US Poison Control Center Calls for Infants 6 Months of Age and Younger

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abstract

BACKGROUND: Anticipatory guidance and prevention efforts to decrease poisonings in young children have historically focused on restricting access to minimize exploratory ingestions. Because infants through 6 months of age have limited mobility, such exposures are expected to be less frequent and therapeutic (or dosing) errors should be more frequent. Although recent prevention efforts target some types of therapeutic errors, the epidemiology of these exposures is not well characterized in this age group. This could have important implications for the effectiveness of current prevention efforts.

METHODS: A 10-year (2004–2013) retrospective review of exposure calls for infants through 6 months of age was conducted on National Poison Data System files.

RESULTS: A total of 271 513 exposures were reported, of which 96.7% were unintentional. Of these, the most common reasons were general unintentional (50.7%), which includes exploratory exposures, and therapeutic error (36.7%). Among the latter, 47.0% involved quantitative dosing errors (a different amount than intended) and 42.8% involved nonquantitative dosing errors (a medication given twice or too soon, the wrong medication, or wrong route). Most exposures (97.5%)occurred in the home but only 85.2% of calls came from the home;80.4% ofself-referrals to a healthcare facility were not admitted.

CONCLUSIONS: General unintentional (including exploratory) exposures and therapeutic errors both comprise a large proportion of calls in this age group. Among therapeutic errors, quantitative and nonquantitative dosing errors are equally concerning. There areappreciablenumbers of patients presenting to healthcare prior topoison centerconsultation. These data can help target future anticipatory guidance and prevention measures.

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Dr Kang conceptualized the study, analyzed the data, drafted the initial manuscript, and revised the manuscript; Dr Brooks obtained and analyzed the data, and reviewed and revised the manuscript; and both authors approved the final manuscript as submitted.

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WHAT'S KNOWN ON THIS SUBJECT: Current anticipatory guidance and poison prevention efforts in children focus on restricting access and decreasing quantitative dosing errors. Little is known about the reasons for exposures in infants ≤6 months of age with inherently limited potential for exploratory ingestions.

WHAT THIS STUDY ADDS: General unintentional (including exploratory) exposures and therapeutic errors comprised 87.4% of poison center calls in this age group. Quantitative and nonquantitative dosing errors had similar frequencies, accounting for 89.8% of therapeutic errors. These findings may guide future prevention efforts.

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The etiology of pediatric poisonings varies by age group such that adolescent exposures are more often intentional whereas younger children and toddlers have a greater rate of unintentional exposures.[1] Because these unintentional exposures are assumed to be due to the exploratory behavior of young children, anticipatory guidance provided by pediatricians encourages parents to keep medications and chemicals inaccessible.[2] Accordingly, office-based counseling for poison prevention becomes a recommendation beginning only with "preschool-aged children" rather than infants.[3] Similarly, Bright Futures recommendations to discuss poison prevention do not begin until the 6-month visit.[4] Moreover, legislative and industry efforts have also focused on restricting access: the Poison Prevention Packaging Act of 1970 required child-resistant packaging, and other innovations have included blister packs for pills and flow-restricted bottles for liquid over-the-counter medications.[5]

Studies of pediatric poisonings usually group all infants <1 year of age together.[1,6–9] However, there is a large variation in motor abilities within the first year of life.[10] An infant who is not yet sitting upright would have a limited potential for exploration compared with one who is cruising or walking. At these early ages, the expectation would be for exploratory behavior to contribute less (fewer exploratory ingestions) and medication errors by caregivers to contribute more (more therapeutic errors). Consistent with this expectation, a previous study of National Poison Data System (NPDS) data of single pharmaceutical product ingestions did show a greater frequency of "therapeutic error" versus "unintentional self-exposure" in younger ages.[9] In that study, the proportion due to therapeutic error was 29.3% in infants <1 year of age, but only 3.1% and 1.6% for infants in their second and third year of life, respectively.

