CROSS-SECTIONAL STUDY

Dental Local Anesthesia-Related Pediatric Cases Reported to U.S. Poison Control Centers

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Abstract: ***Purpose:*** *The purpose of this study was to use National Poison Data System (NPDS) data to identify cases of local anesthetic (LA) adverse events related to dentistry for children.* ***Methods:*** *NPDS data were queried for all human cases from 2004 to 2018 that identified a parenteral LA agent as the substance, in children 12 years old and younger, which led to a medical outcome classification ranging from moderate to death. For cases that met inclusion criteria, deidentified records with case notes were requested.* ***Results:*** *Twenty-seven dental cases that met review criteria and had available case notes were reviewed. Most subjects were female (n equals 20 out of 27, 74 percent), and the average subject age was 6.8 years. Twenty cases (74 percent) had a moderate effect, seven cases (26 percent) had a major effect, and no fatalities were reported. The most common clinical effects classification was a seizure (n equals 13, 48 percent). One case of LA overdose was identified.* ***Conclusions:*** *No cases of permanent damage or fatal outcomes were found. Seizure activity following the administration of local anesthetic was the most common event, suggesting intravascular administration or a toxic dose.* *(Pediatr Dent 2020;42(2):116-22) Received October 4, 2019 Last Revision November 25, 2019 | Accepted November 26, 2019*

KEYWORDS: LOCAL ANESTHETICS, ADVERSE EVENTS, PEDIATRIC DENTISTRY, POISON CONTROL

No quantitative measure for dental-related local anesthetic (**LA**) population safety exists for children.[1-4] Instead, case reports,[5-11] insurance claim reviews,[1,12] surveys of dental boards,[13] analyses of United States Food and Drug Administration (**FDA**) adverse events reporting,[14] provider surveys,[14-18] reviews of media reports,[2] reviews of coroner's reports,[19] and systematic reviews of these sources[20] have been used to describe adverse events related to LA. There are myriad reports of LA events (Figure 1), but the true volume, repetition in reporting, and missed events are unknown due to a lack of a central national clearinghouse, no mandated reporting regulations, fear of litigation, and other factors.

Another monitor of adverse events related to medications is the National Poison Data System (**NPDS**). The NPDS products database contains over 437,000 products ranging from viral and bacterial agents to commercial chemicals and drugs.[21] Regional poison control centers (**PCCs**) provide information and consultation to laypersons and health care providers in health care facilities (**HCFs**). In 2016, 67.7 percent of calls originated from a residence and 24.4 percent originated from an HCF.[21] In 2017, 2,115,186 poisoning cases were managed by poison centers and reported to the NPDS.[21] An analysis of these data has been used to describe analgesic-related medication errors[22] and adverse events.[23]

In the absence of a central registry for outcomes of anesthetics in dentistry,[4] alternative sources should be utilized to identify potential sources of harm. Typically, only events that cause death or permanent harm are captured in existing publications; also, the morbidity of LAs is underestimated. A source that includes less severe complications and potential near misses will inform providers and, ultimately, improve patient safety.

The purpose of this study was to use National Poison Data System data to identify cases of local anesthetic adverse events related to dentistry for children.

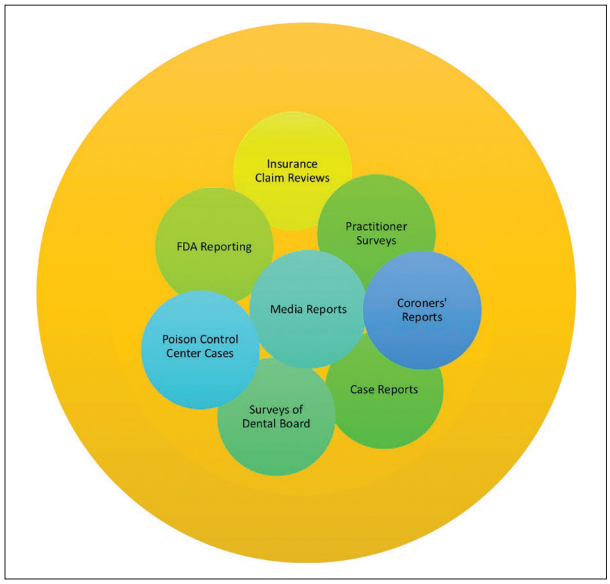

Figure 1. A theoretical model for the sources of information regarding local anesthetic adverse events in dentistry. The true volume, repetition in reporting, and missed events are unknown.

