

# A Case Report and Literature Review: Accidental Ingestion of Local Anesthetic Solutions in Children



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## ABSTRACT

**Introduction:** Anesthetic medications are frequently used in medical procedures to prevent pain and undesired sensations. Local anesthetic agents are widely used in the form of ointment, gel, cream, drop or spray in minor surgical or in-house pain relieving procedures in children and adults.

**Case Presentation:** A 16-month-old boy ingested an unknown amount of lidocaine and became lethargic after about 15 minutes. After a while, he experienced a generalized tonic-clonic seizure and loss of consciousness. He needed a short course of intubation and mechanical ventilation. A short literature review was also performed on local anesthetic intoxication.

**Conclusions:** Safe-seeming local anesthetic agents can cause life-threatening complications, especially when used at home without enough medical knowledge or supervision.

## 1. Introduction

Anesthetic medications are used in medical procedures to prevent pain and undesired sensation. These medications are divided into two categories according to their properties and application. General anesthetics can cause systemic effects and the reversible loss of consciousness; while Local Anesthetics (LA) cause temporary loss of sensation in the site of application. LAs are structurally similar to cocaine, thus, having the suf-

fix "Caine" at the end of their names. They are more advantageous than cocaine because of their safety and less toxicity (1).

LAs are widely used in the form of ointment, gel, cream, or spray in minor medical procedures such as dental surgery or circumcision. Although many studies have documented the safety of LAs, there are few reports that suggest a wide range of complication from dizziness to seizure due to the high dose of application.

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## 2. Case Presentation

A previously healthy 16-month-old boy was found in a room by his mother with a bottle of uncapped lidocaine 2% spray near him. He ingested an unknown amount of lidocaine and became lethargic after about 15 minutes. On the way to the hospital, he experienced a generalized tonic-clonic seizure. The seizure stopped after diazepam administration in the nearest healthcare center. However, he lost consciousness and did not respond to verbal commands and painful stimuli soon after. As a result, he was intubated there and referred to our hospital.

After about two hours, the patient spontaneously regained his consciousness, and self-extubated. The patient was previously healthy with no febrile seizure or previous noteworthy medical history. In addition, he had no medical history of cardiovascular complications or infections that could predispose him to a seizure. At the time of admission, the laboratory data, electrocardiogram and physical examinations demonstrated no abnormalities. His test results were as follows: blood glucose:86 mg/dL; creatinine:0.36 mg/dL; blood urea nitrogen:21 mg/dL; aspartate aminotransferase:9 U/L; alanine transaminase:30 U/L; Na+:137 meq/L; K+:3.7 meq/L; white blood cells:6900/ $\mu$ L; Hemoglobin:10.2 g/dL; and platelet count:263/ $\mu$ L. His blood pressure was 85/60 mmHg and heart rate was 120 beats/min. The evaluation of the methemoglobin level was not accessible in our center.

## 3. Discussion

### 3.1. Pathophysiology

Nerve fibers are categorized into three groups. Group A is responsible for the transmission of pressure and motor sensations. Group B is in charge of myelinated fibers with intermediate size and, Group C of transporting pain and temperature information. LAs inhibit group C fibers, so the patient doesn't feel pain but still reacts to pressure or motion (1). LAs inhibit neuron depolarization by interfering with Na<sup>+</sup> and K<sup>+</sup> function (2). Moreover, by decreasing membrane permeability to these ions, the excitation threshold is never reached an action potential level (3). High levels of LAs in neural structure inhibit excitatory neurons leading to coma, apnea and circulatory failure. Selective block of the cortical inhibitory neuron causes the formation of seizure potential in subcortical structure.

### 3.2. LAs are divided into two groups

Amino ester and amino amide, according to the differences in their intermediate chains. This causes different metabolism pathways. The amino esters group is metabolized by a plasma enzyme, called pseudocholinesterase. Some people cannot synthesize this enzyme due to genetic disorders; thus, they are predisposed to LAs' toxicity (4). Amino amides are metabolized by a microsomal enzyme in the liver. Therefore, hepatic diseases decrease LAs' metabolism and accordingly its toxicity (5). Some medications such as erythromycin, ketoconazole, and cyclosporine inhibit these microsomal enzymes causing toxicity (3, 6, 7).

