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Spinal Anesthesia in Premature Infants Recovering from Respiratory Distress Syndrome

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Reports of spinal anesthesia in children date back to the early part of this century. However, the technique has not achieved widespread popularity and its use has been infrequent.[1–5] We have experience with this technique in 20 premature infants undergoing inguinal hernia repair who were recovering from various stages of respiratory distress syndrome (RDS). Our objective was to avoid endotracheal intubation and general anesthesia with the possible hazard of postoperative apnea requiring mechanical ventilation. We also measured sensory evoked potentials (SEP) in eight patients before, during, and after administration of the spinal anesthetic to document its onset, duration, and recovery.

METHODS

Only premature infants undergoing inguinal hernia repair were selected for spinal anesthesia and SEP monitoring. Appropriate informed consent was obtained from the parents. These patients had a gestational age of less than 36 weeks and one or more of the following characteristics: 1) a history of respiratory distress requiring at least 1 week of mechanical ventilatory support; 2) current enrollment in our apnea monitoring program; 3) bronchopulmonary dysplasia (BPD) documented by radiographic or pathological means (table 1). Patients with a history of severe intracranial hemorrhage (Papile's grades III and IV), with or without hydrocephalus, were excluded. No upper age limit was placed on postconceptional age if the patient continued to exhibit resolved respiratory disease at the time of surgery.

After insertion of a venous canula and appropriate monitoring devices, lumbar puncture was performed with the use of a 1.5 inch 22-gauge spinal needle after infiltration with 1% lidocaine. Hyperbaric tetracaine (1% without epinephrine) was administered below the third lumbar interspace with a dose range of 0.24–0.65 mg/kg. Oxygen and nitrous oxide were administered to some of these infants as required for sedation during lumbar puncture. The spinal anesthetic was considered to be completely successful if the child was assessed to be free of pain during the procedure and if no supplemental agents, other than brief periods of nitrous oxide, were necessary for sedation. Some blocks, although initially adequate, later required supplementation, because surgery exceeded the duration of analgesia. In these cases either 1% lidocaine was injected into the surgical field or less than 0.5% halothane was administered via face mask. If the spinal anesthetic was unsatisfactory through the entire procedure, ketamine was given iv to supplement it.

Neurophysiologic changes were documented using serial short latency sensory evoked potentials elicited with posterior tibial nerve stimulation. Standard recording methods were used from the scalp according to the International 10–20 system. Stimulation current was adjusted to minimal twitch of the foot in the range of 5–10 mA with a frequency of 5/s. The amplitudes and latencies of the early P_1N_2 waves were serially recorded using the Nicolet Ca1000®. Monitoring continued up to 3 h into the recovery period.

RESULTS

Twenty infants underwent 21 inguinal hernia repairs using spinal anesthesia. One child required reoperation for a recurrent hernia (patients 10 and 13, table 1). All patients had significant RDS in the immediate postnatal period and all had episodes of apnea. Twelve of the 20 patients had radiographic and clinical evidence of BPD. Eleven patients were younger than 44 weeks postconceptional age, and eight patients were under 2,500 g in weight. One patient had a recent history of pneumonia, necessitating reintubation of the trachea and mechanical ventilation for a period of 3 weeks. His hernia was repaired 5 weeks after extubation of the trachea (patient 19).

Other preoperative medical history is shown in table 1. Supplementation of the spinal anesthetic was necessary for several patients. One, in whom the spinal blockade was clearly unsatisfactory, received ketamine. One patient

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TABLE 1. Patient Profiles

Patient	Gestational Age in Weeks	Birth Weight (g)	Postconceptual Age (weeks)	Weight at Time of Surgery	Preoperative Medical Management
1	27	880	41	2,280	HAM, steroids, diuretics
2	31	1,600	35	2,400	HAM
3	29	900	51	3,500	HAM
4	32	960	46	5,900	HAM
5	26	1,000	39	2,000	ICN, diuretics
6	26	890	36	2,800	ICN, AM
7	26	770	38	1,920	ICN, diuretics
8	26	880	42	3,500	HAM, steroids, diuretics
9	26	770	38	2,500	ICN, steroids, diuretics
10*	27	850	52	3,100	HAM, O_2, steroids, diuretics
11	28	1,120	45	4,500	HAM, diuretics
12	30	1,230	38	3,190	HAM, theophyllin
13*	27	850	73	5,100	HAM, O_2
14	32	920	44	2,200	ICN, AM
15	26	660	78	3,600	ICN, IMV
16	28	1,240	40	1,820	ICN, steroids, diuretics
17	28	1,000	40	4,500	HAM, theophyllin
18	27	970	51	4,450	HAM
19	32	2,610	52	4,400	IMV, pneumonia
20	27	770	40	1,700	ICN, AM, theophyllin
21	31	2,600	45	3,700	HAM
Mean SD	28.19 ± 2.2	1,117 ± 535	45.90 ± 11.2	3,288 ± 1,155	

HAM = home apnea monitor; AM = apnea monitor; ICN = intensive care nursery; IMV = intermittent mandatory ventilation.

