

Practical perioperative pain control in children and adults

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Pain is soul-destroying. No patient should have to endure intense pain unnecessarily. The quality of mercy is essential to the practice of medicine. Here of all places it should not be strained.

The Quality of Mercy

Introduction

Acute injuries, which include surgical operations, cause a number of physiological changes. Peripheral sensitisation occurs after injury to a nerve (cut skin, surgery to tissue) when an increase in response to stimuli by the peripheral nervous system takes place. Nerve fibres, which do not usually transmit pain, are now more sensitive, and do send painful stimuli. This will impact on the central nervous system, where increased noxious input causes a number of different responses. These include muscle spasms and increased sympathetic stimulation. The resultant increased oxygen and calorie consumption will impact particularly on the growth of neonates and infants.

It is important to differentiate between nociception and pain: nociception is a noxious stimulus, or a stimulus which would be noxious if prolonged; activity induced in a nociceptive pathway by a noxious stimulus is not pain. Pain is an unpleasant sensory and emotional experience which is associated with tissue damage or described in terms of such damage, or both (IASP).

Poorly managed acute pain has a negative impact on many organ systems, and has physical and psychosocial consequences. Increasing evidence points to the development of chronic pain syndromes in individuals (both adult and paediatric) where acute pain has not been well managed.

Consequences of poorly managed pain	
Organ system:	Possible clinical manifestations
Cardiovascular	Tachycardia, hypertension, ↑ systemic vascular resistance, ↑ cardiac workload
Pulmonary	Tachypnoea, hypoxia, hypercarbia, ↓ cough, ↓ VC and FRC, atelectasis, pneumonia, V/Q mismatching
Gastrointestinal	Anorexia, nausea, vomiting, ileus
Renal	Oliguria, urinary retention
Neuroendocrine	↑ adrenergic activity, catabolism and oxygen ↑ consumption, vagal inhibition
Central nervous system	Anxiety, fear, sedation, fatigue, depression
Immunologic	Impaired, especially cell-mediated immunity
Musculoskeletal	Reduced mobility, pressure sores, ↑ risk of DVT's

General principles of perioperative pain control

In general, analgesia should be given in anticipation of pain, and thereafter continuously, or at regular intervals, for the estimated time of duration of pain and discomfort. Simple analgesics alone will not control the pain of major surgery.

Identify what is required: sedation, anxiolysis, analgesia, amnesia, or a combination of one or more of the above. Other factors which should be considered include the type of surgery planned, whether or not this is amenable to a regional or local anaesthetic technique, the medical condition of the patient, and any medication she/he may be taking.

Later in this discussion, differences and similarities between children and adults will be mentioned. Other decisions will involve the route of administration preferred for the type, site and severity of surgery, whether or not the patient will return home after the operation (therefore plan for analgesia to take home), and where the patient returns to after surgery (ward, high care, ICU). The ability of these areas to monitor the patient and care for e.g. epidurals will impact on the decision to use a regional technique or not, and on which drugs can be prescribed safely for the post-operative patient.

Drug administration should be the right drug for the right patient for the right reasons via the right route at the right time.

Pre-emptive analgesia attempts, in theory, to avoid the sensitisation mentioned previously, i.e. to anticipate tissue injury and pain, and to treat it prior to its onset. This is based on the hypothesis that pre-injury afferent blockade or modulation at spinal level (central sensitisation) can reduce the magnitude and duration of post-operative pain. Numerous studies have had equivocal results, the only exception being in the use of high-dose local anaesthetics initiated preoperatively and continued into the postoperative period. Although there is controversy about the science-based evidence of pre-emptive analgesia, its practice makes sound common and neuro-hormonal sense.

Multimodal or balanced analgesia encourages the use of more than one drug or technique in order to improve analgesia and reduce the doses used for any one drug on its own, thus reducing the incidence and severity of side-effects. This is particularly valuable when the components have different sites or mechanisms of action and/or are synergistic.

Preoperative planning

Knowledge of the modalities for providing measures to control pain in the perioperative setting should be a fundamental requirement of any anaesthesiologist. In my opinion anaesthesiologists should be controlling pain management, not the surgeons, but staff constraints are often the limiting factor in following up patients after surgery.

Communication with the patient is vital in developing a successful pain management strategy. In paediatric practice, discussion with the parent(s) is crucial.

