HHS Public Access

Author manuscript

Am J Prev Med. Author manuscript; available in PMC 2020 February 01.

Published in final edited form as:

Am J Prev Med. 2019 February ; 56(2): 288–292. doi:10.1016/j.amepre.2018.10.004.

Ingestion of Over-the-Counter Liquid Medications :

Emergency Department Visits by Children Aged Less Than 6 Years, 2012-2015

Maribeth C. Lovegrove, MPH[1], **Nina J. Weidle, PharmD**[1,2], **Daniel S. Budnitz, MD, MPH**[1]

[1]Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention (CDC), Atlanta, GA

[2]Eagle Medical Services, LLC, Atlanta, GA

Abstract

Introduction: Unintentional medication ingestions by young children lead to nearly 60,000 emergency department (ED) visits annually; 15% involve oral liquid medications. Safety packaging improvements have been shown to limit liquid medication ingestions. Estimated rates of ED visits for pediatric ingestions by product were calculated to help target interventions.

Methods: Frequencies and rates of ED visits for unintentional pediatric ingestions were estimated using adverse event data from the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance project and retail sales/pharmacy dispensing data from Information Resources, Inc. and QuintilesIMS (collected 2012–2015; analyzed 2017). Rates of ED visits for ingestions of over-the-counter (OTC) liquid medications were compared with those for prescription solid medications.

Results: Based on 568 cases, an estimated 6,427 ED visits (95% confidence interval: 4,907–7,948) were made annually after a child <6 years accessed one of the four most commonly implicated OTC liquid medications without caregiver oversight. Nearly two-thirds (63.8%) of these visits were made by children aged ≤2 years and 9.0% resulted in hospitalization. Acetaminophen was the most commonly implicated OTC liquid medication (2,515 estimated ED visits annually). Rates of ED visits for liquid diphenhydramine and acetaminophen ingestions (8.1 and 7.4 ED visits per 100,000 bottles sold) were higher than rates for other common OTC liquids and comparable to high rate prescription solid medications (clonidine and buprenorphine/naloxone [11.1 and 10.5 ED visits per 100,000 dispensed prescriptions]).

Conclusions: Product-specific rates of ED visits for unintentional ingestions can help prioritize preventive interventions, such as enhancing safety packaging with flow restrictors.

Corresponding Author: Daniel S. Budnitz, MD, MPH, Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, 1600 Clifton Road, NE, Mailstop V18-4, Atlanta, GA 30333.

M.C. Lovegrove: conceptualized and designed the study, conducted the analyses, contributed to interpretation of data, drafted the initial manuscript, and reviewed and revised the manuscript. N. J. Weidle: contributed to acquisition and interpretation of data, and reviewed and revised the manuscript. D.S. Budnitz: conceptualized and designed the study, contributed to acquisition and interpretation of data, supervised the study, and reviewed and revised the manuscript. All authors approved the final manuscript as submitted.

Financial Disclosures: No financial disclosures were reported by the authors of this article.

Conflict of Interest Disclosures: The authors have no conflicts of interest relevant to this article to disclose.

Keywords

drug packaging; medication safety; medication ingestion; pediatric poisoning; unintentional overdose; flow restrictor; restricted delivery system

Child-resistant (CR) packaging has contributed to significant declines in pediatric deaths from medication ingestions.[1] However, unintentional medication ingestions by children aged <6 years continue to lead to approximately 450,000 poison center calls and 60,000 emergency department (ED) visits each year in the United States.[2,3] Oral liquid medications are involved in approximately 15% of ED visits for pediatric medication ingestions,[2] and although rare, life-threatening ingestions of over-the-counter (OTC) and prescription liquid products continue to occur.[3, 4] Because the rate of these ingestions relative to units of medication sold has not been previously assessed, rates of ED visits for unintentional ingestions of common oral liquid medications were calculated and compared to rates for commonly ingested solid medications.

METHODS

The numbers of ED visits for unintentional pediatric medication ingestions were estimated using data from the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance (NEISS-CADES) project, a stratified probability sample of hospitals in the U.S and its territories with at least 6 beds and 24-hour EDs.[5, 6] Trained abstractors at the 60 participating hospitals review all ED medical records to identify and record clinician-diagnosed adverse drug events, including pediatric medication ingestions.

