

Lidocaine intoxication in axillary block: similar pharmaceutical form, different concentration

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ABSTRACT

Local anesthetic intoxication is a medical emergency with high mortality. These drugs have not specific antidotes, quick differential diagnosis and supportive treatment required in the case of exposure to toxic doses. We report the complications and anesthetic management of a patient who was scheduled for right carpal tunnel syndrome surgery under regional anesthesia, but mistakenly received injection of 140 mg procaine added to 10% 10 mL lidocaine (10 mL=1000mg) instead of 2% lidocaine (10mL=200 mg) as part of an axillary plexus blockade.

Key words: Axillary blokage; intoxication; lidocaine.

Toxic reactions are among the most prevalent causes of medical emergencies [1]. Development of regional techniques, introduction of new long-acting local anesthetics into clinical use in the practice of anesthesia within the last 20 years, raised awareness among physicians, and patients about the use of regional anesthesia have resulted in increased popularity, and applicability of regional anesthesia. Despite technologies which widen safety margins of regional anesthesia including use of bedside ultrasound which reveals the anatomy of the site of application, and use of peripheral nerve stimulator which directly determines the nerve to be targeted, still intoxications related to local anesthetics in applications of regional anesthesia can be seen as a serious,

and important adverse effects with incidence rates ranging between 0.01, and 0.2% of the cases [2].

Local anesthetics used in the practice of regional anesthesia have usually an amide component, and they induce Na channel blockade in cell membranes, and thus prevent transmission of impulses by way of axons. Lidocaine is an amide group local anesthetic which is preferred in relatively shorter surgical interventions, infiltration anesthesia, extremity blocks, topical anesthesia, and regional intravenous anesthesia (RIVA) with its higher potency, rapid onset, and termination of its action. Its intoxications when used in local anesthesia, emerge frequently during inadvertent intravenous administration of the drug

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in applications of central or peripheral blockade, unnecessarily higher drug dosage, and rapid systemic absorption of the drug. Though central nervous system is firstly, and most frequently affected in local anesthetic intoxications, mortality rates increase due to cardiovascular system involvement. Cardiovascular effects can manifest themselves as enlarged QRS complex due to prolonged Na channel blockade in diastole, prolonged PR interval, AV blocks, and related dangerous arrhythmias. However its central effects appear secondary to cortical stimulation. Early manifestations of cortical stimulation including relatively mild symptoms as metallic taste in the mouth, numbness, disorientation, tinnitus, paresthesia, ataxia, dysarthria, nystagmus, and dose related serious symptoms of cortical stimulation as convulsions, respiratory system depression, serious arrhythmias, deep cardiovascular collapse, and coma can develop [2, 3].

In our article, complications and anesthetic management of a patient who was scheduled for right carpal tunnel syndrome surgery under regional anesthesia, and mistakenly received injection of 140 mg procaine added to 10% 10 mL lidocaine (10 mL=1000mg) instead of 2% lidocaine (10mL=200 mg) as part of an axillary plexus blockade.

CASE REPORT

A 57-year-old-male patient 165 cm tall, and weighing 68 kg in the ASA 1 risk group because of numbness of his left wrist. The biochemical parameters of the patient who was scheduled for operation under regional anesthesia with the diagnosis of carpal tunnel syndrome were as follows; Hb:14.0 mg/dL, Htc:43.0%, Plt:229000/mm³, WBC:6000/mm³, FBG:100 mg/dL, BUN:2817 mg/dL, Creatinine:0.7 mg/dL, AST:20.72 mg/dL, and ALT:12.45 mg/dL. His electrocardiogram (EKG) revealed a HR of 70 bpm with normal sinus rhythm.

Preoperatively the patient was informed about axillary nerve blockade, and his written informed consent was obtained. He didn't receive any preoperative premedication, and in the operating room, his standard EKG, peripheral O₂ saturation (SpO₂), and noninvasive blood pressure (NIBP) were monitors. Using a 18 G branule a vein on the back of his left hand was punctured, and 0.09%NaCl infusion

at a rate of 200 ml/hr was initiated. Right arm to be operated was positioned at 90o abduction with the torso, and forearm was flexed 90°. After cleansing the surgical field with a sterile antibacterial solution, the site was covered with sterile drape, and a single injection was made with a 22 G x 50 mm needle (Stimuplex® Braun, Melsungen, Germany). Retrograde blood was not observed during negative aspiration.

