

PEDIATRIC PHARMACOTHERAPY

A Monthly Newsletter for Health Care Professionals
Children's Medical Center at the University of Virginia

Volume 6 Number 11

November 2000

Patient-Controlled Analgesia: Guidelines for Use in Children

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Patient-controlled analgesia (PCA) permits patients to self-administer small doses of opioid analgesics intravenously or subcutaneously at frequent intervals. PCA is used in the management of moderate-to-severe pain, often in postoperative, burn, sickle cell, and cancer pain. PCA allows the patient to assume control of analgesic administration without the need for nursing intervention, eliminating administration delays. Moreover, PCA can provide a more effective and sustained analgesia than traditional intramuscular (IM) opioid administration.¹⁻⁵

Patient Selection

To use PCA effectively, patients must be able to understand the required instructions and retain that information. The use of PCA in children age 8 years or more is well described. Successful PCA use has been reported in children as young as 6 years of age. Extending PCA to children less than 6 years of age, and to children who are physically and/or cognitively impaired, is limited by their developmental and physical inability to use the pump. The use of PCA in these patients has been attempted, but remains controversial.^{2,6} Parent-/nurse-controlled analgesia (PNCA) is a technique that many institutions have adopted for younger or impaired children. In contrast to patient-controlled analgesia, the parent or nurse provides the supplemental on-demand doses.⁶

Clinical Trials

Several studies evaluating the efficacy and safety of PCA in children have been performed. One of the earliest reports came from the University of Virginia Children's Medical Center. In 1988, Rodgers and colleagues published an evaluation of 15 children, aged 11-18 years, managed with PCA for postoperative pain.⁵ A 10-point self-assessment pain scale was used throughout the study. After an initial morphine "loading" dose of 0.05-0.1 mg/kg, a PCA dose of 0.025-0.05 mg/kg was used with a lockout interval, the period in which no dose is allowed, of 10 to 15

minutes. The mean duration of PCA use was 2.6 days (range 0.75-5.25 days). Pain scale scores were consistently below five. Adverse effects were mild: three patients experienced temporary burning at the injection site and one patient reported nausea. When compared to 15 matched historical controls managed with traditional intermittent opioid dosing, the children receiving PCA required significantly less analgesia during the postoperative period.

In 1991, Berde and colleagues performed a randomized prospective study comparing the efficacy and safety of IM morphine, PCA alone and PCA plus a continuous low-dose infusion (also known as a background infusion or basal rate) for analgesia after orthopedic surgery.⁷ The subjects were randomly assigned to one of three treatment groups: 1) IM morphine 0.1-0.15mg/kg every 3 hours, with an increase to 0.18mg/kg if necessary, 2) intermittent patient-controlled morphine group at a dose of 0.025 mg/kg, or 3) intermittent patient-controlled IV morphine at a dose of 0.018 mg/kg plus a background infusion of 0.015 mg/kg/hr. Both PCA conditions had a lockout period of 10 minutes. Both PCA regimens provided a maximum dose of 0.24 mg/kg over 4 hours.

The analgesics were initiated upon arrival of the subject to the nursing unit. Patients and nurses were asked to assess pain, sedation, nausea, anxiety, and satisfaction every 2 hours utilizing a visual analog scale for each variable. Nurses also recorded the child's alertness hourly and respiratory rate, pulse, and blood pressure every 4 hours.

Eighty-two children between the ages of 7 and 19 completed the study. Twenty-three children were given IM morphine, 32 received PCA alone, and 27 were in the PCA plus background infusion (PCA-plus) group. Mean patient self-report pain score from the first three study periods (the time from arrival on the nursing unit until 3 PM on

postoperative day 1 or approximately the first 24 hours after surgery) were 5.55 ± 2.46 for IM morphine, 4.58 ± 2.45 for PCA alone, and 3.63 ± 2.39 for PCA-plus. Statistical comparisons of the patient self-report data showed that PCA alone and PCA-plus resulted in significantly lower pain scores than did IM morphine. Mean nursing pain scores from the first three study periods were also significantly different (IM morphine 4.59 ± 2.26 , PCA alone 3.20 ± 1.94 , PCA-plus 2.58 ± 1.77). In this analysis, the PCA-plus protocol was significantly better than IM morphine; the other pairwise comparisons did not show significant differences.

Children who received PCA with an additional background infusion had higher ratings of satisfaction than children in the other two groups, but satisfaction ratings for all groups were high. No incidents of clinically significant respiratory depression were noted in any of the groups. Subjects receiving PCA-plus reported significantly less sedation than subjects receiving IM morphine. Finally, there were no significant differences between the treatment groups regarding nausea, vomiting and urinary retention. The authors concluded that PCA appears to be a more effective method of postoperative opioid administration than IM injection in children and adolescents after orthopedic surgery. PCA plus concurrent administration of a low-dose continuous morphine infusion improved pain scores as well as patient satisfaction without increasing the risk of adverse effects.

