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Background. Continuous regional analgesia (CRA) is considered a safe and efficacious technique for postoperative pain relief in children after lower limb surgery. We recently evaluated the feasibility of patient-controlled regional analgesia (PCRA) in a similar acute pain situation and we concluded that PCRA might be advantageous over CRA in terms of lower costs, risk of systemic toxicity while producing similarly adequate analgesia. We therefore prospectively compared both techniques in the paediatric population.

Methods. In total, 30 children undergoing lower limb orthopaedic surgery were randomized to receive PCRA or CRA with ropivacaine 0.2%. Visual analogue scale scores, rescue analgesia, overall satisfaction, motor blockade and plasma ropivacaine concentrations were recorded for 48 h.

Results. Adequate analgesia was achieved with both techniques. No significant difference was noted for rescue analgesia, overall satisfaction and motor blockade. In contrast, children in the PCRA group received significantly less local anaesthetics than those in the CRA group. In addition, total plasma concentrations of ropivacaine were significantly reduced in the PCRA group as compared with the CRA group during the 48 h postoperative period.

Conclusions. Both techniques are efficacious and satisfactory. However, PCRA with ropivacaine 0.2% can provide adequate postoperative analgesia for paediatric orthopaedic procedures with smaller doses of ropivacaine than CRA.

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It is currently common to use regional analgesia for postoperative pain control in children after orthopaedic procedures. The continuous epidural or peripheral infusion of a local anaesthetic provides satisfactory pain relief. However, the goal of either analgesic technique is to achieve adequate analgesia with a minimal amount of drug to decrease any side-effect associated with the local anaesthetic. In adults, patient-controlled epidural analgesia (PCEA) offers the possibility for optimal analgesia with a smaller amount of local anaesthetic than during continuous epidural analgesia (CEA). In addition, we and others have recently showed the benefits of PCEA over CEA in children after major orthopaedic surgery. Moreover, a recent prospective survey of regional anaesthesia stressed the extremely low incidence of complications (zero in the study), after peripheral nerve blocks prompting paediatric anaesthesiologists to use them in the place of a central block. In keeping with this recommendation, several studies have recently suggested the advantage of continuously administered local anaesthetics through a peripheral nerve catheter for postoperative pain relief. The concept of patient-controlled regional analgesia (PCRA) to reduce local anaesthetic administration has been evaluated in adults, and, more recently, we have shown the feasibility of PCRA in children following lower limb surgery. Therefore, we prospectively studied the efficacy of PCRA and continuous regional analgesia (CRA) with ropivacaine 0.2% after paediatric orthopaedic procedures. In addition, we evaluated the toxicity of both
children were then returned to their regular ward, and the perineural infusion was continued for 48 h. During the 48 h study period, the quality of analgesia was assessed by using the VAS, and, when applicable, demand to delivery (D/D) ratios. Children were not awakened for assessment, and ‘asleep’ was recorded on the chart at these times. In addition, children were assessed with regard to the quality of awakening with the following scores: 0=no awakening; 1=pain-free awakening; 2=painful awakening. The degree of motor block in the lower extremities was recorded with a modified Bromage scale (score: 0=no movement; 1=ankle only; 2=ankle and knee; 3=ankle, knee and hip). Finally, satisfaction was evaluated with four chips and scored as follows: 1=totally unsatisfied; 2=moderately unsatisfied; 3=satisfied; 4=very satisfied. Pain scores, motor block scores and volume of ropivacaine infused were recorded every 4 h for 48 h by an independent observer unaware of the infusion regimens delivered. Awakening scores and satisfaction scores were recorded at the end of the 48 h postoperative period. All patients received acetaminophen 15 mg kg\(^{-1}\) and ketoprofen 1 mg kg\(^{-1}\) i.v. every 6 h. Supplemental i.v. analgesia (nalbuphine 0.2 mg kg\(^{-1}\)) was given if patients complained of inadequate analgesia despite activating the demand button. At the end of the 48 h postoperative period, the total consumption of ropivacaine was noted. Specific issues, such as regional catheter-related problems (disconnection, leakage and local inflammation), were also recorded.

