the catheter $S\bar{v}_{O_2}$ with *in vitro* $S\bar{v}_{O_2}$ only at 12-h intervals according to the manufacturers' suggestions. Although more frequent comparisons might help in the control of drifting, time intervals much shorter than 8–12 h would limit the clinical usefulness of such devices. In addition, the variety of severe diseases and therapies our critically ill patients were facing may not have been perfectly modeled by the experimentally manipulated $S\bar{v}_{O_2}$ in the animals.

These findings extend and concur with previous studies in which continuous $S\bar{v}_{O_2}$ monitoring was used in critically ill patients.[7–10] $S\bar{v}_{O_2}$ monitoring can supplement traditional cardiorespiratory monitoring by displaying online trends in oxygen supply-to-demand ratio.[10] We have previously shown in patients in the perioperative period that declining $S\bar{v}_{O_2}$ accurately reflects deteriorating oxygen supply–to–demand ratio.[11]

In summary, two systems for continuous monitoring of mixed venous saturation by fiberoptic reflectance spectrophotometry (Oximetrix® and Edwards®) proved useful for clinical approximation of $S\bar{v}_{O_2}$. Both systems correlated well with an *in vitro* reference $S\bar{v}_{O_2}$ (cooximeter), r = 0.88. Deviations of more than 5% from the *in vitro* $S\bar{v}_{O_2}$ occurred in 20% of the measurements with the Oximetrix® system and in 13% of the measurements with the Edwards® system. This should be a warning against uncritical reliance upon the absolute values of *in vivo* measured $S\bar{v}_{O_2}$, and comparison with a standard *in vitro* $S\bar{v}_{O_2}$ measurement is advisable at 12-h intervals. Nevertheless, either system is suitable for immediate bedside monitoring of trends in $S\bar{v}_{O_2}$ in critically ill patients.

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Anesthesiology
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Plasma Bupivacaine Concentrations Following Ilioinguinal-Iliohypogastric Nerve Blockade in Children

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Blockade of the ilioinguinal and iliohypogastric nerves with bupivacaine is a simple procedure that provides prolonged postoperative analgesia in pediatric patients undergoing inguinal herniorrhaphy.[1] Placement of such a blockade following the induction of general anesthesia and prior to skin incision may decrease inhaled anesthetic requirements and lead to quicker awakening and a quiet, more pain-free stay in the recovery room.[2] Bupivacaine (2 mg/kg) has been recommended for ilioinguinal–iliohypogastric nerve blockade in infants and children,[1] but resulting plasma bupivacaine concentrations have not been previously reported. We therefore designed this investigation to determine peak venous plasma concentra-

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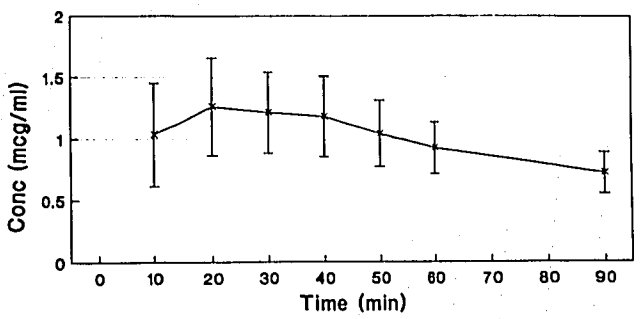

FIG. 1. Plasma bupivacaine concentration following ilioinguinal–iliohypogastric nerve blockade in children. Data are presented as mean ± SD.

tions following the administration of bupivacaine (2 mg/kg) for ilioinguinal–iliohypogastric nerve blockade in children.