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Methods

This retrospective study analyzed data from the NPDS to identify adverse events related to LA use in dentistry for children. Characteristics and trends were identified. Analysis of NPDS data is exempt from Institutional Review Board approval because there is no interaction with subjects and identifiable information is not released.

Data source information. A network of regional PCCs in the U.S., covering all 50 states and the District of Columbia, offers free, confidential medical advice 24 hours per day by telephone through the Poison Helpline. During case management by PCCs, multiple variables are recorded by PCC health care professionals—who may be nurses, pharmacists, and physicians—managing the patients. Variables include age, substance, clinical effects, therapies, and medical outcomes. Information from these cases, including updates from continued follow-up, is uploaded in near real time to the NPDS. Health care providers and HCFs are not mandated to contact PCCs; contact is voluntary when additional information is desired for patient care.

Table. NATIONAL POISON DATA SYSTEM CASES OF LOCAL ANESTHETIC (LA) ADVERSE EVENTS RELATED TO DENTISTRY FOR CHILDREN*

Case no.	Sex	Age (years)	Weight (kg)	Medical outcome	Clinical effects duration (hours)	Status of patient in relation to healthcare facility	LA agents (dose included if known)	Sedation agents used in conjuction	Clinical effects	Therapies
1	Female	6	18.5	Moderate	>8, ≤24	Admitted to noncritical care unit	4% prilocaine	Chloral hydrate, Demerol, Atarax	Tachycardia, drowsiness/ lethargy, urinary retention	Antibiotics, IV fluids, oxygen
2	Female	2	Unknown	Moderate	≤8	Treated/evaluated and released	3% mepivacaine	None	Seizure (single)	Observation only
3	Male	12	Unknown	Moderate	≤8	Treated/evaluated and released	4% articaine w/1:100,000 epi* (136 mg)	Nitrous oxide	Dizziness/vertigo, confusion, erythema/flushed, diaphoresis	Observation only
4	Female	3	15.1	Moderate	≤8	Admitted to noncritical care unit	Lidocaine (2.4 mg/kg), articaine (2.5 mg/kg)	None	Seizure (single)	Food/snack, dilute/irrigate/ wash
5	Female	6	Unknown	Major	>2, ≤8	Admitted to critical care unit	4% articaine w/1:100,000 epi	None	Tachycardia, fever/ hyperthermia	Other (Dantrolene, Kepra)
6	Female	8	48.6	Moderate	≤2	Treated/evaluated and released	Novocain	Chloral hydrate (50 mg), nitrous oxide	Seizure (single)	Oxygen
7	Male	3	Unknown	Major	≤2	Treated/evaluated and released	Prilocaine w/1:200,000 epi	Nitrous oxide	Seizure (single)	No therapy
8	Female	12	Unknown	Moderate	>8, ≤24	Unknown	Novocain	None	Drowsiness/ lethargy	Observation only
9	Male	12	54.5	Major	≤2	Treated/evaluated and released	Lidocaine (0.62 mg/kg)	None	Seizure (single)	Observation only
10	Female	4	20.3	Moderate	Unknown	Treated/evaluated and released	4% articaine w/1:100,000 epi and topical lidocaine	Nitrous oxide	Pain, agitation, ataxia, extrapyramidal symptoms – dystonia	Antihistamines, benzodiazepines
11	Female	5	Unknown	Major	≤2	Treated/evaluated and released	3% mepivacaine (60 mg), 4% articaine w/1:100,000 epi (80 mg)	Nitrous oxide	Seizure (single)	IV fluids
12	Female	3	11.7	Moderate	≤2	Admitted to critical care unit	4% articaine w/1:100,000 epi (5.8 mg/kg)	Meperidine (2.1 mg/kg injection), nitrous oxide	Seizure (single)	Observation only
13	Female	9	38	Moderate	≤2	Treated/evaluated and released	3% mepivacaine (2.8 mg/kg)	None	Confusion, mydriasis, diaphoresis	Observation only
14	Female	8	Unknown	Moderate	≤2	Treated/evaluated and released	4% articaine w/1:100,000 epi (68 mg)	None	Seizure (single)	Observation only

