Time of Observation in Xenobiotic Ingestions in Children
Is 6 Hours Too Long?

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Objectives: Children endure a prolonged observation after xenobiotic ingestions, despite low associated morbidity and mortality. The primary objective was to describe the management and outcomes of acute xenobiotic exposures in asymptomatic pediatric patients presenting to the emergency department (ED). A secondary objective was to explore the impact of vital signs on the patients' management and outcomes.

Methods: We conducted a retrospective review of asymptomatic children (younger than 18 years) presenting to a pediatric ED after a toxic ingestion from 2014 to 2018. Ingestions of hydrocarbons, acetaminophen, salicylates, sulfonylureas, caustic, and/or extended release agents were excluded. Demographic and clinical data were abstracted.

Results: Of 2817 charts, we identified 109 asymptomatic patients with a mean age of 4.7 years. The average observation from registration to disposition was 4.06 hours. Five patients were admitted and were subsequently discharged within 24 hours. Of the discharged patients, 2 returned within 72 hours and were subsequently discharged home. A total of 321 asymptomatic patients presented with ≥1 abnormal vital signs (mean age, 6.6 years) and were observed in the ED for an average of 4.54 hours. They had a higher percentage of ingestions related to suicide attempts (odds ratio, 6.8). Twenty-two were admitted. Of those discharged home, 11 returned to the ED within 72 hours; all were subsequently discharged home.

Conclusions: Prolonged observations may not be necessary after ingestions in asymptomatic children. Vital sign abnormalities at presentation did not impact disposition. Prospective studies are needed to determine the safety and efficacy of this shortened observation.

Key Words: ingestion, observation, xenobiotic

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Pediatric toxic ingestions are a common cause of injury among children and account for approximately 60% of all human toxic exposures reported to North American poison control centers.[1] The 2018 Annual Report of the American Association of Poison Control Centers' National Poison Data System found that children younger than 20 years had more than 4.3 times the number of toxic exposures reported (1483 per 100,000) as compared with adults (340 per 100,000).[2] Adolescents who present for medical care after an ingestion are at a higher risk of morbidity and mortality compared with young children, especially those younger than of 5 years.[1,3] This may be attributed to the fact that ingestions in young children are typically secondary to exploratory behavior rather than suicidal intent, tend to only include 1 xenobiotic agent, and present sooner for medical evaluation.[1,3,4] Although pediatric toxic exposures account for more than half of all reported human toxic exposures, they constitute less than 3% of ingestion-related fatalities with an acute mortality rate of <0.0004%.[2,5] This suggests that the severity of exposures varies greatly, and the majority of ingestions are not life-threatening. The variability in morbidity and mortality may impact the physician's approach to the pediatric unintentional ingestion.

Most patients, adult or pediatric, who present after the ingestion of an immediate-release xenobiotic are observed for 6 hours, which is based on the time-to-peak of the substance. This is based primarily on the principle that individual pharmacokinetics/pharmacodynamics of a xenobiotic and, more specifically, the time-to-peak effects determine the duration necessary for observation.[6] Most of these ingestions can be safely observed in the emergency department (ED) for 6 hours with little concern for delayed presentation of toxicity.[6] However, some studies suggest that this observation period may not be necessary. A prospective study in adult patients by Hollander et al[6] found that a large subset of intentional overdose patients who were observed for 6 hours could have been medically cleared within 2 to 4 hours of presentation. Similarly, a published abstract by Ojo et al[7] found that asymptomatic patients arriving after ingestion rarely developed new symptoms.

To evaluate the efficacy of the 6-hour observation period, the primary aim of this study was to describe the management and outcomes of acute xenobiotic exposures in asymptomatic pediatric patients. We hypothesize that, if patients are asymptomatic upon arrival to the ED, their observation period is unlikely to impact their disposition. As a secondary aim, we will explore the impact of vital signs (VSs) on the outcome and management of these asymptomatic patients.

METHODS

We conducted a retrospective chart review of patients younger than 18 years, who presented to an urban tertiary care pediatric ED after developing a concern for a potentially toxic ingestion from May 2014 to December 2018. Patients were identified based on their *International Classification of Diseases, Ninth or Tenth Revision* (*ICD-9/10*), codes for toxic ingestions. We did not include any encounters with *ICD-9/10* codes that were incorrectly classified as a toxic ingestion (labeled as "bad code" in Fig. 1), as well as any patients lacking sufficient physician documentation (labeled as "no note" in Fig. 1). Lastly, we did not include any patients who were transferred from outside institutions (labeled as "transfers" in Fig. 1), as we could not reliably evaluate their presenting VSs or any initial interventions.

