Poisonings Associated with Intubation: US National Poison Data System Exposures 2000-2013.

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ORIGINAL ARTICLE

Poisonings Associated with Intubation: US National Poison Data System Exposures 2000–2013

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Abstract Patients may be intubated after exposure to a variety of substances because of respiratory failure, CNS sedation, pulmonary pathology, or cardiovascular instability. However, there is little data describing the types of substances that are associated with endotracheal intubation or the rates of intubation after these exposures. Evaluation of this association may inform future research on intubation after exposures to specific substances and guide poison prevention education. Our objective was to determine which exposures were commonly associated with intubation using the data from National Poison Data System (NPDS). The NPDS tracks data from potential exposures to substances reported to all American Association of Poison Control Centers. We performed a retrospective analysis of NPDS data from January 1st, 2000 to December 31st, 2013 to identify human exposures to substances that were associated with endotracheal intubation. Descriptive statistics were used to analyze the data. There were 93,474 single substance exposures and 228,507 multiple substance exposures that were associated with intubation. The most common exposures to substances that were associated with intubation were atypical antipsychotics (7.4 %) for single exposures and benzodiazepines (27.4 %) for multiple exposures. Within each age group, the most common known exposures to substances were for patients under 6 years, clonidine for single and multiple exposures; for patients aged 6–12 years, clonidine for single exposures and atypical antipsychotics for multiple exposures; for patients aged 13–19 years, atypical antipsychotics for single and multiple exposures; and for patients over 19 years, atypical antipsychotics for single exposures and benzodiazepines for multiple exposures. From 2000–2013, the exposures to substances most commonly associated with intubation varied by single versus multiple exposures and by age. This study helps clarify the exposures to substances that are associated with intubation reported to poison centers in the USA.

Keywords Endotracheal intubation · Toxicologic exposure · National poison data system · Poisoning

Introduction

The decision to provide airway management in a patient with poisoning requires careful consideration of a number of factors including altered mental status because of the presence of a sedating xenobiotic, presence of acidosis or severe electrolyte abnormalities, substance-induced respiratory compromise or hemodynamic instability, and drug-induced seizure [1–15]. Reasons for intubation in a poisoned patient may include central nervous system depression, agitated delirium, inability to cooperate with procedures, respiratory compromise, and acute lung injury. Strategies needed to enhance the management of the airway in the poisoned patient depend on several factors, such as the type of exposure, co-exposures, and comorbidities of the patient. These factors can impair oxygenation, ventilation, and airway status in the poisoned patient. While research

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in airway management after toxicologic exposure has been performed, the type of poisonings most commonly associated with intubation is poorly studied [16–19]. Knowledge of the poisonings reported to poison centers that are most commonly associated with intubation may help direct future research into airway management after toxicologic exposure.

The type of exposures to substances that is commonly associated with intubation may reflect a number of factors including severity of exposures, prescribing practices, or poisoning prevention measures. Because the exposure to a substance can vary by the age of a patient, the study of intubation as an outcome might reveal exposures to specific substances that increase the risk for morbidity in particular age groups. Tracking exposures to substances that are associated with intubation may have implications for poisoning prevention by informing prescribing practices or poison prevention education [20, 21].

We characterized the most common substances associated with intubation in poisoned patients by reviewing exposures reported to the AAPCC NPDS. In addition, we reported the annual number of patients poisoned by these substances and the percentage of exposures associated with intubation during the study period.

Materials and Methods

This was a retrospective analysis of the NPDS database, to identify exposures to substances that were most commonly associated with intubation. The study was approved by the Institutional Review Board.

The NPDS tracks data from potential exposures to substances reported to all AAPCC member US poison centers. Exposures are collected by the NPDS on a self-report basis and reflect information provided when the public or healthcare professionals report an actual or potential exposure to a substance (e.g., an ingestion, inhalation, or topical exposure). Data are collected using standardized electronic health record collecting systems with mandatory common data elements and reporting requirements. Data collected includes patient demographic information, substance(s) involved in the exposure, reason for exposure, signs and symptoms, therapeutic interventions, and outcomes. Data collected from callers to the poison center are entered into the electronic health record in real time [22]. In cases of intubation in a health care facility, this information is provided by a healthcare provider.

