14. Opioid minimisation for acute pain management

For at least 10 000 years, opiates derived from the opium poppy were the only reliable analgesics used by humans. During the twentieth century, synthetic opioids were increasingly used, particularly in anaesthesia, to such an extent that editorials were written up to the mid-2007s decrying 'oligoanalgesia' due to unreasonable withholding of opioids.

Subsequently, there are increasing concerns regarding the use of opioids in medical practice, particularly anaesthesia, for two major reasons, namely (i) addiction and overdose and (ii) respiratory depression.

14.1 Prescription opioid addiction and overdose

- This has become a major problem, largely confined to the USA due to unique issues with the prescription of opioids in this country. Despite making up just less than 5% of the world population, Americans consume more than 80% of opiates and opioids used in the world. Regulation has lagged inappropriate industry promotion to the extent that emergency medical services now carry naloxone as a standard drug and even fire services regularly treat opioid overdoses.
- Opioids remain the ideal drug to manage severe pain such as postoperative pain. Presently, drugs which provide analgesia without addictive effects are undergoing trials and the first of these is oliceridine (TRV130). Animal trials have been promising and early human trials are underway.

14.2 Postoperative opioid respiratory depression

This has become an increasing problem in the so-called first world due to the epidemic of obesity:

- A BMI of more than 30 kg/m^2 is associated with an increasing incidence of OSA, which is further increased after surgery under GA.
- As a patient's BMI rises to > 40 kg/m^2, reduction of weight purely through diet and/or exercise is unlikely and procedures such as gastric banding or bypass may be required to significantly reduce caloric uptake. These procedures require GA with persistent risk of airway obstruction from the morbidly obese state.
- However, OSA may also be present without a raised BMI. This may be managed surgically by procedures such as the uvulo-palato-pharyngoplasty (UP-3). Once again, airway patency will persist or be worsened in the immediate postoperative period.

14.3 Interventions to reduce opioid requirements following general anaesthesia

- The interventions discussed below exclude neuraxial, regional and LA blocks as these are extensively covered elsewhere in these guidelines.

- There are two broad categories of intervention: non-pharmacological and pharmacological.

14.3.1 Non-pharmacological interventions

Transcutaneous electrical nerve stimulation

TENS is a pain relief technique that involves passing a low-intensity electric current between cutaneous electrodes through the painful area. TENS devices generate biphasic pulsed currents with adjustable pulse amplitude (1–60 mA), pulse frequency (1–200 Hz), pulse duration (50–200 μs), pulse patterns (continuous, intermittent trains or bursts) as well as modulated amplitude, modulated frequency and modulated duration. There are minor differences in the technical output specifications of standard TENS devices.

TENS can progress from paraesthesia to muscle twitching to pain different from the pain experienced before the application of TENS. It has been used for postoperative pain relief since the 1970s with inconsistent results and it has still not been subjected to a substantial RCT, mainly due to significant difficulties with blinding.

Perioperative language

Humans are sensitive to language use, particularly in stressful situations such as the perioperative period. In particular, negative expressions are not comprehended, the primary concept being understood without the minimising modifier (e.g. when taking blood, if a practitioner tells a patient it will be 'just a little scratch', 'little' will be ignored and 'scratch' will be emphasised).

This has been studied in a perioperative setting where a pain score was compared to a comfort score after a CS. One group of patients were asked to rate their pain from 0 to 10 with 0 = no pain to 10 = worst possible pain, compared to another group of patients who were asked to rate their comfort with a score of 0 = least comfortable to 10 = most comfortable. In the latter group, use of the word 'pain' was limited as far as possible. Pain scores and analgesic consumption were significantly reduced in the comfort group.

Acupuncture

The use of needles in specific locations has been done for centuries, particularly in Asian medicine. Acupuncture is largely applied in outpatient settings to deal with chronic pain. However, there is an increasing application to acute pain in perioperative settings. The major limitation, however, is the availability of practitioners who are able to apply acupunture.

Psychological therapies

Low back pain is a condition that is associated with difficulty in successful treatment, particularly after surgery. In a randomised study of 90 patients from Denmark (59 study patients; 31

controls), CBT of 4 three-hour sessions was compared to standard care. The CBT group had superior mobility and postoperative pain relief. This is similar to studies that demonstrated small but consistent improvement in pain scores.