Therapeutic errors can be divided into quantitative (when an incorrect amount of medication is administered) and nonquantitative dosing errors (eg, medication given twice or too soon, wrong medication given, or wrong route is used). A small retrospective study of poison center calls for infants up to 6 months of age reported 53% of the calls for this age group were due to therapeutic errors. Of these, 28% were due to an "incorrect dose" or quantitative dosing error.[11] Unfortunately, that study was limited by use of a convenience sample, a small number of cases (n = 358), and data from only a single poison control center (PCC).

Because the cause of exposures would have implications on the effectiveness of prevention efforts and appropriateness of anticipatory guidance, we performed a retrospective review of exposures reported to the NPDS in infants ≤6 months of age. We chose this age group because the average infant is unable to pull to stand or cruise until ~8 to 9 months of age.[10] Moreover, the average 6-month-old still requires support to sit, so scooting while seated is also less likely to occur.

METHODS

The NPDS is a near real-time database containing electronic records from all US PCCs. Data were obtained on all human exposures involving patients 0 days to 6 months of age during the period of January 1, 2004, through December 31, 2013. Data were requested by the authors through their association with the American Association of Poison Control Centers. Abstracted data included patient age, gender, exposure acuity, product(s) involved, doses, reason for exposure, scenarios, route of exposure, medical acuity, signs and symptoms related to the exposure, exposure and caller site, management site, treatments, and medical outcome.

In NPDS, each call was assigned a reason for exposure: intentional, unintentional, adverse reaction, or one of several miscellaneous reasons. The default coding for all calls was general unintentional, which included exploratory ingestions (of any type of product, plant, or object), scenarios involving access (eg, sibling providing a substance to the infant or the infant being given a prescription container as a toy), as well as unintentional exposures that did not fit another specific category. Calls were categorized as therapeutic error if a medication dosing error was identified. For this study, therapeutic errors were then categorized as quantitative or nonquantitative dosing errors, or other (breastmilk exposures, drug interactions, and unknown). Because a goal of this study was to compare general unintentional and therapeutic errors, outcomes were analyzed for non–health care facility (HCF) exposures. Some calls had multiple error types checked so these were grouped under the most specific scenario to eliminate duplicates (eg, a call coded for both 10-fold dosing error and incorrect dose was grouped under 10-fold dosing error). Other coding scenarios are optional (accessibility, child-resistance closures, product confusion, pesticide-related, and miscellaneous) and were not analyzed. Supplemental Information provides definitions for many of the terms used in this article.

All included deaths were further analyzed by reviewing the fatality reports included in the American Association of Poison Control Centers' annual reports to determine the exposure's contribution to death. These lists contain only exposures that were "undoubtedly" or "probably" responsible for the fatality (beginning in 2006, "contributory"

cases were also reported). Indirectly reported deaths refers to cases in which the PCC was notified after the death occurred (eg, by a medical examiner) but was not involved in the patient's care.

Descriptive statistics were used to report overall findings. This study was approved by the institutional review board at Banner–University Medical Center Phoenix.

RESULTS

General

Over the 10-year study period from 2004 through 2013, there were 23 900 791 total human exposure calls. Of these, 271 513 (1.1%) were for exposures in infants 6 months of age and younger. Table 1 shows basic demographic information for these infant calls. Boys accounted for approximately half (52%) of the total calls. Most exposures were acute (88.9%) and involved a single substance (97.6%). Ingestion was the most common route of exposure (83.6%). Liquid formulations accounted for the most exposures (60.8%). Although most exposures occurred in a residence (97.5%), a somewhat smaller percentage of calls originated from a residence (85.2%).

Most exposures were unintentional (96.7%), as seen in Table 2. Of these, the 2 most frequent categories were general unintentional (50.7%), which included exploratory ingestions, and therapeutic error (36.7%). Among therapeutic errors, 47.0% involved quantitative dosing errors, whereas 42.8% involved nonquantitative dosing errors (Table 3). Among the nonquantitative dosing errors, giving a medication twice or the wrong medication were the most common reasons.

