Post-operative recovery after inguinal herniotomy in ex-premature infants: comparison between sevoflurane and spinal anaesthesia


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We prospectively studied the post-operative recovery profile of 28 ex-premature infants undergoing inguinal herniotomy. All infants had a post-conceptual age of less than 46 weeks at the time of surgery and were randomized to receive either sevoflurane (group 1, 14 patients) or spinal anaesthesia (group 2, 14 patients). All patients received supplemental caudal analgesia before skin incision. Cardiorespiratory function was continuously recorded in all patients before and after surgery. A blinded observer analysed each paired recording for predefined episodes of apnoea, hypoxaemia or bradycardia and the reports were used to compare the two groups. Spinal anaesthesia was attempted unsuccessfully in four patients in group 2. Five patients in group 1 demonstrated an ‘excess’ number of episodes (median 4, range 3–12) of clinically silent post-operative cardiorespiratory complications. (‘Excess’ in our study was defined as a 3-fold or greater increase in the number of post-operative episodes of bradycardia or apnoea relative to pre-operative occurrence). Three of these patients had pre-existing abnormal respiratory function and accounted for 80% of the episodes (26/32) of post-operative bradycardia and all five episodes of post-operative apnoea identified. All episodes of bradycardia and apnoea were temporally unrelated. None of the remaining patients in group 2 demonstrated an unacceptable number of post-operative cardiorespiratory complications. Our limited study suggests that general anaesthesia with an inhalational agent such as sevoflurane may induce or unmask abnormalities of cardiopulmonary function in predisposed infants. Spinal anaesthesia may be preferable but it is potentially stressful for the infant and associated with a clinically significant failure rate.

Accepted for publication: October 16, 2000

Keywords: anaesthesia, paediatric; anaesthetics volatile, sevoflurane; anaesthetic techniques, subarachnoid

Inguinal hernias are common in former pre-term infants and require early repair to avoid the risks of incarceration. However, the risk of life-threatening apnoea after surgery is significant in this group regardless of the anaesthetic technique used. The reported incidence of post-operative respiratory dysfunction ranges from 20 to 50% and reflects the variation in both anaesthetic technique and study design. Spinal anaesthesia appears to reduce the risk of respiratory dysfunction but does not abolish it. Moreover, the technique requires considerable expertise, is contraindicated in some infants, has a reported failure rate of 10–20%, and can be of insufficient duration for surgery. As a result, the technique may need to be abandoned or supplemented with sedatives or anaesthetic agents, negating any potential benefits. Therefore, despite the perceived advantages of this approach, awake spinal anaesthesia has not gained universal acceptance amongst paediatric anaesthetists and many institutions have rejected it. The introduction into paediatric practice in the UK of sevoflurane and desflurane with their properties of enhanced recovery characteristics may offer a more practical solution. In neonates undergoing pyloromyotomy, it has been observed that recovery after desflurane is twice as fast as isoflurane with less post-operative ventilatory disturbance. Sevoflurane has similar recovery characteristics but unlike desflurane provides excellent conditions for inhalation induction.

We therefore designed a prospective, randomized pilot study that would reflect both clinical practice at our institution and explore the hypothesis that the ‘recovery...
profile’ after sevoflurane anaesthesia is comparable with that after spinal anaesthesia. With neither group experiencing an increase in the number of episodes of apnoea, hypoxaemia or bradycardia relative to pre-operative levels.

Patients and methods

After obtaining Ethical Committee approval and informed parental consent we studied 28 patients undergoing inguinal herniotomy. All infants had been born at less than 36 weeks gestation and had a post-conceptual age (PCA) of less than 46 weeks at the time of surgery. Infants with pre-existing cardiac, neuromuscular or metabolic diseases were excluded from participation in the study. Pre-operative haemoglobin concentration and a history of ‘pre-existing abnormal respiratory function’, with or without an on-going requirement for supplemental oxygen therapy, were noted (Tables 1 and 2). We defined ‘pre-existing abnormal respiratory function’ as the persistence of clinical features of respiratory distress in association with an abnormal chest radiograph beyond the first 28 days of life, either occurring alone or in combination with a ‘current’ history of apnoea (i.e. episodes witnessed within the 2 weeks before surgery).