The following factors will impact on the anaesthesiologist's plan for pain management:

- Ability to communicate with the patient (problems with preverbal children, different language, old patients, mentally challenged individuals)
- Cognitive development: children with special needs
- Previous experiences of pain
- Cultural factors: what is expected behaviour for that group of people

During the preoperative evaluation, plans should already have been considered for intra- and postoperative pain relief. This may necessitate consent for the insertion of catheters for regional techniques, or permission for the use of rectal anti-inflammatory suppositories. Obvious questions of the presence of drug allergies should be routine, and documentation of patient preference for analgesia noted. Previous experience of nausea and vomiting with opioids should be noted, as opioids are the most common group of agents used for pain control in this setting. The side-effects of all agents used should be considered in a risk:benefit ratio. Routine use of anti-emetics with opioids may be preferable in at-risk categories of patients. In general, careful use/choice of alternative drugs can avoid this problem.

If the use of NSAID's is planned, a careful history of sensitivity (idiosyncratic allergic reactions) to these agents, of bleeding (or use of anticoagulants), previous gastric ulceration or gastritis, renal dysfunction, or a history of asthma is vital. Aspirin sensitivity may present as severe bronchospasm, and 10% of people who are sensitive to aspirin are sensitive to tartrazine. The use of aspirin for analgesia and antipyresis in children is not recommended.

When deciding on the use of any drug, the question should be asked "Is there any reason that I should not be using this drug in this particular patient?"

The question of drug interactions is a vital consideration in choosing an analgesic or anxiolytic. Is the patient on any other medication which will impact on the effect of the agents you are administering? Do they share an enzyme pathway (e.g. protease inhibitors and the P450 pathway in the liver) for metabolism? Will they be synergistic, additive, opposing or complementary?

Prior to the use of local anaesthetic techniques, examination of the area to be affected should be assessed for normal sensory and motor activity (especially if the surgery planned is likely to affect nerve function post-op), and any neuronal deficit must be accurately documented.

Nil per mouth instructions should include or exclude any medication the patient may be taking. This is particularly important when patients are taking medications which require their administration with food (for example some of the protease inhibitor antiretroviral agents). Oral analgesic or anxiolytic premedication agents should have specific instructions concerning time to be given, and how much water may be used to swallow the agents. In general, children are allowed free clear fluids until two hours pre-operation, with the last food at least six hours prior to anaesthesia.

Routes of administration

- **Oral:** should/could be used more often perioperatively (especially for smaller procedures), but these drugs need to be given as part of premedication (to allow time for the drugs to work). If given at this time, the details of administration must be documented so that one can factor this into intraoperative drug requirements. Paracetamol and combination drugs containing paracetamol could be used here, e.g. Tramacet® (combination of paracetamol and tramadol).

Many surgeons prefer that non-steroidal anti-inflammatory drugs (NSAIDs) are not administered until surgery is completed. If there are potential problems with gastric emptying, the oral route is not recommended.

- **Transmucosal:** sublingual and intranasal e.g. tilidine HCl (Valoron® drops).
- **Subcutaneous:** this route is more commonly used for chronic pain and palliative care.
- **Transcutaneous:** EMLA® patch (local anaesthetic), Duragesic® (transdermal fentanyl patches), TransAct (flurbiprofen patches).
- **Topical:** eye drops (local anaesthetic or NSAIDs).
- **Skin or wound infiltration:** the use of local anaesthetics before or after surgery.
- **Rectal:** more commonly used for children, mostly paracetamol (Empaped®) or NSAIDs (diclofenac, mefenamic acid); but NSAIDs can also be used in adults. Problems include unpredictable absorption and possible extrusion on patient awaking. Consent for use should be obtained pre-operation.
- **Intramuscular:** pain relief via intramuscular injection should not be an additional source of discomfort, particularly in children. This method produces peaks and troughs in pain control, is a reasonable option for rescue medication, and is more commonly used in adult pain control.
- **Intravenous:** the most common route for post-operative pain control, whether by constant infusion or patient-controlled analgesia (PCA). Nurse- or parent-controlled analgesic options are available for children. The most common modalities include constant infusion, PCA (adult or children), intermittent boluses intravenously, and intermittent intramuscular injection (adults only).
- **Regional plexus or nerve block:** local anaesthetics via single injection or catheter insertion; paravertebral blocks have become increasingly popular.
- **Epidural:** local anaesthetics, opioids, α₂ agonists; single injection or catheter insertion.
- **Intrathecal:** local anaesthetics, opioids.