Ingestions of caustic substances, hydrocarbons, acetaminophen, salicylates, and sulfonylureas were not included because these agents already have established treatment algorithms.[8–10] Cases known to involve extended release agents were also not included because these substances require longer observations.[1] We also did not include any patients who were not normoglycemic if

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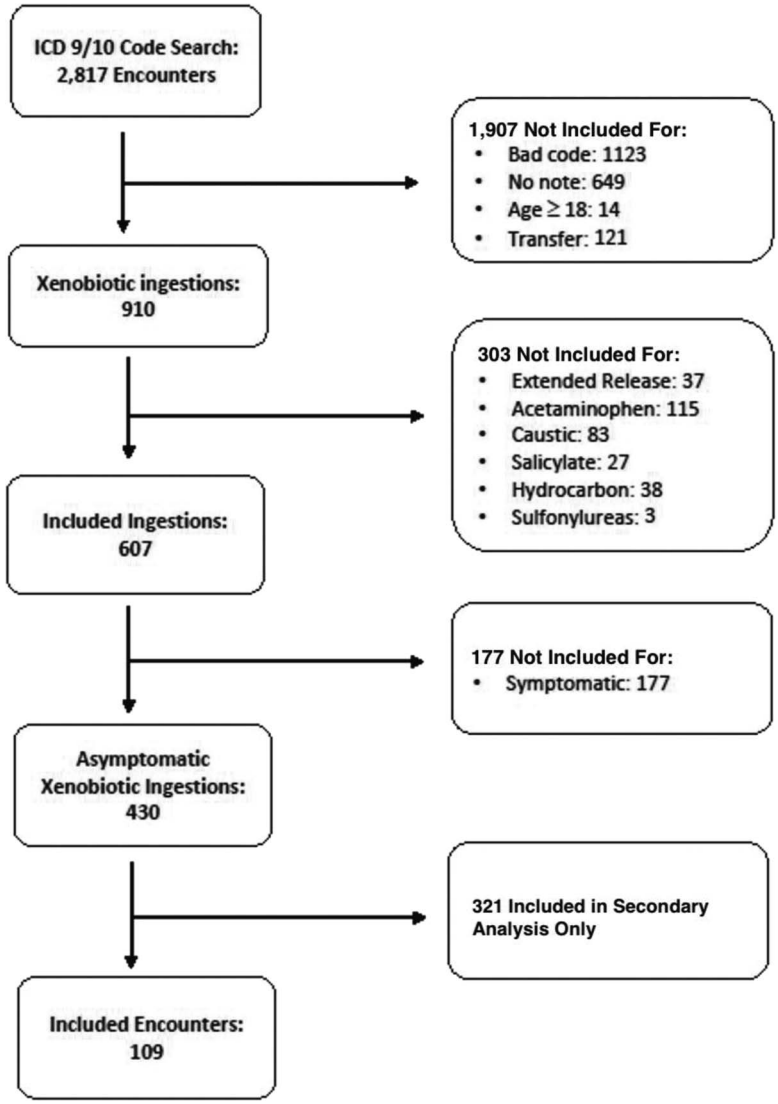

FIGURE 1. Breakdown of included encounters. Note: If there were multiple drug ingestions not included, the authors only counted them once (eg, ranking for inclusion: extended release >acetaminophen >caustic).

obtained on presentation (point of care blood glucose between <70 or >150 mg/dL). Of the remaining patients, only those who were asymptomatic on presentation were included. Asymptomatic was defined as no documented evidence of potential toxodromic symptoms (altered mental status, respiratory distress, emesis, or acute rash) in the physician documentation and normal VSs at triage. We defined normal VSs by the Harriet Lane Handbook (see Figure 2, Supplemental Digital Content 1, http://links.lww.com/PEC/A913), which provided a narrow range of normal values to control for any subjectivity related to the interpretation of those values.[11]

Study data were then abstracted from each patient's chart, including demographics, self-assigned race/ethnicity, past medical history, ingested agent, time of ingestion, presenting VSs, interventions, and length of stay.