In this study, we searched NPDS for calls between January 1, 2000 and December 31, 2013 regarding human exposures to substance(s) (exposures where the caller reported a person was exposed or potentially exposed to a toxicologic substance) with intubation as a therapeutic intervention, including "performed" and "recommended and performed." "Intubation" was used in this analysis to refer to exposures to substances with endotracheal intubation as a therapeutic intervention. We studied numbers of exposures to substances that were associated with intubation by age group for single (reported exposure to one substance) and multiple exposures (reported exposure to multiple substances). Where the substance(s) involved in the exposure was not known by the caller, the exposure was coded as "unknown" and analyzed as such in this study. Where patient age was unknown, data points were excluded from analysis by age group. We performed additional searches for single and multiple exposures to substances that were associated with intubation by age groups: 0–5 years, 6–12 years, 13–19 years, and over 19 years. We recorded the total number of exposures to substances that were associated with intubation by year, sex, substance(s) involved in the exposure, age group, and single versus multiple exposures using a standardized spreadsheet. We summarized distributions for all single and multiple exposures to substances with intubation documented as a therapeutic intervention by age and sex. We identified the five most common single and multiple exposures to substances associated with intubation, overall and by age group, by using the total numbers of single and multiple exposures to substances with intubation as the denominator, and the number of single and multiple exposures to a specific substance that was associated with intubation as the numerator. We performed a second analysis using the number of all substance-specific exposures reported to NPDS as the denominator, which included both exposures to a specific substance managed with intubation, and those managed without intubation. The numerator consisted of the number of substance-specific exposures managed with intubation. The percentage of each of the five most common exposures to substances associated with intubation and associated 95 % exact binomial confidence intervals were then calculated by age group. For example, to calculate the percentage of clonidine exposures associated with intubation among patients age 0–5 years, the numerator was the number of clonidine exposures managed with intubation among patients 0–5 years, and the denominator was the number of all reported clonidine exposures, whether or not associated with intubation, in this age group.

Stata (College Station, TX) was used for statistical analysis.

Results

Single and Multiple Exposures to Substances Most Commonly Associated with Intubation from 2000–2013

A total of 93,474 single exposures and 228,507 multiple exposures to substances had intubation as a therapeutic intervention from January 1st, 2000 to December 31st, 2013. Distribution of single and multiple exposures to substances by

age and sex is included in Table 1. Across all age groups, the five most common single exposures to substances associated with intubation were atypical antipsychotics, amitriptyline, benzodiazepines, ethanol, and acetaminophen combination products. The most common multiple exposures to substances were benzodiazepines, atypical antipsychotics, ethanol, selective serotonin reuptake inhibitors, and other antidepressants (Table 1).

The five most common single and multiple exposures to substances associated with intubation for each age group are included in Table 2. For children under 6 years old, there were 12,008 reported intubations (5517 single exposures, 6491 multiple exposures), and the most common known exposures to substances included clonidine, carbamazepine, and atypical antipsychotics in both single and multiple exposure groups.

There were 2504 children aged 6–12 years with intubation reported as a therapeutic intervention (1059 single exposures, 1445 multiple exposures), and the most common known exposures to substances were clonidine, carbon monoxide, and amitriptyline for single exposures and atypical antipsychotics, clonidine, and benzodiazepines for multiple exposures.

Table 1 Characteristics of NPDS exposures associated with intubation from 2000 to 2013

Characteristic	Number	Percentage (95 % CI)
Single exposures to substances associated with intubation	Number of single exposures to substances associated with intubation	Percentage of total single exposures to substances associated with intubation
Total	93,474	
Age group		
0–5 years	5517	5.9 % (5.8 to 6.1 %)
6–12 years	1059	1.1 % (1.1 to 1.2 %)
13–19 years	8961	9.6 % (9.4 to 9.8 %)
>19 years	76,235	81.6 % (81.3 to 81.8 %)
Unknown	1702	1.8 % (1.7 to 1.9 %)
Gender		
Female	44,415	47.5 % (47.2 to 47.8 %)
Five most common exposures		
Atypical Antipsychotics	6914	7.4 % (7.2 to 7.6 %)
Amitriptyline	5627	6.0 % (5.9 to 6.2 %)
Benzodiazepines	5036	5.4 % (5.2 to 5.5 %)
Ethanol	2370	2.5 % (2.4 to 2.6 %)
Acetaminophen Combination products	2344	2.5 % (2.4 to 2.6 %)
Multiple exposures to substances associated with intubation	Number of multiple exposures to substances associated with intubation	Percentage[a] of total multiple exposures to substances associated with intubation
Total	228,507	
Age group		
0–5 years	6491	2.8 % (2.8 to 2.9 %)
6–12 years	1445	0.6 % (0.6 to 0.7 %)
13–19 years	18,815	8.2 % (8.2 to 8.3 %)
>19 years	198,152	86.7 % (86.6 to 86.8 %)
Unknown	3604	1.6 % (1.5 to 1.6 %)
Gender		
Female	118,700	51.9 % (51.7 to 52.2 %)
Five most common exposures		
Benzodiazepines	62,624	27.4 % (27.2 to 27.6 %)
Atypical Antipsychotics	39,332	17.2 % (17.1 to 17.4 %)
Ethanol	37,619	16.5 % (16.3 to 16.6 %)
Selective serotonin reuptake inhibitors	22,277	9.7 % (9.6 to 9.9 %)
Other antidepressants	17,434	7.6 % (7.5 to 7.7 %)