Patients were allocated randomly, using random number tables, to receive either sevoflurane anaesthesia with caudal analgesia (group 1) or awake spinal anaesthesia with caudal analgesia (group 2). No sedative pre-medication was administered but all patients received paracetamol 15 mg kg\(^{-1}\) per rectum 1 h before surgical incision.

In group 1, general anaesthesia was induced with a 2 MAC equivalent value for age of sevoflurane in 100% oxygen (1 MAC=3.2% in neonates).\(^{14,15}\) Atracurium 0.5 mg MAC equivalent value for age of sevoflurane in 100% surgical incision) and ‘incision to closure’ times were recorded for both patient groups (Table 1). We defined ‘pre-existing abnormal respiratory function’ as the persistence of clinical features of respiratory distress in association with an abnormal chest radiograph beyond the first 28 days of life, either occurring alone or in combination with a ‘current’ history of apnoea (i.e. episodes witnessed within the 2 weeks before surgery).

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In group 2, spinal anaesthesia was established with 0.5% bupivacaine 1 mg kg\(^{-1}\). Patients were placed in the left lateral position and a 25-gauge short bevelled spinal needle inserted in the midline through either the fourth or fifth lumbar interspace until free flowing cerebrospinal fluid was obtained. To ensure that the groups were comparable to one another in terms of the duration and intensity of analgesia provided in the initial post-operative period, both patient groups received before skin incision a single injection of 0.25% bupivacaine 2 mg kg\(^{-1}\) through a 22-gauge cannula inserted into the caudal epidural space.\(^{16,17}\) ‘Induction to incision’ (group 1, start of gaseous induction to surgical incision; group 2, skin penetration with spinal needle to surgical incision) and ‘incision to closure’ times were recorded for both patient groups (Table 1).

Upon completion of skin closure, sevoflurane administration in group 1 was discontinued and residual neuromuscular block antagonized with neostigmine 50 μg kg\(^{-1}\) and glycopyrrolate 10 μg kg\(^{-1}\).

### Table 1 Patient characteristics and intra-operative data. A comparison of post-conceptual age (PCA), gestational age (GA), weight (Wt), pre-operative haemoglobin (Hb) and anaesthetic time (induction–skin closure) for the two groups (median [range]). There was no significant difference between the groups with regard to and variable. \(n=\text{number of patients}\)

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>Group 1 ((n=14)) sevoflurane</th>
<th>Group 2 ((n=10)) spinal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incision–closure (min)</td>
<td>26 [10–45]</td>
<td>28 [12–48]</td>
</tr>
<tr>
<td>Bilateral repairs (a)</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Pre-op 12 h</td>
<td>Post-op 12 h</td>
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</table>

All patients were monitored for a 12 h period pre- and post-operatively using a portable three channel continuous cardiorespiratory monitor (Nellcor Puritan-Bennett EdenTrace II Plus) with internal memory multi-channel recorder interfaced with an EdenTec 3310 Assurance monitor. This integrated monitoring system provided continuous contemporaneous recordings of respiratory effort and pattern (impedance pneumography/airflow thermistor), heart rate (ECG) and haemoglobin oxygen saturation (pulse oximeter) for each patient. In order to allow each patient to

### Table 2 Number of episodes of pre- and post-operative apnoea and bradycardia recorded in each subject. \(a, \text{apnoea lasting } 15 \text{s or longer;} b, \text{bradycardia (less than } 100 \text{ beat min}^{-1}\) for at least 5 s. \(Y, \text{yes;} N, \text{no.} \)

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>Group</th>
<th>Abnormal respiratory function/oxygen therapy</th>
<th>Number of episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-op 12 h</td>
<td>Post-op 12 h</td>
<td></td>
<td></td>
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</table>

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act as their own control, those infants presenting for surgery with an on-going oxygen requirement were prescribed a constant flow rate of supplemental nasal oxygen for the duration of the perioperative period of cardiorespiratory monitoring (Table 2).