As part of our secondary analysis, we evaluated a subset of patients with abnormal VSs as the only outlying variable. We then compared this group of asymptomatic ingestions with abnormal VSs upon presentation, with the original group of asymptomatic patients with normal VSs to evaluate the impact of VSs on the outcome and management of these patients.

The study was approved by the Northwell Health Institutional Review Board.

RESULTS

We reviewed 2817 patient charts, and based on the inclusion criteria previously, 109 patients (3.9%) were determined to be asymptomatic with normal VSs upon presentation to the ED. The mean age of this cohort was 4.7 years, with a median age of 2.7 years (interquartile range, 1.8–5.8 years; Table 1). A total of 103 ingestions (94.5%) were of known agents, and 6 (5.5%) were ingestions of unknown substances. The most common ingestions were nonsteroidal anti-inflammatory drugs (NSAIDs) (13.6%) and cardiac medications (9.7%), and 2 ingestions were disclosed as secondary to suicide attempts. Furthermore, there were 8 coingestions (Table 2).

The average time from ingestion to registration for asymptomatic patients with normal VSs was 2.3 hours. Upon arrival, 24 patients received an intervention within the first 60 minutes, which included laboratory tests, electrocardiograms, medication administration, and/or imaging studies (Fig. 2). No patients were

TABLE 1. Demographics

Characteristics	Normal VSs (n = 109) n (% of Group)	Abnormal VSs (n = 321) n (% of Group)
Sex		
Female	32 (29.4)	168 (52.3)
Male	77 (70.6)	153 (47.7)
Age, y		
0–4	75 (68.8)	192 (59.8)
5–9	20 (18.3)	33 (10.3)
10–15	5 (4.6)	51 (15.9)
16–18	9 (8.3)	45 (14.0)
Mean age	4.70	6.64
Median age	2.71 (IQR*, 1.82–5.83)	3.12 (IQR*, 1.85–13.82)
Race/ethnicity		
Unknown	2 (1.8)	13 (4.0)
White, non-Hispanic	47 (43.1)	125 (38.8)
Hispanic	1 (0.9)	1 (0.3)
Black, African American	31 (28.4)	84 (26.2)
Asian	13 (11.9)	43 (13.4)
American Indian	0 (0.0)	1 (0.3)
Pacific Islander	0 (0.0)	0 (0.0)
Other	15 (13.8)	54 (16.8)

*IQR indicates interquartile range.

admitted during this period. Between 60 and 120 minutes, 12 patients received an intervention, and 1 patient who ingested cabergoline was admitted for monitoring based on extended pharmacokinetics. Between 120 and 180 minutes, 12 patients received an intervention, and no patients were admitted.

Between 180 and 240 minutes, 8 patients received an intervention, and 3 patients were admitted. The first patient was admitted for 24-hour telemetry monitoring because of the ingestion of an unknown substance after consultation with a medical toxicologist. The second patient was admitted for monitoring after an ingestion of clonidine, because of an episode of hypoxia with perioral cyanosis. The patient responded to tactile stimulation, and VSs subsequently normalized in the ED. The third admission in this group was secondary to a disclosed suicide attempt with escitalopram and eszopiclone ingestions and was admitted for telemetry monitoring and the potential for delayed QT prolongation.

Between 240 and 300 minutes, 3 patients received an intervention, and no patients were admitted. Between 300 and 360 minutes, 4 patients received an intervention, and no patients were admitted. After 360 minutes, there were no additional interventions; however, 1 patient with an unknown ingested agent was admitted 7.8 hours after ED presentation for telemetry based on the recommendations of the consulting medical toxicologist.

Overall, patients were observed in the ED from registration to disposition for an average of 4.1 hours and 6.0 hours postingestion. Four of the 5 patients were admitted within 4 hours of presentation. All 5 admitted patients had no additional acute events during admission and were discharged home within 24 hours.

One hundred four asymptomatic patients were discharged. Of this group, 15 (14%) were discharged within 120 minutes of registration, and the predominant xenobiotic ingestions in this rapidly assessed and discharged group were dessicants (3 of 15) and vitamins (2 of 15). One of these 15 patients returned to the ED within 72 hours for an unrelated complaint of a nasal foreign body. In the rest of this cohort (89 patients), there was 1 additional 72-hour return visit. This was for a patient who had ingested multiple laxative chew tablets and returned with 2 episodes of emesis and 3 loose stools. The child was subsequently discharged from the ED without any additional interventions.