[a] Percentage values were rounded to the nearest tenth of a percent

Table 2 Five most common NPDS exposures associated with intubation by age group and as a percentage of total NPDS exposures 2000–2013

Exposure	Number of exposures to substance reported to NPDS associated with intubation	Total number of exposures to substance reported to NPDS	Percentage[a] of total NPDS exposures to substance that were associated with intubation (95 % C.I.)
Age 0–5 years			
Single exposures			
Clonidine	856	21,675	3.9 % (3.6 to 4.2 %)
Carbamazepine	326	11,035	2.9 % (2.6 to 3.3 %)
Unknown	285	61,492	0.5 % (0.4 to 0.5 %)
Lamp Oils	238	25,522	0.9 % (0.8 to 1.0 %)
Atypical Antipsychotics	142	32,083	0.4 % (0.4 to 0.5 %)
Multiple exposures			
Clonidine	1052	6246	16.8 % (15.9 to 17.8 %)
Carbamazepine	367	1994	18.5 % (16.7 to 20.2 %)
Unknown	336	5324	6.3 % (5.7 to 7.0 %)
Atypical Antipsychotics	294	11,304	2.6 % (2.3 to 2.9 %)
Lamp Oils	240	1134	21.1 % (18.8 to 23.7 %)
Age 6–12 years			
Single exposures			
Unknown	122	9817	1.2 % (1.0 to 1.5 %)
Clonidine	77	13,130	0.6 % (0.5 to 0.7 %)
Carbon Monoxide	64	17,674	0.4 % (0.3 to 0.5 %)
Amitriptyline	60	1839	3.3 % (2.5 to 4.2 %)
Atypical Antipsychotics	56	15,209	0.4 % (0.3 to 0.5 %)
Multiple exposures			
Atypical Antipsychotics	550	11,187	4.9 % (4.5 to 5.3 %)
Unknown	146	1187	12.3 % (10.5 to 14.3 %)
Clonidine	106	5410	2.0 % (1.6 to 2.4 %)
Benzodiazepines	102	2810	3.6 % (3.0 to 4.4 %)
Carbon Monoxide	93	773	12.0 % (9.8 to 14.5 %)
Age 13–19 years			
Single exposures			
Unknown	759	26,374	2.9 % (2.7 to 3.1 %)
Atypical Antipsychotics	623	37,615	1.7 % (1.5 to 1.8 %)
Ethanol	612	26,917	2.3 % (2.1 to 2.5 %)
Amitriptyline	590	4674	12.6 % (11.7 to 13.6 %)
Diphenhydramine	315	29,871	1.1 % (0.9 to 1.2 %)
Multiple exposures			
Atypical Antipsychotics	3082	42,425	7.3 % (7.0 to 7.5 %)
Benzodiazepines	2747	45,410	6.0 % (5.8 to 6.3 %)
Ethanol	2347	48,605	4.8 % (4.6 to 5.0 %)
SSRI	2126	56,855	3.7 % (3.6 to 3.9 %)
Anticonvulsants	1385	19,716	7.0 % (6.7 to 7.4 %)
Age over 19 years			
Single exposures			
Unknown	6391	73,085	8.7 % (8.5 to 9.0 %)
Atypical Antipsychotics	5980	116,012	5.2 % (5.0 to 5.3 %)
Amitriptyline	4815	26,020	18.5 % (18.0 to 19.0 %)
Benzodiazepines	4605	223,103	2.1 % (2.0 to 2.1 %)
Acetaminophen Combo	1984	78,624	2.5 % (2.4 to 2.6 %)

Table 2 (continued)

