PERSONAL PRACTICE

Preoperative and postoperative pain control

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Interest in pain management for children in the perioperative period has increased substantially in the past few years and this has led to very significant changes in this area of clinical practice.

The quality of pain control that can be achieved is more often a function of the time and resources devoted to it, rather than the actual regimens employed. A well coordinated multidisciplinary approach will achieve the best results and 'acute pain control teams' are being established in many hospitals with this aim.

Acute pain treatment in children is subject to special problems because they are such a diverse population. The response to analgesics varies with age and side effects are often unpredictable. Pain is difficult to assess in preverbal children which further complicates its management.

Fortunately there have been a number of advances recently that have allowed improvements in pain management. The mechanisms of pain transmission are more completely understood, the pharmacokinetics and pharmacodynamics of analgesic drugs in small children have been described, and new techniques of pain control have come into practice.

Aims of management

Pain has adverse psychological and physiological effects which have been well documented.¹⁻⁴ It is now accepted that patients of all ages are capable of feeling pain and a substantial neuroendocrine response to pain can be demonstrated even in premature neonates.⁵ The full significance of this response is not well understood and although we do have the means to completely ablate it, there is insufficient evidence to justify the potential risks incurred in doing so as a routine.

The beneficial effects of reducing pain to clinically acceptable levels are more obvious and this is the objective in the perioperative period. Patients should be comfortable after surgery and a degree of sedation is particularly important in younger children. It is not always appropriate to remove all sensation of pain as this may mask important clinical information or induce undesirable or dangerous complications. A realistic understanding of what can and should be achieved is important.

Pain assessment

Recognition and quantification of pain are essential steps in pain management. Pain is a

complex sensory experience exclusive to the individual and best assessed by that individual. Assessment by observers is inferior to self assessment, however it is often the only practical method available in children.⁶

In adults postoperative pain is most frequently measured using a linear visual analogue scale. The patient scores his pain on a line with end points 'no pain' and 'worst pain imaginable'.⁷ Sensitive and reproducible results are obtained using this method and it can be used in normal children above the age of 6 or 7 years.⁸ Attempts at self assessment below this age have been made involving diverse and imaginative methods, with varying success. None has yet emerged as superior, and in practice some sort of observer assessment is most often used. A number of observer rated behavioural scales have been devised and they are useful especially when different treatments are being compared.^{8,9} An important effect of recording of pain assessment scores is that it will increase awareness of the need for analgesia which may improve the quality of pain control. Children who cannot communicate how they feel are best assessed by those who know them well and at present this may be the most sensitive measure we have at our disposal.

General principles

A number of considerations have to be reconciled when planning the most appropriate management. The age, physical condition, and capabilities of the patient are important. The presence of preoperative pain and anxiety, the site and extent of surgery, the planned technique of anaesthesia, and likely intensity of postoperative pain must be carefully considered. The intended postoperative monitoring and nursing must be appropriate to the situation and if day case surgery is planned discharge should be suitably timed.

The concept of *balanced analgesia* is to use several drugs together in moderate doses to achieve maximum efficacy with the least side effects. The timing of analgesia in relation to surgery may also be important and the *pre-emptive management* of acute pain is gaining credibility. Analgesia given before injury takes place may be more effective than that given later. The pathophysiology of pain transmission is incompletely understood but the application of what we do know should help in the rational and optimal use of available drugs and

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techniques. The choices are between three groups of drugs: the local anaesthetics, non-steroidal analgesics (NSAIDs) and paracetamol, and the opioid analgesics. These drugs act at different sites and are complementary in effect.