Assessment and measurement of pain

A simple acknowledgement of pain i.e. Is there pain? Yes or no, is often a very good starting point. If the patient has had surgery, pain is a likely consequence. If a patient says he/she has pain, do not refuse treatment because "you may become addicted to the morphine".

Pain control is a basic human right, is humane, and is neuro-hormonally beneficial to the patient.

Pain is a subjective experience and is often based on previous experience. Observer assessment of patient behaviour is unreliable, and in pre- or non-verbal children is particularly difficult. In older children and adults, self-report, visual analogue scales, and verbal numerical ratings have some success. Beware of the Wong-Baker Faces scale as a pain scale in children, as many patients will not separate out anxiety and pain (a crying face expresses their feelings of fear, not necessarily pain). A universal pain scale combines, in tabular form, the Faces scale with a colour coding scale together with a numerical rating, in six different languages.

A. Pain measurement:

• **Categorical scales**

Pain intensity		Pain relief	
Severe	3	Complete	4
Moderate	2	Good	3
Slight	1	Moderate	2
None	0	Slight	1
		None	0

• **Visual analogue scales:**

No relief of pain —————> Complete relief of pain

Usually measured in mm or numbers, it is simple and quick, and avoids imprecise descriptive terms

B. Pain Assessment:

Especially in the pre- or non-verbal child, recognising and assessing pain in children is notoriously difficult. It is important to be aware of the normal behaviour and physiological parameters for various age groups.

- **Physiological parameters** are the most frequently used for non-verbal children, those on ventilators, and those who are mentally challenged. Increases in heart rate, blood pressure, and sweating will reflect painful sensations.
- **Behavioural features** may include grimacing, crying, screaming, and physical withdrawal, but other indicators may be anorexia, sleep disturbances, retrogressive behaviour, inattention, and a reluctance to play.
- **Visual analogue scales** are commonly used as pain rating scales in the older age groups, but are not successful in younger children, those with minimal education, and those with a different interpretation of the conventional understanding of the scale. Caution should be used when using The Faces Scale, as the pain face may be interpreted as a sad face.
- **Parental interviews** are vital in assessing a child's pain, as their knowledge of their child's pain responses will complement the treatment plan.
- **A tactile and visual scale** is an important recognition that watching and touching the child (the "body language") will give the health professional a very good indication of pain and discomfort being experienced. (R Albertyn, personal communication. In press)

Treatment modalities may include non-pharmacological or pharmacological options.

Non-pharmacological methods

- Pre-operative explanation, discussion and education
- Teach coping strategies, especially to children and their parents
- Relaxation therapies
- Distraction techniques: virtual reality
- Splinting and immobilisation of wounds
- Cold or heat
- Transcutaneous electrical nerve stimulation (TENS)
- Hypnosis
- Acupuncture
- Microcurrent electrotherapy: Acustat

Pharmacological therapy

A. Simple analgesics

Paracetamol (oral, rectal in children, intravenous)
Non-steroidal anti-inflammatories (oral, rectal, intravenous, transdermal patches)
Steroid anti-inflammatory drugs (hydrocortisone, methyl prednisolone, dexamethazone) for use intravenously, intramuscularly, and intra-articularly.

B. Opioids

Short acting: remifentanyl, alfentanil, fentanyl, sufentanil
Intermediate acting: morphine, meperidine (Pethidine), tramadol, tilidine HCl (Valoron®), codeine
Long acting: methadone, Duragesic® (fentanyl patches)
Partial agonists: buprenorphine (Temgesic®), nalbuphine: have a ceiling to efficacy.

C. Local anaesthetics

Short-acting or long-acting, with or without adrenaline
Infiltration, nerve block, regional or central blockade; with or without catheters.