Exposure	Number of exposures to substance reported to NPDS associated with intubation	Total number of exposures to substance reported to NPDS	Percentage[a] of total NPDS exposures to substance that were associated with intubation (95 % C.I.)
Multiple exposures			
Benzodiazepines	58,633	476,778	12.3 % (12.2 to 12.4 %)
Atypical Antipsychotics	35,274	212,317	16.6 % (16.5 to 16.8 %)
Ethanol	34,611	446,504	7.7 % (7.8 to 7.8 %)
SSRI	19,661	219,181	9.0 % (8.9 to 9.1 %)
Other Antidepressants	15,708	122,849	12.8 % (12.6 to 13.0 %)

[a] Percentage values were rounded to the nearest tenth of a percent

There were 27,776 patients aged 13–19 years with intubation reported as a therapeutic intervention (8961 single exposures, 18,815 multiple exposures), and the most common known exposures to substances were atypical antipsychotics, ethanol, and amitriptyline in the single exposure group and atypical antipsychotics, benzodiazepines, and ethanol in the multiple exposure group.

There were 274,387 patients over the age of 19 years with intubation as a therapeutic intervention (76,235 single exposures, 198,152 multiple exposures), and the most common known exposures to substances were atypical antipsychotics, amitriptyline, and benzodiazepines in the single exposure group; and benzodiazepines, atypical antipsychotics, and ethanol in the multiple exposure group.

Figures 1 and 2 show the number of exposures over time for the five most common single and multiple exposures to substances that were associated with intubation by age group. For single exposures to substances in the 0–5 years of age group, exposure to clonidine that was associated with intubation appeared to increase over time while exposure to carbamazepine appeared to decrease. There was also an apparent increase over time for single exposure to unknown substances in age 13–19 and over 19 years of age groups (Fig. 1). For multiple exposures, there was an apparent increase over time

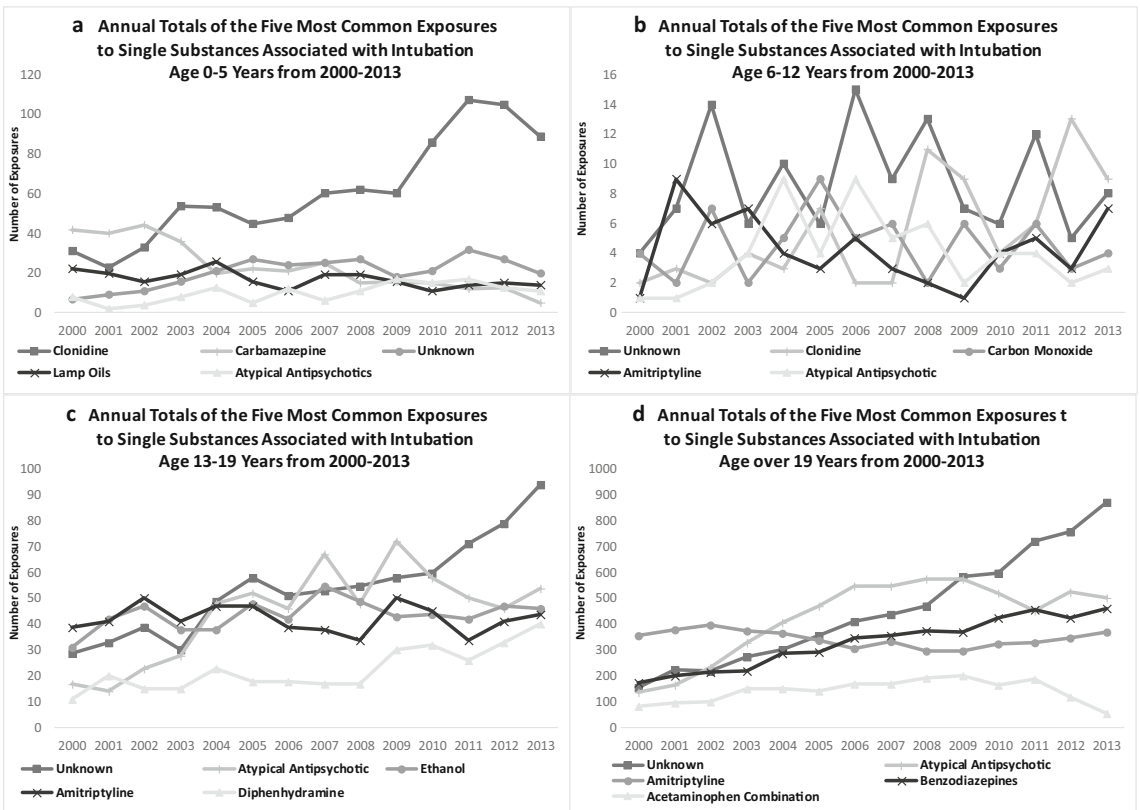

Fig. 1 Annual totals of the five most common exposures involved in single ingestions associated with intubation by age group 2000–2013