* Abbreviations used in this table: AMA=Against medical advice; HCF=health care facility; epi=epinephrine.

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Table. CONTINUED*

Case no.	Sex	Age (years)	Weight (kg)	Medical outcome	Clinical effects duration (hours)	Status of patient in relation to healthcare facility	LA agents (dose included if known)	Sedation agents used in conjuction	Clinical effects	Therapies
15	Male	9	Unknown	Major	>8, ≤24	Treated/evaluated and released	Unknown	Nitrous oxide	Miscellaneous, drowsiness/ lethargy, muscle weakness, paralysis	Oxygen
16	Male	12	Unknown	Moderate	>2, ≤8	Treated/evaluated and released	4% articaine w/1:100,000 epi (104 mg), 2% lidocaine w/1:100,000 epi (35 mg)	None	Chest pain, tachycardia, diaphoresis	Benzodiazepines
17	Female	5	13	Moderate	>8, ≤24	Treated/evaluated and released	3% mepivacaine (16.6 mg/kg)	None	Seizure (single), tremor, respiratory depression	Oxygen
18	Male	10	Unknown	Moderate	>2, ≤8	Observation only	Novocain	None	Numbness	Observation
19	Female	11	Unknown	Moderate	>8, ≤24	Admitted to noncritical care unit	Benzocaine	None	Hypertension, tachycardia, rash, alkalosis, r-CPK elevated, other-miscellaneous, dyspnea	IV fluids
20	Female	4	Unknown	Moderate	> 24, ≤72	Unknown	Articaine	None	Edema, irritation/ pain, pallor	Antibiotics
21	Female	5	Unknown	Major	Unknown	Unknown	Novocain	Triazolam 0.25 mg	Neurological agitation	Unknown
22	Female	9	Unknown	Major	>8, ≤24	Enroute to HCF	4% articaine w/ 1:100,000 epi	None	Bradycardia, seizures (multiple), syncope	Unknown
23	Female	6	Unknown	Moderate	>2, ≤8	Enroute to HCF	4% articaine w/1:100,000 epi	None	Seizure (single)	Observation only
24	Female	5	21.7	Moderate	≤2	In HCF	4% articaine w/1:100,000 epi (3.1mg/kg)	None	Drowsiness/ lethargy, syncope, tremor	Observation only
25	Female	4	16	Moderate	≤2	Unknown	4% articaine w/1:100,000 epi (6.9 mg/kg)	None	Seizure (single)	Observation only
26	Female	6	Unknown	Moderate	≤2	Patient lost to follow-up/left AMA	Novocain	Nitrous oxide	Seizure (single)	Observation only
27	Male	7	19	Moderate	>2, ≤8	Treated/ Evaluated and released	4% articaine w/1:100,000 epi (3.6 mg/kg)	None	Tachycardia	Observation only

* Abbreviations used in this table: AMA=Against medical advice; HCF=health care facility; epi=epinephrine.

The NPDS is the only proprietary database maintained by the American Association of Poison Control Centers (**AAPCC**); it consists of all informational and poison exposure calls received by regional PCCs in the United States and its territories. The NPDS is the only comprehensive poison exposure surveillance database in the United States, and it has extensive internal quality control measures to ensure accuracy and completeness.[21] PCCs use the term "exposure" to designate an individual case/ patient event.