Cases included ED visits from January 1, 2012 through December 31, 2015 in which a child aged <6 years ingested or was suspected of ingesting acetaminophen, diphenhydramine, ibuprofen, or cough and cold medicines (CCMs), as previous analyses found that over 75% of ED visits for unintentional ingestions of liquid medications involved one of these medications.[2] Dosage form, prescription status, and intended age group for each product, were categorized by a study pharmacist based on case narratives, drug databases, and manufacturer websites.[7, 8] The four prescription solid medications most commonly implicated in ED visits for unintentional ingestions were identified for comparison.

National estimates of OTC liquid medication bottles sold were obtained from Information Resources, Inc. (IRI). IRI data include complete point-of-sale data for mass merchandise, club, dollar, and military stores and estimated sales for drug and food stores (based on 92% and 75% coverage, respectively). National estimates of prescriptions dispensed from outpatient retail pharmacies were obtained from QuintilesIMS National Prescription Audit. QuintilesIMS uses proprietary methods to estimate dispensed prescriptions based on data from nearly 48,000 retail pharmacies (representing approximately 80% of prescriptions from drug, food, and mass merchandise stores).

Annual national estimates of ED visits and corresponding 95% confidence intervals (CIs) were calculated using the SURVEYMEANS procedure in SAS, version 9.3 (SAS Institute) to account for sample weights and complex sample design.[9] Rates were calculated by

dividing the estimated number of ED visits (NEISS-CADES) by the estimated numbers of bottles sold or prescriptions dispensed.

RESULTS

Based on 568 cases, an estimated 6,427 ED visits (95% CI: 4,907–7,948) were made annually for unintentional ingestions of one of the four most commonly implicated OTC liquid medications from 2012–2015 (Table 1). During this time, 4,489 estimated visits (95% CI: 3,307–5,670) were made for unintentional ingestions of one of the four most commonly implicated prescription solid medications. The top four OTC liquid medications were implicated in an estimated 10.7% (95% CI: 9.3%−12.1%) of all ED visits for unintentional medication ingestions and the top four prescription solid medications were implicated in 7.5% (95% CI: 6.2%−8.8%).

Acetaminophen was the most commonly implicated OTC liquid medication in ED visits for pediatric ingestions, accounting for an estimated 2,515 ED visits annually (Table 2). While nearly all ED visits for ingestions of OTC liquid acetaminophen (98.7%; 95% CI: 96.2% −100.0%), diphenhydramine (98.1%; 95% CI: 95.2%−100.0%), and ibuprofen (100.0%) involved pediatric formulations; fewer visits attributed to CCMs definitively involved pediatric formations (58.5%; 95% CI: 41.2%−75.9%). There were an additional 920 annual ED visits (95% CI: 392–1,448) for ingestion of the top four OTC medications for which the dosage form was not specified, but even if all were oral liquid products, there were no significant changes in the proportion of estimated visits by patient or case characteristics, or by implicated medication (Appendix).

Estimated rates of ED visits for liquid diphenhydramine and acetaminophen ingestions (8.1 and 7.4 ED visits per 100,000 bottles sold) were significantly higher than rates of ED visits for ibuprofen and CCM ingestions (Table 2). The rate of ED visits involving pediatric CCMs was more than 4-times the rate involving family or adult CCMs or those for which the age group was not specified (2.3 vs. 0.5 ED visits per 100,000 bottles sold). Estimated rates of ED visits for pediatric ingestions per bottle sold for diphenhydramine and acetaminophen were comparable to the rates per prescription dispensed for clonidine and buprenorphine/ naloxone (11.1 and 10.5 ED visits per 100,000 dispensed prescriptions).

DISCUSSION

One reason unintentional ingestions of liquid medications by young children persist despite CR packaging is that most CR packaging in the U.S. uses safety closures/caps on multidose bottles which requires that parents/caregivers immediately and fully re-secure CR closures after every use. To mitigate this limitation, restricted delivery systems such as “flow restrictors,” adapters that narrow bottle openings or create re-closable seals, have been added to some liquid medications.[10–13] These devices add an automatic, passive safety barrier and were voluntarily added to infants’ acetaminophen in 2011 and subsequently added to some children’s acetaminophen products.[13] Based on calls to poison centers, when bottles had flow restrictors, pediatric ingestions of liquid acetaminophen were found to be significantly less likely to involve clinically significant doses.[14, 15]

