Reversal of central nervous system and cardiac toxicity after local anesthetic intoxication by lipid emulsion injection

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Reversal of Central Nervous System and Cardiac Toxicity After Local Anesthetic Intoxication by Lipid Emulsion Injection

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A 91-yr-old man (57 kg, 156 cm, ASA III) received an infraclavicular brachial plexus block for surgery of bursitis of the olecranon. Twenty minutes after infraclavicular injection of 30 mL of mepivacaine 1% (Scandicain®) and 5 min after supplementation of 10 mL of prilocaine 1% (Xylonest®) using an axillary approach, the patient complained of agitation and dizziness and became unresponsive to verbal commands. In addition, supraventricular extrasystole with bigeminy occurred. Local anesthetic toxicity was suspected and a dose of 200 mL of a 20% lipid emulsion was infused. Symptoms of central nervous system and cardiac toxicity disappeared within 5 and 15 min after the first lipid injection, respectively. Plasma concentrations of local anesthetics were determined before, 20, and 40 min after lipid infusion and were 4.08, 2.30, and 1.73 μg/mL for mepivacaine and 0.92, 0.35, and 0.24 μg/mL for prilocaine. These concentrations are below previously reported thresholds of toxicity above 5 μg/mL for both local anesthetics. Signs of toxicity resolved and the patient underwent the scheduled surgical procedure uneventfully under brachial plexus blockade.

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Laboratory investigations have suggested that lipid emulsion infusion may be a treatment option for local anesthetic (LA)-induced systemic toxicity after failure of established resuscitation measures.[1,2] Recently, two case reports described successful resuscitation of patients after ropivacaine- and bupivacaine-related cardiac arrest, respectively.[3,4] The exact mechanism of lipid emulsion reversal of toxicity is unclear; however, recent data support the theory of a "lipid sink" by demonstrating decreased cardiac bupivacaine concentrations after lipid infusion in the isolated heart[5] and a possible positive metabolic effect of lipid infusion.[6] The usefulness of lipid infusion has been reported for the more cardiotoxic LAs ropivacaine and bupivacaine, but not for the less cardiotoxic mepivacaine or prilocaine. We report a case of systemic LA intoxication after infraclavicular plexus block with 30 mL mepivacaine 1%, and 10 mL prilocaine 1%, which was successfully treated by infusion of 200 mL of a 20% lipid solution.

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CASE REPORT

A 91-yr-old man (57 kg, 156 cm, ASA III) with exacerbated chronic obstructive pulmonary disease was admitted for olecranon bursitis surgery. His medical history included hypertension, coronary ischemic heart disease (stage I), myocardial insufficiency (New York Heart Association II) and reflux esophagitis complicated by repeated gastrointestinal bleeding. His medications included ambroxol-HCl, omeprazol, and esomeprazol. In the operating room, a 5-lead electrocardiogram, pulse oximetry, noninvasive arterial blood pressure measurement (5-min intervals), and peripheral venous access were established. An infraclavicular brachial plexus block was performed using a 22-gauge short bevel insulated needle with nerve stimulation. During needle advancement, blood was aspirated and the needle was redirected uneventfully. After eliciting motor responses and a negative aspiration test, 30 mL of plain mepivacaine 1% (Scandicain®, Astra, Wedel) was slowly injected. Because block of the ulnar nerve was incomplete after 15 min, the block was supplemented with 10 mL of plain prilocaine 1% (Xylonest®, Astra) by an axillary approach after a negative aspiration test.

Within 5 min, the patient complained of dizziness, nausea, and agitation, and became unresponsive to verbal commands. He immediately received oxygen by mask and 12.5 mg dolastrone IV. His heart rate increased from 76 to 92 bpm and supraventricular extrasystoles with intermittent bigeminy appeared (Fig. 1A). His arterial blood pressure increased from 160/70 to 190/90 mm Hg and was then measured every minute. LA toxicity was suspected and an IV bolus of 1 mL/kg Intralipid 20%® was injected and repeated after 3 min (total of 100 mL). A continuous Intralipid infusion was started at a rate of 14 mL/min (0.25 $mL \cdot kg^{-1} \cdot min^{-1}$). The patient regained consciousness within 5 min after the first lipid injection. Because extrasystoles were still apparent, lipid infusion was continued up to a total dose of 200 mL when extrasystoles disappeared (Fig. 1B). Blood samples were drawn, centrifugated, and stored at