Case selection criteria. NPDS data from 2004 to 2018 were queried for all human cases that identified: an LA agent as the substance; children aged 12 years or younger; a medical outcome classification of moderate effect, major effect, or death; and a route of exposure as parenteral/injection. Cases with LAs as a substance were identified using the AAPCC generic code of 002000 (LA) and 077762 (unknown anesthetic). For cases that met inclusion criteria, requests were made to the individual PCC for deidentified records with case notes. Cases that did not involve dentistry were excluded.

Study variables. Variables included in this study were age, sex, year of exposure, LA type, presence of additional medications (including sedatives and nitrous oxide), management site, level of health care received, clinical effects duration, and medical outcome.

Medical outcomes (moderate effect, major effect, and death) were classified by a PCC specialist in accordance with standard NPDS definitions.[21] Moderate effect indicates the patient exhibited signs or symptoms, as a result of exposure, that were more pronounced, prolonged, or systemic in nature than minor symptoms and usually required some form of treatment. Major effect signifies the patient exhibited signs or symptoms as a result of the exposure that were life-threatening or resulted in significant residual disability or disfigurement. Data were analyzed using descriptive statistics.

Results

Between 2004 and 2018, PCCs in the United States managed 58 cases in children age 12 years or younger with a moderate, major, or fatal outcome related to LA via injection. Deidentified records of 41 cases (71 percent response rate) were obtained. Eight of the 55 PCCs did not respond, and one PCC had closed. After further analysis, 14 cases were determined unrelated to dentistry and were excluded, leaving 27 dental cases (summarized in the Table).

Twenty cases (74 percent) were females, and seven (26 percent) were males. Age was known in 25 of the 27 cases and averaged 6.8 years. Eleven cases had a recorded weight (mean equals 25.1 kg). Twenty cases (74 percent) reported a moderate effect, and seven cases (26 percent) reported a major effect. No fatalities were reported. The most commonly reported clinical effects duration was less than or equal to two hours (n equals 10, 37 percent).

Articaine was the LA most commonly involved in cases when the agent was known (n equals 14, 52 percent) followed by mepivacaine (n equals 4, 15 percent), lidocaine (n equals 3, 11 percent), prilocaine (n equals 2, 7 percent), and benzocaine (n equals 1, 4 percent). Five cases claimed to have been associated with Novocain. In three cases (11 percent), two different LAs were administered. Twelve cases (44 percent) included an LA dosage. Nitrous oxide was administered in eight cases (30 percent), and sedative agents with or without nitrous oxide were administered in four cases (15 percent). Only one case (case 17) had a verified administration of LA above the maximum recommended dosage. Specifically, a five-year-old female received 16.6 mg/kg mepivacaine (the maximum recommended dose ranges from 4.4 mg/kg to 6.6 mg/kg).[24,25]

The most common clinical effects classification was seizure (n equals 13, 48 percent), tachycardia (n equals five, 19 percent), and drowsiness/lethargy (n equals four, 15 percent). The most common management therapies were observation only (n equals 13, 48 percent) and oxygen supplementation (n equals four, 15 percent).

Discussion

LAs have been reported to be the safest and most effective drugs available for prevention and management of pain.[26] Estimates are that dentists in the U.S. administer more than 300 million LA cartridges annually.[28] In the 14-year period included in this study, the authors were only able to confirm 27 PCC cases regarding dental LAs in children. It is unknown if this low number is due to the safety of LA or nonreporting. Adverse events related to LA vary in severity as well as the morbidity and mortality pyramid modified from Casamassimo et al.[27] (Figure 2). Under a certain threshold, which varies widely among providers, adverse events are unlikely to be reported. Thirteen children in the reported cases had a seizure upon administration of LA, suggesting that the blood level in the brain was excessive.[28] These high blood levels likely resulted from intravenous administration or administration of an excessive amount of a particular drug. It is unlikely these near misses have been captured by surveillance measures other than the NPDS.