Metabolites of LAs are also suspected to Methemoglobin (Met-Hb) formation. Methemoglobin is a form of hemoglobin where the iron ion appears in the form of ferric state instead of the ferrous form due to oxidation and electron depletion. This impaired hemoglobin fails to bind to oxygen, leading to hypoxia and death. Normally, methemoglobin consists of 1% of total hemoglobin, but it increases in LA toxicity. Cyanosis appears when Met-Hb reaches to 10-20%, while dyspnea and tachycardia are noted at 30-50%. Levels greater than 50% are accompanied by coma (8, 9).

### 3.3. Clinical manifestation and treatment

Local anesthetic can cause local or systemic toxicity. The Central Nervous System (CNS) toxicity (seizure) or cardiovascular toxicity are the main manifestations of systemic toxicity. Normally, these manifestations occur approximately one hour after administration. Dizziness, disorientation, muscle twitching, unconsciousness, coma, respiratory depression and arrest, cardiovascular depression and collapse, chest pain, syncope, cyanosis, seizure, rash, and Met-Hb are the prevalent clinical manifestations of anesthetic toxicity (10-12).

The differential diagnosis of local anesthetic toxicity includes anaphylaxis, anxiety disorders, cocaine toxicity, and conversion disorders (13). Additionally, the measurement of anesthetics blood level can be useful in diagnosis. To assess the etiology of seizure, a head computed tomography may be also considered. In patients with local anesthetic toxicity, the first step is to stabilize the potential threats to life. Adequate oxygenation via face mask or intubation must be ensured. The medications of choice to control the seizure are benzodiazepines. Propofol is also helpful but it increases the risk of cardiovascular toxicity. Barbiturates are also successful in seizure management. If seizures persist despite ben-

zodiazepines, small doses of neuromuscular blockers such as succinylcholine should be administrated.

To manage cardiac arrest and ventricular arrhythmias, small doses of epinephrine and amiodarone are preferable, respectively. Methylene blue is also used to decrease Met-Hb level. If mild allergic reactions occur, diphenhydramine must be used. For more serious reactions, subcutaneous epinephrine must be administrated. Corticosteroids are useful in severe allergic reactions (10, 13, 14)

#### 4. Review of Literature

We searched the national library of medicine using the keywords “EMLA OR benzocaine OR dibucaine OR

lidocaine”, and “children OR fetus OR kid OR neonate OR infant”. The English articles or abstracts published from January 1, 2010, to May 11, 2018, were included in this study. A secondary review was performed on the obtained references in literature.

Lidocaine is an aminoamide anesthetic that can cause severe CNS toxicity even in small doses. The maximum safe dose of lidocaine without epinephrine for local anesthesia is 4-4.5 mg/kg for adults and children with at least two-hour intervals for several injections. The serum level of lidocaine must be serially evaluated when used by continues infusion or several intravenous administration, to prevent severe adverse effects (15). Although many studies have reported the safety and efficacy of lidocaine administration, there are some re-

**Table 1.** Cases of lidocaine toxicity

Age	Year	Method of Exposure	Applied Dose	Onset Time	Symptoms	Met-Hb Level (%)	Treatment	Outcome	Hospital Stay (day)	Ref.
8 days	2017	Infusion	32 mg/kg	8 h	Respiratory distress, tachydyspnea, cyanosis, hypoxia	13.8	O2 inspiration, CPAP	Full recovery	-	(16)
17 months	2016	Topical	750 mg	20 min	Seizure	-	Intubation, lorazepam, midazolam, propofol, fentanyl, phenobarbital, Phenytoin, dopamine	Full recovery	-	(17)
10 years	2015	Infusion	Fentanyl 100 µg; lidocaine 50 mg	Immediately	General muscle contraction, rigidity, seizure, lost consciousness	-	Bag-Valve-Mask (BVM) ventilation	Full recovery	3	(18)
2 years	2014	Ingestion	25 mL (500 mg)	40 min	Seizure	-	Diazepam, lorazepam, intubation, CPR, epinephrine	Full recovery	-	(20)
4 months	2014	Topical	-	-	Shaking, lost consciousness, lockjaw, erythematous rash	-	Midazolam, intubation, sodium thiopental, prednisolone	Full recovery	2	(22)
6 weeks	2011	Topical	4.2 mg/kg	2 h	Seizure, apnea, cyanosis	-	Benzodiazepines, intubation, phenobarbital	Full recovery	2	(21)
23 days	2011	Topical	35 mg	30 min	Generalized seizure, facial twitching,	-	Intubation, phenobarbital	Full recovery	3	(21)
3 months	2011	Topical	6 mg/kg	50 min	Seizure	-	Phenobarbital, intubation I	Full recovery	7	(21)
9 years	2011	Topical (aspiration)	2.7 mg/kg	2 min	Dyspnea, hypoxemia, bradycardia	-	Ambu mask bagging, intubation, epinephrine, atropine,	Recovery	1	(23)