Pain transmission after trauma and acute injury

After injury pain receptors are activated by a variety of stimuli including the many substances released as a result of tissue damage. Pain is transmitted by primary afferents to the primary interneurons in the dorsal horn of the spinal cord, which is the site of the physiological 'gate'. At this point signals are enhanced or reduced by facilitatory or inhibitory mechanisms before transmission to the brain where pain is perceived.⁹

At the site of the injury and in neighbouring uninjured areas a state of increased sensitivity occurs manifest as abnormally painful touch sensation, tenderness, and pain on movement of the affected area. In the periphery, substances such as the prostaglandins E_2 and I_2 , peptides, hydrogen ions, and catecholamines do not cause pain but lower the threshold of pain receptors to other stimuli. Similar changes in surrounding areas not directly injured are due to antidromic axoaxonal stimulation and to increased excitability of spinal neurones, that is: central sensitisation. These effects are an example of plasticity within the central nervous system. Events at the periphery have initiated changes in the central nervous system which alter the perception of pain by augmenting inputs from normally innocuous stimuli.^{10 11}

The basis of pre-emptive analgesia is an attempt to prevent the development of these centrally sensitising systems by abolishing the barrage of nociceptive inputs during surgery. This should reduce the degree of postoperative pain, particularly by reducing the hyperalgesia and sensitivity of the surrounding area. Local anaesthetics and opioids have been shown to exhibit this effect in a small number of studies.¹²⁻¹⁴

These mechanisms account for the complementary effects of different analgesics. Local anaesthetics block nerve conduction directly either as peripheral nerve blocks or centrally in spinal and epidural analgesia. Opioids alter the transmission and perception of painful stimuli in the spinal cord and brain. The NSAIDs reduce the prostaglandin mediated sensitisation of pain receptors at the site of injury.

The preoperative phase

At this time the postoperative analgesic plan can be explained to the patient and parent and any questions answered. This is particularly important if the patient is to be expected to actively participate after anaesthesia and surgery, for example, in the use of patient controlled analgesia (PCA, see later).

Psychological factors are known to influence the degree of acute pain reported by patients, fear of the unknown and anticipation of

pain are contributory to this and must be considered.^{15 16} The extent to which discussion and reassurance will allay anxiety varies greatly and often pharmacological aids are necessary. Pre-emptive analgesic administration at this time may be beneficial.¹⁷ Opioid analgesics are indicated for their analgesic, sedative, and anxiolytic effects unless they are going to be used later in the subarachnoid or epidural space, as previous administration tends to increase the likelihood of respiratory depression. The route of drug administration chosen at this time is important. Preoperative medication should be as pleasant as possible to administer and receive, therefore intramuscular injection is rarely indicated. Preoperative fasting does not preclude oral medication and a number of oral preparations of opioids exist that may be used. If venepuncture is intended before the induction of anaesthesia then EMLA cream (lignocaine and prilocaine, Astra) should be applied approximately 90 minutes beforehand.

Treatment for postoperative pain

MILD ANALGESICS

Paracetamol and the NSAIDs are suitable for use after minor surgery, alone or in conjunction with a local anaesthetic nerve block. After major surgery they may complement more potent opioid drugs. Paracetamol and ibuprofen are commonly used in children. Diclofenac and ketorolac, newer, more potent NSAIDs, are entering paediatric practice, although they are not licensed for postoperative use in children at the present.

The exact mechanism of action of these drugs is not known. They are inhibitors of prostaglandin production through their action on the enzyme prostaglandin synthetase (cyclo-oxygenase). Paracetamol has least effect on prostaglandin production. Prostaglandins have many functions including neurotransmission, actions on platelet adhesiveness, and effects on local tissue blood flow particularly in brain and kidney. They are involved in the inflammatory response and in the modification of nociception, they do not cause pain directly but sensitise nerve endings to the effects of pain producing substances. There is a variation in response between individuals to these drugs and all exhibit a maximum efficacy, or ceiling effect, after which further increases in dosage will not improve analgesia.

Oral administration is not normally tolerated for several hours after anaesthesia and gastrointestinal function may not return for several days after major surgery, which limits the use of these drugs. Paracetamol and diclofenac are available in a rectal formulation. Diclofenac and ketorolac can be given parenterally but diclofenac is painful by the intramuscular route.