A 2015 U.S. Food and Drug Administration (FDA) voluntary guidance recommends adoption of container features, such as flow restrictors, to reduce the incidence and magnitude of pediatric ingestions on all pediatric OTC liquid products containing acetaminophen.[16] Recommendations to use such restricted delivery systems for other medicines is currently under consideration by FDA[17] and recommended by other professional and standards organizations.[12, 18] An ASTM Standard Test Method to help manufacturers assess optimal flow restrictors for specific products is under development.[19]

Which products might be candidates for enhanced safety features? ED visits for pediatric ingestion of liquid diphenhydramine products and liquid acetaminophen products occurred at 3-times the estimated rate compared with ibuprofen and pediatric CCM products and at rates comparable to the concerning prescription solid medications clonidine and buprenorphine/naloxone.[20, 21] While voluntary FDA guidelines already recommend such features for pediatric liquid acetaminophen-containing products, acute toxicity of diphenhydramine may be greater than acetaminophen after ingestion of comparable volumes. Based on current guidelines, a child aged <5 years would likely be referred for emergency evaluation only after ingesting a full 120 mL bottle of children's acetaminophen but after just one-half of a 120 mL bottle of children's diphenhydramine.[22, 23] Flow restrictors could be expected to prevent ingestion of such volumes, and need for subsequent ED visits, as in a randomized trial, only 6% of preschool-aged children were able to empty bottles with flow restrictors and no children aged <3½ years removed even 5 mL.[24]

Although CCMs and prescription liquid medications[2] lead to fewer ED visits than other OTC products, ingestion of small volumes of certain products (e.g., liquid opioids) may lead to significant harm, including death.[25] Further investigation of such products for improved safety packaging may be justified based on severity of harm rather than frequency of ED visits. Additionally, improvements in safety packaging should be combined with reminding parents/caregivers to store medications up and away and out of children's reach and sight.[26, 27]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The authors thank Ms. Katie Rose, Ms. Sandra Goring, Ms. Arati Baral, and Mr. Alex Tocitu, from Northrop Grumman (contractor to CDC), for assistance with data coding and programming and Mr. Tom Schroeder, Ms. Elenore Sonski, Mr. Herman Burney, and data abstractors from the U.S. Consumer Product Safety Commission, for assistance with NEISS-CADES data acquisition. We also thank Dr. Ruth Moro of Northrop Grumman (contractor to CDC) for thoughtful review of the manuscript. Lastly, we thank the Consumer Healthcare Products Association for providing over-the-counter sales data obtained from Information Resources, Inc. No individuals named herein received compensation for their contributions.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Funding Source: U.S. Department of Health and Human Services. No external funding.

Abbreviations and Acronyms:

CCM	cough and cold medicine
CI	confidence interval
CR	child-resistant
ED	emergency department
FDA	U.S. Food and Drug Administration
IRI	Information Resources, Inc.
NEISS-CADES	National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance
OTC	over-the-counter

References

1. Rodgers GB. The safety effects of child-resistant packaging for oral prescription drugs. Two decades of experience. JAMA 1996;275(21):1661–5. [PubMed: 8637140]
2. Lovegrove MC, Weidle NJ, Budnitz DS. Trends in Emergency Department Visits for Unsupervised Pediatric Medication Exposures, 2004–2013. Pediatrics 2015;136(4):e821–9. 10.1542/peds.2015-2092. [PubMed: 26347435]
3. Gummin DD, Mowry JB, Spyker DA, et al. 2016 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 34th Annual Report. Clin Toxicol (Phila) 2017;55(10):1072–1252. 10.1080/15563650.2017.1388087. [PubMed: 29185815]
4. Green JL, Wang GS, Reynolds KM, et al. Safety Profile of Cough and Cold Medication Use in Pediatrics. Pediatrics 2017;139(6) 10.1542/peds.2016-3070.
5. Jhung MA, Budnitz DS, Mendelsohn AB, et al. Evaluation and overview of the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance Project (NEISS-CADES). Med Care 2007;45(10 Supl 2):S96–102. 10.1097/MLR.0b013e318041f737. [PubMed: 17909391]
6. Budnitz DS, Pollock DA, Weidenbach KN, et al. National surveillance of emergency department visits for outpatient adverse drug events. JAMA 2006;296(15):1858–66. 10.1001/jama.296.15.1858. [PubMed: 17047216]
7. Wolters Kluwer. Facts & Comparisons® eAnswers http://www.wolterskluwercdi.com/facts-comparisons-online/. Accessed August 3, 2018.
8. US Food and Drug Administration. Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations https://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Accessed August 3, 2018.
9. Schroeder T, Ault K. The NEISS sample (design and implementation) 1997 to present http://www.cpsc.gov//PageFiles/106617/2001d011-6b6.pdf. Accessed August 3, 2018.
10. Budnitz DS, Lovegrove MC. The last mile: taking the final steps in preventing pediatric pharmaceutical poisonings. J Pediatr 2012;160(2):190–2. 10.1016/j.jpeds.2011.09.020. [PubMed: 22056349]
11. Budnitz DS, Salis S. Preventing medication overdoses in young children: an opportunity for harm elimination. Pediatrics 2011;127(6):e1597–9. 10.1542/peds.2011-0926. [PubMed: 21555494]
12. US Pharmacopeial Convention. General chapter <659> packaging and storage requirements http://www.uspnf.com/sites/default/files/usp_pdf/EN/USPNF/revisions/659_rb_notice.pdf. Accessed August 3, 2018.

