prophylactic antacid preparation. To ask some patients to forego this preoperative preparation would not be justified. We can provide, however, pH and volume values from another study of a group of 15 recently (0–8 h) postpartum patients as quasi-control values. All 15 patients had pH values < 2.5. Eleven of the 15 patients had >25 ml of gastric content. Also, 11 of 15 (73%) had both pH values of <2.5 and volumes > 25 ml. Thus, Bicitra<sup>®</sup> appears to be an effective prophylactic antacid.

Finally, no prophylactic antacids can prevent aspiration of gastric contents; they can only ameliorate the consequences. Therefore, all usual preventative measures must be followed, including rapid sequence induction, endotracheal intubation, and cricoid pressure.

Bicitra<sup>®</sup> kindly was supplied for this study by the Willen Drug Company, Baltimore, Maryland.

REFERENCES


Toxic Reaction of Bupivacaine at Low Plasma Concentration

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Toxic reactions from local anesthetics (LA) normally are caused by high plasma concentrations, either from the administration of a high dose or an accidental iv injection. The toxicity of a LA is dependent on lipid solubility, protein binding, pK<sub>a</sub> and, therefore, the pH of plasma.

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Key words: Anesthetics, local: bupivacaine. Complications: convulsions.

We describe a case in which convulsions occurred at a plasma concentration of bupivacaine considered to be nontoxic during regional anesthesia.<sup>2,3</sup>

REPORT OF A CASE

A 28-year-old healthy woman, height 170 cm, weight 56 kg, participated in a study that evaluated the metabolic and cardiovascular changes induced by an iv infusion of bupivacaine at a rate of 2.0 mg·min<sup>–1</sup>. The study was approved by the Regional Ethical Committee. After monitoring equipment was applied and iv catheters were inserted, the patient rested for 90 min before three baseline values including blood pressure (BP), heart rate (HR), and cardiac output (CO) as determined by transesophageal impedance cardiography were measured. Also venous plasma bupivacaine concentrations were measured every half hour (table 1). The determinations of bupivacaine in plasma were performed by selected ion monitoring technique with a 100% specificity.
and a sensitivity of 1.0 ng/ml. Respiratory rate and volumes were measured by an expirograph, tidal volume 350–400 ml with a frequency of 14–17 breaths/min. Two hours after beginning the infusion of bupivacaine, cardiac output decreased 35%, compared with resting control values (table 1); 15 min later generalized seizures and unconsciousness ensued. The bupivacaine infusion was terminated 5–10 s later and ventilation controlled with an FIO₂ of 1.0. Diazepam 5.0 mg was given iv. The convulsions lasted approximately 45 s, after which the patient regained consciousness within 2–3 min without further sequelae.

About 60–120 s after the start of the convulsions, pH was 7.14 (PaCO₂ 34 mmHg and PaO₂ 101 mmHg). No cardiac arrhythmias were observed, and a three-lead ECG was normal. Two weeks later a placebo infusion was performed in this patient, and no hemodynamic or metabolic changes resulted.

**DISCUSSION**

With few exceptions, toxic reactions to bupivacaine do not occur at plasma levels below 4 µg/ml. In mice, bupivacaine convulsions are probably more lethal than convulsions from other LA because the high lipid solubility of bupivacaine may cause myocardial binding of the drug and thereby reduce myocardial reserve. This is supported by reports of several cases with sudden cardiovascular collapse occurring almost immediately after rapid injection of bupivacaine. These cardiovascular complications may be due to severe hypoxia and acidosis that either preceded or occurred concomitantly with the convulsions. In our case there was no reason to believe that acidosis preceded the convulsions, since plasma lactate was unaffected and respiratory rate and tidal volumes were unchanged prior to the convulsive episode. This is in contrast to the substantial rise in plasma lactate during convulsions. A few minutes after convulsions ceased, pH was low, but there was normoxia and normocarbia (table 1).

The plasma concentration of bupivacaine at the time of the convulsive episode was low (1.1 µg/ml). During a normal hemodynamic state, LA are taken up rapidly by all organs. Thus, muscle mass probably accounts for a large portion of the redistribution of LA, although muscle does not show any particular affinity for these drugs. Also the concentration of bupivacaine measured in samples taken from the radial artery are 20–40% higher than those measured simultaneously from the antecubital vein.

We believe the 33% decrease in cardiac output accounts for the untoward effects of bupivacaine in this patient. This could be due to changes in peripheral blood flow with differences in plasma bupivacaine concentrations between venous and arterial blood, though our measurements do not reflect this. Since the venous plasma bupivacaine concentrations remained constant the well perfused organs must have received increasing amounts of the drug. These factors may offer the explanation for the CNS toxicity at a low venous concentration of bupivacaine in this case.

**REFERENCES**