Paracetamol is the most widely used and is the weakest analgesic. First introduced in 1893, it has little peripheral anti-inflammatory activity and does not depress renal or platelet function. It is suitable for all age groups including neonates. Ibuprofen and diclofenac are stronger analgesics and ketorolac may be

even more efficacious.¹⁸ These drugs cause platelet dysfunction and may increase bleeding if given preoperatively, although research in adults suggests this effect is clinically insignificant (it has not been studied in children). Renal dysfunction can occur and is reversible on discontinuing treatment and chronic ingestion is associated with gastrointestinal irritation. The possibility of cerebral and renal vasoconstriction make NSAIDS unsuitable for use in neonates, although little information is available on their effects in this group. Whether they are effective for pre-emptive analgesia is still open to debate.¹⁹ NSAIDS are best introduced early in the postoperative phase.²⁰ They have been shown to reduce opioid requirements after surgery in adults, and intravenous ketorolac is currently being evaluated for this use in children.^{21 22}

LOCAL ANALGESIA

Local analgesic techniques are widely used in paediatrics ranging from simple peripheral nerve blocks to more complex central blocks such as continuous epidurals. Unlike adults, children will usually require general anaesthesia during surgery. Analgesia can be provided intraoperatively and for several hours postoperatively by a single local anaesthetic block performed after the induction of general anaesthesia. These techniques are appealing because they provide high quality analgesia without the administration problems and systemic side effects of opioid drugs and will often be effective until the oral route is available after surgery. If a local anaesthetic block is not possible, infiltration of the surgical incision with local anaesthetic will often substantially reduce further analgesic requirements.

Local anaesthesia is contraindicated in the presence of infection or bleeding diathesis.

PERIPHERAL NERVE BLOCK

Specific nerves usually can be anaesthetised by a single injection, for example ilioinguinal and iliohypogastric nerves for inguinal hernia repair and orchidopexy or the dorsal nerve of penis for circumcision. These are relatively easy to perform and complications and side effects are few.²³ They are particularly suitable for day case surgery.²⁴ Bupivacaine has the longest duration of effect, lasting at least four hours and sometimes much longer.

CENTRAL NERVE BLOCKS

These blocks can provide analgesia at spinal segmental levels from thoracic to sacral depending on the site of the block and the volume and concentration of local anaesthetic used. The duration of effect can be extended by infusion of local anaesthetic and the addition of low dose opioid drugs.

Subarachnoid block

Small volumes of local anaesthetic injected into the cerebrospinal fluid will give profound

analgesia of up to four hours' duration. Some degree of motor block is invariable, causing weakness of the legs. Opioids by this route give prolonged analgesia, however the incidence of respiratory depression is unacceptably high.²⁵

Epidural block

This is a versatile technique with wide applications.²⁶⁻²⁸ Continuous epidural analgesia through a catheter can be used for several days. Access to the epidural space can be gained at the sacral (caudal), lumbar, or thoracic region as required. The first is easiest to perform and is suitable for surgery below the umbilicus; four to six hours analgesia is obtained after a single injection of bupivacaine. The shorter, straighter spine of neonates will allow a catheter to be fed from the sacrococcygeal ligament to the lumbar or thoracic region. In older children catheters are inserted at the required level. Profound analgesia with few systemic side effects can be achieved and hypotension that occurs in adults is rare in children.²⁸ In particular, postoperative respiratory function is excellent, with good preservation of the functional residual capacity of the lungs and cough reflex. Epidurals are also particularly effective in blunting the hormonal and biochemical response to surgery. There are some disadvantages; local anaesthetics alone may produce an uneven degree of analgesia which is difficult to rectify, strong solutions cause unwanted motor weakness and tachyphylaxis occurs. There is little or no sedative effect.

Addition of small doses of opioids will help to reduce these problems but unfortunately introduces a new range of side effects which can be troublesome. Itching, nausea and vomiting, urinary retention, and delayed onset respiratory depression are features of central opioid administration. These side effects can often be effectively treated with low doses of naloxone given systemically which do not reverse the central analgesic effect, but significant numbers of patients are affected and the need for urinary catheterisation in particular can be unacceptably high.^{28 29}

Technical problems can also occur, the fine gauge epidural catheters may become displaced, kinked, or blocked necessitating premature termination of the technique. Management of continuous epidural analgesia requires close supervision by specially trained staff to achieve the best results and for the present, it has a limited place unless these problems can be resolved. Single injection techniques have clearer indications, and are more widely used.

