Pain control with low-dose alfentanil in children undergoing minor abdominal and genito-urinary surgery

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Summary

Background and objective: The aim of this study was to investigate the quality of intra- and postoperative analgesia obtained by alfentanil compared to that produced by peripheral blockade in children.

Methods: During sevoflurane-nitrous oxide atracurium anaesthesia for minor abdominal or genito-urinary surgery, three groups of children aged 0–8 yr received 25 μg kg⁻¹ alfentanil intravenously (n = 28), or peripheral nerve blockade using 1 mL kg⁻¹ ropivacaine 0.475% (n = 24), or 12.5 μg kg⁻¹ alfentanil intravenously with peripheral nerve blockade using 1 mL kg⁻¹ ropivacaine 0.475% (n = 30). Changes in blood pressure and heart rate were measured during the procedures. Postoperative pain was assessed using the face, legs, activity, cry, consolability (FLACC) observational tool for quantifying pain behaviour and a numerical scale scored by nurses, doctors, parents and children.

Results: There was no significant difference in intra- or postoperative analgesic efficacy among the three groups. Patients who received alfentanil had significantly lower heart rates than those who received nerve blockade only (96.0 ± 15.6 vs. 115.9 ± 23.2 beats min⁻¹, P < 0.001). FLACC and numerical scale scores did not differ among the groups. There were no significant differences in incidence of vomiting or use of pain medications.

Conclusions: It was concluded that a low-dose, intravenous bolus of alfentanil may be an efficient alternative to peripheral nerve blockade in controlling pain during and after minor abdominal and genito-urinary surgery.

Keywords: ANAESTHESIA, anaesthesia local, anaesthesia general; PAEDIATRICS ANALGESICS, OPIOID, alfentanil; ANAESTHETICS, LOCAL, ropivacaine; PAIN, POSTOPERATIVE.
herniorraphy. Data concerning alfentanil administered as an intravenous (i.v.) bolus injection in children undergoing short surgical procedures are scarce. Orfei and colleagues [5] investigated the effectiveness of the alfentanil–propofol combination during short surgical procedures. They used an alfentanil bolus dose of 50 μg kg⁻¹ followed by a continuous infusion of 0.50 μg kg⁻¹ min⁻¹. Various groups have investigated the use of alfentanil to facilitate tracheal intubation in adults [6,7] and to reduce the haemodynamic response to intubation [10–12]. The aim of this study was to investigate the quality of intra- and post-operative analgesia obtained by alfentanil as compared to peripheral nerve blockade.

Methods
The study was approved by the Ethics Committee of the Catholic University of the Sacred Heart in Rome, and written informed parental consent was obtained. Eighty-two unpremedicated infants and children, aged 0–8 yr (ASA I and II), undergoing minor abdominal or genito-urinary surgery were studied. Children with a history of liver or kidney disease were excluded. Children were randomly assigned to one of three groups. Group A received alfentanil 25 μg kg⁻¹ i.v. over 30 s; Group B, received ilio-inguinal nerve blockade with ropivacaine 0.475% 1 mL kg⁻¹; Group C received both alfentanil 12 μg kg⁻¹ i.v. over 30 s and ilio-inguinal nerve blockade with ropivacaine 0.475% 1 mL kg⁻¹. Anaesthesia was induced via a face mask using decreasing inhaled concentrations of sevoflurane in 60% nitrous oxide and 40% oxygen, starting with 4% sevoflurane and decreasing to a minimum of 1.5–2% sevoflurane via a Mapleson type D manual circuit. All patients were intraoperatively monitored using peripheral pulse oximeter, automated non-invasive blood pressure (BP) monitor, capnography and electrocardiogram (SC9000XL, Siemens Medical Systems). Once i.v. access was established, atracurium (0.5 mg kg⁻¹) was used in all patients to facilitate orotracheal intubation and alfentanil was administered to patients in Groups A and C. After 90 s, during which the children were gently ventilated manually with 1.5–2% end-tidal PCO₂ between 4.0 and 4.7 kPa and anaesthesia was maintained with 1.5–2% inhaled sevoflurane, 60% nitrous oxide and 40% oxygen. Then, ilio-inguinal blockade was performed in children of Groups B and C. Efficacy in controlling intraoperative pain was evaluated by measuring the changes in arterial pressure and heart rate (HR). An anaesthetist blind to the patient's randomization group, recorded the values on arrival in the operating room (baseline), post-induction, 1 min following tracheal intubation (post-intubation), 1 min following incision (incision +1 min) and 30 min following incision (incision +30 min). Desaturation was defined as an SpO₂ value lower than 92%. At the end of the surgical procedure residual neuromuscular blockade was antagonized with neostigmine (0.05 mg kg⁻¹) and atropine (0.03 mg kg⁻¹). Postoperative analgesia and quality of recovery were evaluated in the recovery room, 6 h after recovery and on the first postoperative day, using two pain scoring systems: a behavioural pain scale for children obtained by the face, legs, activity, cry, consolability (FLACC) tool and a four point numerical score (observer's score). The FLACC is an observational tool for quantifying pain which incorporates five categories of pain behaviours: facial expression, leg movement, activity, cry and consolability, each scored 0–2, for a total score of 0–10 [13]. The child's nurse, blinded to the group allocation of the patient, scored pain with the FLACC tool.

