Lidocaine Toxicity

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Local anesthetics are the most commonly used drugs in dentistry. The number of adverse reactions reported, particularly toxic reactions, are extraordinarily negligible. This article reports a case of lidocaine toxicity with its typical manifestation in a 37-yr-old healthy male. The toxic reaction followed transoral/transpharyngeal topical spraying of lidocaine preoperatively during preparation for general anesthesia. A review of dosages of the most commonly used local anesthetic drugs in dentistry and the management of a toxic reaction is presented. Clinicians need to be in a position to recognize and succesfully manage this potential adverse reaction.

Key Words: Adverse; Complication; Overdose.

Local anesthetics are the most commonly used drugs in dentistry, with the number of lidocaine cartridges used estimated at more than 6 million per week.[1] However, the number of adverse reactions, including toxic reactions, that are reported is negligible. Careful scrutiny of reported adverse reactions usually determines that the majority are epinephrine related or vasovagal responses.[2] The paucity of published case reports for lidocaine toxicity stimulated this article, in which a true convulsive reaction to excessive lidocaine administration is reported. This report will, we hope, reinforce to practitioners the importance of alertness while administering local anesthesia.

CASE REPORT

A 37-yr-old male weighing 78 kg presented to the emergency room at Boston City Hospital with the complaint of "jaw pain." The pain had begun after an assault to the left side of his face sustained 2 days earlier. Past medical and surgical histories were noncontributory, and the patient had no known drug allergies. Laboratory data, chest radiographs, and electrocardiogram were within normal limits. Clinical and radiographic examination revealed a displaced, intraorally compounded fracture of the left mandibular angle. The patient was admitted to the Oral and Maxillofacial Surgery service. He was started on penicillin G (2 million units intravenously every 4 hr) and appropriate pain management.

The patient was brought to the operating room the next day for a planned open reduction and internal fixation (ORIF) with maxillomandibular fixation (MMF). Preoperatively, in preparation for intubation, the patient received 3 mg of midazolam (Versed) 100 μg of fentanyl (Sublimaze), and 0.2 mg of glycopyrrolate (Robinul). He had trismus with an incisal opening of 20 mm secondary to the fracture. A total of 8 ml of 10% lidocaine (800 mg) was sprayed transpharyngeally in multiple doses in anticipation of endotracheal intubation by the anesthesiologist which was to be performed while the patient was awake. After 12 min, the patient had a grand mal (tonic–clonic) seizure. The seizure was controlled with 15 mg of diazepam (Valium) and 500 mg of thiopental, given intravenously in titrated doses. After control of the seizure with these anticonvulsants, the patient's oxygen saturation dropped to 94% despite mask oxygen therapy. He was immediately successfully intubated orally with a size 7.0 oral endotracheal tube fixed at 24 cm. A postintubation arterial blood gas sample revealed metabolic acidosis, with values of pH = 7.22, P_{CO_2} = 42, H_{CO_3} = 16.6, and O_2 saturation = 99.9%. The surgery was delayed, and the patient was admitted to the postanesthesia care unit still intubated. Here, a loading dose

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of 500 mg of Dilantin was administered intravenously. A lidocaine blood level was drawn and found to be 5.3 μg/ml, which is above the toxic overdose threshold.

Hospital Course

The patient was admitted to the medical intensive care unit. The workup performed to rule out possible seizure foci like tumors, intracranial bleeding, or infarcts was negative. This included a head computerized tomography scan and an electroencephalogram, both of which were found to be normal. The patient was extubated the next day and released from intensive care in stable condition. Dilantin therapy was discontinued, as there was no sign of active epileptigenic focus. The patient continued to receive intravenous antibiotic therapy and pain management. He was maintained on a Barton's bandage and a liquid diet with nutrition supplements.

On hospital day 5, the patient was brought to the operating room for a planned ORIF and MMF. Preoperative evaluation showed that he had an interincisal opening of 35 mm. Endotracheal intubation for this procedure was performed nasally under direct vision laryngoscopy. No topical anesthesia was used for the intubation. The patient underwent closed reduction of the fracture with MMF without any complications. Teeth 17, 18, and 19 were extracted intraoperatively. The ORIF was not performed at this stage, as some purulence in the intraorally compound site was encountered during the extraction of teeth. A swab specimen of the purulence was obtained and sent for bacteriological examination. The patient was continued on penicillin G (2 million units q 4h) and intravenous metronidazole (Flagyl, 500 mg q 8h) was added empirically.The extraoral soft tissue swelling decreased, and by hospital day 10, a clinical examination of the patient revealed no signs or symptoms of acute infection.