* Same patient requiring repeat surgery.

required a second dose of tetracaine because of unexpected delay in starting the surgery; another received a second dose because the level of analgesia was demonstrably too low for the procedure. Two patients, early in the series, received a local anesthetic (0.5% lidocaine) supplement at the second hernia site, and three were given halothane (up to 0.5%) via a mask toward the end of the procedure (table 2). Five of the eight patients who required some form of supplemental anesthesia were given a dose of tetracaine that we now consider insufficient for the particular weight group. The patients had a mean birth weight of 1,117 g and a mean weight at surgery of 3,288 g; they were given a mean dose of tetracaine of 0.41 mg/kg. The mean duration of surgery was 51.5 min, and the mean duration of the blockade was 71.5 min (table 3).

The only intraoperative complication was apnea and bradycardia in one patient following injection of the tetracaine. This infant had a history of frequent apnea before surgery. Endotracheal intubation and ventilatory assistance were instigated while excessively high block was excluded. Extubation was possible immediately following the procedure, and no further complication occurred. The solitary postoperative complication was also apnea, developing 8 h after the procedure in a patient with a temperature of 34.2° C (patients 6 and 8, table 1). Intubation and 24 h of ventilatory assistance were required for this child. No children experienced cardiovascular instability and no instances of excessively high blockade were appreciated. In eight patients the SEPs were recorded. The preoperative tracings were appropriate in all cases for the maturity of the infant, each displaying a well-defined P_1N_2 wave form. With the onset of spinal block, all wave formation disappeared. A gradual return of SEP was observed as the block dissipated, and the latency in all eight patients returned to the preoperative level within 3 h from the time the block was first inserted. As delay in short latency time is indicative of neurophysiologic disturbance, this additional information was considered useful in assessing the termination of the block.

TABLE 2. Summary Results of 21 Spinal Anesthetics

Patients	20
Spinals	21
No. requiring second spinal	2 (9.5%)
Unsuccessful spinals	1 (4.8%)
No. requiring supplementation	5 (23.8%)
No. complications	2

TABLE 3. The Dose of Tetracaine in Milligrams per Kilogram and the Duration of Surgery and Anesthesia

No. of procedures	21
Weight in grams	3,288 ± 1,185
mg/kg	0.41 ± 0.12
Total dose	1.24 ± 0.18
Duration of surgery	51.5 ± 20.4
Duration of blockade	71.5 ± 14.09

Values are mean ± SD.

Discussion

Sporadic reports on spinal anesthesia in children have appeared since the turn of the century,[1,2] and until 1951 amethocaine (2% to 5%) and lidocaine (4%) were the most common drugs used.[3–5] In 1951, Berkowitz and Green[6] introduced hyperbaric tetracaine, and subsequent reports have appeared using this agent and lidocaine.[7–10] Calvert[11] reported the use of spinal anesthesia in 26 newborns for meningomyelocele repair. Abajian *et al.*[12] reintroduced subarachnoid blockade in children, including high-risk premature infants. Premature infants are predisposed to apnea, hypoxia, and cardiovascular instability. Respiratory complications occur most frequently.[13] Residual abnormalities were most marked and prolonged after mechanical ventilation and extended into the second year of life.[14] Infants with BPD have poor pulmonary compliance due in part to interstitial fibrosis and they tend to retain fluid.[15] These infants may require steroids and diuretics for successful weaning from ventilatory support, although the latter is a potential source of complication in itself. General anesthesia with the use of inhaled anesthetics or muscle relaxants and narcotics increase the incidence of postoperative apnea attacks. This incidence has been reported by Gregory[16] as 25%. Steward[13] described six postoperative apneic episodes that occurred among 33 premature infants undergoing inguinal hernioraphy. Liu *et al.*[17] found that in 41 premature infants recovering from various types of surgery, eight required reintubation solely for postoperative apneic attacks as opposed to those of their patients who were electively ventilated because of the major nature of the surgery. This has prompted Gregory and Steward to recommend in a recent editorial[18] avoiding elective surgery in children younger than 44 weeks of postconceptional age, although emphasizing the urgent nature of inguinal hernia repair. Episodes of incarceration often demand that a hernia be repaired earlier, and, in fact, the morbidity of inguinal hernias can be reduced by performing the repair early, often before these children are discharged from the intensive care nursery.

