Brief Reviews

Postoperative analgesia: opioid infusions in infants and children

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The purpose of this review is to emphasise the ineffectiveness of traditional analgesic therapy in paediatric patients after surgery, to examine the sensation of pain in infants and children, and to describe the use of intravenous opioids for postoperative analgesia. The management of acute postoperative pain in the paediatric surgical population has been poor. This is despite the knowledge that infants and children have sufficient neurological development at birth to sense pain, and that the same hormonal and metabolic responses to nociceptive stimuli that occur in adult also occur in the neonate. Physicians frequently order analgesics in inappropriate doses, nurses are reluctant to administer opioids, and children themselves frequently compound the problem by refusing injections. The sophisticated techniques for providing postoperative analgesia which have been used so successfully in adults can also be used in paediatric patients. Two of these, continuous intravenous opioid infusion and patient-controlled analgesia, have proved to be very successful. Children older than six months can receive either modality safely with regular monitoring by qualified nursing staff. Infants younger than six months receiving continuous opioid infusions should be monitored in high-dependency units.

La qualité du traitement de la douleur aiguë postopératoire dans la population chirurgicale pédiatrique est douteuse. On sait pourtant que les bébés et les enfants possédent un développement neurologique suffisant dès la naissance pour ressentir la douleur et que les mêmes réponses hormonales et métaboliques aux stimulations nociceptives comme chez les adultes se manifestent chez le nouveau-né. Souvent, les médecins prescrivent des analgésiques à des doses inappropriées, les infirmières sont réticentes à administrer des opiacés, et fréquemment, les enfants eux-mêmes compliquent le problème en refusant les injections. Les techniques sophistiquées d'administration d'analgésie postopératoire utilisées avec tant de succès chez l'adulte peuvent aussi être utilisées chez l'enfant. Deux de celles-ci, la perfusion intraveineuse d'opiacés et l'analgésie contrôlée par le patient ont prouvé leur pleine efficacité. Les enfants au-dessus de six mois peuvent bénéficier de l'une ou l'autre méthode en sécurité avec un monitorage régulier et une équipe soignante qualifiée. Les enfants en-dessous de six mois qui reçoivent des perfusions continues d'opiacés doivent être suivis dans les unités de haute surveillance. L'objectif de cet article est de souligner l'inefficacité de l'analgésie traditionnelle chez les patients pédiatriques après la chirurgie, d'examiner la perception de la douleur chez les bébés et les enfants, et de décrire l'utilisation intraveineuse des opiacés pour l'analgésie post-opératoire.

Key words
ANAESTHESIA: paediatric;
ANALGESIA: postoperative, patient-controlled, infusion;
ANALGESICS: morphine, papaveretum.

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At least fifteen surveys published between 1952 and 1990[1–5] attest to the failure of intermittent intramuscular injection of narcotics to provide adequate postoperative analgesia for adult surgical patients. The traditional techniques of postoperative pain control have been even less successful in paediatric patients. Mather and Mackie[6] found that of 170 paediatric surgical patients 16% did not have a postoperative analgesic ordered, 39% did not receive a postoperative narcotic analgesic, 40% were in moderate to severe pain during the day of surgery, and 27% were similarly uncomfortable on the first postoperative day. Doses of analgesics which were ordered were often inappropriate in amount and/or frequency, and were ordered *pro re nata*, which was interpreted by the nursing staff to mean, "Give as few doses over the longest period of time as possible." Eland and Anderson[7] matched 25 children with 18 adults who were undergoing the same operations. The 25 children received 24 doses of analgesics, of which 11 were narcotics. The 18 adults received

671 doses of analgesics of which 372 were narcotics. Thirteen of the 25 children received no analgesics, including a four-year-old with an amputated foot, a six-year-old who underwent heminephrectomy, and a seven-year-old who had a repair of an ASD. One child received two aspirin tablets following spinal fusion, and two with 65–70% second and third degree burns received one aspirin and one acetaminophen tablet each. Beyer *et al*,[8] comparing 50 children with 50 adults undergoing open heart surgery, showed that the adults received more than twice as many doses of analgesics as the children. Similarly, Schecter *et al.*[9] matched children and adults undergoing inguinal herniorrhaphy or appendectomy or sustaining fractured femurs or second degree burns and, again, the adults received twice as many doses of narcotics per day as the children. These studies, and others in the nursing literature,[10,11] indicate that even when postoperative analgesics are ordered appropriately, nursing staff hesitate to give children narcotics, preferring to administer non-narcotic analgesics, or to use nonanalgesic nursing interventions. A recent study[12] compared patient-controlled analgesia (PCA) with nurse-controlled analgesia using the same PCA device in children aged 5–20 yr undergoing corrective surgery for scoliosis. The nurses' assessment of the patients' pain consistently underestimated that of the patients' and the nurses administered less morphine than did the patients.