As part of our secondary analysis, we evaluated a subset of patients with abnormal VSs as the only outlying variable. Of the 2817 reviewed charts, 321 patients (11.4%) were asymptomatic but presented to the ED with at least 1 abnormal VS.[11] The mean age of this cohort was 6.6 years old, with a median age of 3.1 years (interquartile range, 1.9–13.8 years; Table 1). The most common VS abnormality was blood pressure (82%), and no patients had abnormal oxygen saturation upon presentation (Fig. 3). The most common ingestions were also NSAIDs (13.2%) and cardiac medications (7.3%). Furthermore, 18 (5.9%) were ingestions of unknown substances, and 26 were coingestions (Table 2). A higher percentage of ingestions were categorized as secondary to a disclosed suicide attempt in this group (n = 36 [11.2%]; odds ratio (OR), 6.8; 95% confidence interval, 1.6–28.6).

The average time from ingestion to registration for asymptomatic patients with abnormal VSs was 2.7 hours. Within the first 60 minutes, 128 patients (39.9%) received an intervention (Fig. 4), and 1 patient was admitted for telemetry (see Table 3, Supplemental Digital Content 2, http://links.lww.com/PEC/A914). Between 60 and 120 minutes, 90 patients (28%) received an intervention, and there were no admissions. Between 120 and 180 minutes, 45 patients (14%) received an intervention, and 4 patients were admitted (Supplemental Digital Content, Supplementary Table 3, http://links.lww.com/PEC/A914). Three of the admissions were for monitoring after ingestions of unknown substances, and 1 was for an ingestion of levothyroxine and phenobarbital. Between 180 and 240 minutes, 38 patients (11.8%) received an intervention, and 5 patients were admitted (see Table 3, Supplemental Digital Content 2, http://links.lww.com/PEC/A914). Between 240 and 300 minutes, 23 patients (7.2%) received an intervention, and 1 patient with an

TABLE 2. Distribution of Ingested Xenobiotic Agents

Drug Category	Normal VSs (n = 109) n (% of Group)	Abnormal VSs (n = 321) n (% of Group)
Alcohol	4 (3.9)	2 (0.66)
Antiepileptic	3 (2.9)	8 (2.6)
Antihistamine	5 (4.9)	21 (6.9)
Antipsychotic	0 (0)	10 (3.3)
Benzodiazepines	4 (3.9)	16 (5.3)
Bupropion	0 (0)	0 (0)
Cardiac (CCB, BB, cardiac glycosides)	10 (9.7)	22 (7.3)
Drugs of abuse	5 (4.9)	18 (5.9)
Hormones	7 (6.8)	8 (2.6)
NSAIDs	14 (13.6)	40 (13.2)
Opioids	2 (1.9)	9 (3.0)
SSRI	3 (2.9)	7 (2.3)
Vitamins	9 (8.7)	7 (2.3)
Other	37 (35.9)	135 (44.5)
Known	**103**	**303**
Unknown	**6**	**18**

BB indicates β blocker; CCB, calcium channel blocker; SSRI, selective serotonin reuptake inhibitors.

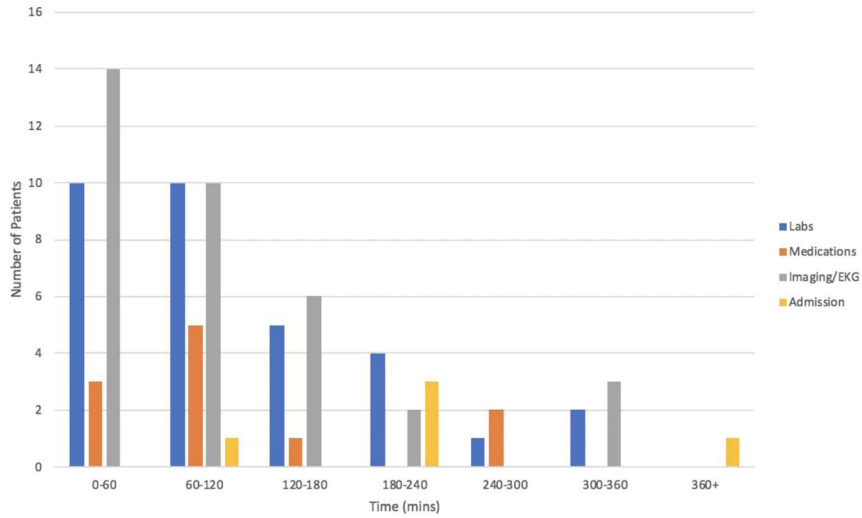

FIGURE 2. Interventions performed on asymptomatic patients with normal VSs.