**Ropivacaine plasma concentrations**

Blood samples of children receiving either regimen were drawn 24 and 48 h after the beginning of the study for total ropivacaine plasma concentrations measurement by high-pressure liquid chromatography as previously described.\(^{10,11}\) Calibration curves were obtained by using human plasma from a blood transfusion centre (Clermont-Ferrand, France). The intra-day coefficients of variation for the assay were 2.4, 2.3, 2.4 and 1.2% for concentrations of 0.3, 0.6, 1.2 and 2.4 mg litre\(^{-1}\), respectively. The inter-day coefficients of variation for the assay were 6.3, 4.7, 3.0 and 0.5% for concentrations of 0.3, 0.6, 1.2 and 2.4 mg litre\(^{-1}\), respectively. The accuracy of the method is correct (<5%), the limit of quantification was 50 \(\mu\)g litre\(^{-1}\) and the ropivacaine recovery rate was better than 90%.

**Statistical analysis**

The proposed sample size was 15 for each group, and the study was powered to 90% to yield a statistically significant result. According to a preliminary report this computation assumes that the mean difference is 25% (corresponding to means of 0.2 vs 0.15 mg kg\(^{-1}\) h\(^{-1}\) of ropivacaine dosage) and that the expected SD is 0.04.\(^{8}\) This threshold was selected as the smallest difference of clinical significance. Data are represented as mean (SD) or median and quartiles as appropriate, and categorical variables are presented as percentage.
Table 1 Patient characteristic and procedure-related data. Variables are presented as mean (SD), as mean (range) or as ratio when appropriate. CRA, continuous regional analgesia; PCRA, patient-controlled regional analgesia

<table>
<thead>
<tr>
<th>Variable</th>
<th>PCRA (n=15)</th>
<th>CRA (n=15)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>9/6</td>
<td>9/6</td>
<td>0.709</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>12.6 (8–15)</td>
<td>11.8 (8–15)</td>
<td>0.363</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>47.8 (9.9)</td>
<td>42.7 (16.7)</td>
<td>0.315</td>
</tr>
<tr>
<td>Type of regional analgesia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sciatic nerve</td>
<td>9/15</td>
<td>10/15</td>
<td>0.998</td>
</tr>
<tr>
<td>Femoral block</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fascia iliaca</td>
<td>6/15</td>
<td>5/15</td>
<td>0.998</td>
</tr>
<tr>
<td>compartment block</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteotomy</td>
<td>5</td>
<td>6</td>
<td>0.998</td>
</tr>
<tr>
<td>Arthroscopy</td>
<td>4</td>
<td>7</td>
<td>0.449</td>
</tr>
<tr>
<td>Cyst or tumour resection</td>
<td>6</td>
<td>2</td>
<td>0.215</td>
</tr>
</tbody>
</table>

with 95% confidence interval. For all statistical analyses, the SigmaStat 3.1 computer software package was used (Systat Software, Point Richmond, CA, USA). Differences between groups within age, weight, gender or type of surgery were analysed using an unpaired t-test (or the Mann–Whitney Rank Sum test for non-normally distributed variables) or χ²-tests when appropriate. Differences between groups and time course within clinical scores, ropivacaine consumption and ropivacaine plasma measurements were analysed using a two-way ANOVA for repeated measures. The Holm–Sidak post hoc correction was used for appropriate multiple comparisons to locate the significance. *P* < 0.05 was considered significant.

Results

In total, 33 children were studied but three patients were excluded and not analysed because of catheter-related issues (failure, disconnection). Patient characteristic data are given in Table 1. The two groups did not differ in age, weight, gender or type of surgery. Both groups obtained effective pain relief with an average VAS value of 1.1 (1.2) for the PCRA group and of 1 (1) for the CRA group during the first 24 h (Fig. 1A; *P* = not significant). On the second day, the average VAS scores were 0.8 (1.2) for the PCRA group and 0.9 (0.9) for the CRA group, respectively (Fig. 1A; *P* = not significant). The total number of boluses received and attempted and the D/D ratio averaged were 15 (15), 33 (43) and 1.8 (0.9) during the 48 h postoperative period, respectively.