In 1993 Doyle and associates compared morphine PCA with or without a background infusion on postoperative analgesia, sleep, morphine consumption, sedation, nausea, vomiting, respiratory depression, and oxygen saturation (SpO_2).⁸ The study enrolled 40 children aged 6 to 12 years undergoing appendectomy. The patients were randomly allocated to receive either PCA with a bolus dose of 0.02 mg/kg and a lockout interval of 5 minutes or the same PCA with a background infusion of 0.02 mg/kg/hr (PCA-plus). Scores for pain, sedation, and nausea were recorded hourly using a 4-point scale.

The total morphine consumption in the PCA-plus group was significantly greater than that in the PCA only group. There was no significant difference in the amounts of morphine self-administered in the two groups. There were no significant differences between the two groups in the hourly pain scores. In contrast to the study

by Berde, there were significantly more incidences of SpO_2 less than 94% in the PCA-plus group than with PCA only. There were four occasions in one PCA-plus patient when ventilatory frequency was <10 breaths per minute. It should be noted, however, that 15% of the SpO_2 values recorded in the PCA only group were also less than 94%.

In addition, patients receiving PCA-plus were more sedated than those in the PCA only group. There was also significantly more nausea and vomiting, as well as time spent asleep in the PCA-plus group. The authors concluded that the use of a morphine PCA background infusion of 0.02 mg/kg/hr for children undergoing lower abdominal surgery produced a significant increase in morphine consumption without improving pain relief, and caused a significant increase in adverse effects.

Doyle and colleagues also performed a randomized study to evaluate different opioid bolus doses in children using PCA.⁹ Forty children undergoing appendectomy were randomized to receive morphine at doses of 0.01 or 0.02 mg/kg. Both regimens included a background morphine infusion of 0.004 mg/kg/hr and a lockout interval of 5 minutes. Hourly recordings of SpO_2 , ventilatory frequency, sedation, number of PCA demands, nausea, and volume of solution infused were made. Pain was scored at rest and during a specified movement, by observers who were unaware of the patient's treatment group.

Patients receiving a morphine dose of 0.02 mg/kg self-administered significantly more total morphine during the study period than those receiving the lower dose. There were no significant differences in pain scores at rest between the groups at any time except for the period 16-20 hours after surgery. However, pain scores during movement were significantly lower in the high dose group during each assessment period. There were significantly more periods when SpO_2 values were less than 94% in the low dose group. There were no significant differences in the incidence of vomiting and the time that patients spent asleep in the two groups after operation. Finally, there were no episodes of oversedation in either group.

The authors concluded that a bolus dose of morphine 0.01 mg/kg was associated with higher pain scores and more hypoxic episodes than a bolus dose of 0.02 mg/kg. They suggest that

there may have been a relationship between these results, with inadequate ventilation occurring as a consequence of pain which restricted thoracic and abdominal movements.

Monitto and colleagues undertook a prospective, observational study to determine patient demographics, effectiveness of analgesia, and the incidence of complications in patients less than 6 years of age receiving parent-/nurse-controlled analgesia (PNCA).⁶ Over a 1-year study period, PNCA was used to treat pain on 240 occasions (118 occasions in 98 females and 122 occasions in 114 males). Choice of opioid was left to the discretion of the attending physician on the Pediatric Pain Service. Three agents were used: morphine, fentanyl, and hydromorphone. All doses were titrated based upon response. Both parents and nurses were allowed to administer bolus doses to patients when they appeared in pain. To compare daily opioid usage patterns, opioid consumption was subsequently converted to "morphine equivalents" using a ratio of 1:40:5 for morphine: fentanyl: hydromorphone. Pain scores were measured by the patient's nurse or by the patient using an objective 6-point scale (pain rating: 0=none to 5=excruciating), and an objective 11-point scale (0-10) or a subjective Wong-Baker FACES Pain Rating Scale (0-5).

PNCA was used in patients for a median of 5 days, with total duration of therapy ranging from 2 to 54 days. Median opioid dosing on Day 1 was 31 µg/kg/hr morphine (range 24-47 µg/kg/hr), 0.86 µg/kg/hr fentanyl (0.6-1.17 µg/kg/hr), and 6.8 µg/kg/hr hydromorphone (4.9-10.2 µg/kg/hr). When these doses were converted to morphine equivalents, comparable hourly patterns of opioid consumption were observed. Median bolus administration frequency decreased over the 5 days of observation, with a peak use of one bolus every 1.3 hours on the first day. Daily maximum pain scores were ≤ 3 of 10 on the objective pain scale or ≤ 2 of 5 on the subjective or self-report pain scales in 81 to 95% of patients.