**Table 2.** The maximum recommended dose of EMLA (24)

Age and Body Weight	Maximum Dose (g)	Maximum Application Area (cm <sup>2</sup> )	Maximum Application Time (h)
Up to 3 months or less than 5 kg	1	10	1
3 to 12 months and more than 5 kg	2	20	4
1 to 6 years and more than 10 kg	10	100	4
7 to 12 years and more than 20 kg	20	200	4

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ports of lidocaine toxicity due to over administration, unintended ingestion by children, or interaction with other medications.

Bohnhorst et al. reported lidocaine toxicity in an 8-day-old infant due to the continuous infusion of lidocaine for the management of neonatal seizures. The patient received 32 mg/kg lidocaine and clinical manifestations appeared after 8 hours. She developed respiratory distress, dyspnea, cyanosis, and hypoxia. The Met-Hb level increased to 13.8% (16). The generalized tonic-clonic seizure has been reported after the topical application of 750 mg lidocaine during dressing change in a 17-month-old child (17).

A 10-year-old girl has received 100 µg of fentanyl and 50 mg of lidocaine for anesthetic induction before teneotomy. Although the lidocaine dose was in normal range, she immediately developed general muscle contraction and seizure (18). Fentanyl can lower the threshold of lidocaine-induced seizure (19). Therefore, the combination of fentanyl and lidocaine should be ad-

ministrated, carefully. Unintended ingestion of lidocaine was reported in a two-year-old boy who developed seizure 40 minutes after ingestion (20).

Menif et al. reported three cases of lidocaine toxicity after analgesic induction for circumcision. Subcutaneous administration of lidocaine and dorsal penile nerve block were the analgesic techniques used in this report (21). More details of lidocaine toxicity cases are listed in Table 1. The EMLA is a eutectic mixture of lidocaine and prilocaine that is widely used under occlusive dressing to provide local anesthesia (24). Guidelines for EMLA application are based on age, weight, skin surface, and the time of application. Table 2 presents the standard dose for EMLA administration.

Cho et al. reported a case of EMLA toxicity. The patient was a 3.5-year-old girl with atopic dermatitis. She received 30 g of EMLA cream for the curettage of molluscum contagiosum. Approximately 1 hour after topical application, she developed a generalized seizure and Met-Hb. Although the recommended dose for this pa-

**Table 3.** Cases of EMLA toxicity

Age	Year	Method of Exposure	Applied Dose (g)	Onset Time	Symptoms	Met-Hb Level (%)	Treatment	Outcome	Hospital Stay (day)	Ref.
3.5 years	2016	Topical	30	1 h	Cyanosis, limp, no respiratory effort, seizure	20.5	Fosphenytoin, phenobarbital, intubation	Full recovery	10	(25)
4 months	2013	Topical	60	75 min	Cyanosis, seizure	22.8	lorazepam, fosphenytoin, intubation, topical decontamination of the EMLA cream, methylene blue, lipid emulsion	Full recovery	4	(26)
2 days	2013	Topical	1	2 h	The edematous foreskin, no discernable corona	-	Decontamination of the EMLA cream	Full recovery	Approximately 1	(27)

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**Table 4.** Cases of benzocaine toxicity