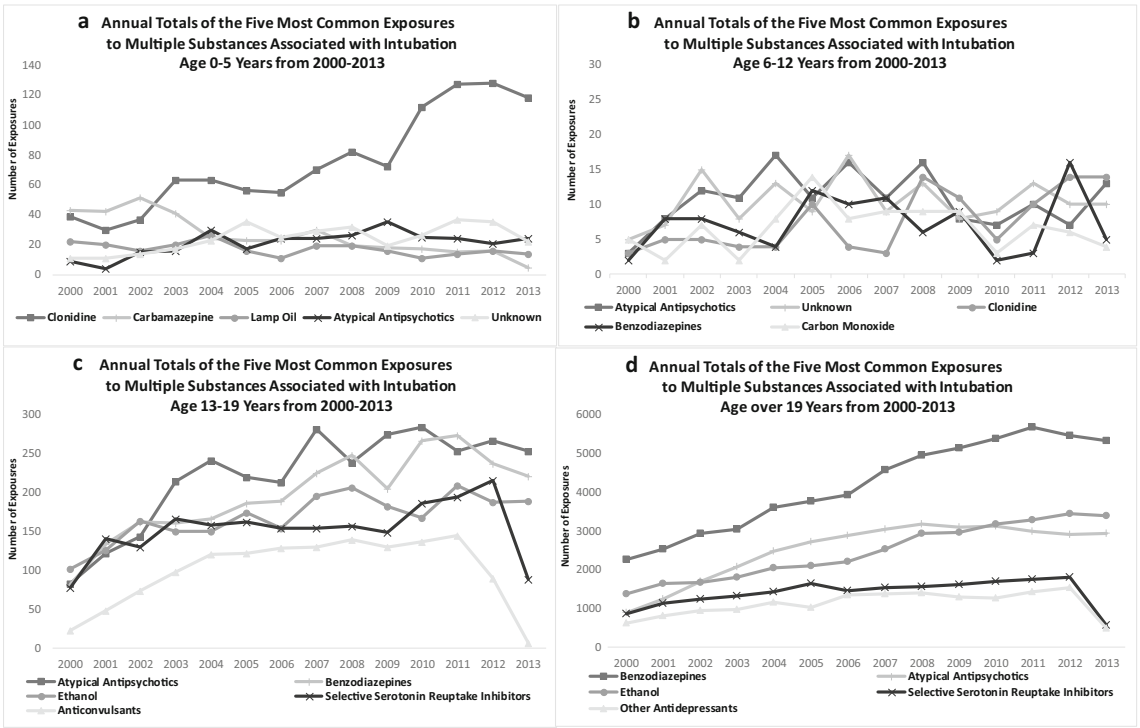

Fig. 2 Annual totals of the five most common exposures involved in multiple ingestions associated with intubation by age group 2000–2013

in clonidine exposures associated with intubation for the 0–5 years age group and benzodiazepine exposures associated with intubation in the age over 19 years group (Fig. 2).

Percentage of Exposures to Substances Associated with Intubation Among all Exposures Reported to NPDS from 2000–2013

For the five most common single and multiple exposures to substances associated with intubation, the percentages among all substance-specific exposures (including both exposures associated with intubation and those not associated with intubation) varied by age group and ranged from 0.4 to 21.1 % (Table 2). Exposures to substances with the highest percentage of patients intubated included lamp oils (21.1 %), carbamazepine (18.5 %), and clonidine (16.8 %) in the age 0–5 years age group for multiple exposures, carbon monoxide (12.0 %) in the 6–12 years age group with multiple exposures, and amitriptyline in both the 13–19 years age group with single ingestions (12.6 %) and the over 19 year group with single ingestions (18.5 %). Among all multiple substance exposures in the age over 19 years age group, 12.3 % of exposures involving a benzodiazepine, 12.8 % of exposures involving other antidepressants (excluding amitriptyline and selective serotonin reuptake inhibitors), and 16.6 % of exposures involving an atypical antipsychotic were associated with intubation.

