Management of post-operative pain

Graham Smith MD FFARCS

The conventional therapy for management of postoperative pain comprises prescription of intramuscular administration of a fixed dose of an opioid on a "prn" (or as required) basis. The failings of this regimen have been well-described¹: poor pain control may ensue because of delegation of patient management to junior staff, withholding of opioids by nursing staff because of fear of inducing drug addiction or respiratory depression, difficulties in quantifying the extent of suffering and difficulty in titrating the dose of opioid to a measured effect. Furthermore, therapy of pain with systemic opioid drugs is difficult because of variation in physiological and psychological factors and inter-individual variability with respect to pharmacokinetics and pharmacodynamics.

Psychological factors which influence the degree of acute pain include social background, motivation and personality. There is a good correlation between the level of anxiety and degree of postoperative pain experienced² and it has been shown that a patient with higher neuroticism scores exhibits greater pain scores after surgery.³ The importance of therapy for the affective component of pain is emphasised by the observation that psychotherapy reduces the requirements for postoperative analgesia⁴ and that diazepam also reduces these requirements.⁵ The importance of physiological factors in influencing the extent of pain is demonstrated by variations in the degree of perceived pain occurring after different types of surgery.

There are considerable pharmacokinetic variations in response to intramuscular administration of an opioid – it has been demonstrated that there may be a 2–5-fold difference in the peak plasma concentration values and a 3–7-fold difference in the rate at which they are attained. Furthermore, the plasma concentrations attained do not correlate with body weight (or lean body mass) which traditionally has been used as one of the major guides to opioid dosage.⁶

It is pharmacodynamic variability which accounts for the major differences in inter-individual opioid requirements. With a constant infusion of an opioid, steady state concentrations are eventually reached at which the receptor drug concentration is in equilibrium with the plasma concentration of the drug. The minimum plasma concentration achieved by this means at which analgesia is produced is termed the minimum effective analgesic

concentration (MEAC). The variation of MEAC level between different patients accounts for the widespread variation in drug demand which is seen when patients use patient-controlled analgesia (PCA systems). This varies between 13 to 44 mg·h⁻¹ meperidine⁷ and 30–100 mg·h⁻¹ for fentanyl.⁸ For morbidly obese patients, morphine requirements vary between 0.8–5.1 mg·h⁻¹ after major surgery.⁹

Pharmacodynamic variability includes that variability produced by differences in psychological profile. Lim and colleagues¹⁰ suggested that certain psychological variables may be related to the ease of activating the endogenous pain suppression system and by analogy Tamsen *et al.* have suggested that the "subjective need for analgesics may also be linked to endogenous pain modulation."¹¹ Evidence for this has been demonstrated by an observed relationship between calculated concentrations of meperidine in the CSF during patient-controlled analgesia and the preoperative concentration of endorphins in CSF.

Therapy for postoperative pain

Conventional intramuscular injections

The quality of postoperative analgesia may be improved by prescription of IM injections on a regular 4-hrly basis as opposed to a "prn" basis¹²). However, whilst this may be associated with improved analgesia for some patients, it is clearly likely to be associated with an increased incidence of side-effects and still may not satisfy the opioid requirements of all patients.

Newer synthetic opioid drugs

The potentially lethal side-effects possessed by the opioids prevent administration of sufficiently large doses to achieve good analgesia in a high proportion of patients. Whilst attempts have been made by the pharmaceutical industry to develop newer opioid drugs which may possess analgesic properties comparable with those of morphine, but with fewer side effects, success has not been achieved to date. Although many of these newer agents have been assessed in studies examining their

Department of Anaesthesia, University of Leicester, England.

efficacy in postoperative pain, for those with a marked ceiling effect to respiratory depression, analgesia has usually been found to be inadequate for severe types of postoperative pain.¹

Continuous intravenous infusions

By assessing the patient's opioid requirements using small intravenous boluses of opioids until adequate analgesia is achieved, various authors have then prescribed a fixed continuous infusion rate based on the initial quantity of opioid administered.^{13,14} It has been demonstrated that this technique is associated with significant periods of apnoea associated with arterial desaturation.¹⁵ More complex regimens have been developed which take into account the pharmacokinetic properties of different agents.

Patient-controlled analgesia

This technique represents one of the most significant advances in management of postoperative pain described in recent decades. The concept was initiated by Sechzer in 1971¹⁶ and essentially may be regarded as a closed-loop system, whereby the patient determines the dose required to maintain adequate analgesia. By controlling the rate of self-administration of drug, the patient maintains a plasma concentration between that required to satisfy subjective requirements for analgesia and that which would produce either unacceptable side effects, such as nausea and vomiting, or such a degree of CNS sedation as to inhibit further activation of the apparatus.