Other studies have shown few cases of LA-related toxicity, but outcomes were more tragic. An analysis of the FDA's adverse drug event reporting system, the U.S. Pharmacopoeia, and a survey of pediatric specialists identified three children with LA overdoses in the dental setting.[14] Three were undergoing dental treatment and received two to three-and-a-half times the maximum recommended doses of either mepivacaine (n equals two) or lidocaine (n equals one);[14] all three children died.[14] Lee et. al found that 9.1 percent of deaths associated with media reports were attributable to LA only.[2]

A review of closed malpractice claims of two liability carriers found 17 cases resulting in adverse anesthesia events. Of these cases, 53 percent (n equals nine) resulted in patient death or permanent brain damage.[1] Thirteen cases were associated with sedation, three with LA only, and one with general anesthesia.[1] In seven of the 17 cases (41 percent), the LA dosage exceeded the maximum recommended dosages either with sedation (n equals four) or without sedation (n equals three).[1] The associated agents were lidocaine (n equals five), mepivacaine plain (n equals one), and prilocaine plain (n equals one).[1]

One issue complicating the determination of LA overdose is conflicting maximum recommended dosages from different sources. In the previously described closed malpractice claims review, the dosages administered in two cases (6.6 mg/kg lidocaine, 5.2 mg/kg mepivacaine plain) were classified as overdoses according to values in an edition of a textbook current at the time the paper was published.[26] However, these dosages do not exceed the maximum recommended dosage described in a later edition of the same textbook.[24] In these cases, only LA was administered and the outcome was death.[1] The American Academy of Pediatric Dentistry (**AAPD**) still recommends a more conservative dosage for children as mentioned in the previous edition of the textbook.[25,26] However, these higher dosages are commonly taught in U.S. dental

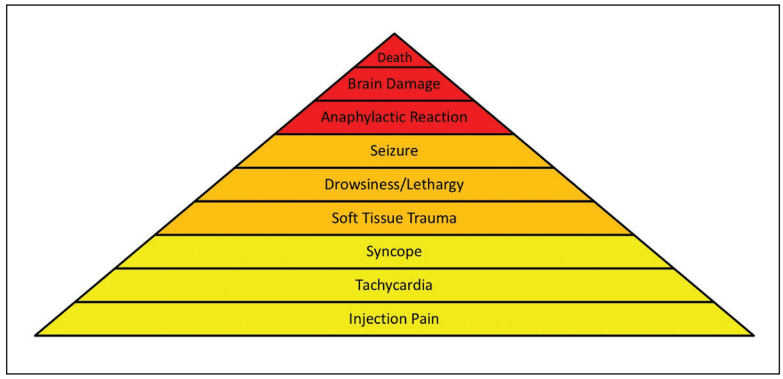

Figure 2. A proposed dental local anesthesia morbidity and mortality pyramid.

schools.[29] Clinicians should not exceed the maximum allowable dose of LA on pediatric patients, and this dose should be weight dependent. Moore and Hersh[30] described a rule of 25, which states that, for healthy patients, a dentist may safely use one cartridge of any marketed LA for every 25 pounds of patient weight. This rule simplifies calculations and is helpful when multiple LAs are used, such as in case four.

In the current study, only one confirmed instance of LA overdose was found. A 13-kg, five-year-old female received four 1.8-mL cartridges of carbocaine (three percent mepivacaine, 216 mg or 16.6 mg/kg) at a dental office. Following administration, the patient experienced apnea of fewer than 30 seconds, tremors in the chair, and a single seizure. Emergency medical services were called, oxygen was administered, and the patient was transported to an emergency department. This dosage exceeds all published maximum dosage recommendations.[24-26] Following observation, the patient was discharged on the same day. A retrospective morbidity and mortality study by Goodson and Moore found that, when the total dose of LA, either alone or combined with narcotics, was exceeded by 300 percent, permanent brain damage or death always resulted.[31] This patient was fortunate, as was another in a reported case of a 22-month-old female who received 21.4 mg/kg of four percent prilocaine plain and did not have any significant postevent sequelae. [1] The review of closed malpractice claims found that three of the claims with the most extreme LA overdoses resulted in only minor outcome severity. [1] Therefore, other factors may contribute to lasting reactions.

