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Continuous Epidural Infusion of Bupivacaine for Postoperative Pain Relief in Children

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Epidural anesthesia is a safe and efficient method to relieve pain in children intra- and postoperatively.[1–3] Continuous epidural infusion of bupivacaine is a technique used commonly with adults,[4,5] but no such studies have been done in children. The aim of our study was to evaluate the efficacy of continuous epidural infusion of low doses of bupivacaine and to measure plasma bupivacaine levels after major surgery in children.

MATERIAL AND METHODS

This study was approved by the committee on human research, and parental consent was obtained. All children were free of respiratory, renal, cardiovascular, hepatic, or neurological disorders (ASA I), and none received medication before the study. We studied 21 children (12 girls and 9 boys) undergoing major orthopedic (14 cases) and genital organ repair (7 cases) operations (table 1). Age ranged from 11 months to 15 yr (mean ± SD: 8.7 ± 4.5 yr), weight ranged from 10–43 kg (mean ± SD: 26 ± 11 kg). All children had a 21- or 20-gauge epidural catheter (Portex Limited, Wilmington, MA) inserted into a mid-lumbar interspace (L3–L4: 16 cases, L2–L3: 5 cases) under nitrous oxide/halothane or enflurane endotracheal anesthesia. The only iv drug given during the course of the study was a single initial dose of vecuronium (80 mcg/kg) or pancuronium (100 mcg/kg) to help intubation of the trachea in children more than 4 yr old. Intraoperative maintainance fluids (dextrose in water and electrolytes) were given at a rate of 5 to 10 $ml \cdot kg^{-1} \cdot h^{-1}$ depending on age.

Before surgery, a loading dose of 0.25% bupivacaine without epinephrine was injected epidurally (0.5 ml/kg) followed 30 min later by an infusion of 0.25% bupivacaine without epinephrine (0.08 $ml \cdot kg^{-1} \cdot h^{-1}$) using a volumetric infusion pump. Infusion was continued at the same rate for 12–72 h during the postoperative period. Children were evaluated postoperatively upon complete awakening and 3 times daily. Arterial blood pressure and heart rate were measured with an automatic blood pressure cuff (Dinamap™), and level of analgesia was tested by the same anesthetist by the pin-prick method. In small infants, repeated withdrawal of a limb was interpreted as a positive reaction to pain. Older children were able to say when the level of analgesia was reached. Pain relief was scored by children who were 10 yr of age or older on a visual analogue scale from 1 to 10. In six of the 21 children, aged 3.25–11 yr (mean ± SD: 8.2 ± 2.5 yr) and weighing 17–43 kg (mean ± SD: 25 ± 9 kg), bupivacaine plasma concentrations were assayed in duplicate from venous blood samples by high-pressure liquid chromatography method§ 24, 28, 32, 36, 40, 44, and 48 h after the start of infusion and 2, 4, 6, 8, and 10 h after infusion was discontinued. The sensitivity of our method is 30 ng/ml, and the coefficient of variation of 4–8% at the concentrations studied.

Total body clearance (CL) was calculated in the six children as follows[6]: $CL = \frac{Ro}{Css}$, where Ro is the bupivacaine epidural infusion rate and Css the bupivacaine plasma concentration at steady state. Css is calculated as the mean of the plasma concentrations at each time interval. After infusion was discontinued, elimination half-life (T $\frac{1}{2}\beta$) was determined using nonlinear least squares analysis. Results are expressed as mean ± SD.

RESULTS

Neither heart rate nor arterial blood pressure was significantly affected in any of the 21 patients at any time of the study (fig. 1). Postoperative initial upper level of analgesia tested when children were fully awake was between T10 and L1 level, and stayed at the starting level throughout the study. Ten children, aged

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§ Bishop W, Oppenheimer RC, Eyres RL: Analysis of lignocaine and bupivacaine in plasma by high pressure liquid chromatography. Asian J Pharmaceut Sci 2:91–94, 1980

TABLE 1. Operations

Urology (n = 7)	
Hypospadias repair	4
Bladder extrophy	1
Ureteral reimplantation	2
Orthopedic (n = 14)	
Club foot bilateral	2
unilateral	1
Lower limb repair (Wagner)	2
Bilateral hip osteotomy	2
Unilateral hip osteotomy	4
Femoral derotation and hip osteotomy	3

8–9.5 yr, evaluated their pain on a visual analogue scale between 1.2 and 1.8 (mean ± SD: 1.4 ± 0.5). Two children with bladder catheters complained of discomfort above T12 level, but did not need additional analgesics. Other children too young to evaluate pain remained calm and slept well throughout the postoperative period. Infusion was continued 12–72 h (mean: 40 ± 17 h) Total dose of bupivacaine 0.25% was 6.0 $mg \cdot kg^{-1} \cdot 24$ h on the first day (intraoperative loading dose + infusion) and 4.8 $mg \cdot kg^{-1} \cdot 24$ h thereafter. Epidural catheters were inspected upon removal. The puncture site appeared unremarkable, and there were no abnormalities. Cultures of catheters and puncture site were negative. Bupivacaine plasma concentrations during the infusion are shown on figure 2. During the infusion, no significant change in bupivacaine plasma concentration was observed. After infusion was discontinued, bupivacaine plasma concentration decreased steadily: terminal half-life (T ½β) ranged from 164–270 min (mean ± SD: 202 ± 56 min). Total body clearance and mean bupivacaine concentrations for each child are shown on table 2. Total body clearance was found to be in the range of values published after single caudal injection of bupivacaine in children of similar age and weight.[7]

DISCUSSION

Throughout the course of the epidural bupivacaine infusion, the infants and children in this study were in no apparent pain. In a group of children receiving intermittent epidural bupivacaine injections, pain recurred as judged by crying and obvious discomfort; those children required repeated intermittent additional doses of bupivacaine.[1] The older children in this study who can describe their pain and score it on a visual analogue scale always had low scores throughout the course of the infusion. Unlike Raj *et al.*'s[4] observations in adults, the upper level of analgesia in our patients was stable throughout the study, with a minimum level around T12.