Using the following analysis criteria, each computer-generated printout was individually analysed for evidence of either movement artefact or electrode dislodgement by an investigator (J.M.W.) blinded to the anaesthetic technique used. An event was defined as being a result of an artefact if one or both of the following occurred: (1) one or more of the above waveforms out of range or unrecognizable and (2) a $\text{SpO}_2$ less than 90% for more than 20 s with no associated bradycardia or apnoea.

Clinical significance was defined as a bradycardia of less than 100 beat min$^{-1}$ for at least 5 s, a haemoglobin oxygen saturation ($\text{SpO}_2$) of less than 90% for more than 10 s and apnoea as a sustained respiratory pause of 15 s or longer, or less than 15 s if accompanied by an $\text{SpO}_2$ less than 90% or bradycardia. These manually validated reports, in which each subject acted as their own control, were then used to draw comparisons between the two groups in terms of the number of ‘excess’ post-operative cardiorespiratory complications recorded. ‘Excess’ in our study was defined as a 3-fold or more increase in the number of post-operative episodes of bradycardia or apnoea relative to pre-operative occurrence.

In accordance with departmental guidelines regarding the routine post-operative observation and care of infants potentially at risk of respiratory dysfunction, real-time apnoea monitoring (Graseby MR10 respiration monitor) in combination with nurse observation was undertaken for all study patients in the post-operative period.

In view of the small sample size, data are reported as median (range). Comparison of cardiorespiratory changes within and between groups (Table 3) was performed using the Mann-Whitney $U$ test. A $P<0.05$ was considered statistically significant.

**Results**

Twenty-eight patients were recruited into the study. Both groups were comparable in terms of PCA, gestational age (GA), weight (Wt), pre-operative haemoglobin level (Hb) and anaesthetic time (induction–skin closure) (Table 1).

Table 3 Comparison of median [range of medians] pre- and post-operative cardiorespiratory changes within and between the groups. There was no statistically significant difference either within or between the groups ($P>0.05$). *Patient 22

<table>
<thead>
<tr>
<th></th>
<th>Sevoflurane group 1 ($n=14$)</th>
<th>Spinal group 2 ($n=10$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-op</td>
<td>Post-op</td>
</tr>
<tr>
<td>$\text{SpO}_2$ (%)</td>
<td>97 [88*–99]</td>
<td>97 [90*–100]</td>
</tr>
<tr>
<td>Per cent time $\text{SpO}_2$ &lt;90%</td>
<td>6 [1–63*]</td>
<td>6 [0–48*]</td>
</tr>
</tbody>
</table>

Five patients (four receiving supplemental oxygen) in group 1 and four patients (three receiving supplemental oxygen) in group 2 fulfilled the study definition of ‘pre-existing abnormal respiratory function’ (Table 2). No patients had a current history of apnoea or were receiving respiratory stimulants in the 2-week period before surgery.

Spinal anaesthesia was attempted unsuccessfully in four patients in group 2 (28% failure rate). All had normal respiratory function and went on to have their surgery successfully completed under general anaesthesia but were excluded from further analysis.

Median pre- and post-operative values for heart rate, $\text{SpO}_2$, relative duration of a decrease of $\text{SpO}_2$, (per cent time
SpO2 less than 90%) and number of episodes of desaturation (SpO2 less than 90% h⁻¹) in group 1 were comparable to values recorded in group 2 (Table 3).

In group 1, three out of the five patients with pre-existing abnormal respiratory function and two out of the nine patients with normal respiratory function experienced an excess of post-operative cardiorespiratory complications (Table 2). In contrast, none of the 10 patients in group 2 exhibited an excess of post-operative complications when compared with their respective pre-operative recordings (Fig. 1).

