CASE REPORTS

PLASMA LIGNOCAIN CONCENTRATIONS ASSOCIATED WITH EXTRADURAL ANALGESIA IN PATIENTS WITH AND WITHOUT MULTIPLE ORGAN FAILURE

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SUMMARY

We have measured plasma concentrations of lignocaine after thoracic extradural analgesia with continuous infusion of lignocaine in eight intensive care patients with chest wall trauma or after major upper abdominal surgery. Four patients developed multiple organ failure (MOF). Plasma concentrations of lignocaine in arterial blood were measured 4, 8, 24 and 48 h after a continuous infusion of lignocaine was commenced in the extradural space. Plasma concentrations of lignocaine were greater in all patients with MOF (range 2.7-5.1 ng ml⁻¹) than in patients without MOF (range 0.8-1.2 ng ml⁻¹). Because plasma concentrations in patients with MOF were within the low toxic range, extradural infusion of lignocaine should only be considered in intensive care patients without MOF or when plasma concentrations of lignocaine are monitored. (Br. J. Anaesth. 1992; 69: 513-516)

KEY WORDS


Extradural administration of either local anaesthetics or opioids has been shown to be effective for pain management in patients with thoracic injury [1, 2] and in high risk patients requiring intensive care after upper abdominal surgery [3]. However, these patients may be at risk of developing multiple organ failure (MOF).

Extradural administration of local anaesthetics may be associated with systemic toxic effects [4]. Differences in the plasma concentrations of local anaesthetics may be caused by organ dysfunction [5]; there are no data on the plasma concentrations of local anaesthetics during extradural analgesia in patients developing MOF. We have measured, therefore, plasma concentrations of lignocaine during continuous extradural infusion of lignocaine in patients with and without MOF.

PATIENTS AND METHODS

We have studied patients admitted to our intensive care unit with chest wall trauma or after major upper abdominal surgery. All had required ventilatory support for adequate gas exchange and thoracic extradural analgesia was considered appropriate for pain management. Organ failure was defined as severity grade 2 in the multiple organ failure score originally described by Goris and colleagues [6]. Multiple organ failure was present when at least two organ failure was present. Sepsis was diagnosed according to the definition of Montgomery and colleagues [7]. Patients were excluded from the study if they had neurological injury, spinal injury, sepsis or coagulopathy.

The study was explained in detail to each patient, and informed consent was obtained for all procedures.

All patients were placed in a lateral decubitus position and a 16-gauge Tuohy needle was introduced in the extradural space at the T5-6 or T6-7 level. A therapeutic dose of 2% lignocaine 10 ml without adrenaline was injected extradurally and an 18-gauge extradural catheter was advanced approximately 4-5 cm into the extradural space. A continuous infusion of 2% lignocaine 0.5-0.6 ml kg⁻¹ h⁻¹ (1-1.2 mg kg⁻¹ h⁻¹) without adrenaline [8, 9] was begun 3-5 min after the test dose had been given. In four patients, an additional extradural infusion of fentanyl 1 μg kg⁻¹ h⁻¹ [10] was required to achieve adequate analgesia (table I).

Arterial blood samples were collected 4, 8, 24 and 48 h after the continuous infusion of lignocaine was started and their plasma concentrations of lignocaine were measured. (Br. J. Anaesth. 1992; 69: 513-516)

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Patients with MOF

Patient No. 1. A 52-yr-old male with acute alcoholic-related necrotizing pancreatitis underwent laparatomy...
A continuous extradural infusion of lignocaine (table I) was started immediately after admission. The plasma lignocaine concentration which exceeded the stated lower toxic concentration of 3 \( \mu g \) ml\(^{-1}\) [13]. The plasma lignocaine concentrations for patients with and without MOF are shown in table II.

### Patients without MOF

**Patient No. 1.** A 21-yr-old male with bilateral multiple rib fractures and pulmonary contusion received ventilatory support (\( F_iO_2 0.6, PEEP 12 \text{ cm } H_2O \)) to achieve adequate gas exchange. On the second day, a continuous extradural infusion of lignocaine (table I) was started. Subsequently, administration of midazolam was reduced from 20 to 5 mg h\(^{-1}\) i.v. and i.v. infusion of fentanyl was discontinued. The patient was weaned from the ventilator to a CPAP of 6 cm H\(_2\)O by the third day.

**Patient No. 2.** A 27-yr-old female with multiple rib fractures and pulmonary contusion received continuous extradural infusion of lignocaine (table I) immediately after admission. Mask-CPAP of 5 cm H\(_2\)O was applied to prevent development of atelectasis.

**Patient No. 3.** A 35-yr-old female with multiple rib fractures and pulmonary contusion received a continuous extradural infusion of lignocaine (table I) immediately after admission. Mask-CPAP of 5 cm H\(_2\)O was applied to prevent development of atelectasis.

**Patient No. 4.** A 30-yr-old male with multiple rib fractures and pulmonary contusion received ventilatory support (\( F_iO_2 0.5, PEEP 10 \text{ cm } H_2O \)) to provide adequate gas exchange. A continuous extradural infusion of lignocaine (table I) was started immediately after admission.

### RESULTS

There were no adverse local or systemic effects of lignocaine in either the MOF or the non-MOF patients.

We terminated the study because four patients developing MOF had plasma lignocaine concentrations which exceeded the stated lower toxic concentration of 3 \( \mu g \) ml\(^{-1}\) [13]. The plasma lignocaine concentrations for patients with and without MOF are shown in table II.
We have found that administration of a continuous extradural infusion of 2% lignocaine was associated with toxic plasma concentrations of lignocaine (≥ 3 μg ml⁻¹) [13] in patients with MOF. In contrast, plasma lignocaine concentrations remained smaller than toxic values in patients without MOF.

The plasma concentration of a local anaesthetic during continuous extradural infusion is determined mainly by absorption into the systemic circulation, its distribution and its rate of clearance by the liver [14]; all of these factors may be altered in the presence of MOF. Body weight and renal disease [5] are reported to have minor effects on the elimination of lignocaine, whereas hypovolaemia [15], cardiovascular disease [16] and hepatic cirrhosis [5] are associated with a decrease in plasma clearance. Clearance of lignocaine is mainly flow dependent [14]. Liver blood flow is determined principally by cardiac output, which in our patients was kept in a higher range (cardiac index > 3.5 litre min⁻¹) to increase oxygen delivery by adequate volume replacement and if necessary by positive inotropic therapy. Thus the presence of either cardiovascular failure or hepatic failure alone may not explain the increased plasma lignocaine concentrations in our MOF patients. Drugs (e.g. H₂-blockers, sedatives) have been shown to decrease both hepatic blood flow and enzyme activity [17] and these factors may also have reduced lignocaine clearance in our MOF patients (table II).

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Organ failure</th>
<th>ASAT† (u litre⁻¹)</th>
<th>Bilirubin† (mg dl⁻¹)</th>
<th>Arterial pH</th>
<th>Plasma lignocaine conc (μg ml⁻¹)</th>
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</tr>
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REFERENCES