unknown ingestion was admitted after an episode of hypoxia and transient hypotension. Between 300 and 360 minutes, 13 patients (4%) received an intervention, and 2 patients were admitted for observation. After 360 minutes, 16 patients (5%) received an intervention, and 9 patients were admitted (see Table 3, Supplemental Digital Content 2, http://links.lww.com/PEC/A914).

These patients were observed in the ED from registration to disposition for an average of 4.5 hours and 7.1 hours from time of ingestion. Twenty-two (6.8%) were admitted. Ninety-five percent (21 of 22) of admitted patients were discharged within 24 hours of admission. One patient was admitted for 48 hours and subsequently transferred to a psychiatric facility for further management. There was no significant difference in the OR for admission when comparing patients with normal VSs to those with abnormal VSs (OR, 1.5; 95% confidence interval, 0.57–4.15).

Two hundred ninety-nine asymptomatic patients with abnormal VSs were discharged home. Of this group, 55 (18%) were discharged within 120 minutes of registration, and the predominant xenobiotic ingestions in this rapidly assessed and discharged group were rat poison (7 of 55) and NSAIDS (3 of 55). Three of these 55 patients returned to the ED within 72 hours, all of which were rat poison ingestions and were instructed to follow-up for repeat laboratories. In the rest of this cohort (244 patients), 8 additional patients returned to the ED within 72 hours. Three patients returned with symptoms of emesis and/or diarrhea after their ingestion of furosemide, metoprolol, and guanfacine, respectively, and the symptoms were deemed unlikely related to the ingestion. All were subsequently discharged from the ED. An additional 3 patients were advised to come back for repeat laboratories and/or additional consultations within the 72-hour window: 1 ingested valproic acid and 2 ingested rat poison (super warfarins such as brodifacoum). All of these patients were ultimately discharged home again. Finally, 2 patients came back within the 72-hour window for psychiatric and/or behavior health evaluations, unrelated to the ingestion.

DISCUSSION

Pediatric toxic ingestions are a common cause of injury, yet those that are secondary to exploratory behavior in infants or young children rarely result in morbidity or mortality.[1] Although there are

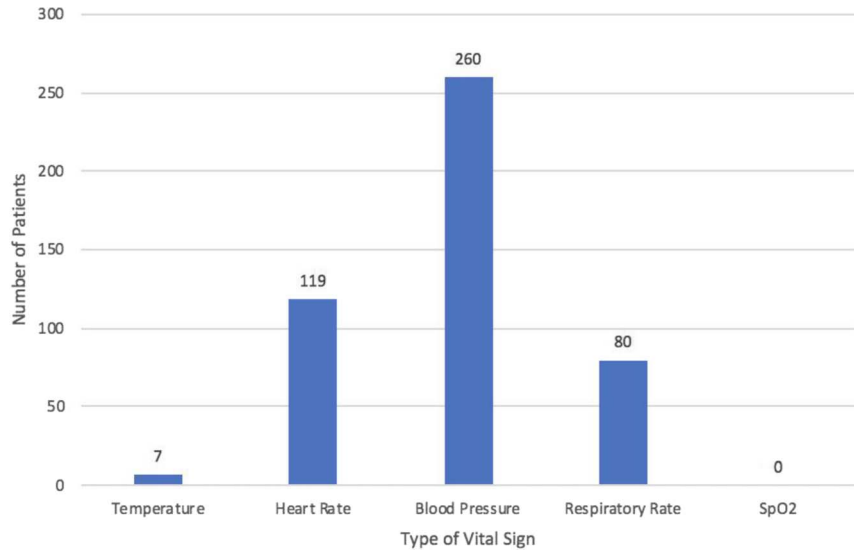

FIGURE 3. Distribution of abnormal VSs.