Using a peripheral nerve stimulator (Stimuplex A; B.Braun Melsungen AG, B.Braun Medical AG CH-6021, Germany) at an intensity of 1.5 mA the nerve was localized. When the intensity of the electrical current was reduced to 0.5 mA, nervous stimuli were observed which made us to think that we were on the innervation site of the nerve to be blocked. Then 40 mL anesthetic solution preprepared by anesthesia technician which we thought to be our routinely used mixture i.e. [20 mL 1% lidocaine (2 ampoules of 2% lidocaine, and 10 mL NaCl 0.09%) and 20 mL 1% prilocaine (10 mL 2% prilocaine, and 10 mL 0,09% NaCl)] was injected to the patient with negative suctions after each application of 5 mL. Injection site was compressed for 5 minutes. Nearly 10 minutes later the patient felt numbness on his tongue, irritability, restlessness, agitation, he uttered meaningless words, and moved his arms, and legs senselessly. Decreased peripheral oxygen saturation and presence of peripheral cyanosis led us to make an initial diagnosis of methemoglobinemia, and supportive O₂ therapy was initiated via oxygen mask at a rate of 6 lt per minute. We couldn't measure methemoglobin levels because of lack of necessity facilities. Arterial blood gas measurements were as follows. pH: 7.43 pO₂:60.1, and pCO₂:44.0. Respiratory distress of the patient increased, and deepened, with a drop in his SpO₂ to 76, was intubated under 1 mg/kg propofol, 1 µ/kg fentanyl, and 0.5 mg.kg⁻¹ rocuronium anesthesia to enjure the patency of his airway. For the post-intubation maintenance of anesthesia 50 oxygen – nitrogen, and 1 mac sevoflurane were used. Following induction of anesthesia, hypotension (NIBP: 60/40 mmHg), and bradycardia (HR:40 bpm) developed which required administration of 0.5 mg atropin, and intermittent IV injections of ephedrine (total dose 30 mg). When his health state was stabilized, NIBP values improved, and his HR dropped to 70 bpm with SpO₂: 95%, he was amenable for surgery. At the end of the operation which lasted

for nearly half an hour, the patient was awakened with injections of 10 µg/kg atropine, and 40 µg/kg neostigmine. Though the patient still continued to articulate meaningless words, and make senseless movements, since he was more cooperative we transferred the patient into the intensive care unit.

When we discerned that in place of 2% lidocaine ampoule which we always requested as a local anesthetic from the pharmacy, 10% lidocaine ampoule was sent, and anesthetic mixture was prepared without checking whether it was 2% lidocaine, we made the diagnosis of local anesthetic intoxication related to wrong formulation of lidocaine rather than methemoglobinemia

During 24-hour monitorization in the intensive care unit his hemodynamic parameters were stable, and his complaints resolved. Then the patient was transferred to his service with relevant recommendations.

DISCUSSION

Ninety-eight percent of systemic reactions that might develop against local anesthetic agents are related to higher plasma concentrations of the drugs used. Higher plasma concentrations can be observed when doses higher than the maximum daily doses are used or in cases of unwanted intravascular injections during central or peripheral nerve blocks [4]. Lidocaine is a local anesthetic with an amide component which induces Na channel blockade in nerve cell membranes. Because of its higher potency, lesser systemic toxic reactions, its safety in IV use unless toxic doses are not exceeded, lidocaine is frequently used local anesthetic in anesthesia practice. Lidocaine at doses exceeding 4 mg/kg, and doses above 7.5 mg/kg of its combined form with adrenaline used in local anesthesia have toxicity effects [1].

In CNS toxicity related to local anesthetics, firstly excitatory, then depressive symptoms become evident. Presence of hypoxia, hypercapnia, and acidosis further facilitates development of convulsion. Besides cardiovascular collapse can be seen because of the impact of local anesthetic on vascular smooth muscle resulting in vasodilation, and bradycardia due to its direct effect on myocardium. Symptoms of cardiac toxicity are more frequently seen in patients with a history of cardiovascular disease [5].

In our case occurrence of mild hypoxia, and cyanosis at the onset made us to think of the development of methemoglobinemia related to prilocaine injection. Regression of cyanosis after delivery of 100% O₂ made us to drift away from the diagnosis of methemoglobinemia.