13. OTC industry support FDA advisory committee recommendations on new dosing instructions [press release] Washington D.C: Consumer Healthcare Products Association https://www.chpa.org/05_18_11newdosinginstructions.aspx. Accessed August 3, 2018.
14. Geller RJ, Hon SL, Reynolds KM, et al. Do new child resistant closures reduce injury following accidental ingestion [NACCT abstract 6]? Clin Toxicol (Phila) 2015;53(7):641–642.
15. Brass EP, Reynolds KM, Burnham RI, et al. Frequency of Poison Center Exposures for Pediatric Accidental Unsupervised Ingestions of Acetaminophen after the Introduction of Flow Restrictors. J Pediatr 2018 10.1016/j.jpeds.2018.02.033.
16. US Food and Drug Administration. Guidance for industry: over-the-counter pediatric oral liquid drug products containing acetaminophen https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM417568.pdf. Accessed August 3, 2018.
17. US Food and Drug Administration. Guidance agenda: new & revised draft guidances CDER is planning to publish during calendar year 2018 https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm417290.pdf. Accessed August 3, 2018.
18. Paul IM, Neville K, Galinkin JL, et al. Metric Units and the Preferred Dosing of Orally Administered Liquid Medications. Pediatrics 2015;135(4):784–787.
19. ASTM International. Controlling the flow. ASTM Standardization News https://www.astm.org/standardization-news/?q=update/controlling-the-flow-ja15.html. Accessed August 3, 2018.
20. Bar-Oz B, Levichek Z, Koren G. Medications that can be fatal for a toddler with one tablet or teaspoonful: a 2004 update. Paediatr Drugs 2004;6(2):123–6. [PubMed: 15035652]
21. Michael JB, Sztajnkrycer MD. Deadly pediatric poisons: nine common agents that kill at low doses. Emerg Med Clin North Am 2004;22(4):1019–50. 10.1016/j.emc.2004.05.004. [PubMed: 15474780]
22. Scharman EJ, Erdman AR, Wax PM, et al. Diphenhydramine and dimenhydrinate poisoning: an evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila) 2006;44(3):205–23. [PubMed: 16749537]
23. Dart RC, Erdman AR, Olson KR, et al. Acetaminophen poisoning: an evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila) 2006;44(1):1–18.
24. Lovegrove MC, Hon S, Geller RJ, et al. Efficacy of flow restrictors in limiting access of liquid medications by young children. J Pediatr 2013;163(4):1134–9 e1. 10.1016/j.jpeds.2013.05.045. [PubMed: 23896185]
25. Henry K, Harris CR. Deadly ingestions. Pediatr Clin North Am 2006;53(2):293–315. 10.1016/j.pcl.2005.09.007. [PubMed: 16574527]
26. UpAndAway.org Put your medicines up and away and out of sight http://www.upandaway.org/. Accessed August 3, 2018.
27. Safe Kids Worldwide. Simple steps to safe medicine storage https://www.safekids.org/video/simple-steps-safe-medicine-storage. Accessed August 3, 2018.

Table 1.

