Title: PHARMACOKINETICS OF BUPIVACAINE IN CHILDREN FOLLOWING INTERCOSTAL BLOCK

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Introduction. The present study investigated the pharmacokinetics of bupivacaine hydrochloride in children following intercostal nerve blocks.

Methods. Intercostal nerve blocks were performed on 23 occasions with bupivacaine, 0.5% with epinephrine 1:200,000 in 22 children following elective cardiovascular surgery performed through a thoracotomy incision. The average age of the group was 55±11 months. All children were anesthetized with halothane for the operative procedure. Following skin closure the nerves in five interspaces were blocked during continuous electrocardiographic and blood pressure monitoring. Three doses of bupivacaine were used: 2mg/kg (n=7), 3mg/kg (n=5) and 4mg/kg (n=11). Samples of arterial blood were obtained from indwelling radial artery catheters immediately prior to performing the block (control) and 5, 10, 15, 30, 60, 120 and 180 minutes following completion of the block. In 3 children samples were obtained for a total of 360 minutes. Simultaneous central venous and arterial samples were obtained in 4 children. Bupivacaine (base) concentration in whole blood was assayed by gas chromatographic methods. A two compartment model was used and apparent volume of distribution (VOL), clearance (Cl), and elimination half-life (T 1/2) were determined. All data are reported as mean ± SEM. The study was approved by the Human Investigation Committee, and parenteral consent was obtained.

Results. There were no changes in heart rate or blood pressure during the performance of the block. Arterial whole blood concentrations (ug/ml) were:

Dose	5"	10"	15"	30"
2mg/kg	0.65±.07	0.74±.09	0.63±.08	0.54±.10
3mg/kg	1.30±.11	1.22±.08	1.38±.13	1.21±.20
4mg/kg	1.87±.16	1.83±.16	1.71±.18	1.47±.14

Dose	60"	120"	180"
2mg/kg	0.43±.09	0.31±.08	0.24±.10
3mg/kg	0.91±.15	0.63±.14	0.40±.10
4mg/kg	1.02±.15	0.74±.15	0.53±.10

The mean peak concentrations achieved were 2mg/kg: 0.77±.09, 3mg/kg: 1.39±.12 and 4mg/kg: 1.99±.16. The highest peak concentration was 3.20 ug/ml. Occurrence of peak concentration with respect to dose and time is shown below.

Dose	5"	10"	15"	30"
2 mg/kg	1	5	1	
3 mg/kg	1	2	1	1
4 mg/kg	7	3	1	

Arterial concentrations of bupivacaine were greater than the venous concentrations in the 5, 10 and 15 minute samples. Concentrations were equal in samples obtained after 15 minutes. VOL, Cl and T 1/2 were determined for 16 children. VOL was 2.8±0.2 L, Cl was .28±.06 L/min and T 1/2 was 136±24 minutes. There was no correlation between clearance and body weight or surface area.

Discussion. Rapid absorption of bupivacaine from the intercostal space occurred in this population. Peak concentrations occurred earlier than has been previously reported in adults. (1) Two factors may account for this observation. Cardiac output per kilogram is greater in children than in adults and this may make uptake of drug more rapid. Although our blocks encompassed a smaller number of ribs than in the adult studies, the volume and dose of drug per interspace was relatively greater in our study. Our data suggests a trend for peak concentrations to occur earlier at the highest dose and volume used and thus volume of drug may influence the rapidity of uptake. Rapid uptake of local anesthetic by the lung from venous blood and subsequent release of drug into pulmonary blood occurred. Net uptake of drug by lung was completed by 5 minutes, and net release ceased 15 to 30 minutes following completion of the block. In this study VOL and T 1/2 were similar to and Cl was less than the values obtained in adults (2,3). The lack of correlation of Cl with weight or surface area probably represents individual variation in metabolism and excretion of drug as well as the influence of surgery and anesthesia on hepatic and renal function. No adverse cardiovascular or central nervous system effects were seen during this study although one child had a peak concentration that approached the range that is considered potentially toxic in adults. We recommend that 4mg/kg is the upper dose limit of bupivacaine for intercostal block in children.

References.

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