The observer's score was based on the pain assessment scored by nurses, doctors, parents and children if able to self-report, according to the following scale: absent, mild, moderate and severe (0–3).

The decision to treat pain was based on routine practice and was taken by a physician unaware of the rating procedures. If the pain was assessed as severe or if the child asked for an analgesic, a suppository of paracetamol was administered.

Results
Mean age, body weight and duration of surgery were similar in the three groups (Table 1).

No significant differences were observed between the groups in HR or BP at baseline. Sequential changes in HR and systolic pressure during surgery are shown in Figures 1 and 2. Group B patients had significantly higher HR, compared to Groups A and C, throughout the surgical procedure (t-test for unpaired data P < 0.01 in each stage, for B vs. A and P < 0.03 for B vs. C). After induction of anaesthesia, HR decreased significantly in the groups who received alfentanil (Group A: 96.0 ± 15.6 vs. 120.4 ± 10.8 beats min⁻¹, P < 0.02; Group B: 115.9 ± 23.1 vs. 118.8 ± 10.9, P > 0.1; Group C: 99.7 ± 16.4 vs. 118.4 ± 15.6, P < 0.01, t-test for paired data) while it remained virtually unchanged in those who only had nerve block (Group B). Tracheal intubation resulted in a significant increase in HR in Group B (P < 0.001, t-test for paired data) compared to pre-intubation values, while there was a
difference between the groups.

Changes in systolic BP

Figure 2.
Changes in systolic BP (mean ± SEM) for the alfentanil group (○), nerve blockade group (□) and alfentanil + nerve blockade group (●). Incision + 1 min = 1 min after skin incision; incision + 30 min = 30 min after skin incision. *P < 0.01 alfentanil vs. nerve blockade; †P < 0.03 alfentanil + nerve blockade vs. nerve blockade.

slight but non-significant increase in Groups A and C. No significant haemodynamic responses were observed after surgical incision in any of the groups. After the induction of anaesthesia systolic BP decreased by approximately 10% in all groups (P < 0.001, t-test for paired data), but remained quite stable throughout the rest of the procedure. Diastolic pressure did not differ among the three groups. Nine patients required supplemental analgesia for postoperative pain control (two in Group C, three in Group B, four in Group A), and they received paracetamol suppositories (200 mg). There was no difference between the groups in the quality of postoperative analgesia or in recovery assessment. Table 2 shows the results of FLACC scores; no significant differences were observed in the FLACC scores at any time between the groups (U-test, non-parametric test for unpaired data). At recovery, Group A showed higher FLACC scores than B and C; median (interquartile range) 4 (1-5) for Group A, 3 (1-4) for Groups B and C, but the differences did not reach statistical significance. A similar result was obtained by the four point numerical scale in the recovery room (Table 3). The scores obtained 6 h after recovery and the first postoperative day did not differ significantly from zero.