The most common substances involved in general unintentional and therapeutic error exposures (outside of a HCF) are listed in Table 4. Diaper care and rash products were the

TABLE 1 Exposure Demographics

Category	Total	% of Total
Gender		
Male	141 189	52.0
Female	127 912	47.1
Unknown	2412	0.9
Acuity		
Acute	241 410	88.9
Acute-on-chronic	19 381	7.1
Chronic	9653	3.6
Unknown	1069	0.4
No. of products		
1	265 077	97.6
2	5581	2.1
3	607	0.2
4–9	240	0.1
Route of Exposure		
Ingestion	227 077	83.6
Inhalation/Nasal	19 525	7.2
Dermal	16 389	6.0
Ocular	15 280	5.6
Parenteral	2382	0.9
Bite/Sting	1813	0.7
Other	1781	0.7
Unknown	852	0.3
Formulation		
Liquid	165 144	60.8
Solid (including capsules)	29 747	11.0
Cream, lotion, gel	27 753	10.2
Aerosol, mist, gas	17 641	6.5
Powder	8457	3.1
Patch	287	0.1
Other	25 072	9.2
Unknown	5168	1.9
Exposure site		
Residence	264 781	97.5
HCF	2839	1.0
Other	3438	1.3
Unknown	455	0.2
Caller site		
Residence	231 384	85.2
HCF	24 667	9.1
Other	15 225	5.6
Unknown	237	0.1
Management site		
On site (non-HCF)	232 547	85.6
Referred to HCF by PCC	10 832	4.0
Already en route/in HCF	23 810	8.8
Other	2978	1.1
Unknown	1346	0.5
Level of HCF care		
Treated/Evaluated and released	22 932	66.2
Admitted to non-ICU	2807	8.1
Admitted to ICU	2415	7.0
Patient refused/No show	1560	4.5
Lost to follow-up/Left AMA	4914	14.2
Medical outcome/Clinical effects		
Not followed (nontoxic or minimal effect)	172 343	63.5
No effect	60 211	22.2
Minor effect	22 213	8.2
Moderate effect	3066	1.1
Major effect	438	0.2
Death (including indirect report)	73	0.0
Unrelated effect	7476	2.8

TABLE 1 Continued

Category	Total	% of Total
Confirmed nonexposure	588	0.2
Unable to follow (potentially toxic)	5105	1.9

Basic information about all calls is listed. Note that a single exposure may involve multiple formulations and/or routes of exposure. For route of exposure, "other" includes aspiration, otic, vaginal, and rectal. For formulation, "other" includes household items like plants and toys. For exposure and caller site, "other" includes school, public area, workplace, and restaurant. Note that level of care applies only to calls that were referred to or already at an HCF. AMA, against medical advice.

TABLE 2 Reasons for Exposures

Reason for Exposure	Total	% of Total	Group Total, %
Unintentional			
Unintentional - General	137 725	50.7	
Unintentional - Therapeutic error	99 705	36.7	
Unintentional - Environmental	12 268	4.5	
Unintentional - Misuse	7180	2.6	
Unintentional - Food poisoning	3556	1.3	
Unintentional - Bite/Sting	1818	0.7	
Unintentional - Occupational	14	< 0.1	
Unintentional - Unknown	406	0.1	96.7
Intentional			
Intentional - Misuse	434	0.2	
Intentional - Abuse	66	< 0.1	
Intentional - Suspected suicide	23	< 0.1	
Intentional - Unknown	111	< 0.1	0.2
Adverse Reaction			
Adverse reaction - Drug	3611	1.3	
Adverse reaction - Food	1044	0.4	
Adverse reaction - Other	887	0.3	2.0
Miscellaneous			
Other - Contamination/Tampering	1213	0.4	
Other - Malicious	460	0.2	
Other - Withdrawal	151	0.1	
Unknown reason	841	0.3	1.0
Total	271 513	100	

The reasons for exposures are listed and organized by major categories. Abuse and suspected suicide are likely misclassifications in this age group.

most common causes of general unintentional exposures, whereas acetaminophen alone was the most common cause of therapeutic errors. The most common products resulting in major clinical effects were ethanol, for general unintentional, and combination cough and cold preparations for therapeutic errors (Table 5). Of note, ibuprofen was the sixth most common product involved in therapeutic errors and its exposure frequency increased over the study period.