ED Visits for Unintentional Ingestions Involving Commonly Implicated Oral Medications, Children <6 Years, 2012–2015[a]

Patient and Case Characteristics	ED Visits Involving the Top 4 Commonly Implicated Liquid Medications[b]				ED Visits Involving the Top 4 Commonly Implicated Prescription Solid Medications[c]			
	Cases	Annual National Estimate			Cases	Annual National Estimate		
	No.	No.	%	95% CI	No.	No.	%	95% CI
Age (Years)								
<2	124	1,693	26.3	(21.7 – 31.0)	166	1,771	39.5	(30.5 – 48.4)
2	217	2,405	37.4	(32.2 – 42.7)	129	1,646	36.7	(30.8 – 42.5)
3	148	1,657	25.8	(20.4 – 31.2)	45	736	16.4	(9.7 – 23.1)
4–5	79	672	10.5	(6.5 – 14.4)	34	335	7.5	(4.7 – 10.2)
Sex								
Female	283	3,161	49.2	(41.9 – 56.4)	194	2,460	54.8	(46.0 – 63.6)
Male	285	3,267	50.8	(43.6 – 58.1)	180	2,029	45.2	(36.4 – 54.0)
No. of Implicated Medications								
1	555	6,311	98.2	(96.5 – 99.8)	305	3,659	81.5	(74.9 – 88.1)
2 or more	13	--	--	--	69	830	18.5	(11.9 – 25.1)
Disposition								
Hospitalized	81	578	9.0	(5.2 – 12.8)	189	1,883	41.9	(31.6 – 52.3)
Treated and released or left against medical advice	487	5,850	91.0	(87.2 – 94.8)	185	2,606	58.1	(47.7 – 68.4)
Total	**568**	**6,427**	**100.0**	**NA**	**374**	**4,489**	**100.0**	**NA**

[a]Estimates of ED visits for unintentional pediatric medication ingestions based on data from the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance project (2012–2015). Estimates based on <20 cases are not shown (--). ED=Emergency department; NA=not applicable.

[b]Most commonly implicated (top 4) oral OTC liquid medications: single-ingredient acetaminophen, diphenhydramine allergy products, and ibuprofen, and single- or multi-ingredient cough and cold medicines.

[c]Most commonly implicated (top 4) oral prescription solid medications: clonidine, clonazepam, lisinopril, and buprenorphine/naloxone.

Table 2.

ED Visits for Unintentional Ingestions Involving Commonly Implicated Oral Medications, Children <6 Years, 2012–2015[a]

Most Commonly Implicated Liquid Drug Products[b]	Annual National Estimate		Rate per 100,000 Bottles Sold[c]	
	No.	95% CI	Rate	95% CI
Acetaminophen	2,515	(1,532 – 3,498)	7.4	(4.5 – 10.3)
Diphenhydramine Allergy Products[d]	1,200	(817 – 1,583)	8.1	(5.5 – 10.7)
Ibuprofen	1,197	(862 – 1,531)	3.3	(2.4 – 4.2)
Cough and Cold Medicines	1,561	(1,025 – 2,096)	0.9	(0.6 – 1.1)
Pediatric Products	914	(450 – 1,378)	2.3	(1.1 – 3.5)
Family/Adult/Unspecified Age Products	653	(349 – 956)	0.5	(0.2 – 0.7)
Total	**6,427**	**(4,907 – 7,948)**	**NA**	**NA**
Most Commonly Implicated Prescription Solid Drug Products	**Annual National Estimate**		**Rate per 100,000 Dispensed Retail Prescriptions[e]**	
	No.	**95% CI**	**Rate**	**95% CI**
Clonidine	1,417	(1,011 – 1,824)	11.1	(7.9 – 14.3)
Clonazepam	1,232	(799 – 1,664)	4.7	(3.0 – 6.3)
Lisinopril	979	(516 – 1,442)	1.1	(0.6 – 1.7)
Buprenorphine/Naloxone	861	(423 – 1,299)	10.5	(5.1 – 15.8)
Total	**4,489**	**(3,307 – 5,670)**	**NA**	**NA**

[a]Estimates of ED visits for unintentional pediatric medication ingestions based on data from the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance project (2012–2015). The sum of estimates for individual products may be greater than the total because ED visits may involve >1 commonly implicated OTC liquid medication. ED=Emergency department; OTC=over-the-counter; NA=not applicable.

[b]Pediatric formulations were implicated in nearly all ED visits attributed to single-ingredient acetaminophen (1 case involved a product with unspecified age group) and diphenhydramine (2 cases involved a family product), and in all visits attributed to ibuprofen.

[c]Estimates of bottles sold based on data from Information Resources, Inc. (2012–2015).

[d]Excludes 1 case involving an OTC liquid diphenhydramine adult sleep aid.

[e]Estimates of dispensed oral retail prescriptions based on data from the QuintilesIMS National Prescription Audit (2012–2015).