No patients suffered adverse effects from the administration of alfentanil such as haemodynamic instability, bradycardia, chest wall rigidity or vomiting. One patient in the alfentanil group had an episode of arterial desaturation after extubation, which was brought under control with manual ventilation using 100% inhaled oxygen. This patient recovered

Table 1. Patients' data.

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (month)</th>
<th>Weight (kg)</th>
<th>Duration of surgery (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfentanil (A, n = 28)</td>
<td>30 (1-96)</td>
<td>13.0 (2.7-34.5)</td>
<td>42 (20-180)</td>
</tr>
<tr>
<td>Nerve blockade (B, n = 24)</td>
<td>18 (2-96)</td>
<td>13.7 (4.0-47.0)</td>
<td>60 (15-165)</td>
</tr>
<tr>
<td>Alfentanil + nerve blockade</td>
<td>24 (2-72)</td>
<td>14.3 (4.8-36.2)</td>
<td>60 (25-160)</td>
</tr>
</tbody>
</table>

Data are presented as median (range). There was no significant difference between the groups.

Table 2. Median (interquartile range) of FLACC, after surgery.

<table>
<thead>
<tr>
<th>Group</th>
<th>Recovery</th>
<th>6 h after recovery</th>
<th>First postoperative day</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>4 (1-5)</td>
<td>0 (0-0)</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>B</td>
<td>3 (1-4)</td>
<td>0 (0-0)</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>C</td>
<td>3 (1-4)</td>
<td>0 (0-0)</td>
<td>0 (0-0)</td>
</tr>
</tbody>
</table>

Postoperative pain evaluation by FLACC scores obtained in the recovery room, 6 h after recovery and in the first postoperative day. FLACC is obtained as a combination of five pain behaviours: face, legs, activity, cry and consolability, each scored 0-2. Total score 0-10.

Table 3. Median (interquartile range) of four point numerical scale, at recovery.

<table>
<thead>
<tr>
<th>Evaluation of pain score</th>
<th>Group</th>
<th>Parents</th>
<th>Nurse</th>
<th>Doctor</th>
<th>Child</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>1 (1-1)</td>
<td>0 (0-1)</td>
<td>0 (0-1)</td>
<td>1 (0-2)</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>1 (0-1)</td>
<td>0 (0-1)</td>
<td>0 (0-1)</td>
<td>1 (0-2)</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>1 (0-1)</td>
<td>0 (0-1)</td>
<td>0 (0-1)</td>
<td>1 (0-3)</td>
</tr>
</tbody>
</table>

Postoperative pain evaluation by observers' scores, obtained in the recovery room. Pain is evaluated as: absent, mild, moderate and severe (scores: 0-5).
within 2 min without further difficulty and did not require treatment with naloxone.