MATERIALS AND METHODS

After obtaining informed parental consent and with the permission of our Institutional Review Board, 14 healthy, unpremedicated children scheduled to undergo unilateral or bilateral inguinal herniorrhaphy were enrolled in this study. The patients ranged in age from 13 months to 10 years, and weighed between 9.5 and 36 kg. Anesthesia was induced *via* a mask with oxygen, nitrous oxide, and halothane and followed by the insertion of a 20-gauge iv catheter, which was used both for administration of fluids and withdrawal of blood samples. Dead space in the tubing was cleared by at least three times the volume required for blood to appear in the syringe; a second syringe was then used to obtain the blood sample. All patients received atropine (10 μg/kg iv), and those whose tracheas were intubated were given pancuronium (0.1 mg/kg iv). Unilateral or bilateral ilioinguinal–iliohypogastric nerve blockades (depending on the site of surgery) were performed (by R.H.E.) using epinephrine-free bupivacaine (2 mg/kg) immediately after induction of anesthesia. Bupivacaine 0.25% or 0.50% was selected so that the minimum volume utilized per side blocked was 4 ml. The blockades were placed 2 cm medial and 2 cm superior to the anterior superior iliac crest using a short bevel 22-gauge needle. Patients were monitored following surgery for one hour for signs or symptoms of neurologic or cardiovascular reactions to bupivacaine; all procedures lasted at least 45 min. Blockades were considered to be successful if no analgesics were required in the recovery room.

Heparinized blood samples (3 ml) were obtained at 10-min intervals for the first 60 min following the blockade, with a final sample drawn in the recovery room at 90 min. The samples were centrifuged, and the plasma collected and stored at −20° C until analysis.

Plasma bupivacaine concentrations from the first five patients were measured by high performance liquid chromatography (HPLC) utilizing the method of Weigand and Chou[3] with the following modifications: mobile phase consisted of 37.5% methanol, 62.5% sodium phosphate monobasic (0.05 M), and etidocaine was used as an internal standard. Sensitivity of this assay in our laboratory is 0.05 μg/ml with a coefficient of variation of 6.2% and 3.1% at 0.15 μg/ml and 2.5 μg/ml, respectively. This assay requires 1.0 ml of plasma. The plasma bupivacaine concentrations in the remaining nine patients were measured by HPLC utilizing a slightly different mobile phase (43% methanol, 57% ammonium phosphate [0.1 M]). This assay requires 100 μl of plasma and has a lower sensitivity of 0.05 μg/ml with a coefficient of variation of less than 6% and less than 1% at 0.05 μg/ml and 3 μg/ml, respectively. We found no interference with either assay by any of the other drugs that these patients received.

All bupivacaine concentrations are reported as mean ± SD. Bupivacaine concentrations following unilateral and bilateral ilioinguinal–iliohypogastric nerve blockades were compared using an unpaired t test, with $P < 0.05$ considered significant.

RESULTS

No toxic neurologic or cardiovascular reactions were observed either in the operating room or the recovery room following administration of the blockades. All blockades were judged to be successful because no narcotics or other analgesics were given in the perioperative period and all patients appeared to be pain-free in the recovery room.

Maximum plasma bupivacaine concentrations were observed between 10 and 40 min following the ilioinguinal–iliohypogastric blockade (mean time 26 ± 10 min); the highest individual concentration observed was 2.29 μg/ml (fig. 1, table 1). The mean peak bupivacaine concentration was 1.35 ± 0.35 μg/ml (95% confidence interval 0.66–2.04 μg/ml); each patient's peak bupivacaine concentration was greater than 0.9 μg/ml. The mean peak bupivacaine concentration following bilateral nerve blockades (1.25 ± 0.22 μg/ml) was not significantly different than that following unilateral nerve blockade (1.41 ± 0.40 μg/ml).