Age	Year	Method of Exposure	Applied Dose	Onset Time	Symptoms	Met-Hb Level (%)	Treatment	Outcome	Hospital Stay (day)	Ref.
4-year-old	2016	Topical	400 mg	10 min	Disorientation, confusion, cyanosis, tachycardia, tachypnea	74	Intubation, methylene blue	Full recovery	3	(28)
8-year-old	2014	Topical	Not reported	1 hour	Cyanosis	32.9	Intubation, methylene blue	Full recovery	-	(29)
7-month-old	2012	Topical	-	5 h	Anxiety, dyspnea, cyanosis	42	Decontamination of gel, oral ascorbic acid, a packed red blood cell transfusion	Recovery	-	(30)
6-year-old	2012	Topical	-	5 days	Cyanosis	35.5	Decontamination of gel, Methylene blue	Recovery	-	(30)
4.5-year-old	2011	Topical	-	1 h	Afebrile, greyish-cyanosis, agitation, tachycardia, tachypnea	13	Saline	Recovery	-	(31)
5-year-old	2011	Topical	-	2 h	Bluish skin, mild dyspnea, agitation	38.5	Supplement O <sub>2</sub> , methylene blue	Recovery	6	(32)
6-year-old	2010	Topical	-	3 h	Cyanosis, vomiting, and lethargy, tachycardia, tachypnea	69.9	Methylene blue	Full recovery	2	(33)

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tient was 10 g, the medical team decided to apply 30 g due to a large amount of lesion. Atopic dermatitis may also increase absorption (25). In another report, a 4-month-old girl with extensive vascular malformation received 60 g of EMLA. Seventy-five minutes later she became cyanotic and developed a seizure and Met-Hb. Vascular malformation may have increased EMLA absorption (26).

Plank et al. reported 2 cases of EMLA toxicity after topical application and an occlusive dressing. Both of them received EMLA before circumcision. They both developed edematous foreskin with no discernible corona. After these manifestations, EMLA was removed to prevent systemic toxicity (27) (Table 3). Benzocaine is an amino ester LA that is widely used in dentistry and surgical operations such as endoscopy, gastric tube placement, or endotracheal intubation.

Met-Hb is the most prevalent complication of benzocaine. Lipton reported a massive Met-Hb in a 4-year-old girl who received 2 mL of 20% benzocaine (400 mg) before gastrostomy tube replacement. Her physician declared that the benzocaine dose was standard for pediatric surgery; however, 10 minutes after the application, she developed acute onset disorientation and confusion. The Met-Hb level also increased to 74% which was the highest level of the reported local anesthetic toxicity in children since 2010 (28). Cyanosis and somnolence were reported in an 8-year-old boy after the application of multiple doses of aerosolized benzocaine 20% solution. He received this LA for nasogastric tube replacement (29).

Kaczorowska et al. reported 7-month-old and 6-year-old boys with stage IV neuroblastoma. Both of them received a topical oral gel due to neutropenia and local infection. The gel contained glycerin, doxycycline, nystatin, and benzocaine. Their clinical manifestation of toxicity appeared in 5 hours and 5 days, respectively. The 7-month-

old boy developed dyspnea, cyanosis and anxiousness and Met-Hb level reached 42%. The 6-year-old boy had milder manifestations. His Met-Hb increased to 35.5% and developed blue cyanotic skin discoloration. After these reports, the oral gel, containing benzocaine, was withdrawn from the hospital medication protocols (30).

Poredos et al. reported a 4.5-year-old boy with 44% of total body surface flame burn. Burn cream containing 1.2% benzocaine was applied. In 46 days post-surgery, he used the cream in all the burn and donor regions. After one hour, he became lethargic and greyish. He also developed tachycardia. His Met-Hb level was 10 times higher than the normal rate (31). In another report, a 5-year-old girl received topical benzocaine powder orally, to relieve the pain after an adenotonsillectomy. Two hours later, she developed agitation and dyspnea. Her skin became bluish and her Met-Hb level increased up to 38% (32). Chung et al. also reported another case of benzocaine toxicity. A 6-year-old boy received benzocaine for toothache. After 3 hours, he developed grayish skin, lethargy, and vomiting. His Met-Hb level increased up to 69.9% (33) (Table 4).

Potentially, local anesthetic agents can cause life-threatening complications, especially when used at home without enough medical knowledge or supervision. Besides attention to the indication and safe medical dose, adequate information must be provided to the patients or their parents even for safe-seeming local anesthetic agents.

## Ethical Considerations

### Compliance with ethical guidelines

There is no ethical principle to be considered doing this research.

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### Authors contributions

Conceptualization: Mohammad Reza Navaeifar; Investigation: All authors; Writing-original draft: Afrouz Alipour; Writing-review & editing: All authors; and Supervision: Mohammad Reza Navaeifar.

## Conflict of interest

The authors declare no conflict of interest.

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