D. Inhalational agents: Entonox (scavenging is essential)

E. Others:

- Ketamine

- Steroidal anti-inflammatories: dexamethasone (150 mcg/kg), hydrocortisone and others
- α_2 adrenoreceptor agonists
Clonidine
Dexmedetomidine: highly selective, intravenously administered α_2 agonist
- Cannabinoids: tetrahydrocannabinol (THC)
- Combinations of drugs: numerous options such as Stopayne®, Myprodol®, and others
- Dextrose (25%), breast milk

A. Simple analgesics

These are either used alone for mild to moderate pain, or used to supplement other analgesics for more severe pain. They are usually given orally or rectally, but can be used intravenously and in adults intramuscularly.

Neonates and infants: Dextrose on a dummy, breast milk, paracetamol, selective NSAIDs. Monitoring is essential if using opioids.

• Paracetamol

Paracetamol is an analgesic with anti-pyretic activity. Its action is mainly central inhibition of prostaglandin F (amongst others). It lacks peripheral action, so has very little anti-inflammatory effect; neither does it have the gastro-intestinal tract or renal side-effects classically described with the NSAIDs. COX-3 is weakly sensitive to paracetamol but this action only partly explains the analgesic effect of paracetamol. Other mechanisms of action of paracetamol include activity at the cannabinoid receptors at spinal level, as well as involvement at the serotonergic and nitric oxide systems.

The major drawback in the use of this drug has been the administering of inadequate drug dosages. For children, a loading dose is recommended, followed by a maintenance dose not exceeding a maximum of 90 mg/kg/day in infants and older children and 60 mg/kg/day in neonates. (These maximum doses are reduced in the use of Perfalgan® (see below). The adult maximum dose is 4 – 6 g per day.

Many oral preparations containing paracetamol also now contain a dose of N-acetyl cysteine so that the problems of overdose and production of the toxic metabolite of paracetamol N-acetyl-p-benzo-quinone imine (NAPQI) is countered. (N-Acetyl-cysteine is the pro-drug for glutathione which irreversibly inactivates NAPQI).

Perfalgan® (intravenous paracetamol) is a new product to the South African market, and has an important role to play in perioperative pain management, in both children and adults. It is available in two sizes: 100 ml (1000 mg) and 50 ml (500 mg), with a concentration of 10 mg/ml.

Dosage: Neonates 7.5 mg/kg/dose 6 hourly (maximum 30mg/kg/day)

Children 15 mg/kg/dose 6 hourly (maximum 60 mg/kg/day)
Adults 1 g 6 hourly (maximum 4 g/day)

• Non-Steroidal Anti-inflammatory Drugs

NSAIDs are classified by chemical group or mode of action. The different groups include the following:

1. Carboxylic acid:

- Salicylates: aspirin
- Phenylacetic acids: diclofenac, fenclofenac, alclofenac
- Carbo- and heterocyclic acids: indomethacin, sulindac
- Propionic acids: ibuprofen, naproxyn, ketoprofen, fenoprofen, flubiprofen
- Fenamates: mefanamic acid, meclofenamic acid

2. **Pyrazolones:** phenylbutazone, propazones (This group is no longer in use in SA.)

3. **Oxicams** (selective): tenoxicam, piroxicam, meloxicam, isoxicam, lornoxicam

4. **Specific COX-2 inhibitors** (COXIBS): celecoxib (Celebrex®), paracoxib (Rayzon®), etoricoxib (Arcoxa®), valdecoxib

Vioxx® and Brexican® (piroxicam) were taken off the market because of cardiovascular side-effects. Many of the Coxibs are under investigation for this.

Important facts about NSAIDs

COX 1 is present in most tissues as a “housekeeper” enzyme. COX 2 is inducible by inflammation and increases in response to trauma, surgery and inflammatory disease (arthritis). Both have the same affinity to convert arachidonic acid to prostaglandin. COX 1 maintains gastric mucosal integrity and influences renal function, so inhibition of this COX 1 is undesirable. Inhibition of COX 2, however, is desirable because of its anti-inflammatory consequence. The concept of a COX 2:COX 1 ratio looks at a balance of inhibition of the inducible COX 2: the lower the ratio, the lower the COX 1 inhibition and the lower the overall side-effect profile.

Questions around perioperative bleeding and possible increased incidence of wound infection and poor bone healing do not generally apply to perioperative use, but the long term use may impact on both aspects. If there is any concern about potential for bleeding, administer the NSAID at the end of the surgical procedure (e.g for ENT procedures).