Three patients in the PCRA group and eight in the CRA group received supplemental analgesia (Fig. 1B; *P* = not significant). In terms of quality of awakening and overall satisfaction scores, no significant differences were found between either group (Fig. 1C and D, respectively). One motor blockade was present in either group.

Ropivacaine consumption and plasma dosages

Patients in the PCRA group received half the hourly local anaesthetic compared with those in the CRA group [0.1 (0.06) mg kg⁻¹ h⁻¹ vs 0.2 (0.01) mg kg⁻¹ h⁻¹; *P* < 0.05]. There was no difference in the average hourly dose of perineural ropivacaine between the first and second day [0.11 (0.06) mg kg⁻¹ h⁻¹ vs 0.1 (0.07) mg kg⁻¹ h⁻¹] in the PCRA group. The total dose of perineural ropivacaine was 230 (138) mg 48 h⁻¹ [4.99 (3.04) mg kg⁻¹ 48 h⁻¹] for the PCRA group vs 410 (161) mg 48 h⁻¹ [9.6 (0.01) mg kg⁻¹ 48 h⁻¹] for the CRA group (*P* < 0.05).

Total plasma concentrations of ropivacaine obtained in children 24 and 48 h after the beginning of the perineural infusion were significantly greater in the CRA group compared with the PCRA group at either time point (Fig. 2; *P* < 0.05).

Discussion

This study shows for the first time that PCRA offers similarly adequate pain relief when compared with CRA in children following lower limb surgery. In addition, this self-administered regional anaesthetic technique permits a statistically significant reduction in total ropivacaine requirements during the first 48 h after surgery, and therefore enables theoretically lower systemic toxicity, as evidenced by diminished total ropivacaine levels in plasma.

Ropivacaine 0.2% has been widely used in children and several studies have reported its clinical efficacy and safety when administered for peripheral anaesthesia or analgesia.12,13 In this study, we confirm that the peripherally self-administered infusion yields adequate analgesia with minimum local anaesthetics consumption and rare adverse effects.8 Moreover, our findings show that PCRA offers advantages over continuously administered local anaesthetics with respect to local anaesthetics consumption, as evidenced by a reduction by 50% of total perineural ropivacaine obtained during the 48 h postoperative period in the PCRA group compared with the CRA group. It is conceivable that lower continuous doses regimen of ropivacaine 0.2%, that is 0.075 or 0.05 ml kg⁻¹/C0 h⁻¹ up to 0.2 ml kg⁻¹ h⁻¹ of ropivacaine 0.2% (with or without adjuvant) is more likely to be found.5,11,15 Hence, the lower consumption of ropivacaine obtained in the PCRA group might lead to substantial advantages over CRA, that is, a theoretical reduction of cost and risk of adverse effects of local anaesthetic, and over morphine patient-controlled analgesia, that is, a reduction of nausea and pruritus. However, further study is required to evaluate the advantages of PCRA over CRA when a minimum infusion rate of ropivacaine 0.2%, that is below 0.1 ml kg⁻¹ h⁻¹, is used in that paediatric population to relief postoperative pain.