Outcomes

Outcomes of general unintentional and therapeutic error calls that occurred outside of an HCF are listed in Table 6. Most exposures (88.0%) were managed on-site and did not need referral to an HCF. There were 16 501 exposures (7.0%) where the patient had self-referred (taken by a caregiver) to an HCF (ie, management site listed as en route to or already in an HCF). Among these patients, 80.4% were released and 13.3% were admitted to the hospital (data not shown). Calls coded as "admitted to psychiatry" (n = 10) were excluded because they likely represent inaccurate coding in this age group.

In examining clinical effects, 65.8% of calls were not followed by a PCC because it was deemed a nontoxic exposure or one with minimal anticipated effect. A further 22.0% of exposures had no effect, and 0.9% of calls resulted in a moderate or severe effect, or death.

There were 73 total deaths in this infant age group. Of these, 12 were due to an out-of-hospital general unintentional exposure (3) or therapeutic error (9); however, only 2 were rated undoubtedly or probably responsible and 1 was deemed contributory (methadone, azithromycin, lipid emulsion). Of the remaining 61 deaths, the exposure was thought to be undoubtedly or probably responsible in 20 of them. The reasons included in-hospital therapeutic error (5), in-hospital adverse reaction (1), intentional or malicious (5), dog bites (1), and carbon monoxide (1). An additional 7 had an unknown reason, but 3 of these were neonatal deaths (1 day old) related to methamphetamine or phencyclidine.

DISCUSSION

One of the Healthy People 2020 goals is a 10% decrease in medication overdose–related emergency department visits by children <5 years of age.[12] Although there has been a steady decline in the number of calls across all ages, US PCCs continue to receive a large number of calls for infants 6 months of age and younger. Among the calls analyzed in this study, 97.5% of the exposures occurred in the home, yet only 85.2% of calls originated from the home. This discrepancy suggests that these cases self-triaged to an HCF without calling a PCC. Of the 16 501 non-HCF general unintentional and therapeutic error exposures that self-referred to an HCF, 80.4% were released. Inevitably, some of these visits were unnecessary and may have been prevented with early PCC involvement. However, because guidelines typically do

not recommend specific poison prevention education (including providing the PCC phone number) until at least 6 months of age, parents (especially first-time parents) may not be aware of PCCs. A potential intervention can be early parental education about the availability of PCCs as a resource for medical guidance, perhaps beginning at discharge from the nursery, along with frequent reinforcement.

In addition to decreasing the number of patients seeking unnecessary medical care for benign exposures, enhanced primary prevention may assist with meeting the Healthy People 2020 goal. The current study found 36.7% of calls were due to therapeutic error, somewhat greater than the 29.3% found in infants <1 year of age by Bond et al.[9] Among these, 47.0% consisted of quantitative dosing errors and 42.8% consisted of nonquantitative dosing errors. Although recent prevention efforts, such as providing appropriate-size syringes for liquid medications and standardization of measurements for liquid medications,[13] directly target some of the quantitative dosing errors, they are unlikely to prevent nonquantitative dosing errors (such as being given a medication twice).

General unintentional exposures comprised 50.7% of all calls. This category includes exploratory ingestions (of any type of product, plant, or object) as well as other scenarios involving access (eg, sibling providing a substance to the child), child-resistant closures (eg, child accessing a prescription container that was given as a toy), calls that do not fit any of the other unintentional reasons, and calls that did not change the default coding. This latter possibility of PCC specialists accepting the default of general unintentional is a potential source of misclassification. Unfortunately, it is impossible to estimate how many calls were coded this way using the high-level NPDS data and would require obtaining individual records from a PCC to compare the coding to any provided narrative entries. To the extent that stereotypical acceptance of general unintentional (ie, the default) occurs, therapeutic errors should