Discussion

The control of intra- and postoperative analgesia in children undergoing minor abdominal or genitourinary surgery can be effectively obtained by peripheral or central nerve blockade. Although these procedures have recently become popular, several factors still limit a wider use. Neural blockades require highly trained operators, may increase the duration of the surgical procedures and may induce complications such as toxicity due to accidental intravascular injection or dural puncture. Alternatively, the use of high-dose opioids provides effective analgesia and rapid recovery, but the incidence of side-effects is high [2]. Data concerning the optimal dose of alfentanil for intra- and postoperative analgesia in children and babies are scarce, while several groups have used an alfentanil bolus for facilitating tracheal intubation at dosages ranging from 10 to 40 μg kg⁻¹ [8,10,14]. Gronert and colleagues [4] used a 100 μg kg⁻¹ bolus followed by an i.v. infusion at 2 μg kg⁻¹ min⁻¹, in infants undergoing inguinal herniorrhaphy. Orfei and colleagues [5] used an alfentanil bolus dose of 50 μg kg⁻¹ followed by a continuous infusion of 0.50 μg kg⁻¹ min⁻¹, and concluded that it allowed good control of surgical analgesia without the risk of early respiratory depression in the postoperative period. We investigated the use of low dosage alfentanil as a single i.v. analgesic agent. We used an alfentanil dose of 25 μg kg⁻¹ in a group of children undergoing minor abdominal and genito-urinary surgery, and compared it to an age-matched group in which analgesia was obtained by peripheral nerve blockade, and to a third group which received a lower dose of alfentanil (12.5 μg kg⁻¹) together with a peripheral nerve blockade. Anaesthesia proceeded smoothly in the three groups. Intrubating conditions did not differ, all groups received atracurium consequently we cannot assess any effects of alfentanil on tracheal intubation. Hiller and Saarnivaara [15] and Ng and Wang [12] showed that pretreatment with alfentanil diminished haemodynamic responses to tracheal intubation. We observed a similarly attenuated response in both groups who received alfentanil. Respiratory side-effects associated with the use of alfentanil were not specifically monitored in this study, however none of the patients but one had clinical evidence of respiratory depression. In this patient, approximately 5 min after extubation, we observed slow breathing and a decrease of arterial oxygen saturation to 86%. This child had received 25 μg kg⁻¹ of alfentanil at the beginning of the procedure, without any additional bolus. Two minutes of manual ventilation resulted in a complete recovery.

The HR in the children who received alfentanil (Groups A and C) decreased by approximately 20 beats min⁻¹ after induction and remained virtually unchanged throughout the procedure. In the group which received only nerve blockade (Group B) the HR remained virtually unchanged after induction. Other studies have reported a decrease in HR and BP after administration of alfentanil exceeding 30 μg kg⁻¹ [14,16]. In this study we used lower doses: 25 μg kg⁻¹ in the alfentanil alone group and 12.5 μg kg⁻¹ in the alfentanil and nerve blockade group. Arterial pressure decreased by approximately 10% after induction in all groups and remained virtually unchanged. Thus, on the basis of arterial pressure and HR trends, alfentanil gave intraoperative pain control comparable to peripheral nerve blockade.

Postoperative recovery data and follow-up data the next day did not differ among the three groups, although in the recovery room, children treated only with alfentanil showed, according to FLACC and observer's scores, slightly higher pain scores than the others. We had no cases of vomiting. Data concerning incidence of postoperative vomiting after alfentanil anaesthesia are controversial. White and colleagues [17] and Davies and colleagues [18] have reported high incidence in adults and children, while Gronert and colleagues [4] reported no cases of vomiting in infants receiving 100 μg kg⁻¹ of alfentanil. Patel and Hannallah [19] reported a 30–40% incidence of vomiting in children 7 months to 6-year-old, which dropped to less than 8% in infants younger than 7 months.

There were no episodes of recurrent respiratory depression in the present study but one case of oxygen desaturation, in a patient belonging to the alfentanil group. It occurred approximately 5 min after extubation and resolved within 2 min. Sternlo and Sandin [20] described two cases of recurrent respiratory depression in adults after continuous infusion of alfentanil and propofol, and reviewed 16 published cases of recurrent respiratory depression after alfentanil infusion. They concluded that the incidence is low and that the majority of cases are patients treated with rather high dosages. den Hoolander and colleagues [21] used alfentanil 20 μg kg⁻¹ by i.v. bolus injection followed by i.v. infusion of 1 μg kg⁻¹ min⁻¹ in 11 children undergoing heart surgery. They did not report cases of early or recurrent respiratory depression with dosages higher than those used in the present investigation. FLACC and observer's postoperative pain scores did not show significant differences, indicating that alfentanil provided satisfactory analgesia in most cases.

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In conclusion, our results indicate that low-dose alfentanil bolus (25 μg kg⁻¹) offers an attractive alternative technique for children undergoing minor abdominal or genito-urinary surgery. At this low-dose alfentanil appears to be effective and haemodynamically well tolerated without inducing postoperative vomiting.

References