The most basic form of PCA apparatus administers only single bolus doses in response to activation of the machine, but the fluctuation in plasma concentration produced with this system may be reduced further by machines which deliver a continuous low-dose infusion, on top of which the patient adds a patient-activated bolus. For safety, it is best to accept an infusion rate which falls short of maintaining analgesia.

Experience with PCA is expanding rapidly and there is little doubt that a better quality of analgesia is produced than that affected by conventional intramuscular injections. Although the technique of PCA is inherently safer than other forms of IV administration of opioids, cases of severe respiratory depression have been reported as a result of programming errors.¹⁷ Not all patients are suitable for the technique, notably the very young and those who cannot understand what is required. It is clear that the low-dose infusion plus bolus technique with morphine yields better analgesia than the bolus alone technique.¹⁸ The technique may be used to administer opioids subcutaneously, intramuscularly, intravenously or by extradural routes.

Other routes of administration

ORAL

This is unsuitable for administration of strong opioids to patients in the early postoperative period, but is used commonly with non-opioid analgesics.

SUBLINGUAL

This has been used successfully for administration of sublingual buprenorphine as a sole analgesic for major abdominal surgery producing analgesia comparable with that following PCA with meperidine.¹² This technique offers the advantage that tablets may be removed from the mouth in the event of overdosage and that accidental swallowing does not result in toxicity because of high first pass metabolism. However, the major disadvantages of buprenorphine are a relatively high degree of sedation and nausea.

RECTAL

This route has been used for administration of sustained release preparations of morphine and a philosophy suggested that this may be equivalent to providing a continuous low-dose background infusion inadequate to provide analgesia in all patients, but on top of which satisfactory analgesia may be achieved by administration of smaller doses of opioids.¹⁹

TRANSDERMAL

Recently a transdermal delivery system has been developed for rate-controlled administration of fentanyl²⁰ and encouraging results have been obtained in the treatment of postoperative pain.²¹ The system has been designed to provide a sustained release of $100 \mu\text{g} \cdot \text{h}^{-1}$; however, it must be applied two hours before the expected pain or stimulus and a bolus IV dose of fentanyl is necessary as a loading dose. Again it has been suggested that transdermal fentanyl may provide a significant degree of background analgesia but that supplementary analgesia may be required in many patients (i.e., a dose large enough to provide adequate analgesia in the majority of patients would undoubtedly cause toxicity in a small proportion).²¹ However, the ease of administration may be a major advantage for this route of administration.

Local analgesic techniques

In recent years there has been increased enthusiasm for the use of somatic nerve blocks to provide postoperative analgesia. With bupivacaine, useful postoperative analgesia may be produced for 8–12 hours following a single administration. Prolongation of further analgesia using local analgesic agents is dependent upon either repeated

injections (e.g., intercostal nerve blocks) or the use of catheter techniques.

Single somatic nerve blocks with bupivacaine have found particular favour in paediatric day-case surgery and in adults following surgery to the upper or lower limbs. Examples of these techniques are described in recent publications.²²

Spinal and extradural opioids

Both subarachnoid and extradural injection of opioids have been used to provide prolonged postoperative analgesia. This technique possesses the advantages of prolonged analgesia without the motor autonomic block produced by local anaesthetic injected into the extradural space, but possesses the disadvantages of respiratory depression, itching and urinary retention. The most significant side-effect is that of respiratory depression which is more common with the more lipid insoluble agents, and encouraged by the supine posture, administration of further systemic opioids, and increased age of the patient.²³

Recently it has been suggested that the quality of postoperative analgesia is significantly better with an intravenous extradural infusion of diacetylmorphine and bupivacaine than with the opioid or local anaesthetic alone.²⁴

Other methods

Acupuncture has been employed in the treatment of postoperative pain, but it has not been shown to produce the same quality of analgesia as that using opioids.

A variety of psychological methods has also been described. Many have been shown to improve postoperative analgesia, but not to the extent of totally obviating the need for opioids.²⁵

Conclusion

Although traditional methods of administering postoperative analgesia may be inadequate, they do have the merit of simplicity and familiarity carries a degree of inherent safety. Of the newer techniques which have been introduced, perhaps patient-controlled analgesia has the greatest degree of inherent safety but mishaps may arise as a result of programming error or machine failure. Extradural techniques employing either local analgesic agents or opioids require enhanced patient monitoring.

For many years, advanced techniques of analgesia have been employed safely by retaining patients in intensive care units or, in many European centres, in high dependency nursing areas for 24–48 hours after surgery. The ability to finance time spent in treating patients in surgical wards postoperatively has recently enabled Ready and his

colleagues to develop and operate an acute pain team to supervise patient-controlled analgesia and extradural opioid analgesia on normal surgical wards.²⁶ This work may help to identify those groups of patients who may be treated safely with advanced analgesic techniques on the normal wards and those who require high dependency nursing units.

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