TABLE 3 Most Common Scenarios for Therapeutic Error Exposures

Type of Therapeutic Error	Total	% of Total	Group Total, %
Quantitative dosing error			
Incorrect dose[a]	19 616	19.7	
Confused units of measure	10 053	10.1	
Incorrect formulation or concentration given/dispensed	6783	6.8	
Dispensing cup error	5405	5.4	
10-fold dosing error	5010	5.0	47.0
Nonquantitative dosing error			
Inadvertently given medication twice	18 539	18.6	
Inadvertently given someone else's/wrong medication	14 540	14.6	
Medication doses given too close together	7049	7.1	
Incorrect dosing route	2093	2.1	
More than 1 product containing same ingredient	427	0.4	42.8
Other			
Unknown	6030	6.0	
Iatrogenic error	3257	3.3	
Exposure through breastmilk	845	0.8	
Drug interaction	58	0.1	10.2
Total	99 705	100	

Therapeutic errors were categorized as a quantitative dosing error, nonquantitative dosing error, or other. Calls coded with multiple scenarios were categorized under the most specific scenario.
[a] Incorrect dose indicates a quantitative dosing error that is not described by the other categories.

TABLE 4 Ten Most Common Out-of-Hospital Exposures From General Unintentional or Therapeutic Error

Substance	No. of Calls
General Unintentional	
1) Diaper care and rash products	7495
2) Acetaminophen alone	4871
3) GI preparation (excluding H2-blocker and PPI)	4250
4) Plants: oxalates	3800
5) Creams, lotions, and make-up	3552
6) Topical antifungal	3295
7) Foreign body, toy, or miscellaneous substance	2752
8) Pens or inks	2527
9) Soaps (bar, hand or complexion)	2483
10) Combination cough/cold product	2279
Therapuetic Error	
1) Acetaminophen alone	22 208
2) H2-blocker	13 746
3) GI preparation (excluding H2-blocker and PPI)	9380
4) Combination cough/cold product	8609
5) Systemic antibiotic (PO, IM, IV)	6145
6) Ibuprofen	5229
7) Antihistamine alone	3927
8) PPI	2344
9) Topical antifungal	1907
10) Albuterol	1671

GI, gastrointestinal; IM, intramuscular; IV, intravenous; PPI, proton pump inhibitor; PO, by mouth.

TABLE 5 Five Most Common Out-of-Hospital Exposures Causing Major Clinical Effects for General Unintentional or Therapeutic Error Calls

Substance	No. of Calls
General Unintentional	
1) Ethanol (beverages)	5
2) Acetaminophen alone	3
2) Amphetamines	3
2) Botulism	3
2) Carbon monoxide	3
2) Cocaine	3
2) SSRI	3
Therapeutic Error	
1) Combination cough/cold product	11
1) GI preparation (excluding H2-blocker and PPI)	11
3) Acetaminophen alone	7
3) Methadone	7
5) Systemic antibiotic (PO, IM, IV)	7

GI, gastrointestinal; IM, intramuscular; IV, intravenous; PPI, proton pump inhibitor; PO, by mouth; SSRI, selective serotonin reuptake inhibitor.

TABLE 6 Outcomes

	General Unintentional		Therapeutic Error		Total	% of Total
	n = 137 550		*n* = 97 424			
	No. of Calls	% of Total	No. of Calls	% of Total		
Management Site						
On site (non-HCF)	121 659	88.4	85 098	87.3	206 757	88.0
Referred to HCF by PCC	4577	3.3	3489	3.6	8066	3.4
Already en route/in HCF	8875	6.5	7626	7.8	16 501	7.0
Other	1819	1.3	817	0.8	2636	1.1
Unknown	620	0.5	394	0.4	1014	0.4
Level of HCF Care						
Treated/Evaluated and released	9604	71.4	8011	72.1	17 615	71.7
Admitted to non-ICU	672	5.0	863	7.8	1535	6.3
Admitted to ICU	493	3.7	620	5.6	1113	4.5
Patient refused/No show	787	5.9	393	3.5	1180	4.8
Lost to follow-up/Left AMA	1891	14.1	1224	11.0	3115	12.7
Medical Outcome / Clinical Effects						
Not followed (nontoxic or minimal effect)	88 544	64.4	66 091	67.8	154 635	65.8
No effect	29 340	21.3	22 378	23.0	51 718	22.0
Minor effect	12 458	9.1	5086	5.2	17 544	7.5
Moderate effect	1011	0.7	871	0.9	1882	0.8
Major effect	102	0.1	97	0.1	199	0.1
Death (including indirect report)	3	< 0.1	9	< 0.1	12	< 0.1
Unrelated effect	3021	2.2	1699	1.7	4720	2.0
Confirmed nonexposure	305	0.2	138	0.1	443	0.2
Unable to follow (potentially toxic)	2766	2.0	1055	1.1	3821	1.6

