Postoperative extradural analgesia in children: comparison of morphine with fentanyl†

C. LEJUS, G. ROUSSIÈRE, S. TESTA, M. F. GANANSIA, M. MEIGNIER AND R. SOURON

SUMMARY
We have compared the efficacy and side effects of extradural morphine with extradural fentanyl for postoperative pain relief. Thirty children (ages 1–16 yr) were allocated randomly to receive, after extradural administration of 0.5% bupivacaine 0.75 ml kg⁻¹ and before surgical incision, extradural morphine 0.75 μg kg⁻¹ (group M), with an additional dose administered 24 h later or extradural fentanyl 2 μg kg⁻¹ (group F) followed by a continuous extradural infusion (during 48 h). There was no major complication (respiratory depression). Pain scores were satisfactory in both groups for 48 h. Ventilatory frequency was greater in group M 20, 21, 22, 23 and 25 h after the beginning of analgesia (P < 0.05). Pruritus, nausea and vomiting were less common with extradural fentanyl (20% vs 53%, P < 0.05 and 0% vs 33%, P < 0.05) than with morphine. Urinary retention occurred with equal frequency (25%) in the two groups. After a bolus of 2 μg kg⁻¹, continuous extradural infusion of fentanyl 5 μg kg⁻¹ day⁻¹ provided analgesia comparable to that from a daily bolus of extradural morphine 0.75 mg kg⁻¹ and produced fewer side effects. (Br. J. Anaesth. 1994; 72: 156–159)

KEY WORDS

Extradural opioids have been shown to provide effective postoperative analgesia in paediatric patients. Morphine is perhaps the opioid used most widely for this purpose in children [1, 2]. Because of its greater lipid solubility, fentanyl has been suggested as one of the opioids least likely to cause side effects [3]. The onset of analgesia is quicker than with morphine (around 13 min) [4], but the duration of action of a single dose is shorter (6 h) and there is a need for a continuous infusion. Satisfactory analgesia has been provided in adults by continuous extradural infusion of fentanyl [5]. Because fentanyl has not been assessed extensively in children [6, 7], we have compared the efficacy and side effects of equipotent doses [8] of extradural morphine and fentanyl for postoperative analgesia in children.

PATIENTS AND METHODS
The study was approved by our Human Studies Ethics Committee and written informed consent was obtained from all parents. We studied 30 children (ASA I and II, aged 6 months to 15 yr) undergoing major orthopaedic, urological, abdominal and thoraco-abdominal surgery. Children with infectious diseases, coagulopathy, neurological diseases and vertebral anomaly were excluded. Premedication consisted of rectal midazolam 0.3 mg kg⁻¹ 20 min before arrival in the surgical room. For children younger than 6 yr, anaesthesia was induced with halothane; for children older than 6 yr, a choice was given of halothane or i.v. injection of thiopentone 5 mg kg⁻¹. Tracheal intubation was facilitated by administration of atracurium 500 μg kg⁻¹ and anaesthesia was maintained with isoflurane and nitrous oxide in oxygen (FIO₂ 0.5). Ventilation was controlled to maintain normocapnia. Children were turned to the lateral position and a lumbar (L4–5) extradural catheter placed before surgery, except in three subjects (lung lobectomy, Nissen fundoplication and diaphragmatic hernia repair) in whom it was inserted at a thoracic level. For children weighing more than 20 kg, a 19-gauge extradural catheter was introduced in the extradural space via an 18-gauge needle. For children weighing 20 kg or less, a 22-gauge extradural catheter was introduced in the extradural space via a 19-gauge needle. For intraoperative analgesia, all children received an extradural bolus of 0.5% bupivacaine 0.75 ml kg⁻¹ with adrenaline (1:200000).