OPIOID ANALGESICS

Morphine is the prototype opioid analgesic and is still the mainstay of postoperative pain treatment. It has been in use for many years and its effects are well known if incompletely understood. It is the standard to which others are compared. A degree of respiratory depression is common and this effect should be monitored whenever the drug is used in the

perioperative period. Morphine clearance reaches adult values between 6 months and 2.5 years of age.³⁰ At younger ages the effects of opioids are less predictable and respiratory support is often required. In neonates plasma concentrations are very variable and rebound increases can occur between 10 minutes to 15 hours after a single dose of some opioids.^{31 32} Repeated administration causes marked cumulation and very high concentrations can be achieved.^{33 34} About 70% of intravenous morphine is metabolised in the liver to the conjugated metabolites morphine-3-glucuronide (M3G, 55%) and morphine-6-glucuronide (M6G, 15%). M6G is a potent analgesic (200 times stronger than morphine in animal studies) and causes respiratory depression. In contrast M3G is not analgesic, it has excitatory effects and caused respiratory stimulation in an animal model.³⁵ Age, pharmacogenetic and other factors influence the relative proportions of these metabolites produced by an individual. It is possible that alterations in the balance of M3G to M6G can explain some of the differences seen between individuals in response to morphine.

Oral administration

Morphine, codeine, and dihydrocodeine are popular choices for oral administration in children, particularly in liquid form. However, in the early postoperative period, parenteral treatment is generally required as gastrointestinal absorption is unreliable.

Intramuscular administration

Numerous painful injections are obviously to be avoided. There is declining acceptance of intramuscular opioid injections, although they have a long record of safety. Administration is simple and special equipment is not required, absorption is reliable and predictable, reaching therapeutic concentrations soon after injection. The drug must be given regularly and the dose flexible if analgesia is to be satisfactory, but this rarely occurs and can be difficult to achieve. Indwelling cannulas can be placed during anaesthesia for subsequent use, this practice has not been widespread, however, and there are concerns that absorption of some drugs may become unpredictable after a time. Administration algorithms can improve the quality of analgesia obtained by intramuscular dosing. The technique has a place but is really only suitable for short periods of time unless other methods are not available.

Intravenous administration

All intravenous techniques require continuous direct supervision by specially trained staff. Various infusion techniques are available and are increasing in popularity as different facilities become available. A simple continuous morphine infusion adjusted as necessary is often satisfactory but may be too inflexible. Analgesic requirements vary widely between patients and for the same patient depending on the circumstances. Adjustments to the rate of

infusion of morphine within narrow limits will only very slowly change the plasma concentration and clinical effect. Subtherapeutic or unnecessarily high concentrations may be inadvertently obtained. Delivery of the drug is more easily tailored to an individual's requirements using a programmable syringe pump or PCA.

PCA

Specially designed tamper proof pumps allow a preset continuous infusion or background infusion to be supplemented by bolus doses, triggered from a patient operated handset. A minimum dose interval known as the lockout period is also preset together with a maximum total dose within a defined period.

This technique is becoming popular in paediatric practice after its successful use in adults.^{36 37} Normal children above the age of 6 years are usually able to understand the concept and physically accomplish PCA. Before starting PCA the patient is first made pain free by a suitable loading dose of morphine, this is normally done in the operating theatre or the recovery room where the pump is programmed and started. The greatest safety feature of PCA is that *only the patient* operates the handset. The requirement for a small background infusion varies and tends to be inversely related to the age of the patient. The technique is very safe provided staff are properly trained and clear protocols devised for the management of complications, such as nausea and vomiting, excessive sedation, and respiratory depression.

