Analgesic strategies

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Introduction

Acute postoperative pain remains a major problem. Undertreatment can lead to serious consequences including persistent postoperative pain, impaired rehabilitation, and increased length of hospital stay, sympathetic overdrive and immunosuppression. Overtreatment can lead to serious adverse events related to analgesic use such as sedation and respiratory depression. It is therefore imperative to prevent and treat postoperative pain, but at the same time not to cause harm from our treatment.

When forming a strategy to deal with postoperative pain, one has to take several factors into consideration:

- Your own skill set and what you are comfortable with.
- The patient and any comorbidity they may have.
- Your environment in which you work and the support staff around you.
- Equipment at your disposal.

Regional anaesthesia and peripheral nerve blocks remains the cornerstone of effective postoperative analgesia. However, this is not always possible due to lack of skills, equipment or, the patient or procedure is not amenable. I have chosen to explore further various other modalities of analgesia.

Spinal morphine

Effectiveness

There is no doubt that morphine provides 12-24 hours of effective postoperative analgesia.[1]

Adverse effects

Adverse effects include pruritus, nausea and vomiting and respiratory depression.[1] Of these, respiratory depression is the most feared. The difficulty in reviewing the literature is that the term "respiratory depression" has no clear definition.[2] Consequently, determining the exact incidence is not a perfect science. In one study, neither 100 µg nor 250 µg intrathecal morphine affected minute ventilation or the ventilator responses to CO_2, whereas both measurements were depressed for 3 hours after 8 mg subcutaneous morphine.[3]

The mechanisms of respiratory depression include:[4]

- Vascular uptake by the epidural or subarachnoid venous plexuses and circulation to brainstem respiratory center.
- Arachnoid penetration and movement into the spinal cord.
- Rostral spread via the aqueous cerebrospinal fluid to the brainstem.
- Rostral spread via direct perimedullary vascular channels.

The incidence of respiratory depression correlates with the dose of intrathecal morphine. Meta-analysis indicates a reduced frequency of hypoxaemia when lower doses (vs. higher doses) of single-shot, intrathecal opioids are used.[5] The optimal dose (balancing effective analgesia and a low incidence of adverse effects) most probably being between 75-150 µg.[6]

Contraindications[4]

- Obstructive sleep apnoea
- Morbid obesity
- Elderly
- Cardiopulmonary disease
- Patients on $MgSO_4$

Guidelines

The American Society of Anesthesiologists has published guidelines for the postoperative morphine of patients who have had intrathecal morphine[5] This should be done hourly for the first 12 hours and then 2 hourly for the next 12 hours. Monitoring should include respiratory rate as well as level of consciousness. Pulse oximetry is not more sensitive than clinical monitory. Capnography is sensitive, but has severe practical limitations.

Patient controlled analgesia (PCA)

Morphine has been the drug of choice for PCA, but it is associated with many problems:

- Slow onset, therefore, patients become frustrated.
- Patients press PCA very often and become sedated.
- Side effects – nausea, itching, sedation (especially in the elderly), mental clouding.

- Not ideal for patients with renal dysfunction or obstructive sleep apnoea (OSA).

We will further explore different types of PCA:

- Fentanyl PCA
- Tramadol PCA
- Remifentanil PCA
- Subcutaneous PCA

Fentanyl PCA

Fentanyl is more lipid soluble than morphine and has a faster onset of action.[7] The duration of action is short due to redistribution. During the early phase of administration, fentanyl is redistributed from the plasma within 5 minutes to highly vascular tissues and then finally to muscle and fat where it is then slowly released back into the circulation. Eventually, the duration of action is prolonged as tissues become saturated. The elimination half-life then becomes longer than morphine.

Fentanyl is metabolised in the liver. Patients with renal failure are suitable candidates for fentanyl PCA. Liver transplant patients must have reduced doses of fentanyl PCA in keeping with their degree of liver dysfunction.[8] Dose reduction must also be used for the elderly. In a randomised, double-blind, multicenter study, Camu et al have compared the safety and efficacy of three administered, demand-dose size of fentanyl (20, 40 and 60 µg) in 150 patients after major surgery.[9] In each group, a maximum of six doses per hour were allocated. The authors decided that based on combined safety and efficacy considerations, a demand fentanyl dose of 40 µg was the most appropriate for PCA management of postoperative pain.

Box 1: Fentanyl PCA protocol:*

- Bolus:
  - Adults: 25 µg (reduce to 20 µg if elderly, liver dysfunction or frail)
  - Children: 0.25 µg/kg to a maximum of 25 µg
- Lockout: 6-8 minutes depending on pain and type of surgery and patient
- Limits: Use a limit if the lockout is 6 minutes. Limit to 8-9 doses per hour

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Tramadol PCA

Tramadol is a synthetic opioid of the aminocyclohexanol group. It is a centrally acting analgesic with weak opioid receptor agonist properties. It binds to the µ-receptor approximately 6 000-fold less than morphine and has a weaker affinity for the opioid κ- and δ-receptors. This explains the absence of respiratory depression with the use of clinical doses of tramadol.[10]

Common adverse effects seen with tramadol are nausea, vomiting, sweating, dry mouth, and drowsiness. However, tramadol PCA would be the drug of choice in patients with OSA.