Local anesthetics can be marketed in many pharmaceutical forms as cream, gel, liposomal capsule, tablet, and spray. Tablet formulation of mexyletine, and tocainide which is a derivative of lidocaine have been used in antiarrhythmic, and neuropathic pains. Besides, 10% solution of lidocaine (Xylocain® pump spray) is used as an aerosol, and each puff contains 10 mg lidocaine. In topical anesthesia EMLA® (2.5% lidocaine, 2.5% prilocaine) cream has been applied.

Lidocaine solution is marketed in ampoules each containing 2%, or 10% concentrations. Similar appearance of ampoules can easily result in erroneous applications. Injections of higher doses of lidocaine are one of the most frequent erroneous drug applications. Packaging of bolus, and concentrated dosage forms of these types of drugs is still problematic [6]. In our case, instead of injecting 2% lidocaine formulation which is used routinely for the purpose of peripheral blockade, the ampoule with similar appearance except for an extra yellow line on the neck of the ampoule which contained 10% lidocaine was inadvertently prepared for injection, and our patient received 5-fold higher dose than our estimate.

Kudo et al. [7] presented a 76-year-old patient with known paroxysmal ventricular dysrhythmia who was injected 5 ml 10% lidocaine (599 mg) instead of 2.5 ml 2% lidocaine (50 mg) for the treatment of his dysrhythmia. They reported tonic-clonic convulsions immediately after high doses of lidocaine injection, then cardiac arrest developed. Despite initiation of resuscitation without delay the patient died.

Ludot et al. [8] planned knee surgery using posterior lumbar plexus block in a 13-year-old patient, and at 15. minute of lidocaine, and ropivacaine injection heart rate of the patient increased up to 150 bpm, and ventricular tachycardia with a wide QRS complex emerged. Preoperatively measured arterial blood pressure (88/45 mmHg) rised up to 12/92, while SpO₂ dropped from 99% to 92 percent. The patient was given 150 ml IV (3mg/kg) 20% lipid emulsion (Medialipid 20%, Braun, Germany) with

the initial diagnosis of local anesthetic intoxication. At 2nd minute of the infusion, her heart rate regressed to 100 bpm, and arterial blood pressure to 100/48 mm Hg, and SpO₂ increased to 97 percent. After stabilization of her vital signs, and inability to detect any additional sign, we proceeded with the operation. The patient was discharged on postoperative 2. day without any sequelae.

Safe use of lipid emulsions in intoxications of local anesthetics was reported by Rosenblatt et al. [9] in the year 2006. In this presentation, brachial plexus blockade was applied using bupivacaine, and mepivacaine combination. After the blockade, cardiac arrest was developed in the patient, and cardiopulmonary resuscitation was initiated. The patient didn't respond to 20 minutes of resuscitation, then 100 ml 20% Intralipid® fat emulsion (Fresenius kabi, Uppsala, Sweden) was administered through intravenous route, a little while after initiation of lipid therapy her hemodynamic parameters started to return to normal levels.

In the practice of anesthesia, lipid emulsions are marketed as total parenteral nutrition solutions and in formulations with propofol. However in the literature, clear-cut information about effective, and safe use of these emulsions in lipid rescue treatment is lacking [10]. In our case in consideration of potential beneficial effects of lipid solutions, we urgently requested these solutions from the pharmacy of our hospital, but we were unable to use them for the patient because of difficulties in its procurement.

Anesthetic pharmacotherapy requires constant care, and it is not exempt from erroneous applications. Erroneous applications, and unnecessarily higher doses can frequently lead to serious adverse effects, besides confusing infusion, and single dose applications, and dosage calculation errors can be also frequently seen. Blendon et al. [11] investigated faulty drug applications, reported physicians or family members (35%), civilians (42%) for these erroneous usage of drugs.

Even though literature information does not absolutely support, we think that in pharmacy departments of hospitals where day-care surgeries, and regional techniques are frequently applied, lipid solutions should be available for immediate use so as to protect the patients from adverse outcomes of drug use.

CONCLUSION

Finally, we think that preventive measurements including standardization, separation of different forms of the drugs (intrathecal, topical, and intravenous), drugs used in different dosages should be marketed in different coloured, and sized ampoules, controlled application of the drugs at every step of their usage, regular, meticulous, and updated pharmacological training of health personnel should be developed.

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