Nurse controlled analgesia

In children too young to use PCA the apparatus can be used as a modified continuous opiate infusion known as nurse controlled analgesia. The pump is programmed to deliver a moderate background infusion with the option of one or two extra boluses per hour to be triggered by the named nurse who is caring for the patient. Analgesia is supplemented before painful procedures while the constant infusion remains at a relatively low level. The system has flexibility and is efficient particularly as the nursing staff are not required to spend long periods of time checking and administering controlled drugs.

Subcutaneous administration

The techniques described above can also be used to administer morphine subcutaneously provided suitably high concentration, low volume solutions are used. An intravenous cannula is sited in the subcutaneous tissue and covered with a clear occlusive dressing. The site should be changed when necessary (weekly is usual) and EMLA cream makes this less uncomfortable.

The future

Improvements in the current techniques of pain management are constantly being

described. New analgesic drugs are being researched. Antagonists to neuropeptide mediators in pain transmission such as substance P and neurokinin A have been discovered and these may lead to new drugs with novel mechanisms of action. Opioids and NSAIDs with more specific effects are also a possibility with enhanced therapeutic effect and decreased liability to side effects.

A recent report on the management of pain after surgery emphasised that a named individual or individuals should take responsibility for the safe and adequate provision of analgesia in every institution and that outcomes should be carefully audited.³⁸ In its publication *Children First* the Audit Commission has outlined its proposals to assess the quality of care given to children in hospital; pain relief is named as one of 10 indicators to be used and is further suggested to be the subject of continuous appraisal.³⁹ It is likely that we can expect further interest and development in the field of acute pain management in the coming years.

