BUPIVACAINE 0.125% IN EPIDURAL BLOCK ANALGESIA DURING CHILDBIRTH: MATERNAL AND FOETAL PLASMA CONCENTRATIONS

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SUMMARY
The maternal plasma concentration of bupivacaine has been determined in 19 patients receiving a continuous epidural block during labour, using bupivacaine 0.125% with adrenaline 1:400,000. The plasma concentration of bupivacaine rarely exceeded 0.18 µg/ml. Bupivacaine does not accumulate in the maternal blood when such low concentrations are used. The plasma concentration of bupivacaine has also been determined in umbilical venous and arterial blood at birth. The concentration ratio (umbilical venous/maternal venous) at delivery ranged from 0.09 to 0.49 (mean 0.28).

Bupivacaine hydrochloride 0.25 and 0.5% with and without adrenaline has been used successfully in epidural block for several years. Maternal and neonatal blood concentrations of the drug have been studied (Hyman and Shnider, 1971; Moore et al., 1970, 1971; Reynolds and Taylor, 1970, 1971; Thomas, Climie and Mather, 1969). Bupivacaine 0.125% with adrenaline 1:400,000 has been used successfully in our department for epidural block during childbirth (Vanderick et al., 1974).

The purpose of this investigation was to determine the maternal plasma concentration of bupivacaine at various times after the injection of the drug into the epidural space, and to compare maternal and umbilical arterial and venous plasma concentrations at birth.

MATERIAL AND METHODS
Nineteen patients, in whom no obstetric problem was anticipated, were selected for the elective induction of labour at term under epidural block analgesia. Their ages ranged from 20 to 33 years. Seventeen were primiparae.

Labour was induced in each patient by means of an intravenous infusion of oxytocin. Amniocentesis was performed early in the first stage of labour. A Portex plastic catheter was inserted through a Tuohy 17-gauge needle into the epidural space (Van Steenberge, 1969). The free end of the catheter was attached to a Millipore filter. A 5-ml test dose of bupivacaine 0.125% (6.25 mg) with adrenaline 1:400,000 was then given.

Maternal arterial pressure and pulse rate were checked at regular intervals. Signs of toxicity or abnormal reactions were noted. Foetal heart rate and uterine contractions were monitored whenever possible with a cardiotocograph.

Continuous epidural analgesia was started as soon as labour was established as evidenced by regular uterine contractions and cervical dilatation of at least 2 cm. Bupivacaine 0.125% (12.5 mg) with adrenaline 1:400,000 in 10 ml was injected at intervals (45-90 min) to give continuous pain relief to the mother. At the end of the first stage of labour or early in the second stage 15 ml (18.75 mg) of bupivacaine was given, with the patient in the sitting position to produce perineal anaesthesia. Delivery was achieved within 70 min after the last dose.

Maternal blood samples were drawn from an antecubital vein at specified times after each injection of the anaesthetic:

(1) In 5 patients blood samples were taken at 5-min intervals during the first half-hour and at 60 min after the first 10-ml dose. Thereafter samples were drawn before and at 10, 20 and 40 min after each repeat injection. At the time of delivery blood was taken from the mother and from the umbilical vein.
(2) Seven patients had blood sampled at 10-min intervals for the first half-hour after each injection and at delivery.

(3) Sampling from the mother, the umbilical vein and the umbilical arteries, at delivery only, was performed in another 7 patients.

All blood samples were placed in a refrigerator until processed. Plasma bupivacaine concentration was determined by one of us (R.B.) using gas chromatography and a modification of the method described by Tucker et al. (1970).

RESULTS

All patients except one (patient no. 8) experienced complete analgesia from the onset of the epidural block until after delivery and perineal repair. No major side effects were noted. Delivery was spontaneous in 9 patients, and the vacuum extractor or forceps were used in the remaining 10, usually because of prolongation of the second stage. Monitoring by cardiotocography showed no notable abnormalities of foetal heart rate and all babies were in good health at birth (Apgar score range 8 to 10). Details of a more extensive clinical study may be found in a previous paper (Vanderick et al., 1974).

Figures 1 and 2 illustrate the plasma concentrations of bupivacaine in 2 patients (nos. 2 and 10). Figure 3 shows the plasma concentration of bupivacaine in 8 patients in whom epidural block lasted for longer than 3 hours.

Placental transfer.

Table I lists the plasma concentrations of bupivacaine in the maternal blood and in the umbilical venous and arterial blood immediately after cord section.

The mean concentration of the drug in the maternal peripheral blood at delivery was 0.154 µg/ml plasma (range 0.093–0.265 µg/ml). The mean concentration of bupivacaine in the umbilical vein was 0.040 µg/ml plasma. Patient no. 8 had an unsuccessful sensory block even after greater doses of the anaesthetic were injected. If this case is disregarded the mean concentration in the umbilical vein is 0.035 µg/ml (range 0.01–0.06 µg/ml) (figs. 4 and 5).