DISCUSSION

The threshold arterial plasma concentration of bupivacaine that may cause a seizure in human adults is generally thought to be 4 μg/ml.[4,5] There are no reports in infants or children in which the seizure threshold of bupivacaine has been determined; therefore, we have made an assumption that the value is similar to that in adults. Although venous plasma bupivacaine concentrations may

TABLE 1. Peak Bupivacaine Concentration after Ilioinguinal–Iliohypogastric Nerve Blockade for Herniorrhaphy

Age (yr)	Weight (kg)	% Bupivacaine Injected	Site of Surgery	Peak Concentration (μg/ml)	Time of Peak Concentration (min)
1.2	10.9	0.25	Bilateral	1.41	30
2.1	12.5	0.25	Bilateral	1.54	20
2.2	11.8	0.25	Bilateral	1.19	20
3.2	14.5	0.25	Bilateral	1.12	30
8.0	18.0	0.50	Bilateral	0.91	10
1.1	9.5	0.25	Unilateral	0.99	40
3.0	15.5	0.50	Unilateral	1.28	10
4.5	21.4	0.50	Unilateral	1.11	20
4.6	10.9	0.50	Unilateral	1.27	20
6.0	18.0	0.50	Unilateral	1.76	40
6.6	23.0	0.50	Unilateral	1.68	30
9.0	25.0	0.50	Unilateral	1.06	30
9.8	36.0	0.50	Unilateral	1.27	40
10.0	33.0	0.50	Unilateral	2.29	20
Mean 5.1	18.6	—	—	1.35	26
SD 3.0	8.0	—	—	0.35	10

be as much as 19% lower than simultaneous arterial concentrations,[6] it is unlikely that even the peak bupivacaine concentration observed in this study (2.29 μg/ml) could result in a convulsion. However, mild to moderate CNS excitation can be evident in some adult patients at bupivacaine concentrations as low as 1.6 μg/ml.[7] Such reactions (*e.g.*, perioral numbness, disorientation, muscle twitching, nystagmus, slurred speech, lightheadedness, *etc.*) would not pose a clinical problem during general anesthesia but could potentially cause difficulties in the recovery room. If the ilioinguinal–iliohypogastric nerve blockade is performed prior to the start of surgery, in most cases bupivacaine concentrations will be below 1.6 μg/ml by the time the patient is admitted to the recovery room. However, if the ilioinguinal–iliohypogastric blockade with bupivacaine is given by the surgeon near the end of surgery, the peak concentration will occur postoperatively and mild neurologic reactions in the recovery room are possible. For this reason we advocate performing the blockade at the beginning rather than at the end of the surgical procedure.

The mean peak venous plasma bupivacaine concentration reported in our study (1.35 ± 0.35 μg/ml) was slightly higher than that reported after the caudal administration of epinephrine-free bupivacaine (2.5 mg/kg) in children (1.25 ± 0.54 μg/ml).[8] Following caudal injection uptake of bupivacaine resulted in peak concentrations between 10 and 40 min, just as observed in our study. We were unable to make a direct comparison with uptake of bupivacaine following intercostal blockades in children as reported by Rothstein *et al.*[9] due to their addition of epinephrine to the local anesthetic and sampling arterial whole blood. However, based on the venous arterial and whole blood plasma bupivacaine ratios they observed,[9] we estimate that the peak venous plasma concentrations we obtained would be similar to those following intercostal blockades using bupivacaine (2–3 mg/kg with 1:200,000 epinephrine). Uptake from the intercostal sites was considerably more rapid, however, with peak concentrations occurring approximately 10 min following the block.

Although plasma bupivacaine concentrations achieved during an intersample period may have been higher than the peak concentrations measured, the area into which the ilioinguinal–iliohypogastric nerve blockade is placed is not highly vascular, and the rise, plateau, and slow fall in bupivacaine concentrations we observed leads us to conclude that the intersample peak concentrations would not be much higher than those observed.

In the absence of kinetic data demonstrating the safety of larger amounts of bupivacaine, a dose greater than 2 mg/kg of plain bupivacaine cannot be recommended. Consideration should be given to routinely adding epinephrine to minimize systemic absorption of this drug.[10]

Extrapolation of our findings to infants younger than 13 months should be made with some caution, because no patients younger than 13 months were studied. However, we have never observed any signs or symptoms of neurotoxicity in patients less than one year of age following ilioinguinal–iliohypogastric nerve blockades with bupivacaine (2 mg/kg).