Discussion

Across all age groups, atypical antipsychotics were the most common single exposure to a substance associated with intubation, while benzodiazepines were most common among multiple substance exposures. Our finding that clonidine was the most common exposure associated with intubation for patients under 6 years old supports a recent study that demonstrated increasing pediatric exposures to central alpha-2 agonists between 2000 and 2011 [23]. Apparent increasing numbers of clonidine exposures associated with intubation may be due to increasing prescriptions of this medication during the study time period, resulting in increased inadvertent pediatric exposures [24, 25]. Further research into this relationship may inform prescribing practices and poisoning prevention practices for high-risk medications like clonidine. Apparent decreasing numbers of pediatric exposures to carbamazepine associated with intubation may reflect decreasing prescribing frequency of carbamazepine [26–28]. A high percentage of exposures to carbamazepine, clonidine, and lamp oils in young children, carbon monoxide in older children age 6–12, and amitriptyline in patients over the age of 13, were managed with intubation and may represent exposures at increased risk for respiratory failure or failure to protect the airway because of a change in mental status. It is important for medical providers, including prescribers, poison center personnel, and medical toxicologists, to be aware of exposures to substances that are commonly associated with intubation

because this may inform prescribing practices, research on intubation practices, public education provided by toxicologists and poison centers, and resource allocation in the acute care setting.

Knowledge of exposures to substances most frequently associated with intubation may inform airway management recommendations given to emergency providers by toxicologists. For example, the high percentage of amitriptyline poisonings reported to NPDS that are associated with intubation suggests that these may be exposures that are likely to present with respiratory compromise, hemodynamic instability, or central nervous system depression. Toxicologists and poison center personnel advising emergency providers on airway management for such patients should warn that management with intubation can place patients at risk for worsening acid-base status—a significant consideration given the high percentage of amitriptyline exposures associated with intubation in this study.

This study had several significant limitations. This was a retrospective study using a convenience sample of exposures to substances reported to the NPDS from 2000 to 2013 and was therefore limited by the use of pre-existing records not explicitly designed for this study and which may not be representative of the general population. Limitations included potential unstable population estimates because of biased reporting and potential for misclassification because data were not verified. For example, data collected by poison centers are not verified by either the NPDS or AAPCC and are based on self-reported information from the public or health care professionals, which may be limited and lack medical decision-making information, such as reason for intubation [29]. The estimates of exposures to substances in NPDS are not representative of the general US population. Because identification of the substances involved in exposures relies on the caller, there may be considerable error, particularly in cases where intubation may limit patient history. Laboratory testing of clinical specimens to confirm the exposure to a substance is rarely performed. Further, exposures to substances that are reported to poison centers may have more severe manifestations of toxicity, resulting in reporting bias. On the other hand, exposures reported do not necessarily represent a poisoning or overdose. Further understanding of indications for, and underlying mechanisms of the respiratory, cardiac, or central nervous system deterioration leading to intubation of patients with poisoning is needed in order to change provider practice, awareness, and preparedness. Analysis of provider medical decision-making should be used in future studies of poisonings associated with intubation. Further knowledge of exposures to substances commonly associated with intubation as a therapeutic intervention in poisoned patients may direct future research in airway management of the poisoned patient. Awareness of such high morbidity exposures to substances may guide the approach taken by healthcare providers in preparing a patient for intubation and provide insight for toxicologists advising emergency clinicians in the airway management of poisoned patients. Further, knowledge of types of exposures to substances with increasing or decreasing association with intubation may inform prescribing and poisoning prevention practices for medical providers.

Conclusions

From 2000 to 2013, exposures to substances reported to NPDS most commonly associated with intubation varied by single vs. multiple exposures and by age. Substances with the highest percentage of exposures associated with intubation included lamp oil, clonidine, and carbamazepine exposures in patients aged 0–5 years and amitriptyline exposures in patients aged 13 years and older. This study helps to clarify which substances are associated with intubation from a national dataset, which has not been previously reported in the literature.

Acknowledgments The authors acknowledge The American Association of Poison Control Centers (AAPCC, www.aapcc.org), which maintains the national database of information logged by all US poison control centers which was used in this study.

Case records in this database are from self-reported calls; they reflect only information provided when the public or healthcare professionals report an actual or potential exposure to a substance (e.g., an ingestion, inhalation, or topical exposure) or request information. Exposures do not necessarily represent a poisoning or overdose. The AAPCC is not able to completely verify the accuracy of every report made to member centers. Additional exposures may go unreported to poison control centers and data referenced from the AAPCC should not be construed to represent the complete incidence of national exposures to any substance(s).

Compliance with Ethical Standards

Conflicts of Interest The authors declare that they have no competing interests.

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