Pain sensation in infants and children

Longstanding misconceptions surround the traditional approach to postoperative analgesia in children. The myths persist that (a) children do not feel as much pain as adults, (b) children will not remember pain, (c) children may become narcotic addicts, (d) narcotics are not safe for children, and (e) children who do not act as if they are in pain are not in pain. Children will often lie quietly rigid, denying pain, because of their overwhelming fear of getting "a shot." Eland and Anderson[7] found that 55% of paediatric patients identified injections as the worst part of their hospitalization. Children admitted to the investigators that they had lied to the nursing staff about how much pain they were in because they were so afraid of receiving an injection.

The view that the nervous system of neonates and infants is developmentally immature has been used to support the practice of providing little or no anaesthesia or analgesia for painful invasive procedures. More recently, Anand and Hickey[13] have provided a well referenced review of pain in neonates. The density of cutaneous nociceptive nerve endings in neonates is at least that of adults. The lack of myelination of peripheral nerves, which would slow conduction velocity, is offset by the shorter distances impulses must travel. Nociceptive tracts in the spinal cord and brain have completed myelination by the end of the third trimester. Substance P and its receptors are detectable in the fetal dorsal horn at 12 to 16 wk of gestation. Endogenous opioids are present in the plasma and CSF of term infants and the concentrations of beta-endorphin increase in response to stress. Increases in heart rate and blood pressure, decreases in transcutaneous oxygen tension and increases in palmar sweating are observed in neonates undergoing painful procedures such as circumcisions and heel pricks. These changes can be prevented by providing analgesia. Similarly, a marked release of catecholamines, growth hormone, cortisol and glucagon occurs, and this hormonal stress response can be attenuated when adequate anaesthesia is provided. Altered complex behavioural patterns seen following circumcision are absent when local anaesthesia is used. In summary, the neural pathways and neurotransmitters responsible for nociception and its modulation, as well as the evoked hormonal, metabolic and cardiorespiratory responses, are fully present in neonates.[13]

Postoperative analgesia

The goal in providing postoperative analgesia is to achieve consistent pain relief while limiting toxicity. Inter- and intrapatient variations in the pharmacokinetic and pharmacodynamic behaviour of opioids, as well as psychological and sociocultural differences, make it impossible to achieve consistent analgesia reliably with intermittent intramuscular injections.

Recently, the sophisticated analgesic interventions that have been so successful in adults have also been applied to paediatric patients. These include regional anaesthetic techniques, subarachnoid and epidural opioids, continuous narcotic infusions, patient-controlled analgesia and patient-controlled epidural analgesia.

Continuous intravenous opioid infusions

Miser[14] described the use of continuous infusions of morphine in children with terminal malignancy in 1980. In 1983, Bray[15] randomized 20 children undergoing major abdominal or thoracic surgery. In one group, a loading dose of morphine 200 $\mu g \cdot kg^{-1}$ was followed by a continuous infusion at a rate of 20 $\mu g \cdot kg^{-1} \cdot hr^{-1}$. The second group received *im* injections of morphine 200 $\mu g \cdot kg^{-1}$ q4hr *prn*. Pain scores in the latter group were higher over the first 48 hr postoperatively. Their technique was subsequently used in over 200 patients aged 1–15 yr with good results.[15]

Beasley and Tibballs[16] reported a series of 121 children who underwent major surgery, 13 of whom were under one year of age. Nursing staff were allowed to vary an infusion of morphine between 10 and 40 $\mu g \cdot kg^{-1} \cdot hr^{-1}$. Pain scores assessed by patients were low (median scores