A blood sample was also taken from the umbilical artery in 8 patients. Bupivacaine concentrations were slightly less in the umbilical arteries (mean 0.035 µg/ml plasma) than in the corresponding veins (mean 0.044 µg/ml plasma).

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**Fig. 1.** Plasma concentration of bupivacaine during continuous epidural analgesia. Arrows indicate doses. UV = Umbilical vein. (Patient no. 2.)
Fig. 2. Plasma concentration of bupivacaine during continuous epidural analgesia. Arrows indicate doses.

UV = Umbilical vein. (Patient no. 10)

Fig. 3. Maternal concentration during continuous epidural analgesia using bupivacaine 0.125% with adrenaline 1:400,000 (8 patients in whom the epidural block lasted longer than 3 hours). Arrows indicate doses.
### Table I. Clinical details and plasma concentrations of bupivacaine during continuous epidural analgesia.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Total dose of bupivacaine (mg)</th>
<th>No. of injections</th>
<th>Duration of block (min)</th>
<th>Plasma concentrations (µg/ml)</th>
<th>Ratio UV/mat.</th>
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FDD = first dose delivery. LDD = Last dose delivery. UV = umbilical vein. UA = umbilical artery.

**DISCUSSION**

Bupivacaine hydrochloride, when injected into the extradural space, is quickly absorbed into the maternal blood (Hyman and Shnider, 1971; Moore et al., 1970; Reynolds and Taylor, 1970). This study suggests that when bupivacaine 0.125% is used the maximum plasma concentration occurs 10 to 20 min after injection and that the value of the peak rarely exceeds 0.18 µg/ml (table I). This is considerably lower than when bupivacaine 0.5% is used (Hyman and Shnider, 1971; Moore et al., 1970; Reynolds and Taylor, 1970). Provided the total dose of bupivacaine does not exceed 100 mg the maternal plasma concentration at delivery is always less than 0.20 µg/ml. In our practice the total dose of bupivacaine administered exceeds 100 mg in less than 5% of patients.

This study also suggests that cumulative concentrations of bupivacaine in the maternal blood are minimal (fig. 3). This is a marked advantage over other anaesthetics such as mepivacaine (Reynolds, 1971), lignocaine (Reynolds and Taylor, 1971; Reynolds, 1971) or even bupivacaine 0.5% (Hyman and Shnider, 1971; Reynolds and Taylor, 1971) and 0.25% (Hyman and Shnider, 1971).

Because the plasma concentrations of bupivacaine in this study were small the concentrations in the umbilical cord were much less than in previously published reports. Using bupivacaine 0.5% with adrenaline 1:200,000, Reynolds and Taylor (1971) found umbilical vein concentrations of 0.092–0.337 µg/ml plasma (mean 0.180 µg/ml). Using bupivacaine 0.125%, with adrenaline 1:400,000 we found a mean umbilical vein concentration of 0.040 µg/ml plasma. Our results suggest that, provided the total amount of bupivacaine administered does not exceed 100 mg, the umbilical vein concentration of the drug will not exceed 0.060 µg/ml plasma (fig. 4).

![Fig. 4. Maternal □ and umbilical vein ○ plasma concentration of bupivacaine at delivery related to the total dose administered.](image)
Table I lists the ratio of umbilical vein/maternal plasma concentration. It varies from 0.09 to 0.49 (mean 0.28). This figure is comparable with the ratio 0.2–0.4 usually described in the literature (Hyman and Shnider, 1971; Moore et al., 1971; Reynolds and Taylor, 1970, 1971) when bupivacaine 0.5% is used. This suggests that the ratio is constant (roughly 1/3) regardless of the circulating amount of the drug. This would suggest that, by decreasing the amount of drug administered by using lower concentrations, the risk of foetal toxicity will be reduced.

However, Reynolds and Taylor (1970) demonstrated that the addition of adrenaline increased the umbilical vein/maternal plasma ratio from 0.23 to 0.40. Why adrenaline increases the proportion of transferred bupivacaine is not yet explained and needs further investigation.

Neither the duration of the block nor the time between the last refill dose and delivery are related to the umbilical vein concentration. This was also described by Reynolds and Taylor (1970, 1971). Even if the maternal plasma concentration of the drug increases with the time between the last dose and delivery, the umbilical vein concentrations are all at a value of less than 0.06 µg/ml (fig. 5).

When the plasma concentrations of bupivacaine in the umbilical vein and artery are compared, it appears that the umbilical artery carries about 20% less bupivacaine than the corresponding umbilical vein. Moore et al. (1970) have demonstrated the same phenomenon in adults: the arterial blood contains 20–40% more bupivacaine than the venous blood. This similarity between adult and foetus supports the hypothesis that the foetus is able to metabolize or store the drug.

CONCLUSION

The advantages of using bupivacaine 0.125% in continuous epidural analgesia during labour and delivery are obvious. The low concentration still provides a clinically satisfactory sensory block, side effects are decreased and toxicity of the drug to mother and newborn is reduced.

REFERENCES