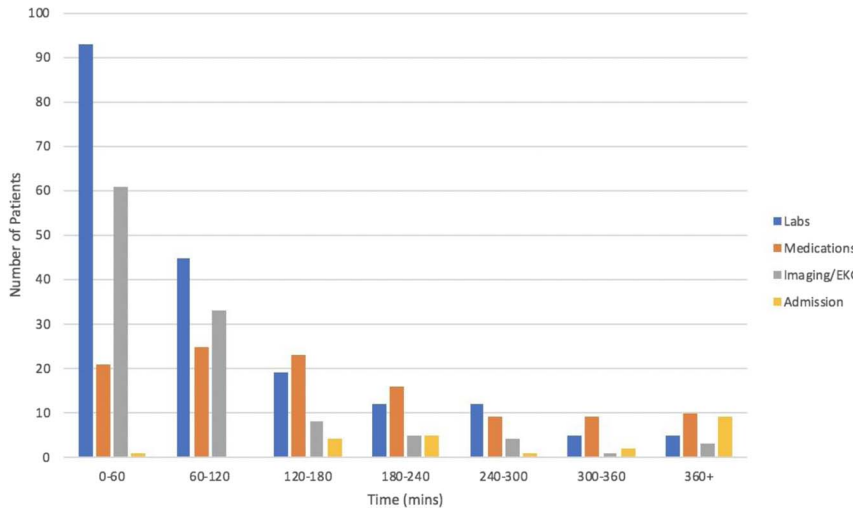

FIGURE 4. Interventions performed on asymptomatic patients with abnormal VSs.

studies in adult literature that assess the observation period after an ingestion, the authors did not encounter any similar studies in pediatrics or any widely accepted evidence for the duration of observation in asymptomatic pediatric patients.[6]

There were 2817 charts reviewed, yielding a cohort of 109 asymptomatic patients with normal VSs upon presentation to the ED. A second cohort, based on our secondary objective, included 321 asymptomatic patients presenting with abnormal VSs. A higher percentage of our patients presented to the ED with abnormal VSs, making it difficult to compare the 2 groups. Accordingly, we analyzed each group individually and subsequently compared rates of admissions/discharges/returns. The majority of diagnostic interventions such as laboratory tests, electrocardiograms, imaging, and/or medication administrations occurred within the first 2 hours after presentation, but there was no clear association between intervention and admission (see Figure 2, Supplemental Digital Content 1, http://links.lww.com/PEC/A913).

Admissions

There were 5 admitted patients (4.6%) in the asymptomatic group with normal VSs. Four (80%) of the admissions were determined within 4 hours of presentation, consistent with our hypothesis that providers can identify most patients requiring admission or further medical interventions in less than 6 hours. One patient was not admitted until 7.8 hours postregistration. After chart review, there were several features of this case, which limit its applicability to the rest of the study. First, this child had an unwitnessed ingestion of an unknown substance. Additional history later revealed medications in the home, including a β blocker and a sulfonylurea. This child was ultimately admitted for monitoring for bradycardia or hypoglycemia. As stated in the methods, disclosed sulfonylurea ingestions were not included in this study because of their preestablished treatment algorithms and prolonged pharmacokinetics.[1] However, because of the nature of this unknown ingestion, it was included in the cohort initially. In this case, the risk of a sulfonylurea ingestion, although quite low, warranted admission for monitoring by the toxicology team. Over the course of the admission, this child had no acute events and was discharged within 24 hours. Because of the retrospective nature of this study, the authors were unable to determine if the providers had planned this disposition earlier in the clinical course or if there was a change after 7 hours of observation when the medications were disclosed.

There were 22 admissions (7%) within our cohort of patients with abnormal VSs. There was no significant difference in the OR for admission when comparing patients with normal VSs with those with abnormal VSs. This could be attributed to 2 main factors—the first is that admission, as an outcome variable, is subjective, and admission thresholds may differ between providers. The second explanation is that VSs, when interpreted in isolation, may be poor predictors of life-threatening conditions in pediatric patients. Particularly in the ED, toxicity, anxiety, and the uncooperative pediatric patient may contribute to abnormalities in VSs. One study found that nonhospitalized children, including those in the ED at triage and in primary care settings, had higher heart rates than hospitalized children even when accounting for body temperature.[12] This was even more notable in children younger than 2 years.[12] The authors attributed some of those differences to the emotional stress of young children who are ill and being assessed by strangers, and the effect of this stress on heart rate. In addition, the study's narrow range of normal VSs may have impacted this result, as the 2 groups may not have actually represented markedly different populations upon presentation. For these reasons, the authors sought to describe the reasons for admission, as well as the clinical course, to provide context to the disposition decisions.