The patient had an unfavorable displacement of the fracture with malocclusion not correctable by the closed reduction performed previously. This necessitated further surgical treatment in the form of an open reduction, which was performed without complications on hospital day 11. The MMF was released and general anesthesia was again provided with an naso-endotracheal tube placed under direct vision laryngoscopy. No topical lidocaine was needed for this intubation. The patient's subsequent clinical course was unremarkable and he was discharged on hospital day 15. He was followed as an outpatient and continued to progress well.

DISCUSSION

Local anesthetics have traditionally been considered to be rationally safe drugs. Lidocaine, the first of the non-ester compounds, has long been the standard of comparison and is rated to be twice as potent and toxic as procaine.[3] Classically, drug overdose toxic reactions have been described as those clinical signs and symptoms that result from overly high blood levels of a drug in various organs or tissues. For an overdose to occur, the drug must gain access to the affected organs or tissues in the concentration needed.

Predisposing factors to local anesthetic overdose can be broadly outlined as follows:[1]

1. *Patient Factors*

- Age (under 6 yr and over 65 yr).[2]
- Lean body weight (lower weight increases risk).
- Presence of pathology (eg, liver, pulmonary and cardiovascular diseases).[4]
- Genetics (eg, atypical pseudocolinesterase for ester type local anesthetics).[5]
- Mental attitude (anxiety decreases seizure threshold).[1]
- Pregnancy (slightly increased risk in pregnant women).

2. *Drug Factors*

- Vasoactivity of drug (higher lipid solubility and protein binding decreases risk while vasodilation increases the risk).
- Route of administration (varies with route and intravascular injection increases risk).
- Rate of injection, if intravascular (increases the risk).[1]
- Vascularity of administration site (increases the risk).
- Presence of vasoconstrictor (decreases the risk).

All these factors should be borne in mind while using local anesthetics. It should also be understood that it is often difficult to control the amount or area of membrane sprayed with topical sprays.

In the case reported, due to the trismus present, a blind awake nasal intubation was deemed prudent by the anesthesiologist. To make the procedure tolerable for the patient, the clinician needs well-anesthetized oropharyngeal and laryngeal soft tissue structures. This is usually achieved by topical local anesthetic sprays (eg, 4–10% lidocaine), which deliver a metered dose with each spray. Because of the difficulty of intubation in individual cases, multiple attempts may be required before successful intubation. It is easy to become casual about the dose of topical anesthetic administered as the anesthetist's concentration shifts toward intubating the patient successfully. Repeated doses of local anesthetic spray often result in a cumulative effect. This is further compounded by the fact that these sprays do not contain vasoconstrictors and are used in highly vascularized areas of the body.

The Council of Dental Therapeutics of the American Dental Association (ADA) revised the maximum permis-

sible dosages for local anesthetics and no longer adjusts doses for the inclusion of vasoconstictor.[1] Table 1 lists the present recommendations of the ADA for intraoral injections. This is contrary to the medical and anesthesia literature, which still allows for increased doses to be given when a vasoconstrictor is included in the preparation. As recommended by the ADA, these reduced dosages are perhaps based on the hypothesis that the orofacial region has a richer blood supply, which could result in more rapid drug absorption and higher peak blood concentrations than would occur with identical doses elsewhere.[6]

Signs and Symptoms of Lidocaine Overdose

In general, local anesthetics produce a depression of excitable membranes. The cardiovascular system and central nervous system are highly susceptible. The usual clinical presentation entails an initial, fleeting apparent stimulation followed by depression. Although the excitatory phase generally precedes the depressive phase, it is possible for the former to be extremely short or even absent. This may be true especially for lidocaine and mepivacaine.

In previous studies, it has been shown that following injection of 40–60 mg of lidocaine intraorally, blood levels of approximately 1.0 μg/ml are attained. As the blood level of the drug increases from 4–5 up to 7 μg/ml, definite central nervous system stimulation can be seen. With a further increase of drug levels in the blood greater than 7.5 μg/ml, seizure activity is seen. Levels above 10 μg/ml cause marked central nervous system depression. It is generally accepted that toxic effects from lidocaine occur in conscious subjects at a plasma level in excess of 5 μg/ml. Anesthetized subjects, however, may not show signs of toxicity until a level of 10 μg/ml, when circulatory depression becomes evident. Effects on the cardiovascular system are likewise concentration-related, and blood levels of 1.8–5 μg/ml cause electrophysiological antiarrythmic changes. Levels of 5–10 μg/ml result in prolongation of conduction time and increased diastolic threshold. These can be seen on an electrocardiogram as increased principal deflection intervals with sinus bradycardia. Peripheral vasodilation, negative inotropic effects, negative chronotropic myocardial effects, decreased cardiac output, and decreased blood pressure may also occur. There may be a wide margin between central nervous system toxicity and cardiovascular-respiratory depression. In fact, while the former causes apnea, the latter is often the result of hypoxia itself, compounded by the direct effect of the drug.