- Bond MR. Psychological and psychiatric aspects of pain. *Anaesthesia* 1978; 33: 355-61.
- Owens ME. Pain in infancy: conceptual and methodological issues. *Pain* 1984; 20: 213-30.
- Anand KJS, Hickey PR. Halothane-morphine compared with high dose sufentanil for anaesthesia and postoperative analgesia in neonatal cardiac surgery. *N Engl J Med* 1991; 326: 1-9.
- Dixon S, Snyder J, Holve R, Bromberger P. Behavioural effects of circumcision with and without anaesthesia. *J Dev Behav Pediatr* 1984; 5: 246-50.
- Anand KJS, Hickey PR. Pain and its effects in the human neonate and fetus. *N Engl J Med* 1987; 317: 1321-9.
- Beyer JE, McGrath PJ, Berde CB. Discordance between self-report and behavioural pain measures in children aged 3-7 years after surgery. *Journal of Pain and Symptom Management* 1990; 5: 350-6.
- McGrath PJ, Cunningham MA, Goodman JT, Unruh A. The clinical measurement of pain in children: a review. *Clinical Journal of Pain* 1985; 1: 221-7.
- Beyer JE, Wells N. The assessment of pain in children. *Pediatr Clin North Am* 1989; 36: 837-53.
- Wall PD. The gate control theory of pain mechanisms. A re-examination and re-statement. *Brain* 1978; 101: 1-18.
- Raja SN, Meyer RA, Campbell JN. Peripheral mechanisms of somatic pain. *Anesthesiology* 1988; 68: 571-90.
- Woolf CJ. Recent advances in the pathophysiology of acute pain. *Br J Anaesth* 1989; 63: 139-46.
- Jebeles JA, Reilly JS, Gutierrez JF, Bradley EL, Kissin I. The effect of preincisional infiltration of tonsils with bupivacaine on the pain following tonsillectomy under general anaesthesia. *Pain* 1991; 47: 305-8.
- Ejlertsen E, Bryde Andersen H, Eliassen K, Mogensen T. A comparison between preincisional and postincisional lidocaine infiltration and postoperative pain. *Anesth Analg* 1992; 74: 495-8.
- Richmond CE, Bromley LM, Woolf CJ. *Lancet* 1993; 342: 73-5.
- Parbrook GD, Steel DF, Dalrymple DG. Factors predisposing to postoperative pain and pulmonary complications. A study of male patients undergoing elective gastric surgery. *Br J Anaesth* 1973; 45: 21-33.
- Bond MR. Psychological and psychiatric aspects of pain. *Anaesthesia* 1978; 33: 355-61.
- Kiss IE, Kilian M. Does opiate premedication influence postoperative analgesia? A prospective study. *Pain* 1992; 48: 157-9.
- Maunukela EL, Kokki H, Bullingham RES. Comparison of intravenous ketorolac with morphine for postoperative pain in children. *Clin Pharmacol Ther* 1992; 52: 436-43.
- Murphy DF, Medley C. Preoperative indomethacin for pain relief after thoracotomy: comparison with postoperative indomethacin. *Br J Anaesth* 1993; 70: 298-300.
- Murphy DF. NSAIDs and postoperative pain. Sooner is better than later. *BMJ* 1993; 306: 1493-4.
- Owen H, Glavin RJ, Shaw NA. Ibuprofen in the management of postoperative pain. *Br J Anaesth* 1986; 58: 1371-5.
- Gilles GWA, Kenny GNC, McArdle CS. The morphine sparing effect of ketorolac tromethamine. *Anaesthesia* 1987; 42: 727-31.
- Arthur DS, McNicol LR. Local anaesthetic techniques in paediatric surgery. *Br J Anaesth* 1986; 58: 760-78.
- Shandling B, Steward D. Regional analgesia for postoperative pain in pediatric outpatient surgery. *J Pediatr Surg* 1980; 15: 477-80.
- Jones SEF, Beasley JM, Macfarlane DWR, Davis JM, Hall-Davies G. Intrathecal morphine for postoperative pain relief in children. *Br J Anaesth* 1984; 56: 137-40.
- Dalens B, Tanguy A, Haberer J. Lumbar epidural anesthesia for operative and post-operative pain relief in infants and young children. *Anesth Analg* 1986; 65: 1069-73.
- Ecoffey C, Dubousset A, Samii K. Lumbar and thoracic epidural anesthesia for urologic and upper abdominal surgery in infants and children. *Anesthesiology* 1986; 65: 87-90.
- Dalens B, Chrysostome Y. Intervertebral epidural anaesthesia in paediatric surgery: success rate and adverse effects in 650 consecutive procedures. *Paediatric Anaesthesia* 1991; 1: 107-17.
- Glenski JA, Warner MA, Dawson B, Kaufman B. Postoperative use of epidurally administered morphine in children and adolescents. *Mayo Clin Proc* 1984; 59: 530-3.
- McRorie T, Lynn A, Nespeca M, Opheim K, Slaterry J. The maturation of morphine clearance and metabolism. *Am J Dis Child* 1992; 146: 972-6.
- Brandom BW, Davis PJ. Changes in drug requirements during growth. *Current Opinion in Anesthesiology* 1992; 5: 374-9.
- Koehntop DE, Rodman JH, Brundage DM, Hegland MG, Buckley JJ. Pharmacokinetics of fentanyl in neonates. *Anesth Analg* 1986; 65: 227-32.
- Lynn AM, Slaterry JT. Morphine pharmacokinetics in early infancy. *Anesthesiology* 1987; 66: 136-9.
- Bhat R, Abu-Harb M, Chari G, Ulali A. Morphine metabolism in acutely ill pre-term newborn infants. *J Pediatr* 1992; 120: 795-9.
- Osborne R, Joel S, Trew D, Slevin M. Analgesic activity of morphine-6-glucuronide. *Lancet* 1988; i: 828.
- Gaukroger PB, Tomkins DP, Van Der Walt JH. Patient controlled analgesia in children. *Anesthesia and Intensive Care* 1989; 17: 264-8.
- Vetter TR. Pediatric patient controlled analgesia with morphine versus meperidine. *Journal of Pain and Symptom Management* 1992; 7: 204-8.
- Royal College of Surgeons of England and College of Anaesthetists. *Pain after surgery*. London: RCS, 1990.
- Audit Commission. *Children first*. London: HMSO, 1993.