Four hours later, a continuous extradural infusion was started with fentanyl 5 μg kg⁻¹ day⁻¹ (not ex-
ceeding 300 μg day⁻¹) in group F and with saline in group M. The extradural infusion was maintained at the same rate (1 ml h⁻¹ for children weighing 20 kg or less and 1.5 ml h⁻¹ for children weighing more than 20 kg) for the next 48 h. The extradural drugs were prepared by a physician who did not participate in pain evaluation. Monitoring comprised arterial pressure (Dinamap), continuous ECG monitoring (Siemens), end-tidal carbon dioxide (Datex), continuous transcutaneous arterial oxygen saturation (SaO₂) and nasopharyngeal temperature. After tracheal extubation, when the children were awake, they were transferred to the surgical ward. Twenty-four hours after the beginning of postoperative analgesia, children in group M were given an extradural dose of morphine 75 μg kg⁻¹ and those in group F received a bolus of saline. Postoperative monitoring included continuous SaO₂ with pulse oximetry (Nelcor), hourly ventilatory frequency and hourly sedation on a three-point scale graded from 0 (no sedation) to 2 (profound sedation). Pain was evaluated every 2 h with three scores: a visual analogue pain scale (VAS) graded from 0 to 10 for children older than 5 yr (group M, n = 7; group F, n = 6), a verbal pain score (0 = asleep; 1 = awake but no pain; 2 = light pain; 3 = moderate pain; 4 = severe pain) for children older than 3 yr (group M, n = 8; group F, n = 12) and a five-point pain score for all children [1] (1 = laughing/euphoric; 2 = happy/playful; 3 = calm/asleep; 4 = crying/grimacing/can be distracted by toy, food or parents; 5 = crying/screaming/inconsolable). When children were asleep VAS scores were not performed. At the end of the study, the quality of analgesia was evaluated also, by a questionnaire given to the parents and the nurses, who were asked if they found analgesia very good, good or inadequate. No opioid was administered to the children by any route other than extradural. If analgesia was inadequate (Krane pain score ≥ 4), an i.v. bolus of paracetamol 25 mg kg⁻¹ was administered (not exceeding 100 mg kg⁻¹ day⁻¹). If pain persisted despite this injection, the double-blind procedure was broken and the choice of analgesic was left to the physician on call. Side effects such as nausea, vomiting, urinary retention or pruritus were recorded. Urinary retention of more than 8 h duration and requiring bladder catheterization was considered significant.

### Statistics

Data were statistically analysed using chi square and analysis of variance followed by Scheffé’s test, Student’s t test for unpaired data and Kruskall–Wallis analysis followed by Mann–Whitney U test as appropriate. All values were expressed as mean (SD), except for ventilatory frequency, which was expressed as mean (SEM) percentage of theoretical values [9]. P < 0.05 was considered as significant.

### RESULTS

We studied 30 children (22 males), mean age 5.7 (SD 5.1) yr (range 6 months to 15 yr) and mean weight 20.3 (13.3) kg (range 4.5–63 kg). Both groups

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<th>Table I. Patient data (mean (range or SD))</th>
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<td>Fentanyl group (n = 15)</td>
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<td>Age (6 mo–15 yr)</td>
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<td>Sex (F/M)</td>
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<th>Table II. Type of surgery</th>
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<td>Fentanyl group (n = 15)</td>
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![Fig. 1. Mean pain scores during the first 48 h after major surgery with an extradural bolus of morphine (M) 75 μg kg⁻¹ day⁻¹ (●) or an extradural bolus of fentanyl (F) 2 μg kg⁻¹ + continuous infusion of 5 μg kg⁻¹ day⁻¹ (○). Krane scale (n = 15, both groups): 1 = laughing/euphoric; 2 = happy/playful; 3 = calm/asleep; 4 = crying/grimacing/can be distracted by toy, food or parents; 5 = crying/screaming/inconsolable. Verbal pain scores (n = 8 group M; n = 12 group F): 0 = asleep; 1 = awake but no pain; 2 = light pain; 3 = moderate pain; 4 = severe pain. Visual analogue pain scores (n = 7 group M; n = 6 group F): graded from 0 (no pain) to 10 (severe pain).](image)
were comparable in characteristics (table I) and type of surgery (table II). Two children were excluded from the study: one in group F at 12 h because of accidental withdrawal of the extradural catheter, and one in group M at 32 h because pain persisted despite administration of paracetamol (partial loss of the morphine bolus at the antimicrobial filter had occurred). There was no significant difference in pain scores between the two groups (fig. 1). Pain relief was good in both groups. Among the 568 Krane's pain scores (79% of the planned Krane's scores) performed by the nurses, only 1% were graded 5 and 16% were graded 4. Analgesia was graded equally by parents and nurses (table III). Forty percent of patients in group F and 53% in group M (ns) did not need additional analgesics (paracetamol) for the first 48 h after operation.

