prophylactic antacid preparation. To ask some patients to forgo 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® appears to have a prophylactic effect.

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

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

REFERENCES


Anesthesiology
61:99–100, 1984

Toxic Reaction of Bupivacaine at Low Plasma Concentration

LARS J. HASSELSTRÖM, M.D., AND TORBEN MOGENSEN, M.D.

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, pKa, and, therefore, the pH of plasma.

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

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⁻¹. The study was approved by the Regional Ethical Committee. After monitoring equipment was applied and iv catheters were inserted, the patient rested for 30 min before three baseline values including blood pressure (BP) heart rate (HR), and cardiac output (CO) as determined by transthoracic 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.
TABLE 1. Intravenous Infusion of Bupivacaine 2 mg/min

<table>
<thead>
<tr>
<th>Time</th>
<th>-30</th>
<th>-15</th>
<th>0</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>120</th>
<th>138</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial blood pressure (mmHg)</td>
<td>110/70</td>
<td>118/70</td>
<td>125/75</td>
<td>110/79</td>
<td>127/81</td>
<td>128/80</td>
<td>127/83</td>
<td>140/80</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td>83</td>
<td>86</td>
<td>85</td>
<td>90</td>
<td>96</td>
<td>96</td>
<td>95</td>
<td>100</td>
</tr>
<tr>
<td>Heart rate/minute</td>
<td>72</td>
<td>74</td>
<td>79</td>
<td>76</td>
<td>80</td>
<td>83</td>
<td>80</td>
<td>120</td>
</tr>
<tr>
<td>Cardiac output (1/min)</td>
<td>5.9</td>
<td>4.2</td>
<td>6.0</td>
<td>8.7</td>
<td>6.9</td>
<td>6.1</td>
<td>3.6</td>
<td>3.6</td>
</tr>
<tr>
<td>Blood bupivacaine (μg/ml)</td>
<td>0.75</td>
<td>0.60</td>
<td>0.51</td>
<td>0.60</td>
<td>0.71</td>
<td>0.70</td>
<td>0.80</td>
<td>1.03</td>
</tr>
<tr>
<td>P-lactate (mmol/l)</td>
<td>4.1</td>
<td>3.8</td>
<td>4.2</td>
<td>3.8</td>
<td>3.3</td>
<td>3.5</td>
<td>3.3</td>
<td>4.8</td>
</tr>
<tr>
<td>P-glucose (mmol/l)</td>
<td>4.1</td>
<td>3.8</td>
<td>4.2</td>
<td>3.8</td>
<td>3.3</td>
<td>3.5</td>
<td>3.3</td>
<td>4.8</td>
</tr>
</tbody>
</table>

Convulsions started at time 155 min. Infusion was started at point 0.

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 33%, compared with resting
control values (table 1); 15 min later generalized seizures and uncon-
sciousness ensued. The bupivacaine infusion was terminated 5–10 s
after 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 Paco2 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 meta-
abolic 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 solu-
bility 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 (ta-
ble 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 sam-
ple 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 measure-
ments do not reflect this. Since the venous plasma bu-
 pivacaine 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 bu-
pivacaine in this case.

**REFERENCES**

1. Covino BG, Vasallo HG: Local anesthetics—mechanisms of action
and clinical use. New York, Grune and Stratton, 1976

2. Moore DC, Mather LE, Bridenbaugh PO, Bridenbaugh LD, Balfour RI,
Lysons DF, Horton WG: Arterial and venous plasma levels of bupivacaine
following epidural and intercostal nerve blocks. ANESTHESIOLOGY 45:31–
45, 1976

3. Moore DC, Mather LE, Bridenbaugh LD, Balfour RI, Lysons DF,
Horton WG: Arterial and venous plasma levels of bupivacaine following

4. Moore DC, Thompson GE, Crawford RD: Long acting local an-
esthetic drugs and convulsions with hypoxia and acidosis.
ANESTHESIOLOGY 56:230–232, 1982

5. DeJong RH, Bonin JD: Deaths from local anesthetic-induced con-


6. Albright GA: Cardiac arrest following regional anesthesia with
etidocaine or bupivacaine. ANESTHESIOLOGY 51:285–287,
1979

7. Moore DC, Crawford RD, Sculrocl JE: Severe hypoxia and acidosis
following local anesthetic-induced convulsions. ANESTHESIO-
LOGY 53:259–260, 1980

8. Katz J: The distribution of C14 labelled lidocaine injected intra-
venously in the rat. ANESTHESIOLOGY 29:249–253, 1968

9. Moore DC, Bridenbaugh LD, Bridenbaugh PO, Tucker GT: Bu-