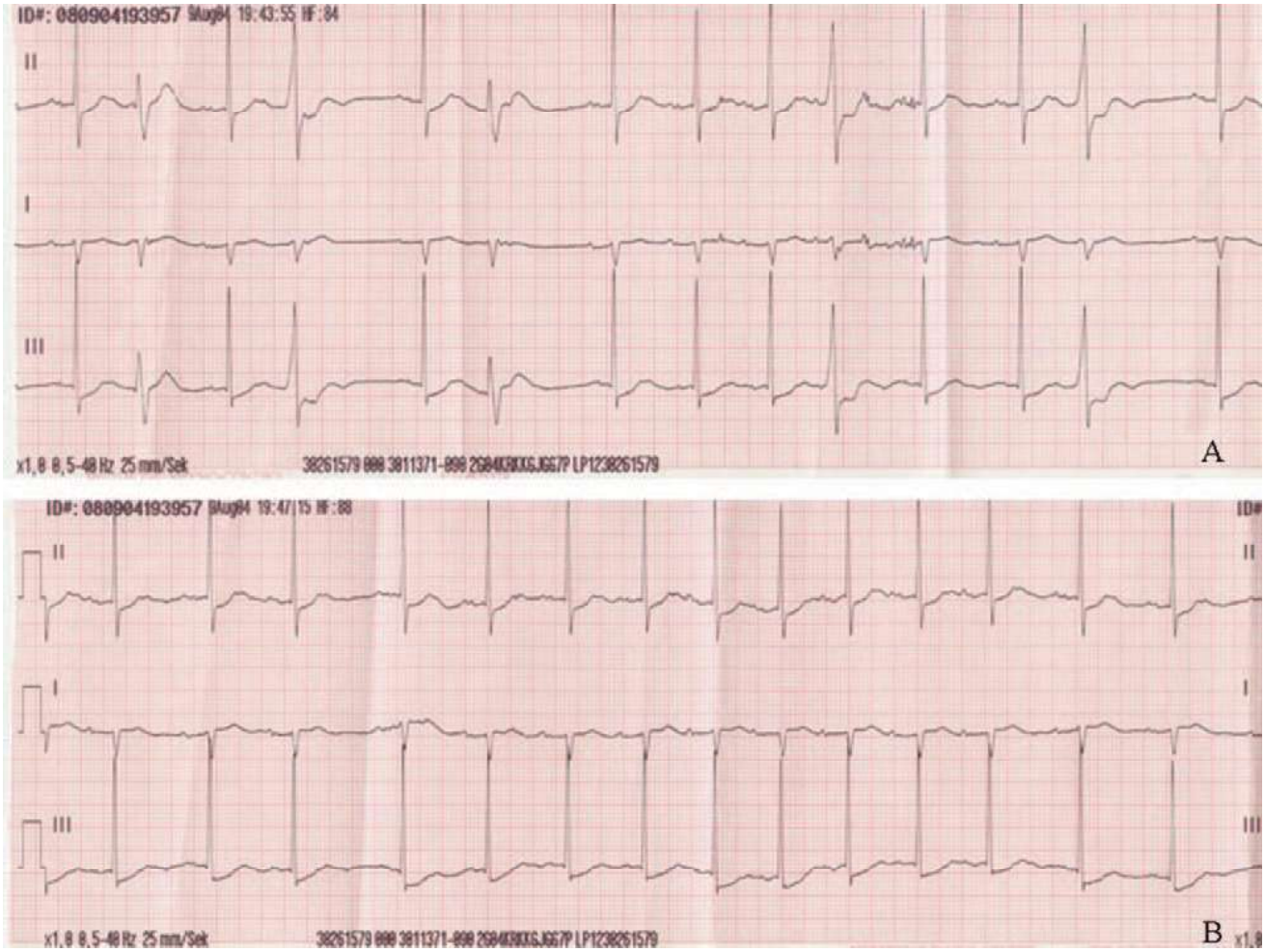

Figure 1. A, electrocardiogram (ECG) at onset of central nervous system toxicity and before lipid emulsion infusion showing supraventricular extrasystoles with intermittent bigeminy. B, ECG after administration of 200 mL of lipid emulsion showing sinus rhythm with respiratory variation. Supraventricular extrasytoles are no longer present.