We did not observe any case of clinical respiratory depression and naloxone was not required. Ventilatory frequency (fig. 2) always exceeded 75% of the theoretical values according to age [9]. However, in group M, ventilatory frequency was greater ($P < 0.05$) than that in group F 20, 21, 22, 23 and 25 h after the beginning of analgesia (fig. 2). In all patients, haemodynamic variables remained within the normal range. There was no difference in mean arterial pressure and heart rate between groups. Side effects were more frequent in group M than in group F: nausea or vomiting 53% vs 20%, respectively ($P < 0.05$); pruritus 33% vs 0%, respectively ($P < 0.05$). Two patients in group M had urinary bladder catheters placed in the operating room for surgical procedure. In the 28 remaining patients, the rate of urinary retention was not statistically different between groups (30% in group M vs 20% in group F). Sedation was similar in the two groups except at 6 h, when it was greater ($P < 0.05$) in group M than in group F without a decrease in mean ventilatory frequency. When sedation was graded 2, the child was sleepy but always arousable.

**DISCUSSION**

In this study we found that continuous extradural infusion of fentanyl 5 μg kg$^{-1}$ day$^{-1}$ after a loading dose of 2 μg kg$^{-1}$ provided postoperative analgesia similar to that obtained with a bolus of morphine 75 μg kg$^{-1}$ day$^{-1}$ during the first 48 h after major paediatric surgery.

Pain scoring (Krane's scores, VAS, verbal scores) did not reveal any difference in analgesia between the two groups, perhaps because of our small sample size. Quality of analgesia was good in the two groups. Krane's scores were less than 4 in 83% of the scores performed during the first 48 h after operation. Unfortunately, we were unable to use VAS in children younger than 5 yr, but VAS and verbal scores mean values were less than 3 and 2, respectively, in older children. Quality of analgesia assessed by parents and nurses seemed at first sight to be at variance with these results as 21% of nurse questionnaires rated analgesia as insufficient, but these results are consistent with 17% Krane's scores equal to or greater than 4.

Ventilatory frequency was greater with morphine than with fentanyl at 21–30 h after the beginning of the study. In order to explain this increase in group M, we suggest that analgesia was more stable in group F as an increase in ventilatory frequency is considered a sign of pain [10]. The duration of action of extradural morphine is variable [1, 11, 12], and may explain the attenuation of analgesia in group M at the end of the first day of the study. Continuous administration of morphine, as proposed recently [13], may be a solution to this problem.

The dose of morphine 75 μg kg$^{-1}$ used was intermediate in the range (30–100 μg kg$^{-1}$) reported

![Fig. 2. Mean (SEM) ventilatory frequency (%) of theoretical values according to age) during the first 48 h after major surgery. ● = Extradural bolus of morphine 75 μg kg$^{-1}$ day$^{-1}$ (n = 15); □ = extradural bolus of fentanyl 2 μg kg$^{-1}$ + continuous infusion of 5 μg kg$^{-1}$ day$^{-1}$ (n = 15). * $P < 0.05$ between groups.](image-url)
in the literature to be efficient in children [1, 2, 14, 15]. Determination of the extradural dose of fentanyl was difficult because there are few paediatric data available. Fentanyl is used in children essentially by extradural bolus (1 μg kg⁻¹) in combination with local anaesthetic [16]. Continuous extradural infusion of fentanyl has been reported for postoperative analgesia, but in association with bupivacaine [6, 7]. Our choice of the extradural dose of fentanyl was based on conclusions by Chrubasik and colleagues [8], who demonstrated that the analgesic potency of continuous extradural fentanyl compared with continuous extradural morphine was about 10.

The choice of the maximal daily dose of 3 mg for morphine (for a weight of 40 kg) and of a maximal bolus of 100 μg for fentanyl (for a weight of 50 kg) did not introduce any bias, as only two children exceeded 40 kg in group M and none exceeded 50 kg in group F. In our study, the volume of continuous extradural infusion was determined only by practical and technical reasons. The effect of various volumes of extradurally injected opioid on the onset, duration and quality of analgesia is not known. For morphine, various volumes (2–10 ml) have been used [11, 17, 18], but there are no data in the literature for children. The choice of the bolus dose of bupivacaine was based upon recommendations and pharmokinetic data of Ecoffey, Dubouset and Samii [19].

It is well known that the two opioids we used cause respiratory depression [14, 20], but there was no instance of this complication in our study.

Pruritus, nausea and vomiting were less frequent with fentanyl than with morphine. The greater lipid solubility of fentanyl [21] may explain these results. The low incidence of vomiting or nausea and of pruritus is an advantage with fentanyl. Pruritus caused by extradural morphine was moderate and did not require treatment.

Urinary retention was similar in the two groups. Retention is influenced by type of surgery and gender [2] and it seems to occur more frequently in children [14] than in adults. It is not always caused by extradural opioids, but may be induced by factors such as postoperative posture or inflammation. In our study, catheterization of the bladder was not followed by traumatic or infectious urinary complications.

REFERENCES