of stay (including ED patients) was 11 hours, and 26 hours for those admitted.

The Colorado RPC cases increased significantly post-legalization, with a mean increase in marijuana calls of 34% per year, compared to 19% increase per year for the rest of the US. A third (37%) of cases originated from patient’s home while 60% originated from a health care facility. Most children had no ($n = 45$; 28%) or minor ($n = 75$; 46%) effects. The most common clinical effects were drowsiness/lethargy (49%), ataxia (12%) and agitation (8%). There was one reported death in an 11-month-old patient, although it is unclear if marijuana was causative.

Conclusion Unintentional marijuana exposures increased in the first 2 years after legalization in Colorado, with edible products frequently being involved. As other states move to legalize marijuana, the consequences of unintentional pediatric exposures must be acknowledged.

Critique By examining data from a single hospital and a RPC, the authors increased the generalizability of the study (including rural and urban areas). The overall numbers of the study are impressive, and data are up to date with information from 2015 presented.

The study lacks detailed clinical information on the patients who were seen at CHC. Similarly, the number and type of interventions that occurred at CHC were not provided. This type of detailed information is not routinely available from poison center-based studies but could have been extracted directly from hospital records. The data discussing hospital testing are presented in two different forms for pre- and post-legalization. The authors failed to

define if “recreational marijuana” represents non-medical dispensary products and/or those illegally obtained?

Implication for Toxicologists Unintentional marijuana exposure should be included in the differential diagnosis for pediatric patient with acute toxic encephalopathy. Poison centers and toxicologists must play an active role in educating emergency medicine and pediatric providers on the clinical effects of marijuana exposure among kids. Emphasis on the safe storage of all marijuana, particularly edible preparations, is necessary.

Kamboj A, Spiller HA, Casavant MJ, Chounthirath T, Smith GA. Pediatric Exposure to E-Cigarettes, Nicotine, and Tobacco Products in the United States. *Pediatrics*. 2016;137(6):e20160041.

Background Electronic cigarettes (e-cigarettes) entered the US marketplace in 2007 with total sales expected to approach \$10 billion dollars by 2017. Looking only at combined cigarette and e-cigarette exposure calls to US Poison Control Centers (PCCs), the proportion of e-cigarette exposures increased from 0.3% in September 2010 to 41.7% in February 2014. Liquid nicotine is an emerging public health threat as electronic cigarettes become more popular.

Research Question What are the epidemiologic characteristics and outcomes of exposures to electronic cigarettes, nicotine, and tobacco products among young children in the US?

Methods A retrospective analysis of single substance exposures, involving nicotine and tobacco products among children <6 years of age, called to the National Poison Data System (NPDS; representing all US PCCs). The study period was January 1, 2012 through April 30, 2015.

Results The NPDS received 29,141 nicotine/tobacco calls during the study period for children <6 years old, averaging 729 pediatric exposures per month. Cigarettes accounted for 60.1% of calls, tobacco products (chewing tobacco/snuff) for 16.4%, and e-cigarettes for 14.2%. The vast majority (95.5%) of calls involved an ingestion, and 39% originated from the Southern region of the US. The scenario associated with e-cigarette exposures was known in 5.1% of cases; product storage within sight of the child took place in 44.8% of these exposures. Ten percent of households reported that e-cigarettes were always left out in sight and 8.6% stated the products were temporarily open while in use. More than three-quarters (79.6%) of exposed children were <2 years old. Dramatically, the monthly e-cigarette exposure rate rose by 1492.9% between January 2012 ($n = 14$) and April 2015 ($n = 223$).

Approximately three-quarters (75.9%) of the exposed children were managed on site (typically at home), 16.6% were treated and released from a healthcare facility (HCF), 0.4% admitted to a floor bed, and 0.2% required critical care admissions. Children with e-cigarette exposures were more commonly referred to HCFs by PCCs compared to those with exposures to conventional cigarette/tobacco products. In addition, children with e-cigarettes exposures were more likely to be admitted to a HCF compared to cigarettes (OR 5.19, 95% CI 3.60–7.48) or other tobacco products (OR 4.69, 95% CI 2.71–8.12). Among all exposed children, 1.2% suffered severe outcomes and a 1-year-old child died after access to a refill container of liquid nicotine. Children exposed to e-cigarettes (OR 2.60, 95% CI 1.96–3.46) or other tobacco products (OR 3.05, 95% CI 2.35–3.96) were more likely to have severe outcomes compared to those exposed to cigarettes. The most common clinical effect was vomiting (22%); the serious clinical effects included coma ($n = 6$), seizure ($n = 6$), respiratory arrest ($n = 3$), and cardiac arrest ($n = 1$).

Education and prevention techniques, as well as governmental actions, were reviewed. These included the Child Nicotine Poisoning Prevention Act, signed into law in January 2016, requiring child-resistant packaging for e-liquid containers.

Conclusion The frequency of e-cigarette and liquid nicotine exposures have increased significantly. These exposures,

when compared to cigarettes, are more likely to require medical attention and result in serious effects.

Critique The paper acknowledges limitations inherent to retrospective PCC work, including reporting bias that may underestimate the frequency of these exposures and/or overestimate clinical effects. Also, reported exposures do not necessarily mean that an ingestion, inhalation, or dermal/ocular contact occurred. There were, however, 355 subjects (1.2% of total) with severe outcomes and one death.

Implication for Toxicologists It is important for PCCs and toxicologists to be aware of the growing public health threat associated with liquid nicotine products. Keeping nicotine on the differential is paramount for clinical bedside care and when reviewing safe medication/chemical storage with families. If toxicologists and PCC staff use “teachable moments” after pediatric exposures, they further emphasize the importance of primary poisoning prevention strategies.

Compliance with Ethical Standards

Conflicts of Interest None

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