General anesthesia exerts a potentially adverse effect on the postoperative course of these infants through a variety of mechanisms. Halothane depresses the chemoreceptor response to hypoxia,[20] enhances paradoxial rib cage movement and distortion prevalent in infants, and contributes to intercostal muscle fatigue by preferential depression of the spinal intercostal neuron pool.[21] Although the diaphragm is more resistant to depressant agents than the intercostal muscles, its ability to sustain contraction is limited even in the term infant because of the low percentage of high oxidative fibers.[22] Prematurity and superimposed lung disease further limit effective respiratory function. Other complications related to general anesthesia and intubation include atelectasis, aspiration, extubation stridor, and depression of baroreceptor response by halothane.[23]

A distinct relationship has been found between the severity of BPD and the length of intubation and mechanical ventilation following RDS. Histologic changes in the air passages differing from the effect of high inspired oxygen concentration have been identified. A temporal relationship exists between the severity of these changes and the length of intubation.[24]

Endotracheal intubation and ventilation beyond 24 h often worsen the existing lung pathology. Complications ranged from mild squamous cell metaplasia in the trachea to more severe histologic changes and infectious episodes.[25,26] According to Rhodes *et al.*,[27] such changes were not seen in infants who were ventilated via a mask alone. Although no evidence exists that a brief period of intubation during general anesthesia causes lasting damage to the air passages, these reports suggest that infants who require continued postoperative mechanical ventilation because of apneic attacks suffer a setback in the already slow recovery from residual lung disease. Recognizing these risk factors, we were encouraged by the work of Abajian *et al.*[12] to search for an alternative technique.

Patients in our series underwent hernia repair as early as the 35th postconceptional week of age and as late as the 78th week. The latter patient had severe unresolved lung disease requiring intermittent mandatory ventilation (patient 15, table 1). Eight patients had not yet been discharged from the intensive care nursery. Eleven were receiving drugs for management of their residual lung disease, and all were on the apnea monitoring program. The average weight at surgery was 3,240 g (1,820–5,900 g), and the mean postconceptional age was 46.4 weeks (35–78 weeks). The wide range in values in these values underscores the diversity of this group of patients consistent with the spectrum of lung disease.

Tetracaine is a safe and effective agent for spinal anesthesia. Berkowitz and Green[6] recommended 0.2 mg/kg of hyperbaric tetracaine, but this study did not include children under 2 years of age. Abajian *et al.*[12] quotes 0.32 mg/kg for "high-risk" infants with an average weight of 3,420 g (±250 g) and 0.22 mg/kg for infants who weigh more (4,740 ± 260 g). The total dose varied from 1.0 to 1.2 mg for lower limb, perineal, and abdominal procedures that included inguinal hernia repair. We found that using the above dose range and not exceeding 1.2 mg did not always provide sufficiently high levels or durations of anesthesia. This difference may be explained, in part, by the larger proportion of infants under 3,000 g in our series (table 1) and the uniformity of the surgical procedure. In our series, a total dose of up to 0.65 mg/kg in the lowest group was associated with the best results, as this patient group neither received supplementation nor experienced signs of overdosage. The duration of surgery

and spinal blockade was measured from the insertion of tetracaine to the reappearance of hip flexion, as the earliest indicator of returning motor function, this averaged 70 min (±14 min) (table 3).

Establishing the upper level of anesthesia by response to needle prick is difficult because of the natural irritability of these patients. A successful blockade is recognized when these patients do not react to surgical stimulation with sustained crying and are easily comforted by a pacifier or a brief period of nitrous oxide administration. We encountered two respiratory complications (table 2). The incident of intraoperative apnea occurred in an infant who suffered a dozen such monitored episodes during any 24-h period. There were no signs and symptoms of tetracaine overdose, and endotracheal intubation was performed (patient 6, table 1). The single postoperative apneic episode occurred 8 h after full recovery from the spinal anesthetic when the patient became hypothermic (T 34.2° C). A casual relationship does not appear to exist with the spinal anesthetic itself (patient 8, table 1).

It must be emphasized that with this technique, as with general anesthesia, postoperative monitoring is imperative because postoperative apnea may occur irrespective of the anesthetic technique used.