Adverse events were reported when dosages below the maximum recommended dosage were administered. Malamed identified that 15 percent of persons are hyperresponders to an average dose of a given drug and within this group another 15 percent are extreme hyperresponders.[28] These patients may fall into this group. In case nine, a 12-year-old, 54.5-kg child received 34 mg of LA. The initial report indicated that Novocain was used, but this was updated to lidocaine. After 10 to 15 minutes, the dentist was about to give a second dose and the child began to seize. The reported dose and timing of the seizures are not consistent with overdose. However, LA doses on the order of one-fiftieth of the recommended upper limit have resulted in a seizure when placed where unintended.[28]

Articaine was the most commonly used agent in the reported cases; in two of the cases, the children were three years old (cases four and 12). In both cases, other agents were used. According to the product instructions for articaine in America, use in pediatric patients younger than four years of age is not recommended.[32] Brickhouse et al.[33] found that 18 percent of dentists surveyed currently used articaine in two- to three-year-olds in 2008; that number is likely higher today. It must be noted that reports of Novocain use were almost certainly erroneous, so articaine may have also been mistakenly reported as the agent.

The strengths of the current study include the use of a highly reliable database. The accuracy of coding in NPDS for demographics and reason for exposure is greater than 95 percent.[34] This database is a novel source of information about morbidity related to LA in dentistry. Utilization identified an additional case of LA overdose that has not been previously published. The use of sources such as NPDS can help find cases of near misses demonstrating that dentists need more awareness and education regarding weight-based LA calculations for children.

The use of databases avoids methodologic problems with other data sources. Surveys may not accurately gather information about all adverse events due to nonparticipation, relocation, or underreporting.[18] For example, there were 10 deaths in Illinois related to dental sedation and/or general anesthesia procedures, but none of these were reported in a survey of anesthesia permit holders examining the same 10-year time period.[18] Data from state dental boards have limited use due to variations in surveillance.[4] Surveillance mechanisms that monitor from the limited perspective of fatal outcomes may lead to disproportionate attention to modalities that result in death and underemphasize the morbidity associated with other sources.[35]

There are several limitations to this study. One was the inability to review full records for all cases in the database. Additionally, the NPDS database depends on accurate information from callers. Five cases in this review reported the administration of Novocain or procaine HCL. Procaine is not available in dental cartridges in North America, and injectable ester anesthetics including procaine HCL were removed from the marketplace in 1996.[26] Reports of Novocain use were likely due to incorrect information relayed to the PCC. In the 27 cases, detailed agent and dosage information was not always available from dentists, and this lack of information likely impacted treatment. Some information was disclosed after initial therapy had started. For example, in case six, the dentist clarified the dosage of the sedation medication via a text message to the patient's mother approximately 30 minutes after seizure management had started, and the dosage of the LA remains unknown. In case 10, the name of the LA and administration of diphenhydramine by the dentist in the office were not reported until 24 hours after the child presented to the emergency department. In case 15, the LA name and dosage were obtained 3.5 hours after presenting to an HFC.

The American Academy of Pediatrics' Annual Leadership Forum included a resolution on preventing deaths in dentists' and oral surgeons' offices as one of their top 10 resolutions.[36] Organized dentistry has called for an emphasis on patient safety, including the formation of the AAPD Safety Committee.[4] This current review of NPDS data suggests that, overall, LA is safe in the dental setting. However, it identifies cases where the LA administration dosage and/or technique was likely incorrect. Better communication with patients regarding drugs administered could improve timely and appropriate emergency management when needed. Thus, patients would benefit from discharge summaries that list all drugs and dosages administered, including LAs and a contact phone number for the dentist in case of adverse events.

Conclusions

Based on this study's results, the following conclusions can be made:

1. No cases of permanent damage or fatal outcomes were found.
2. Seizure activity following the administration of local anesthetic was the most common event and suggests intravascular administration or a toxic dose.
3. Multiple cases lacked vital information such as agent and dosage, and this information should be provided in patient discharge summaries to ensure timely and appropriate care.

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