20–30/100) and respiratory depression was not detected, although vital signs were only taken at four-hour intervals. Lynn[17] studied 44 children aged 14 mo to 17 yr following cardiac surgery. The patients received morphine infusions ranging from 10 to 50 $\mu g \cdot kg^{-1} \cdot hr^{-1}$ for an average of 35 hr. Of 39 patients receiving 10–30 $\mu g \cdot kg^{-1} \cdot hr^{-1}$, only one had a $PaCO_2$ greater than 50 mmHg after ventilator rates (intermittent mandatory ventilation) had been decreased to less than eight breaths per minute. Three of five children receiving 40–50 $\mu g \cdot kg^{-1} \cdot hr^{-1}$ developed mild hypercarbia ($PaCO_2$ values of 48, 54 and 66 mmHg). Dilworth and MacKellar[18] reported on the first 144 patients of an experience of over 600, aged 6 mo to 15 yr. In their series, papaveretum in a dose of 50–70 $\mu g \cdot kg^{-1} \cdot hr^{-1}$ was the most commonly used opioid. In seven patients (5%) there was a decrease in respiratory rate below a set minimum which responded to a reduction in dosage. Hendrickson *et al.*[19] compared 20 children receiving morphine 100 $\mu g \cdot kg^{-1}$ *im* q3hr with 26 children receiving morphine 10–40 $\mu g \cdot kg^{-1} \cdot hr^{-1}$ *iv*. Pain scores for the *im* group were consistently higher for three days postoperatively. There were no differences between the two groups with respect to side effects, and no cases of respiratory depression were reported.

Despite the success of this technique in children over six months of age, there has still been concern with the use of opioids in patients under this age. Koren *et al.*[20] gave morphine infusions to 12 newborns at a rate of 6–40 $\mu g \cdot kg^{-1} \cdot hr^{-1}$ for 59.5 ± 10.2 hr. A large interpatient variability in plasma concentrations, elimination half-life and clearance was observed. Two patients with high serum concentrations (61 and 90 $ng \cdot ml^{-1}$) had generalized seizures which stopped after the narcotic was discontinued. They recommended a maximum infusion rate of 15 $\mu g \cdot kg^{-1} \cdot hr^{-1}$. Similarly, Lynn and Slattery[21] found longer elimination half-lives and slower clearance in seven term infants less than seven days of age compared with three infants older than three weeks of age. Olkkola *et al.*[22] also found interpatient variations in the pharmacokinetic behaviour of morphine, with two infants less than two months old having prolonged clearance and elimination half-life. The authors of these papers felt that the pharmacokinetic profile of morphine reached that of the older child or adult by one or two months of age, but the number of infants studied was quite small. A summary of pharmacokinetic variables from these studies is presented in the Table.

It has been suggested that the infant brain is more sensitive than adults to opioids, on a pharmacodynamic basis. Kupferberg and Way[23] demonstrated a lower morphine LD_{50} in 16-day-old rats than in 32-day-old rats, and found brain concentrations of morphine were higher in the younger rats following equal doses based on weight.

TABLE Morphine pharmacokinetic behaviour in newborns and infants

Reference	*n*	*Age*	$t_{1/2}\beta$ *(hr)*	*Cl* $(ml \cdot kg^{-1} \cdot min^{-1})$
20	8	newborn	13.9 ± 6.4	7.8 ± 1.9
21	7	<4 d	6.8	6.3
	3	>1 mo	3.9	23.8
	31	1–17 yr		23.4
22	2	<3 mo	4	5.2
	4	3–6 mo	1	29.6

They suggested that an incompletely developed blood brain barrier allowed greater penetration of morphine to the infant brain. However, the endpoint for comparison was death, not respiratory depression or analgesia. As well, the blood brain barrier in the newborn rat is relatively incompletely developed compared with higher mammals such as sheep.[24] Their findings may not be applicable to the human neonate.

It would seem reasonable to use continuous opioid infusions in children over six months of age on paediatric wards, with hourly monitoring of vital signs, level of consciousness and pain scores by trained nursing staff. Although the literature suggests that this may be safe in infants as young as two months of age, larger studies will have to be performed to demonstrate that safety. Until then, these infants should be monitored in a high-dependency unit.

Patient-controlled analgesia

The theory underlying the use of PCA is that only the patients (but not the nurses or physicians) know when they are in pain, how much pain they have, and when and how much analgesia they need. Patients can titrate their analgesic intake to match fluctuating degrees of pain, with short intervals between drug administration and therapeutic effect. An individual balance between the need for analgesia and the severity of side effects is reached. The ability to maintain control of this therapy is an important factor in its success, particularly in an environment where so much control has been taken away.[25]

The first report of the use of PCA in paediatric patients was in 1987.* The initial reports described PCA use in adolescents,[26–28]* but since then the lower age limit has been steadily decreasing, and selected patients as young as five years of age can use PCA successfully.[29–31]† A typical

**Brown RE, Broadman LM.* Patient-controlled analgesia (PCA) for postoperative pain control in adolescents. Anesth Analg 1987; 66: S22.