We have used SEP monitoring in eight patients in this series. Somatosensory evoked potentials have been shown to be reliable indicators of ascending sensory pathway dysfunction in children.[28] Moreover, the maturation of the central nervous system can be followed by serial SEPs in the premature as well as in early infancy. The short latency SEP is well defined and correlates with maturity.[29,30] Measurement of this latency before and after spinal anesthesia allows the observer to detect adverse changes in afferent sensory pathways. This would be indicated by a change in the amplitude and latency of the potential. In the patients studied to date with this technique, the SEP latencies have returned to baseline value within 3 h; at this time by gross neurologic assessment there was full return of motor function in the legs. It is encouraging that the onset and reversible nature of such blockade can be recorded in the clinical setting by an electric marker.

We conclude that subarachnoid blockade with hyperbaric tetracaine for the repair of inguinal hernias is a satisfactory alternative to general anesthesia in our hands for selected premature infants. This method of anesthesia may avoid the increased incidence of postoperative respiratory complications associated with general anesthesia and reduce the requirement for postoperative mechanical ventilatory support. It does not change the need for intensive postoperative monitoring. Infants in the 2,000–3,000-g weight range require higher doses of tetracaine compared with those more than 3,000 g. SEP monitoring perioperatively may provide further information on the physiology of the premature infants' nervous systems in response to spinal anesthesia.

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Comparison of Alfentanil with Fentanyl for Outpatient Anesthesia

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Alfentanil (Alfenta®) is a new, rapid and short-acting synthetic analog of fentanil that may offer advantages over the parent compound in the outpatient surgery setting.[1,2] Previous authors have described the use of this new opioid compound by either repeated injection or continuous administration as a supplement to nitrous oxide.[1–3]

The administration of ketamine or fentanyl by continuous infusion provided for more precise regulation of anesthetic or analgesic dose, and hence drug effect, when compared with conventional intermittent injection techniques.[4] The continuous infusion technique lessened the total amount of drug administered and thereby decreased recovery times for outpatients. The present study was designed 1) to compare the clinical effects and therapeutic concentration ranges for alfentanil and fentanyl when administered with nitrous oxide for maintenance of anesthesia during brief outpatient surgical procedures; and 2) to determine whether a continuous infusion of alfentanil (or fentanyl) would offer any advantages over the traditional intermittent injection technique.

MATERIALS AND METHODS

After informed consent was obtained, 100 healthy (ASA physical status I or II) young women presenting for midtrimester therapeutic abortion by dilatation and extraction were randomly assigned to one of four treatment groups: Group 1—fentanyl bolus (FB), n = 25; Group 2—fentanyl infusion (FI), n = 25; Group 3—alfentanil bolus (AB), n = 25; Group 4—alfentanil infusion (AI), n = 25.

This double-blind, open-parallel protocol was approved by the local institutional review board. The surgeon, anesthesiologist monitoring the patient,§ physician–observer, and patient were unaware of which analgesic drug was being administered. The four groups were comparable (mean ± SEM) with respect to age (25 ± 3 yr), weight (63 ± 4 kg), and gestation (16 ± 1 week). Before surgery, patients were asked to complete a baseline Trieger test[5] (used to measure psychomotor function[6]) and a series of analog scales[7] (Appendix 1), which were used to assess the degree of pain and sedation.

These unpremedicated outpatients were taken to the operating room, where an 18-gauge intravenous catheter was inserted into a forearm vein and routine monitoring devices were applied (*e.g.*, Dinamap® blood pressure cuff, precordial stethoscope, and ECG). All patients were administered droperidol, 0.625 mg iv. In addition, Groups 1 and 2 received fentanyl, 100 μg iv, and Groups 3 and 4 were given alfentanil, 500 μg iv, as a loading dose 2–3 min before induction of anesthesia.

In all groups, anesthesia was induced with thiopental, 4 mg/kg iv (over 30–60 s), and when the patient became unresponsive (*i.e.*, loss of eyelid reflex), nitrous oxide (N_2O) 70% in O_2 was administered *via* a tight-fitting face mask with the use of conventional circle absorber system. When the patient resumed spontaneous ventilation, a maintenance infusion of fentanyl (Group 2) or alfentanil

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§ The opioid solutions were prepared so that the anesthesiologist administering the drugs used similar volumes for the bolus injections (*e.g.*, fentanyl 50 μg/ml or alfentanil 250 μg/ml) and the maintenance infusions (*e.g.*, fentanyl 2 μg/ml or alfentanil 10 μg/ml).