Box 2: Tramadol PCA protocol:[10]

- Bolus: 10-20 mg
- Lockout: 5-10 minutes
- Limits: 400-500 mg in 4 hours

Remifentanil PCA

Remifentanil is a selective µ-receptor agonist with an analgesic potency similar to that of fentanyl. It is structurally unique because of its ester linkage, which renders it susceptible to hydrolysis by nonspecific plasma and tissue esterases to inactive metabolites. Remifentanil thus has brevity of action, precise and rapidly titratable effects, no accumulation and rapid recovery after discontinuation. This makes it ideal for situations requiring a short acting drug with predictable termination. Examples of this would be PCA for labour analgesia and extracorporeal shock wave lithotripsy.[10] However, it must be stressed, that remifentanil is a potent respiratory depressant and adequate and continuous monitoring must be available.

Box 3: Remifentanil PCA protocol[11]

- Bolus: 0,5 µg/kg
- Lockout: 2 minutes

Subcutaneous PCA

Subcutaneous PCA is a useful alternative to intravenous PCA and negates the need for a patent intravenous line. Doses required seem to be equivalent to intravenous doses.[12] It may be useful to use a higher concentration of drug and give a smaller volume if using the subcutaneous route.[12]

Analgesic adjuvants

- Lignocaine
- Pregabalin and Gabapentin
- Intra-articular local anaesthetic

Lignocaine

Lignocaine is an amide local anaesthetic. It seems that local anaesthetics reduce inflammation and the perception of pain. They act peripherally by decreasing the release of inflammatory mediators and centrally, by modifying neuronal responses in the dorsal horn.[13] A recent review looked at the literature from 1966-2009.[14] In open and laparoscopic abdominal surgery, as well as in ambulatory surgery, intravenous perioperative anaesthetic infusions resulted in significant reductions in postoperative pain intensity and opioid consumption (reduced by up to 85%). In addition, there was earlier return of bowel function, earlier rehabilitation and shorter hospital stay. The administration of lignocaine did not result in toxicity or clinically significant adverse events. Lignocaine has no impact on postoperative analgesia in patients undergoing tonsillectomy, hip arthroplasty and coronary artery bypass grafting. It has been mooted that different types of pain (neuropathic versus nociceptive) respond differently to

lignocaine, with neuropathic being more "sensitive" to lignocaine.[10]

There in so clear consensus regarding dose and duration of lignocaine. My own personal protocol is as follows:

Box 4: Lignocaine protocol

- Loading dose: 1,5 mg/kg before incision
- Infusion: 2 mg/kg/hr for at least the duration of surgery. Ideally for 24 hours

Pregabalin (Lyrica®) and Gabapentin (Neurontin®)

Pregabalin and gabapentin bind to the alpha-2-delta subunit of the voltage dependent calcium channel in the central nervous system. They thus decrease neurotransmitter release and attenuate postsynaptic excitability. A recent review which looked at the use of these drugs for the management of acute post-operative pain, concluded that:

- Gabapentin resulted in better post-operative analgesia as well as rescue analgesia sparing in 6 of 10 randomised controlled trials (RCTs) that administered pre-emptive analgesia only.
- Pregabalin provided better post-operative analgesia and rescue analgesia sparing than placebo in 2 of 3 RCTs.
- Gabapentin and pregabalin reduce pain and opioid consumption when compared to placebo but the data is still insufficient when compared to other post-operative regimens.[15]

The most problematic adverse effect of these drugs remains sedation. Dr Scott Reuben carried out a large proportion of the research into these drugs. Unfortunately, his research done between 1996 and 2009 has been found to be fraudulent. This has left the research into these drugs in shambles.

In summary, the main role for gabapentin and pregabalin remains as the treatment for chronic, neuropathic pain. There is no clear role for these drugs in the setting of acute postoperative pain.

Intra-articular local anaesthetic

Our orthopaedic counterparts frequently use intra-articular local anaesthetic injections. However, recent data suggest that local anaesthetics may affect chondrocyte viability in a time- and concentration-dependent manner. Prolonged infusions of local anaesthetic agents into a joint are no longer advocated as this may lead to chondrolysis.[16] In addition, local anaesthetic agents are more chondrotoxic in degenerate versus intact cartilage.[17] Chondrotoxicity increases from ropivicaine, to mepivicaine, to bupivacaine, without clearly correlating with analgesic potency.[17]

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