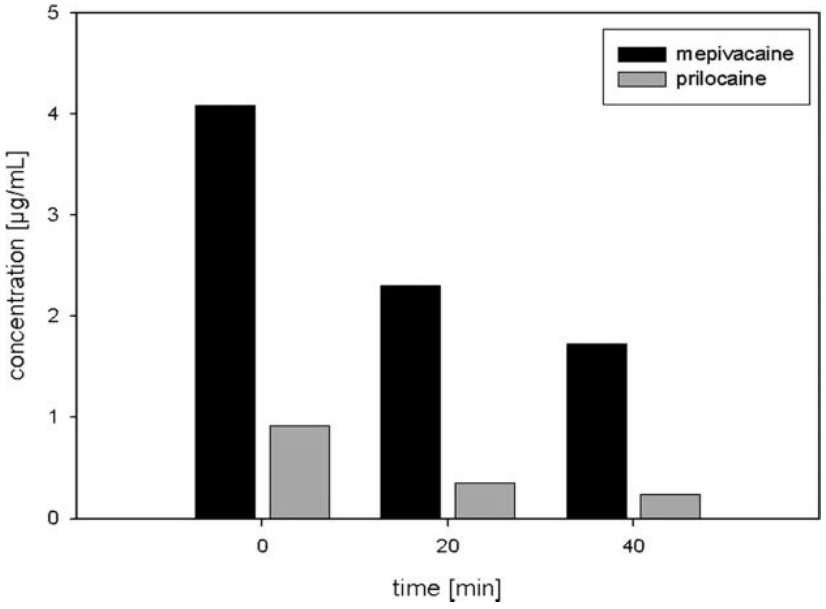

Figure 2. Time course of the plasma concentration of mepivacaine and prilocaine at the start and 20 and 40 min after administration of lipid emulsion.

−20°C to determine the plasma concentration of LAs by means of high-performance liquid chromatography immediately before, 20, and 40 min after lipid administration (20, 40, and 60 min after mepivacaine injection, respectively; Fig. 2): Serum concentrations for mepivacaine were 4.08, 2.30, and 1.73 µg/mL and 0.92, 0.35, and 0.24 µg/mL for prilocaine and, therefore, below previously reported toxic concentrations.

The block was tested again and judged adequate. Therefore, surgery was started and performed uneventfully. The

further postoperative course was uneventful. The patient's electrocardiogram showed regular sinus rhythm and he was transferred to a medical ward for further treatment of the exacerbated chronic obstructive pulmonary disease.

DISCUSSION

This is the first report of the clinical effect of lipid emulsion infusion on reversal of central nervous system (CNS) and cardiac toxicity with sequential LA plasma concentrations. The plasma concentration of mepivacaine was below 6 μg/mL, generally considered a threshold for mepivacaine CNS toxicity.[7] Similar thresholds have been suggested for prilocaine toxicity.[8] However, thresholds for onset of LA toxicity are subject to a wide interindividual range.[9–11] Toxicity has been reported with a peak mepivacaine plasma concentration of 5.1 μg/mL,[12] and comparable serum concentrations of prilocaine have been associated with CNS toxicity after cuff deflation in IV regional anesthesia.[10] Notably, the plasma concentration of prilocaine 5 min after injection of only 100 mg was surprisingly high in our patient, suggesting possible intravascular injection, since peak plasma concentrations after absorption should occur 20–30 min later.[13] Hence, the toxic effects of mepivacaine could have been enhanced. Although no definite studies concerning the effects of LA mixtures on toxicity have been reported in humans, such additive effects of LAs have been demonstrated in animal models.[14] Unfortunately, no epinephrine was added as a marker for intravascular injection.

Yamamoto et al. described the time course of plasma mepivacaine concentration after axillary plexus block and described a 50% reduction after 120 min.[11] In our patient, the plasma concentration of both mepivacaine and prilocaine was decreased by half within 20 min. This finding supports Weinberg's hypothesis of a "lipid sink" effect.[15] Unfortunately, no fourth sample was obtained, and we were therefore not able to calculate the pharmacokinetics as described previously.[16]

Lipids are readily available in the operating room at our institution because of a previous positive experience with LA toxicity.[3] Lipid infusion was immediately started after onset of symptoms, but before seizures occurred. The onset of arrhythmia at small doses of LAs implies reduced tolerance to the cardiac effects of both LAs. There could have been a significant influence of age on tolerance of LA. It remains unclear whether cardiac events were caused only by direct LA toxicity or possibly also caused by a secondary sympathetic response to CNS excitation. In our patient, CNS toxicity was reversed after injection of two boluses of 1 mL/kg each of Intralipid 20%. To reverse cardiac toxicity, a further dose of 2 mL/kg was required, given as a continuous infusion, which was in accordance with the dose used in both case reports[3,4] and Weinberg's recommendations for treatment of LA related toxicity (http://www.lipidrescue.org).[15,17]

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