Effective adjunctive preventative therapy with NSAIDs

- Misoprostil: is a synthetic prostaglandin E1 analogue that enhances several of the factors that maintain gastro-duodenal integrity. Its use is contraindicated in women of child-bearing age and in those who are pregnant (it stimulates uterine contractions and premature labour, and may also cause premature closure of the ductus arteriosus of the foetus), or in those women who are lactating. It is often used with NSAIDs to prevent their gastric side-effects (e.g Arthrotec®: diclofenac + misoprostil).
- Antacids have not been shown to prevent NSAIDs-related gastropathy (ulcers, gastritis)
- H2 antagonists in standard doses reduce duodenal ulceration, but not gastric ulcers. Famotidine at high doses (not at normal doses) has some effect in reducing both gastric and duodenal ulcers.
- Gastric acid proton pump inhibitors (PPIs) are used in the treatment of NSAID-induced ulcers, but have not yet been proven to prevent this complication.

Appropriate prescribing

NSAIDs are not all the same, and have very different toxicity profiles. Risk factors have been identified in:

- Persons 65 years or older
- History of previous gastrointestinal symptoms with NSAIDs
- Concomitant use of oral corticosteroids
- High NSAID doses

The more COX 2 selective, the fewer the gastrointestinal side-effects. When there are cardiac risk factors, cardioprotection with low-dose aspirin (Ecotrin®) is required. This will obviously have an impact on perioperative bleeding tendency.

The ideal NSAID should be able to act both centrally (by crossing the blood brain barrier) as well as peripherally. Tissue trauma induced by surgery results in the production of pro-inflammatory mediators that induce COX-2 release. Increased levels of prostaglandins may induce peripheral sensitisation of nociceptors, but also induce secondary sensitisation in the dorsal horn by blockade of the inhibitory action of glycine. Used in combination with opioids or on their own, they play an important role in perioperative pain control. Rectal or intravenous (occasionally intramuscular) routes are most commonly used perioperatively.

Commonly used NSAIDs used in SA include:

- Diclofenac (rectal suppository, oral, imi)
- Ibuprofen (oral)
- Coxflam® (meloxicam)
- Paricoxib (Rayzon®) (ivi, imi)
- Loroxicam (Xefo®) (ivi, imi, po)

Intravenous preparations available include Rayzon® (paricoxib, which is the prodrug for valdecoxib), and Xefo® (loroxicam) but none of these formulations is available for use in children. Thus for paediatric practice, rectal suppositories and pre- or postoperative oral preparations are available (diclofenac suppositories, oral ibuprofen (Brufen®, Nurofen®). In other countries, ketoprofen (ketorolac) is available for paediatric use.

Side-effects: gastritis, peptic ulceration, decreased renal function (inhibition of vasodilatory prostaglandins), idiosyncratic allergic reactions, aspirin-sensitivity syndrome: asthma, interference with blood clotting, inhibit platelet function, fluid retention.

B. Opioids

- **Short-acting** agents (see above) are commonly used for the severe pain during the intra-operative period, but plans should be made for postoperative comfort.
- **Intermediate:** as mentioned above, morphine and pethidine are the mainstays of analgesic therapy, with Valoron® (tilidine HCl) another common agent in paediatric practice. Tramadol is used ivi, imi and po but has a high incidence of nausea and vomiting.

Simple analgesics are commonly used as adjuncts (paracetamol, NSAIDs). Local anaesthetic agents should always be considered.

Pethidine: caution is recommended with postoperative use (either by infusion or intermittent bolus). The active metabolite, nor-meperidine, causes central excitation, and may result in confusion, delirium and convulsions after 2 – 4 days of pethidine use. It also has anti-muscarinic activity (atropine-like) which may cause confusion in the elderly. It blocks neuronal uptake of serotonin so should not be used in patients on monoamine oxidase inhibitors.

- **Long-acting:** methadone is most commonly used for the weaning from prolonged use/abuse of opioids, but is a very good analgesic in its own right and can be given as either an infusion or a twice-daily oral dose. Duragesic patches are more commonly used in chronic pain, but are useful in the patient with a prolonged postoperative recovery time.