Management site, level of care, and clinical effects are reported for each exposure that occurred outside of an HCF. Indirectly reported deaths refers to cases where the PCC was notified after the death occurred (eg, by a medical examiner) but was not involved in the patient's care. Note that level of care applies only to calls that were referred to or already at an HCF. AMA, against medical advice.

be even more frequent than what was found in this study. Among the top substances involved in general unintentional exposures (Table 4), many would not be affected by this type of error because they are not used therapeutically (eg, oxalate plants, foreign body/toy, pens/inks, soaps). Although substances such as acetaminophen (#2) or combination cough/cold products (#10) could be affected by such misclassification, these substances were already among the most frequently involved in therapeutic errors, so there would be little overall effect to the list of products involved. Ultimately, these general unintentional exposures appear frequent enough in this young age group that early poison prevention education may be considered.

Of note, because exploratory ingestions are not specifically coded, it is not possible to obtain precise data on its frequency. Perhapsfuture NPDS data may offer insight into the efficacy of novel education and prevention efforts.

Several of the substances involved in general unintentional exposures (outside of an HCF) causing major effects (Table 5) were drugs of abuse, including ethanol, amphetamines, and cocaine. Despite the low prevalence, this is a concerning finding. Among therapeutic errors causing major effects, methadone was 1 of the top 5 products and was also responsible for 1 of the therapeutic error deaths. Because this is typically used as outpatient treatment to prevent opioid withdrawal in infants (whether due to neonatal abstinence syndrome or after a prolonged ICU stay during which opioids were used), it does suggest a potential danger of home use. A further observation was that ibuprofen was the sixth most common product involved in therapeutic error calls, and these exposures have been increasing. This increase is surprising given the lack of recommendations for ibuprofen in infants younger than 6 months of age.[14]

Limitations for this work share the inherent flaws associated with retrospective database studies. These data depend on exposures being reported to the PCC. Because most calls originated from a non-HCF, data depended on the reliability of the caller. There was no mechanism to validate the information provided except possibly during follow-up calls to an HCF. It is apparent that inaccurate data entry by PCC staff also occurs because some calls were coded as abuse (ie, of a recreational drug) or suicide, which do not apply in this age group. However, there is no reason to believe that such errors disproportionately affect this age group. The potential of accepting default values was discussed in depth earlier. Some calls also had missing, or "unknown," data. Because the number of calls coded with "unknown" for any category was <1% (except for unknown formulation comprising 1.9% in Table 1), the conclusions of this study are not materially affected. Because some asymptomatic calls may actually have been nonexposures, caution is warranted when drawing conclusions about clinical effects. Regardless, even calls mistakenly thought to involve an exposure can be used to guide prevention efforts because they are potential exposures after all.

CONCLUSIONS

A retrospective review of 10 years of US PCC data showed that exposures in infants ≤6 months of age were almost all unintentional and primarily due to either general unintentional exposures (including exploratory ingestions) or therapeutic errors. Among the therapeutic errors, quantitative dosing errors comprised 47% and nonquantitative dosing errors comprised 42.8%, making them equally concerning. There was also adiscrepancy between the number of exposures occurring at home compared to the number of calls originating from the home, suggestingself-referralto an HCF prior to PCC consultation. These findings may help guide future poison education and prevention efforts.

ABBREVIATIONS

AMA: against medical advice.
HCF: health care facility
NPDS: National Poison Data System
PCC: poison control center

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