Music

Music has proven useful to reduce the perception of pain, particularly of procedural pain such as dressing changes for burns. Several anaesthesiologists will ask patients to bring their music player with their favourite tracks to the operating room with them. The practitioners can then play the music at a comfortable level during the time of induction. As hearing is the last sensation to be anaesthetised and the first to return, the music is continually played even in the recovery room. The pleasant sounds appear to improve postoperative outcomes.

Hypnosis

Hypnosis is defined as inducing a state of consciousness in which a person apparently loses the power of voluntary action and is highly responsive to suggestion or direction. It is used in therapy typically to allow modification of behaviour. In the context of this section, it is used to modify the response to pain. The usefulness of hypnosis is limited by the following:

i. The unavailability of suitably trained therapists.
ii. Up to 20% of patients do not respond to hypnosis.
iii. The effect of a hypnotic treatment varies in duration and may require frequent repetition.

Sleep disorders

Insomnia is exceedingly common in all hospital settings but particularly in HCUs. A consistent complaint from patients discharged from HCUs is the dreaded bath between 3 and 4 am. A major cause of disorientation leading to delirium in patients over the age of 60 is sleep deprivation. Yet this is very common in modern ICUs and a point which all can improve.

Manual therapies

This is beyond the scope of this guideline.

14.3.2 Pharmacological interventions

NSAIDs and paracetamol

These have been extensively covered in this guideline and will not be discussed further. These have a central role in reducing opioid requirements for pain relief.

Ketamine

The NMDA receptor antagonist, ketamine, is a drug widely used in veterinary practice. Since this drug causes the least CV depression of available anaesthetic agents, it is particularly useful in the management of unstable trauma and septic patients. Oral as well as relatively painless IM and SC administration make it a useful drug in paediatric applications such as suturing and establishing IV access.

For the management of acute pain, ketamine can provide profound analgesia, with a dose of 2 mg/kg intravenously, allowing for procedures as extensive as a CS to be performed. Ketamine is useful as an adjunct to other agents in analgesic regimens (e.g. an infusion of 0.2 mg/kg/hour and PCA with a bolus of 2.5–5 mg and a lockout time of 5–10 minutes).

Lignocaine

LA provided by lignocaine is well-recognised. Less well-known is that, as a sodium channel blocker, lignocaine is also an extremely effective analgesic. Owing to its short duration of action, lignocaine needs to be given as a continuous infusion (CI) at a rate of 1.0–1.5 mg/kg/hr.

Dexmedetomidine

The α_2-receptor agonist, dexmedetomidine, has largely replaced clonidine, particularly in South Africa, where clonidine is not available as an IV preparation. The oral formulation (Dixarit®) is a 25 µg tablet used for migraine treatment which is impractical for use in sedation.

Dexmedetomidine provides a unique form of sedation that includes profound analgesia. The patient is sedated but rousable, returning to sleep within a short time. RR and haemoglobin oxygen saturation are unaffected.

Sedation is initiated by a bolus dose of 0.5–1 mcg/kg delivered over 15–30 minutes. A push injection bolus can cause severe *hyper*tension and bradycardia. Maintenance will require an infusion of 0.2–0.9 µg/kg/hr. Onset and offset of sedation is slow and functions as a baseline for other sedative agents. The requirement for other sedatives such as ketamine, lignocaine or opioids (rarely required) is reduced by at least 40%, up to 80%. During the management of difficult airways, dexmedetomidine is an extremely useful adjunct, improving patient comfort and cooperation without affecting airway obstruction.

Magnesium sulphate

The second most common intracellular cation is magnesium. In terms of pain management, magnesium acts synergistically with ketamine as an NMDA-receptor antagonist. Administration requires an LD of 30–50 mg/kg over 15 minutes followed by an infusion of 10–30 mg/kg/h aiming for a serum level of 2–4 mmol/l. Clinically, deep tendon reflexes can be monitored.

Magnesium administered to patients with postoperative pain reduces opioid consumption but has less effect on reducing opioid-related side effects.