†*Gaukroger PB, Tomkins DP, van der Walt JH.* Letter. J Pediatr Surg 1988; 23: 1227-8.

programme uses a bolus of morphine 10–20 $\mu g \cdot kg^{-1}$ with a lockout period of ten minutes. Patient-controlled analgesia has been used with[29,31,32] and without[26–28,30,32]* a continuous background infusion, although this is presently an area of controversy in the adult literature. Three authors found that the use of a background infusion did not improve pain scores, did not decrease the number of demands by the patients, nor decrease the number of patients who had difficulty sleeping or who had nocturnal awakening due to pain.[33–35] On the other hand, two studies[36,37] showed better pain scores when background infusions were used. The only paediatric study which examined this question[32] found no differences in pain scores between patients who did and did not receive a background infusion. Although the risk of respiratory depression may theoretically be increased with the use of background infusions, no study to date has documented this.

All the published series have claimed consistent success. Those that have compared PCA with intermittent *prn im* injection[26,28,32] have demonstrated superior analgesia without an increase in side effects. Rogers[26] and Broadman[28] found that children using PCA received twice as much narcotic as those undergoing similar operations and receiving intermittent *intramuscular* injections. This underscores the inadequacy of the traditional management of postoperative pain in children.

Patients quickly learn to administer a dose before painful procedures such as dressing changes, removal of drains or physiotherapy. Children usually indicate that they want to use PCA again on subsequent hospital admissions. Studies in adults[38,39] have indicated better postoperative recovery and earlier hospital discharge when patients receive PCA rather than *intramuscular* injections, but no such studies have been performed in paediatric patients.

Considerable preparation is required in order to establish a PCA programme. Convincing hospital administration and surgical staff that this therapy will be beneficial usually requires a pilot project. Nursing staff must receive sufficient inservice education and be comfortable with the machines. Nurses are often reluctant to become involved with PCA, being concerned both with the technology required and the anticipated increase in workload. However, experience has shown that nursing time spent in providing analgesia is actually reduced.[40] Once the nurses see how effective PCA is, they become enthusiastic advocates.

Candidates for PCA are children who are at least five years of age, undergoing major surgical procedures after which considerable pain is anticipated. (Patient-controlled analgesia is also being used for painful medical conditions such as sickle cell crises, palliative care in oncology, and in burn victims.) Preoperatively, the patients and their parents are interviewed, and the purpose and operation of the machine are explained. These instructions should be reinforced by the nursing staff. The PCA device is programmed, loaded and waiting for the patient in the post-anaesthetic recovery room. An order sheet is completed describing the menu with which the machine has been programmed, monitoring orders, instructions for inadequate analgesia or excessive sedation, treatment of side effects, and the person to contact in case problems arise. Other CNS depressants are not given without consulting the anaesthesia staff responsible for the patient. Patients are usually monitored hourly: pain, side effects, somnolence and respiratory rate are assessed.

One important piece of information which is available from the memory of many PCA machines is the number of attempts and doses that the patient has received. This is important when assessing a patient who complains of inadequate analgesia. If the patient is using the maximum that the programmed menu could deliver, then the menu is inadequate and should be increased. However, if the patient is hardly using the device at all, the reason for his/her reluctance to press the trigger must be found. It may be that the patient needs reeducation or reassurance about the use of the machine, or that the parents, who may be discouraging their child from triggering, need to be reassured. This problem was brought home most vividly by one of our cases early in a pilot project at the British Columbia's Children's Hospital. An eight-year-old girl underwent an Ilizarov leg-lengthening procedure. Upon return to the floor, her nurse instructed her to, "Push the button whenever you have pain, and you'll get a shot." Needless to say, the poor child pushed no buttons, and received no analgesia. A few moments reassurance were all that were necessary.

Parent-assisted PCA

Rogers[26] and Broadman[41] discussed the use of "parent-assisted" PCA. This modification introduces two potential problems. On the one hand, it bypasses one of the safety features of PCA, that the sedated patient will not trigger the machine.* It also introduces the possibility of parental bias which may limit narcotic administration as with nursing staff.[12] The use of parent-assisted PCA also means that a parent must be continuously present 24 hr a day.

Summary

Until recently, the record of health care professionals in the provision of postoperative analgesia in paediatric patients has been poor. We have many new strategies available, which give our patients superior and more

**Gaukroger PB, Tomkins DP, van der Walt JH.* Letter. J Pediatr Surg 1988; 23: 1227-8.

consistent pain relief. Continuous intravenous opioid infusion and PCA are two extremely effective techniques. It is important to convince our colleagues, surgeons, nurses and hospital administrators of the value of instituting programmes for acute pain management in children.

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