Table 4 relates the total number of post-operative episodes of apnoea and bradycardia recorded to the pre-operative respiratory function of those patients in group 1 identified as exhibiting an excess of post-operative cardiorespiratory complications (Table 2). The three patients with abnormal respiratory function accounted for 80% of the episodes (26/32) of post-operative bradycardia and all five episodes of post-operative apnoea identified. All recorded episodes of apnoea (five in group 1 and two in group 2) were temporally unrelated to the recorded episodes of bradycardia and haemoglobin oxygen desaturation (SpO2 less than 90%) (Tables 2 and 3).

One patient in group 1 (patient no. 22), presented for surgery with a median SpO2 less than 90%. This level of hypoxaemia persisted throughout the post-operative period and accounted for the wide range in the duration of hypoxaemia (median per cent time SpO2 less than 90%; 63 versus 48%) recorded for each study period (Table 3).

The concurrent use post-operatively, as per hospital policy, of real-time apnoea monitoring in combination with nurse observation failed to detect any of the above recorded episodes of cardiorespiratory disturbance. All resolved spontaneously without intervention.

Discussion
We have endeavoured to design a study that reflects as closely as possible clinical practice at The Royal Hospital for Sick Children in Bristol. After the work conducted at our institution by Peutrell and Hughes, a combined approach of separate spinal and caudal epidural injections has been the preferred method of anaesthesia for those infants presenting for lower abdominal surgery who are thought to be at risk of post-operative cardiorespiratory complications.17 We have found this approach provides anaesthesia of a sufficient quality and duration to permit the completion of bilateral inguinal herniotomies without the need for additional incremental boluses of local anaesthetic. The dosing regime (bupivacaine 3 mg kg⁻¹) in the awake-spinal–caudal group has been used without untoward sequelae at our institution for at least the last decade. It is less than the 3.8 mg kg⁻¹ dose used by Gunter and colleagues16 to establish single injection caudal epidural anaesthesia and compares favourably with the mean total dose of bupivacaine 2.8 mg kg⁻¹ (range 2.5–3.7 mg kg⁻¹) used by Peutrell and Hughes in their study of a combined spinal–epidural technique.17

Several studies to date have determined that the incidence of clinically significant post-operative apnoea falls exponentially with time from the completion of surgery.2,6,19 Proposed aetiological factors for this include the hang-over effect of residual anaesthetic agents combined with an elevated plasma level of circulating endorphins. The contribution of the latter is in turn related to the intensity and duration of the surgical insult.5,19 By attempting to ensure that both groups were comparable in terms of the duration and intensity of analgesia provided, we hoped to be able to detect in the initial post-operative period any excess cardiorespiratory complications attributable to residual anaesthesia alone.

The results of our pilot study suggest that despite the enhanced recovery characteristics of sevoflurane, the recovery profile in this vulnerable age group may not be comparable to that of ‘awake’ spinal anaesthesia in all infants. However, balanced against this, was our inability to establish spinal anaesthesia in four subjects (28%), despite the technique being performed by experienced paediatric anaesthetists. This highlights the considerable expertise and practice required and is one of the primary reasons why the seemingly advantageous procedure of spinal anaesthesia has not gained universal acceptance in many paediatric institutions.3,17 These findings need to be interpreted within the context of the limited size of the study and, therefore, require further comment.

Viewed as a whole, the recovery profile of both groups appeared comparable with neither group experiencing a significant number of episodes of hypoxaemia (SpO2 less than 90% h⁻¹) relative to pre-operative levels (Table 3). It must, however, be appreciated that these results were based on computer generated recordings and are therefore susceptible to artefact.20 The addition of real-time video surveillance in a sleep study unit would have helped to limit the impact of the undefined noise-to-signal ratio of the recording system, but because of the unpredictable scheduling of surgery this was not a feasible option. An observer blinded to the anaesthetic technique used, therefore checked the validity of each recording manually.