The smaller dose of total peripherally infused ropivacaine in the PCRA group resulted indeed in a significantly lower plasma concentration at 24 and 48 h when compared with
the CRA group. In addition, ropivacaine is thought to be less toxic than bupivacaine because higher doses of ropivacaine compared with bupivacaine are required to produce central neurological disorders and cardiovascular changes when i.v. administered in adult volunteers. The pharmacokinetic profile of ropivacaine has been extensively evaluated in children mostly after caudal blockade and more recently after peripheral nerve block suggesting ropivacaine up to 3 mg kg\(^{-1}\) to be safe. However, recently, Paut and colleagues reported high values of venous plasma ropivacaine in four children after single injection of ropivacaine 3.5 mg kg\(^{-1}\) for fascia iliaca compartment blockade suggesting a potential toxic effect of ropivacaine pending the peripheral nerve block performed and, of course, the dose administered although no clinical evident signs were noticed. In this study, the maximally infused ropivacaine dose in the CRA group failed to reach toxic plasma levels suggesting either analgesic regimen, that is PCRA and CRA, to be safe. However, we cannot totally exclude systemic toxicity of ropivacaine 0.2% in the PCRA group as we did not measure peak plasma levels 30–60 min after each bolus; rather, we measured total ropivacaine plasma levels

![Fig 1](A) Mean (SD) 4-hourly total pain scores [VAS (in cm)] in the PCRA (open circle) and the CRA (black squares) groups. (n) Proportion of children requiring rescue analgesia in the PCRA (open bars) and the CRA (black bars) groups. Error bars represent the upper limit of the 95% confidence interval. (c) Proportion of children experiencing painful awakening during the night period in the PCRA (open bars) and the CRA (black bars) groups. Error bars represent the upper limit of the 95% confidence interval. (d) Satisfaction score in the PCRA (open bars) and the CRA (black bars) groups. Error bars represent the upper limit of the 95% confidence interval.

![Fig 2](Time course of total ropivacaine plasma concentrations obtained 24 and 48 h after the beginning of the infusion. Each bar represents the mean (SD) of 15 children in either group. *P<0.05. CRA (black bars), continuous regional analgesia; PCRA (open bars), patient-controlled regional analgesia.)
24 and 48 h after the beginning of the infusion while the 0.1 ml kg\(^{-1}\) delivered boluses of plain ropivacaine 0.2% averaged 7.8 (7.6) and 7.5 (8), respectively. The D/D ratio has been used as an indirect indicator of pain relief during PCA or PCEA and adequate analgesia is usually provided with a D/D ratio less than 2.\(^9\) Although we failed to record virtual additional boluses in the CRA group, this study reports a mean D/D ratio of 1.8 (0.9) in the PCRA group below the satisfactory ratio of 2 and confirms recent similar findings in children receiving PCRA or PCEA for postoperative pain relief after major orthopaedic procedures.\(^{28}\) It is very likely that children in the CRA group have attempted to access additional ropivacaine because supplemental rescue analgesia was greater in that group, although it just missed statistical significance. Thus, as in adults, PCRA may help to reduce local anaesthetic doses by adjusting analgesia to demand.\(^7\) Our findings failed to show any significant benefit of PCRA over CRA to improve the quality of awakening. With regard to the combination of boluses injection plus continuous fixed-rate infusion used in our study, this method has shown to be associated with a better sleep pattern than without a background infusion when using either PCEA or i.v. administered opiates.\(^2\)\(^{20}\) However, in this latter work, background infusion of morphine combined with supplemental boluses has led to greater sedation scores likely contributing to a better sleep pattern.\(^{20}\) Finally, postoperative local anaesthetics-related motor blockade occurrence is undesirable in children undergoing orthopaedic procedure. In our study, we failed to show any significant benefit of PCRA over CRA to improve motor blockade avoidance possibly because ropivacaine, especially at these dosages, appears to be associated with a lower propensity for motor block when compared with other long-acting amide local anaesthetics.\(^15\)

In summary, our findings suggest that the use of PCRA of the lower extremity provides satisfactory pain relief after orthopaedic surgery in children. Either PCRA or CRA technique provides adequate analgesia without altering overall satisfaction, supplemental analgesia and sleep pattern. However, boluses combined to fixed-infusion of ropivacaine 0.2% in that setting offers some advantages over continuously administered local anaesthetics such as less overall drug consumption and diminished plasma concentrations of ropivacaine. Further extensive study is required to show benefits of one technique over another in terms of clinical adverse-event occurrence and cost.

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