Of the 36 patients who disclosed suicidality in the context of their ingestion, 7 (19.4%) were admitted. Therefore, patients who disclose suicidality after an ingestion likely represent a vulnerable population with unreliable history and may require longer observations and/or admissions, even if the psychiatric concerns have been addressed.

Discharges

Disposition is a critical part of ED management. Although the investigators of this study are evaluating if a shorter observation time would be appropriate, it is also critical to ensure safety when discharging a patient. Return visits may be one indicator of potential medical management errors associated with inappropriate assessment or treatment.[13] Our study demonstrated that none of the discharged patients, regardless of their VSs or admission status, required any unanticipated medical interventions postdischarge. This supports the disposition decisions made by providers.

Limitations

Our study had several limitations. First, because this was a retrospective chart review, we were limited by the information

available in the medical chart. We were unable to determine the reasoning for certain clinical decisions, including the time a patient was medically cleared for discharge or why a patient received specific treatments or interventions. We also could not be certain that time of admission was captured with the level of precision required for a time-to-event analysis; therefore, we instead calculated OR of admission between our groups. Similarly, when selecting the relevant encounters, we found multiple unrelated *ICD-9/10* codes likely due to the variability in the wording of discharge diagnoses. The data were also limited to include those cases where documentation was able to obtained, with 649 potential subjects excluded for lack of complete documentation (denoted as "no note" in Fig. 1). The authors were unable to determine if these patients would have otherwise fit the inclusion criteria and, as such, cannot postulate on whether they would have impacted the data set. In addition, given the retrospective nature of this study, we were only able to account for patients who return to care within the hospital network. However, given the catchment area of the hospital network, this likely represented the majority of return visits requiring acute care interventions.

Second, there is an innate limitation when evaluating ingestions in pediatric populations who cannot reliably disclose the ingested agent. Investigators rely predominantly on secondary history from a caretaker, and there may be secondary gain from withholding information because of fear of allegations of child endangerment or negligence. Similarly, investigators cannot be certain that the patient actually ingested the alleged substance. Nonetheless, the investigators used the most consistent information available to them.

Finally, the authors recognize that using abnormal VSs as a method of identifying a potentially at-risk patient group is met with challenges. Vital sign norms are highly variable and are constantly changing because of the scope of patients presenting to the ED. A recent study from Sepanski et al[14] found that heart and respiratory rates from 1.2 million nonadmitted patients presenting to their EDs were higher than previously published norms in the Pediatric Advanced Life Support guidelines. Furthermore, they advocated for using centile ranges rather than dichotomous "normal" and "abnormal" cutoffs.[14] Another study by Fleming et al[15] found that existing reference ranges for heart rates and respiratory rates in children were inconsistent, and the ranges did not agree with centile charts derived from their systematic review of observational studies. Nonetheless, given the lack of a widely accepted source for normal VSs, the authors decided to use the guidelines based on The Harriet Lane Handbook. The authors acknowledged that this may provide a falsely high number of patients with abnormal VSs but would be unlikely to miss those with VS changes that may not meet the "abnormal" values in other published ranges. This would lead to increasing the sensitivity at the cost of the specificity of the patient population.

CONCLUSIONS

Xenobiotic ingestions (not involving acetaminophen, salicylates, hydrocarbons, caustic substances, and/or extended release medications) in asymptomatic pediatric patients are often observed for 6 hours postingestion based on pharmacokinetics. Of 910 toxic exposures presenting to the ED of this pediatric hospital, about one third will have a predetermined, defined evaluation pathway and about one fifth will be symptomatic. Out of the remaining cases, when children are asymptomatic at presentation or only have minor VS abnormalities, it is unlikely that their observation in the ED will alter their disposition. Our current study suggests that such extended observation periods may not be necessary. Furthermore, none of the discharged patients, in either group, required any unanticipated medical interventions postdischarge. Patients who disclose suicidal intent upon presentation represent a potentially at-risk and sometimes unreliable group and should be monitored accordingly. Prospective studies evaluating the shortened observation period in asymptomatic patients are needed and will help clinicians determine necessary observation periods, as prolonged length of stay in an ED comes with additional risks and costs.

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