Contraindications

- Sensitivity to opioids in general or any one in particular. The naturally-occurring opioids (morphine, codeine) release histamine more than the semi-synthetic agents (pethidine, fentanyl).
- Porphyria.
- Caution in the hypotensive, hypovolaemic patient. Start with half of the recommended dose, and reassess as resuscitation progresses.
- Renal failure: morphine metabolises to renally excreted products which may accumulate in kidney failure and cause respiratory depression. This effect is more likely with prolonged use over hours to days, thus constant reassessment is vital.
- Liver failure: decreased metabolism results in higher serum levels and a greater incidence of side-effects.
- Severe head injury and/or raised intracranial pressure. Consult with the neurosurgeon.
- Respiratory depression, of whatever aetiology.
- Surgery of the biliary tree.

C. Others

Combination medications

Stopayne®: Tablets (paracetamol 320 mg, codeine phosphate 8 mg, meprobamate 150 mg, caffeine 32 mg). The capsule has more caffeine.

Syrup: paracetamol 125 mg, codeine 5 mg and promethazine 6.25 mg per 5 ml

Myprodol®: ibuprofen, paracetamol, codeine (suspension, tablets, capsules)

Tramacet®: (paracetamol 325 mg, tramadol 37.5 mg)

Synap Forte®: (paracetamol 500 mg, dextropoxyphene 50 mg,

Management of the side-effects of opioids	
Anticipation and management of the side-effects of the drugs that anaesthesiologists administer is of paramount importance for good patient care.	
1. Over-sedation:	Stop, or decrease the dose of opioid. Methylphenidate (stimulant)
2. Respiratory depression	Stop opioid. Airway management. Naloxone: 0.2 – 0.4 mcg/kg/dose, up to 2 mg
3. Dysphoria	Change opioid, or select another group of analgesics.
4. Constipation	Stool softeners (Duphalac®), prune juice, osmotic agents (Movicol®) prokinetic agents (metoclopramide).
5. Nausea and vomiting	Promethazine: 0.25 mg/kg, max 25mg. Droperidol: 20 mcg/kg/dose. Long acting Ondansetron: 0.1 mg/kg/dose. Max 4 mg. Adults 4 – 8 mg
6. Pruritis / itching:	Diphenhydramine: 0.5 mg/kg/dose. Max 25 mg Chlorpheniramine: 0.1 mg/kg/dose (not for infants under 1 year.) Hydroxyzine (Aterax®): 2 mg/kg/dose po 6-8hrly Promethazine (Phenergan®): 0.2 – 0.5 mg/kg/dose. Narcan: low dose to effect, from 2 – 4 mcg/kg/dose Chlorpromazine: 0.5 – 2 mg/kg/dose po 6 – 8 hrly (max 100 mg)
7. Urinary retention	Catheterise bladder
8. Seizures	Stop opioids. Anticonvulsants
9. Tolerance or physical dependence	Change opioids and/or analgesics. Wean off slowly
NB: Promethazine is contraindicated in children under 2 years of age. (MCC, June 2008)	

diphenhydramine 5 mg, caffeine 50 mg)

There are many and various combinations of OTC (over-the-counter) medications, with a variety of trade names available for clinical use in both adults and children.

Many adult patients will be taking these medications of their own accord, so questioning them prior to surgery is essential. Use of herbal and complimentary medications should also be noted.

α_2 agonists

Clonidine orally in paediatric practice and dexmedetomidine (ivi only) in adults (and in many other countries in paediatric use as well) are very useful agents for pain relief, anxiolysis and sedation.

Anti-depressants and anticonvulsants

Gabapentin, pregabalin, the tricyclic antidepressants and carbamazepine have all traditionally been used as secondary analgesics for neuropathic and chronic pain, but recent reports of the use of both gabapentin and pregabalin in the perioperative period have shown promising results. They are both expensive in SA but may have a role in the future. Gabapentin is an excellent antipruritic in children with burns.

Anaesthetic and analgesic techniques

- TIVA
Caution: remifentanyl: acute tolerance, ensure good analgesia on awakening
- Regional anaesthesia and local anaesthetics
Epidurals: with or without catheters, with or without additives
Paravertebral blocks
Nerve blocks: with or without catheters
Caudals: with or without additives (ketamine, clonidine, opioids): mostly paediatrics
Spinals: catheters, additives (opioids)
- IV Paraceramol (Perfalgan®)
- Intravenous NSAIDs: not often available in the “state” hospitals
- Combinations: regional + general anaesthesia (GA); this is common in children.