It should be kept in mind that acidosis can develop rapidly after seizures as a result of hypoxia and hypercarbia. This lowering of the pH decreases the plasma protein binding of the local anesthetic and also increases the free anionic part the drug, leading to increased plasma levels. Elevated levels of carbon dioxide in the blood cause cerebral vasodilation, resulting in more of the toxicologic agent reaching the brain. The acidotic, hypercapneic, and hypoxic states can also potentiate the negative ionotropic and chronotropic effects of the local anesthetic.

Commonly encountered clinical features of an overdose may be categorized as follows.[1] A low to moderate overdose results in clinical signs of dizziness, disorientation, excitement, speech changes, nystagmus, elevated blood pressure, increases in pulse and respiratory rates, flushing, and loss of consciousness. A moderate to severe overdose results in generalized tonic-clonic seizures, followed by central nervous system depression along with a depressed cardiovascular status, including blood pressure, heart and respiratory rates, disorientation, drowsiness, and loss of consciousness.

The overdose thresholds that result in central nervous system signs and symptoms for common local anesthetics are as follows:[1] bupivacaine and etidiocaine, 1–2 μg/ml; prilocaine, 4 μg/ml; and lidocaine and mepivacaine, 5 μg/ml.

Management of Toxic Reactions

In most cases, the reaction is mild and transitory and requires no specific treatment. The blood level of the anesthetic decreases as the reaction progresses because of biotransformation and redistribution. As previously mentioned, hypoxia, hypercarbia, and acidosis develop rapidly in anesthetized patients with local anesthetic–induced seizures. Clinicians should attempt to recognize the toxic reaction immediately and institute therapy to minimize other potentially adverse sequelae.

Though management should be individualized, in general it should encompass the following protocol. First, the patient should be placed in a supine position with elevated legs; the patient should be protected from injuries. Second, the ABCs of basic life support should be provided as needed. Third, if prolonged seizures occur, oxygen should be administered. It has been shown in dogs that the minimum lethal dose can be up to fourfold as high for well-ventilated lungs as compared with an apneic subject.[7] And finally, an appropriate anticonvulsant should be considered in prolonged seizures. Usually intravenous titrated doses of benzodiazepines are given. Diazepam has long been used with success to control active seizures. Rapidly acting barbiturates such as thiopental can also be used if readily available. Following seizures, there may be a post ictal state of depression; the administered anticonvulsants further add to this phe-

Table 1. The Presently Acceptable or Recommended Maximum Dosages of Commonly Used Local Anesthetic Drugs for Intraoral Injections, as Recommended by the American Dental Association

Drug	*Common Concentration Available %*	*Maximum Recommended Dose*	*Amount of Drug in Dental Cartridges (mg)*
Lidocaine	2.0[a]	2.0 mg/lb (max. 300 mg)	36
Mepivacaine	3.0	2.0 mg/lb (max. 300 mg)	54
Bupivacaine	0.5	0.6 mg/lb (max. 90 mg)	9
Etidocaine	1.5	3.6 mg/lb (max. 400 mg)	27
Prilocaine	4.0	2.7 mg/lb (max. 400 mg)	72
Articaine	4.0	3.2 mg/lb (max. 500 mg)	72

[a] With or without vasocons.

nomenon. Thus, the patient must be adequately observed and managed as required during the post ictal period for signs and symptoms such as apnea, hypotension, and cardiovascular collapse.

CONCLUSIONS

Lidocaine, as well as other local anesthetics, are reasonably safe agents. The routine use of these agents and the low number of reported adverse reactions confirm this fact. However, injudicious use of these drugs can cause toxic reactions. Though rare, systemic toxicity is a potentially serious, even fatal, complication from regional anesthesia.

The operator must clearly understand the pharmacology of the anesthetic agent and be in a position to prevent and treat any adverse or toxic reactions that might occur. The best way to treat local anesthetic overdose complications is to prevent it altogether by using the right technique. Aspirating before injection remains the single most important factor in preventing inadvertent intravascular injections. Patients' predisposing factors for toxicity should be carefully ascertained for each case beforehand. Extra caution is recommended while using topical anesthetics, as the area sprayed and the degree of absorption are usually not controllable.

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