Magnesium is excreted by the kidneys. Therefore, special care should be taken in patients with impaired renal function.

Gabapentinoids

These anticonvulsant drugs used extensively in chronic pain management, showed initial promise in the management of acute pain. However, after a comprehensive meta-analysis, these are no longer recommended.

Esmolol

Decreased opioid requirements with subsequent decrease in opioid side effects, both intra- and postoperatively. Intraoperatively a patient will respond to a noxious stimulus through increased heart rate, BP or both. Esmolol and fentanyl have similar haemodynamic effects, both reducing the heart rate and BP. Studies reviewed in a 2018 meta-analysis have demonstrated similar analgesic efficacy whether esmolol or fentanyl were administered in response to predetermined haemodynamic changes. Patients given esmolol had significantly fewer opioid-related side effects, including sedation, nausea and vomiting.

Unanswered questions, however, include the following:

1. Is the effect of esmolol on perioperative pain a class effect common to all β-blockers or unique to esmolol?
2. Should β blockade with esmolol or another β-blocker be extended into the postoperative period? If so, for how long?

14.4 Opioid-free analgesia

LA techniques were pioneered in KwaZulu-Natal, South Africa and remain the mainstay of postoperative pain relief from simple infiltration to complex ultrasound-guided blocks.

Baseline systemic analgesia is based on paracetamol 1 g 6-hourly in adults and an NSAID as indicated according to specific comorbidities.

J-P Mulier pioneered the concept of OFA (opioid-free anaesthesia/analgesia) in his hospital in Brugge, Belgium. This interest was born out of necessity, as he was anaesthetising an increasing number of super morbidly obese patients (BMIs > 60 kg/m^2) with significant OSA who were exquisitely sensitive to opioids. He found no difficulty in providing OFA and very rarely resorted to a remifentanil infusion. Usually, he succeeded with a combination of desflurane and dexmedetomidine intraoperatively. During the latter stages of the operation, patients received IV paracetamol and ketorolac if there was no renal impairment.

In anticipation of the postoperative multimodal analgesic, infusion LDs of the component drugs would be given as follows:

1. Ketamine 0.5 mg/kg
2. Lignocaine 1 mg/kg
3. Magnesium 30 mg/kg

The infusion recommended by Dr Mulier is given in Appendix 1. This infusion commenced during the closing stage of surgery. At the end of surgery with muscle relaxation reversed and adequate breathing established, the patient was extubated.

Any complaints of pain were carefully evaluated and, if required, treated with no more than 1 mg of morphine at 30-minute intervals so that not all, but the vast majority of anaesthetics were opioid-free. Tramadol (50 mg) may be preferred. In the ward, the patient could be out of bed within two hours, walking in the ward within six hours and fully mobilised within 24 hours.

Dr Mulier's results are reproducible as demonstrated by pro vs con articles assessing the efficacy of OFA in breast reduction surgery.

14.5 Conclusion

Pain is something we all have or will experience at some point in time. This short summary provides a few interventions that may assist not only the patients, but also the practitioner when that most terrible of masters makes its appearance.

Appendix 1

24-hour background analgesic infusion

J-P Mulier, Oostende-Brugge, Belgium

Based on an 80 kg patient over 24 hours (multiplication factor for each drug = 24 x 80 = 1 920).

Amounts are rounded off to available ampoule sizes.

Drug	Dose/kg/hour	kg	Hours	Total/24 h	Volume
Ketamine	0.05 mg	80	24	100 mg	2 ml of 50 mg/ml
Lignocaine	1 mg	80	24	2 000 mg	20 ml (10%; 100 mg/ml)
Dexmedetomidine	0.1 µg	80	24	200 µg	2 ml (100 µg/ml)
$MgSO_4$	2.5 mg	80	24	5 g	10 ml (50%; 0.5 g/ml
Dextrose 5%					500 ml
Total volume					534 ml
Infusion rate					534/24 = 22 m/hour

(Remark: As far as the author knows, DW5% 500 ml is not available in South Africa. Therefore, the total drug volumes (34 ml) can be added to 200 ml of DW5% = 234 ml and administered at 234 ml/24 hours = 9.75 ml/h ≈10 ml/h).)

Reviews

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