Title: PLASMA BUPIVACAINE CONCENTRATIONS DURING CONTINUOUS EPIDURAL INFUSIONS

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Introduction. Epidural analgesia has an established role for pain relief in labor. However the danger period in the maintenance of continuous epidural blockade is immediately following the administration of an intermittent top-up dose. Moreover this technique is extremely time-consuming and may be delayed if staff are not immediately available. It has been suggested that epidural infusions are safer than top-up doses[1] and that the supervision of infusions is simpler[2]. Bupivacaine 0.08% solution infused at 25 ml h^{-1} has been shown to provide long periods of uninterrupted analgesia[3]. It appears, therefore, that infusions produce greater safety and are more effective in providing uninterrupted analgesia than intermittent doses.

A recent report on the clinical effects of 0.08% and 0.25% solutions of bupivacaine administered as continuous epidural infusions[4] showed that the weaker solution produced better analgesia with fewer side effects. Since both solutions were infused at a dose rate of 20 mg h^{-1} we have compared plasma concentrations during continuous epidural infusion of 0.08% and 0.25% bupivacaine solutions.

Methods. Twenty patients who had requested epidural analgesia for labor were randomly allocated to receive either 0.08% or 0.25% bupivacaine. All patients were fit and healthy and at 37 weeks gestation or more. All gave informed consent and the protocol was approved by the University Medical Ethical Research Committee.

After correct insertion of the epidural catheter through the L3-4 interspace, an initial bolus of 50 mg (10 ml of 0.5%) bupivacaine was given. This was followed immediately by the infusion of either 25 ml h^{-1} of 0.08% or 8 ml h^{-1} of 0.25% bupivacaine via an infusion pump (Imed 960). Each patient thus received 20 mg h^{-1}.

Venous blood samples were taken from an indwelling cannula in the non-infused arm at 0, 15, 30, 60, 90, 120, 180 and 300 minutes. Bupivacaine analysis was by High Pressure Liquid Chromatography.

Blood pressure, EKG, height of sensory block and the extent of muscle weakness were monitored continuously in all patients. Data are presented as the mean in each series and the significance of the differences was calculated using the unpaired students 't' test.

Results. The two groups of patients were comparable in terms of mean age, weight and parity. Two patients in each group who experienced some discomfort during the 5-hour sampling period required a single top-up dose of 30 mg after 3 hours. From 30 minutes onwards the mean plasma levels were significantly higher in those patients receiving the more concentrated solution (Table 1).

Table 1. Mean plasma levels of bupivacaine (ng ml^{-1} ±SD) during epidural infusion (n=10).

min	INFUSED CONCENTRATION 0.08%	0.25%	P
15	402±65	545±273	0.12
30	368±80	534±200	0.03
60	321±67	522±203	0.008
90	314±42	528±201	0.004
120	323±85	540±216	0.008
180	341±97	553±205	0.008
300	277±83	539±177	0.001

A hypotensive episode occurred in one patient in each group. Cephalad spread beyond T6 occurred in one patient receiving the more dilute solution and in two patients given 0.25%. Loss of motor power occurred more often with the stronger solution (5/10 compared with 2/10).

Discussion. The use of 0.08% solution bupivacaine was associated with fewer side effects than the more concentrated solution. This could be related to the lower plasma concentrations. Although the subjects received the same total dose of drug per unit time the concentration gradient should be greater with the 0.25% solution thus favoring tissue uptake. However, there was a greater surface area for absorption with the higher volume of weaker solution. This study would suggest that the significantly lower plasma levels associated with the weaker solutions reduces the risk of toxicity.

References

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