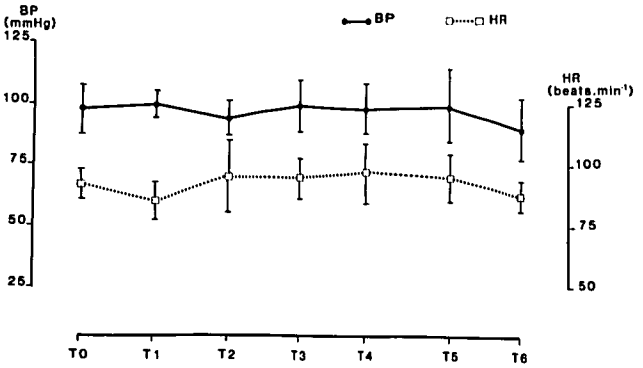

FIG. 1. Systolic arterial blood pressure and heart rate variations during continuous epidural infusion of bupivacaine (time between two measurements: 3 h).

Bupivacaine plasma concentration was first measured after 24 h of infusion in order to eliminate any interaction of drug metabolism with residual anesthesia, and to ensure that plasma bupivacaine level would have achieved a plateau.[6] Bupivacaine plasma concentrations were not measured during the first 24 h, as pharmacokinetic studies[1,8] have shown that maximum bupivacaine plasma concentration after a single epidural injection of a similar dose of bupivacaine is well below toxic levels. In the six children who had bupivacaine plasma concentration measured after 24 h of continuous epidural infusion, the bupivacaine plasma concentrations remained level with no significant change during the course of the infusion, showing that there was no accumulation of bupivacaine in plasma after 48 h of infusion. Total body clearance calculated in those six children was in the same range as the results published by Ecoffey *et al.*[8] These findings are consistent with those published by Denson *et al.*,[7] who showed that total body

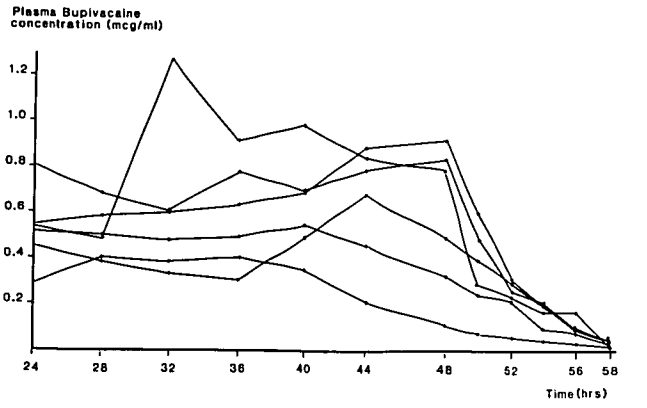

FIG. 2. Bupivacaine plasma concentration ($mcg \cdot ml^{-1}$) during continuous epidural infusion of 0.2 $mg \cdot kg^{-1} \cdot h^{-1}$ of bupivacaine 0.25% (mean ± SD) (n = 6). First measurement was done at 24 h of infusion and infusion was discontinued at 48 h.

TABLE 2. Mean Plasma Bupivacaine Concentrations and Total Body Clearance

Patient	Css (mean ± SD) mcg · ml^{-1}	CL, ml · min^{-1} · kg^{-1}
1	.47 ± .07	7.09
2	.45 ± .12	7.40
3	.73 ± .07	4.56
4	0.30 ± .11	11.11
5	.69 ± .14	4.83
6	.84 ± .29	3.96

clearance of bupivacaine exhibited no significant change throughout the course of long-term infusion.

We conclude that continuous epidural infusion of bupivacaine is a safe and effective method of pain relief in children undergoing major lower extremity and genitourinary operations. It requires an anesthesiologist trained in regional anesthesia in children, repeated examination of the child, dependable infusion pumps and attention to measures which prevent infection.

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Influence of Balloon Inflation and Deflation on Location of Pulmonary Artery Catheter Tip

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Catheter perforation of the pulmonary artery represents a serious and sometimes lethal complication of invasive hemodynamic monitoring; it is seen predominantly in patients with pulmonary hypertension.[1,2] Two initiating mechanisms have been proposed: 1) eccentric balloon inflation, causing impingement of the catheter tip into the vessel wall,[3–5] and 2) high intraballoon pressures, causing direct vessel disruption during balloon inflation.[4,6,7] We believe that other forces acting on the catheter tip may contribute to causing this complication.

Several reports have described catheter-induced rupture through the pulmonary artery, with extension into the pleural cavity, causing massive hemothoraces.[1,4,8,9] One possible explanation of the hemothorax is the formation of a dissecting hematoma by the catheter perforating the pulmonary artery, with dissection into the pulmonary parenchyma and extension into the pleural space. Another explanation is direct penetration of the catheter tip through the pulmonary artery and parenchyma into the pleural space.[8] In the latter circumstance, the hemodynamic forces causing this excessive

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