PNCA usage was associated with an 8% incidence of pruritus and a 15% incidence of vomiting on the first day of treatment. Vomiting was not associated with a particular opioid or surgical site; however, children ≥ 2 years of age had significantly more vomiting on Day 1 than patients < 2 years of age (26% versus 4%, P<0.05). Nine children (4%) studied received naloxone, five for treatment of PNCA-related apnea or oxygen desaturation. All had

improvement of their symptoms after naloxone administration. The authors concluded that PNCA produced effective analgesia in more than 80% of children under 6 years of age who were experiencing moderate-to-severe pain.

Adverse effects

Adverse effects with PCA are consistent with those commonly seen with opioid use. In general, adverse effects associated with PCA include respiratory depression, drowsiness, dry mouth, constipation, nausea, vomiting, urinary retention, and pruritus. In the studies of PCA use in children published to date, the most frequently reported adverse effects have been oversedation, nausea, and pruritus.⁷⁻⁹ Small doses of an opioid antagonist (ie, naloxone, nalbuphine, or nalmefene) administered intravenously can reduce morphine-induced adverse effects without compromising analgesic efficacy.^{1-4,10-12}

PCA Orders

The dosing of opioids for effective analgesia requires careful titration to patient response. A dose that is adequate for one patient may be too much or too little for another. Moreover, a specific dose, given by continuous IV infusion cannot be expected to meet the patient's analgesic needs at all times. The methods of PCA prescribing should be tailored to suit the needs of the individual child.

Morphine appears to be the agent used in most pediatric hospitals. Bolus doses of 0.015 to 0.02 mg/kg are commonly used as a starting point.⁶ Lockout intervals have not been formally studied, but a 5 to 15 minute lockout period has been widely used without any compromise in efficacy or safety. The use and dosing of a background infusion depends on the age of the child, the opioid selected, the type of surgery, and the type of pain. The dose of morphine most frequently used as a background infusion for postoperative pain is 0.01 to 0.04 mg/kg/hr. A higher dosing range, 0.025 to 2.6 mg/kg/hr, has been used for sickle cell or cancer pain, where patients are often opioid tolerant.^{6-10,12}

Summary

The use of patient controlled analgesia in children and adolescents has been shown safe and effective. PCA may be the preferred method of pain management in many children, as it allows the nurse to spend more time with other aspects of nursing care and results in fewer delays in analgesic administration to the patient.

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Pharmacology Literature Review

Enteral administration of growth factors

It has been suggested that endogenous G-CSF and erythropoietin, present in the amniotic fluid, may stimulate development of the intestines *in utero*. Several investigators have proposed that enteral administration of recombinant growth factors, such as filgrastim (rG-CSF) and epoetin alfa, to premature infants may mimic this effect. This study examined the stability of both recombinant growth factors in an electrolyte solution designed to simulate amniotic fluid. Both agents were stable in the solution of normal saline, sodium acetate, potassium chloride, and albumin for up to 24 hours when refrigerated and 18 hours at room temperature. The results of this preliminary work suggest that this method of growth factor administration is feasible and clinical trials are possible. Calhoun DA, Juul SE, McBryde EV, et al. Stability of filgrastim and epoetin alfa in a system designed for enteral administration to neonates. **Ann Pharmacother** 2000;34:1257-61.

Managing antiemetic therapy

The authors of this paper present a novel way of dosing antiemetics in children using a computerized outcomes-based approach which incorporates emetogenic potential of common chemotherapeutic agents, cost, and efficacy. Data collection and analysis were done at the bedside with a handheld computer. Compared with traditional methods, the computerized system resulted in fewer symptomatic patients and required less time. Holdsworth MT, Adams VR, Raisch DW, et al. Computerized system for outcomes-based antiemetic therapy in children. **Ann Pharmacother** 2000;34:1101-8.

Formulary Update

The following actions were taken by the Pharmacy and Therapeutics Committee during their meeting on 10/27/00:

1. A review of the selective serotonin reuptake inhibitors was conducted. Citalopram (Celexa[®]) was added to the Formulary for the treatment of depression. Fluvoxamine (Luvox[®]) was removed.
2. Risedronate (Actonel[®]), a bisphosphonate used for hypercalcemia and osteolytic bone lesions, was added with restriction to patients unable to tolerate alendronate.
3. The use of a generic preparation of cyclosporine (Gengraf[®]) was approved. Sandimmune[®] will no longer be stocked.

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