Five out of the 14 patients (36%) in group 1 compared with none of the 10 patients in group 2 exhibited an excess of post-operative cardiorespiratory complications (Table 2). In patients with pre-existing abnormal respiratory function, three out of five patients in group 1 demonstrated an excess of post-operative cardiorespiratory complications compared with none of four in group 2 (Fig. 1). We propose a number of possible explanations to account for this difference between the groups.

First, with reference to a standard premature infant growth chart, we established that those patients in group 2 with pre-existing abnormal respiratory function were born ‘small-for-gestational-age’ (less than 10th percentile) as opposed to ‘appropriate-for-gestational-age’ (10th–90th percentile) at birth. These infants were at increased risk of developing clinical signs of respiratory distress compared with ‘appropriate-for-gestational-age’ infants.21 In addition, the technique of sequential administration of incremental boluses of local anaesthetic was used in group 1. This was not the case in group 2 where we used a single injection caudal epidural anaesthesia with a bolus of 2 mg kg⁻¹ in addition to the spinal anaesthesia. The incremental boluses of local anaesthetic in group 1 were used as adjunctive therapy to ensure the delivery of adequate analgesia for the anticipated surgical insult.
operative apnoea.19 Infants seem to have a somewhat lower risk of postoperative apnoea.19 22 Therefore, it is possible that the observed differences between the two subgroups are purely a function of the level of monitoring. In our study, the concurrent use of standard real-time post-operative apnoea monitoring in combination with nurse observation, as per hospital policy, failed to detect any of the subsequently computer identified adverse episodes (Tables 2 and 4). This raises the interesting question whether cardiorespiratory complications only detectable by sophisticated techniques are clinically important; particularly when they appear to resolve spontaneously without intervention.

Third, the study of relatively rare events requires a large patient population that is impossible to acquire at any one institution. Using a statistical approach recommended by Hanley and Lippman-Hand, Coté and colleagues determined that a sample size of at least 300 patients would be necessary to detect a 1% incidence of apnoea with 95% confidence in a particular age group.19 22 Therefore, considering the limited size of this pilot study, it is possible that we have rejected our hypothesis when it is, in fact, true. In other words, the observed difference between the two groups is not significant and our results are, at best, inconclusive.

Impedance pneumography is the most widely used form of respiratory monitoring but has limitations for detecting obstructive airway problems and a high incidence of false alarms.20 The importance of upper airway obstruction in the pathophysiology of apnoea and bradycardia is well described in infants with periodic breathing and low PCA.23 24 It is, therefore, reasonable to conclude that general anaesthesia, which can decrease upper airway muscle tone, may contribute to the development of cardiorespiratory complications in susceptible infants.9 Given the limitations of impedance pneumography for detecting obstructive airway problems, this may account for why the incidence of apnoea was comparable between the groups and may also, in part, explain the excess of temporally unrelated episodes of bradycardia in group 1 (Tables 2 and 4).

It is clear even from our limited study that post-operative cardiorespiratory complications occur frequently in former pre-term infants after relatively minor surgical procedures. Allowing for the high detection rate with sophisticated computer-assisted continuous recording devices, it is also apparent that general anaesthesia even with modern evasive agents such as sevoflurane can induce or unmask abnormalities of cardiopulmonary function in predisposed infants. Recent work by O’Brien and colleagues has been more encouraging.12 They suggest that desflurane, in terms of the quality of recovery that it offers, may be the most appropriate potent inhalational agent with which to maintain general anaesthesia in high risk infants.

In conclusion, spinal anaesthesia may be preferable to general anaesthesia for ex-premature infants undergoing lower abdominal surgery within the first weeks of life. But until this has been demonstrated in large prospective, controlled studies in comparison with modern low solubility potent inhalational agents, we will continue to have reservations about routinely subjecting our patients to an awake technique that is potentially stressful for the infant and associated with a clinically significant failure rate.

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