The use of local anaesthetics should be considered for every case.

Practical information

- One needs to know the “pre-morbid” personality pain appreciation prior to surgery.
- Pain control: for intense pain intraoperatively vs postoperative pain after surgery e.g remi/fentanyl/sufenta vs morphine/pethidine ± local anaesthetics .
- Acute tolerance: most commonly remifentanyl or sufenta but also reported after single morphine dose.
- Type of surgery is greatest predictor of increased requirements for analgesia. Thoracic and abdominal surgery > neurosurgery, orthopaedics > lumps and bumps.
- If there are increased analgesic requirements intraoperatively, there will usually be increased requirements postoperatively.
- Aim: plan the analgesic regimen for *that* person having *that* particular surgery. Use LA whenever possible.
- Adjuvants for epidural/caudal analgesia to prolong action of local anaesthetic: ketamine, clonidine, opioids.
- Children with epidurals may require supplemental sedation for ease of nursing or additional analgesia for discomfort (urinary catheter, invasive monitoring lines, etc). This is not an indicator of poor regional technique, rather it as a reflection of a child who is so well relieved of the pain that he/she wants to move and be “normal”.
- Adults are more likely than children to have physiologic organ dysfunction, concomitant disease, and a history of opioid and /or other medication use.
- The safety of the patient in the postoperative period is a priority.
- Any patient who has been taking opioids for longer than 7 – 10 days should have the drugs weaned, not stopped abruptly.

Many patients have individual idiosyncratic reactions to some of the combination formulae: confusion, nausea and vomiting, extreme sedation, or itching. Be aware of the stabilising/preservative agent (e.g. tartrazine in Vallergan®, alcohol in many agents).

Many combination medications may not have the same components or drug dose for each formulation of the product e.g. Stopayne® capsules, tablets, and syrup are different from each other.

- Caffeine has analgesic effect of its own and is not merely added to keep the patient awake after the sedative action of other drugs. A recent ruling (June 2008) from the MCC in South Africa states that any formulation which contains promethazine (Phenergan®) is contraindicated for use in children under two years of age, because of reported respiratory depression.

Combination formulae may contain any one or more of the following:

- Aspirin
- Paracetamol
- Caffeine
- Meprobamate
- Promethazine
- Codeine phosphate
- Dextropropoxyphene napsylate
- Diphenhydramine HCl
- Tramadol
- Tartrazine
- Alcohol
- Sugar

Most patients will not volunteer information to you about their pain: ask them regularly. In children, this may be more difficult, and looking at their “body language” may well be the most informative. Check the results of your analgesia once it has been administered.

In adults, the use of herbal preparations is common. It is vital that any use of these agents is known about and documented, as many have anti-platelet activity.

Comfort issues in the perioperative period

- Intravenous drips: method of insertion, site chosen (preferably not over a joint) is important for the patient when it is planned for the drip to be kept in for more than a day.
- Central venous catheters: correct placement and securement can add considerably to the longevity of the line.
- Infiltration, nerve blocks, epidurals and spinals: give the local anaesthetics time to work before you do the block. Secure catheters properly and comfortably.
- Nasogastric tubes: do not have the tube pulling on the side or upper part of the nostril, especially in patients who are, or are likely to be, hypotensive (e.g. cardiacs, major trauma).
- Urinary catheters: secure to avoid traction as this may cause urethral damage.
- Bandaging and strapping: tight, loose, splints not fitting or hurting over joints or bony prominences.
- Chest drains: insertion, maintenance, removal: make a plan for each phase.
- Distraction techniques: TV, virtual reality, play stations, blowing bubbles etc.
- Depression will impact on pain management.
- Thirst and prolonged starvation times impact negatively on both the comfort and lack of calories for the patient (NB burns children).
- Itching, whether as a side-effect of opioids or as a consequence of a healing wound can be seriously debilitating.

Pharmacogenomics and pain

Understanding the correlation between an individual’s genetic make-up and his/her response to a particular drug will allow for the development of patient-specific therapies, population-specific treatments, avoidance of adverse effects of some drugs, reduced inefficiency of drugs (why some drugs do not work in some people), and targeted drug design (analgesics tailor-made to individuals). A patient’s response to a drug may depend on one or more factors, which can vary according to the alleles that an individual carries.