In summary, we have determined that bupivacaine (2 mg/kg) injected percutaneously for ilioinguinal–iliohypogastric nerve blockades in children results in peak plasma venous concentrations below the estimated adult convulsive concentration of bupivacaine. Based on the peak bupivacaine concentrations that developed and the absence of any observed CNS toxicity, a dose of 2 mg/kg appears to be safe in children older than 12 months.

However, because of the potential of mild nervous system toxicity at peak concentrations measured, we recommend that a 2 mg/kg dose of plain bupivacaine for ilioinguinal–iliohypogastric nerve blockade not be exceeded, that strong consideration be given to using bupivacaine with epinephrine, and that the blockade preferably be performed near the beginning of the surgical procedure.

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Anesthesiology
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Refractory Bradycardia during Aspiration of a Tracheal Cyst in a Young Infant

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We recently anesthetized an infant with an unusual cause of stridor, a bronchogenic cyst, who also developed severe intraoperative bradycardia, which did not respond to iv atropine despite the absence of hypoxemia.

Case Report

A 7-week-old, 4.2-kg infant born at 42 weeks gestation was scheduled for diagnostic bronchoscopy. Soon after birth she became stridorous without other evidence of respiratory distress. Her parents were told that she had a "floppy" airway and would outgrow the problem.

After discharge she was occasionally stridorous when agitated. This was intermittently accompanied by gasping respirations, tachypnea, and peripheral cyanosis. At four weeks of age the patient had an apneic spell and was admitted to another institution. She was stridorous with an intermittent cough. A chest radiograph and barium swallow were unremarkable. She was referred to our institution for further evaluation and scheduled for elective bronchoscopy.

On examination she appeared to be a healthy 4.2-kg infant without stridor, tachypnea, retractions, or cyanosis. The vital signs were unremarkable. The external airway was normal in appearance, breath sounds were equal and clear, and the remainder of the physical examination was equally unremarkable. The hemoglobin content was 12 g/dl. Atropine 0.1 mg im was used as premedication. Intraoperative monitoring included a precordial stethoscope, ECG, pulse oximeter, and blood pressure cuff. Induction of anesthesia was performed by inhalation of nitrous oxide, halothane, and oxygen without difficulty. We encountered no problems with ventilation, and the pulse oximeter indicated 100% saturation. A 22-gauge iv line was started and the N_2O discontinued. The trachea and vocal cords were topically anesthetized with 4% lidocaine administered by atomizer. With the patient spontaneously breathing, a Hopkins rod–glass telescope was introduced without difficulty, revealing a large midtracheal cyst originating from the right posterolateral wall occluding 80% of the trachea. The telescope was then removed and a Storz® ventilating bronchoscope was passed easily. Equal bilateral breath sounds and chest expansion were obtained with assisted ventilation *via* the bronchoscope side port. A needle was introduced through the bronchoscope and 7–10 ml of fluid aspirated. Prior to aspiration the systolic blood pressure was 80 mmHg and the heart rate 140 beats/min. With aspiration the heart rate acutely fell to 50 beats/min and the systolic blood pressure to 50 mmHg. The pulse oximeter showed 100% saturation. No P-waves could be seen on the ECG, indicating a nodal rhythm. Controlled ventilation revealed bilateral breath sounds. Atropine 0.1 mg (~25 μg/kg) was immediately administered iv. When no response was seen after 60 s an equal dose of atropine was repeated. Again no response was noted after another minute. Because of continuous bradycardia and hypotension, epinephrine 50 μg (~10 μg/kg) was given iv, with an immediate increase in heart rate to 180 beats/min and systolic blood pressure to 80 mmHg. Repeat tracheoscopy revealed a decompressed cyst and posterior tracheomalacia.

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