Responses to endogenous opioids are dependent on genetic factors, which are likely to influence susceptibility to pain. Thus individual responses to pain may vary, and depend on variations

in the expression of receptors, enzymes that activate the drugs, and those enzymes responsible for terminating the effects of those drugs.

Examples in this category of patient include those who are unable to metabolise codeine to its active form morphine, thus administering codeine to these patients will not provide them with any pain relief.

Differences between children and adults

The main difference lies in the psychological development of the child, but other areas of differences include the following:

- Some techniques are less appropriate in children: PCA, intramuscular injections.
- Many medications available for use in adults are not recommended for use in children, are contraindicated, or have not been tested for use in any of the paediatric age groups. Neonates and infants are particularly disadvantaged. Off-label and unlicensed use of medications is more common in paediatric practice than adult practice.
- Much of the equipment used regularly in adults may not be available for use in smaller children: only recently have size-appropriate catheters become available for paediatric use (e.g. central venous catheters, epidural catheters).
- Drug pharmacodynamics and kinetics for the various paediatric age groups may differ from each other and from adults.
- Miscalculated doses, and inadvertent administration of adult preparations to children are the more common reasons for drug toxicity in children.
- Children cannot always answer for themselves and be understood. They also have parents who expect the anaesthetists to communicate with them as well.
- Psychological development impacts on anaesthetic management and pain control in the following ways:
 - Pain means different things at different ages: pain may be interpreted as punishment.
 - Anxiety impacts on analgesic requirements.
 - Communication is a major challenge but trust can be established. Care-givers can be very helpful in “interpreting” for a non-verbal patient.

What is new?

- Gabapentin/Pregabalin
- Perfolgan: intravenous paracetamol
- Gene therapy
- PROSPECT (procedure-specific postop pain management)
- Iotophoretic fentanyl patches
- Nitric oxide releasing NSAIDs: NO is gastro-protective and protects against the vasoconstrictive effects of the NSAIDs (Nitroaspirin, Nitroflubiprofen etc)
- Dual COX and LOX inhibitors: Licofelone inhibits COX 1, COX 2 and LOX 5
- Other uses of NSAIDs: spinal cord injury - new COX and LOX inhibitors (IL10 is neuroprotective); intestinal CA – over-express COX enzyme; Alzheimer’s disease: COX 1 inhibition may prevent progression
- Other analgesic mechanisms of action of NSAIDs: Tissue acidosis is a major cause of pain via acid-sensing ion channels (ACIS). NSAIDs desensitise ACIS. Bradykinin: new NSAIDs block bradykinin thus decreasing visceral and ureteric pain.

Summary

- Poorly managed pain affects virtually every organ system.
- Successful pain management requires a continuum of care and change of delivery systems as the process of recovery takes place.
- Opiates are the mainstay of perioperative pain management, and are administered by a variety of routes. Antagonists are available which reverse actions of both endogenous and exogenous opioid ligands. Side-effects should be anticipated and treated.
- Use of local anaesthetic techniques should be considered in every case, especially in children, where LA blocks are usually performed under GA.

- Other management approaches include physical therapies, non-opioid medications, and psychosocial modalities.
- Rehabilitative therapies aimed at improved function after surgery should be the long-term aim, with these being done within the pain threshold of each patient.
- Do the simple things well: this may generate great benefits for patients without requiring expensive high-tech interventions.

Conclusion

Anaesthetists should take their pain management responsibility seriously. Be kind and considerate. You never know who you will have taking care of you if/when you have to go to hospital. Assess and measure pain, as well as the response to therapy. Do not use NSAID's when you anticipate poor renal perfusion, significant perioperative blood loss, or the possibility of gastric irritation. Multimodal pain control is usually the most successful. Think about what your patient will require for that particular procedure, and make your analgesic choice accordingly. Especially in children, but in many adults as well, anxiety and fear will increase analgesic requirements, so anticipate and treat this problem timeously.

Complications of pain control interventions can be minimised by appropriate training and education of staff and parents, the use of protocols or guidelines, monitoring the patients according to the drugs used, and the ability to resuscitate patients if the need arises.

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