

Analgesia And Sedation

R Mackenzie

Introduction

The principle aims of pre-hospital care are to preserve life, minimise complications resulting from injury and reduce pain and suffering (1). To achieve this, the pre-hospital practitioner should be confident in the safe use of a limited range of analgesic and sedative drugs (1,2). In this article, a summary of effective and safe techniques for analgesia and sedation in both the civilian and military pre-hospital environments is presented. In the military context, the material is relevant primarily to role one and role two medical support. Pre-hospital anaesthesia will be discussed in later articles in the series. Although every effort has been made to ensure that the doses stated are correct, readers should always check these with current product information and unit or departmental policy.

Analgesia

The neurobiology of pain and the use of analgesic agents in the pre-hospital and military environment have recently been reviewed (3-6). This article revisits these issues because pain is important and there is evidence that it is inadequately managed in both the pre-hospital (7-9) and hospital settings (10-13). This is reflected by wide variations in pre-hospital practice (7,14). Pain relief is important for practical, physiological and humanitarian reasons (15-17). Controlling pain facilitates assessment of injuries, helps reduce rescue and extrication times and permits medical interventions. Good analgesia also reduces sympathetic overactivity and circulating catecholamines in the acute phase of injury. The peripheral vasoconstriction, tachycardia and increased oxygen consumption associated with excess catecholamines exacerbates the effects and consequences of hypovolaemia. Improvements in ventilation and a reduction in psychological stress can also be achieved. Pain relief is, to the casualty, one of the most critical aspects of their care. Effective analgesia is therefore a fundamental component of quality emergency care (3,15-17).

Pain is a complex phenomenon comprising physiological, emotional, psychological and behavioural components (Figure 1). In physiological terms, mechanical, chemical or thermal injury to tissue initiates an acute inflammatory cascade that is then sustained by multiple chemical mediators. There is increased activity of nociceptive neurons (specialised nerve endings which receive and transmit noxious stimuli) and other peripheral sensory neurons such as temperature and touch (whose threshold is

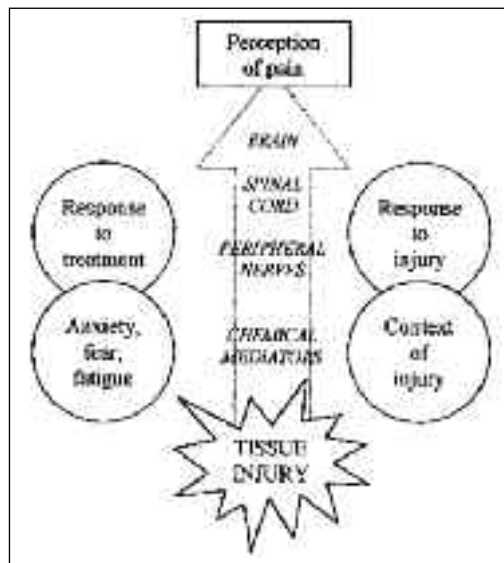


Fig 1. The factors influencing the perception of pain. Individual variations in physiology, response to injury and response to treatment, the context of the injury (e.g. combat vs training) and the presence of other factors such as anxiety, fear and fatigue all modulate pain perception. Adapted from reference 17.

reduced by inflammation). This sensory information is integrated in the dorsal horn of the spinal cord. Ascending pathways then relay the information to the thalamic, limbic and cortical structures responsible for the perception of and response to pain. Control of pain reduces the extent and duration of this entire nociceptive cascade (15-17).

Although the physiological responses predominate in pain associated with physical injury, the impact of the other components should not be underestimated. Anxiety, fear, anger, sadness, depression and fatigue all lower the pain threshold. The casualty's personality and beliefs about the significance of the pain also influence this threshold. This was most strikingly demonstrated by the observation that soldiers wounded in battle requested less analgesia than civilian casualties with comparable injuries (18-20). To the soldier in battle, being wounded was associated with being released from a frightening and life threatening environment. The soldier could expect repatriation, treatment and the end of the war. In contrast, injuries represent a personal and possibly financial disaster to civilians (18-20). A less dramatic (but more common) example is the casualty who believes that they have broken a bone whose pain and analgesic requirement diminishes on reassurance that there is no fracture. The management of pain therefore requires a combination of psychological, physical and pharmacological treatments. Psychological treatments in the acute phase include reassurance and explanation. To quote the British Association for Immediate

Maj R Mackenzie
PhD, MRCP, Dip IMC
RCSEd, RAMC(V)

254 (City of
Cambridge) Field
Ambulance (V), 450
Cherry Hinton Road,
Cambridge, CB1 8HQ

e-mail:
roderick.mackenzie@doctors.org.uk

Care (BASICS) Monograph on Pain Relief: 'It takes little effort to hold the patient's hand and say, "I am the doctor and I am here to help you" (1). Physical treatments include simple measures such as immobilisation by splinting or supporting wounds, covering wounds (especially burns), applying dressings and, in some cases, providing definitive treatment (e.g. reducing a dislocation or trephining a sub-ungual haematoma). The remainder of this article focuses on the pharmacological treatment of acute pain.

Before discussing selection and administration of analgesic drugs, it is worth re-emphasizing three key principles of treatment of acute pain in the pre-hospital setting. Firstly, assessment and aggressive treatment of life threatening conditions according to the Battlefield Advanced Trauma Life Support philosophy (21) should always precede pain relief (with the caveat that pain relief may facilitate assessment and treatment). Secondly, in emergency circumstances, only those drugs and preparations that are familiar to the practitioner should be used. Thirdly, severity of pain should be measured and analgesia titrated against severity in a logical and stepwise manner. Despite the complexity of pain, simple subjective scales such as the 'pain ruler' (Figure 2) have been shown to be valid assessment tools (6,8,22,23). Despite this, few ambulance services use pain scales on patient report forms and there is no provision for the evaluation of pain and its treatment on either the BASICS patient report form or the tri-service FMed 826 field medical card. In the absence of a formal pain scale, it is reasonable to measure the effects of treatment using a simple verbal rating of pain (17).

There are numerous randomised trials of

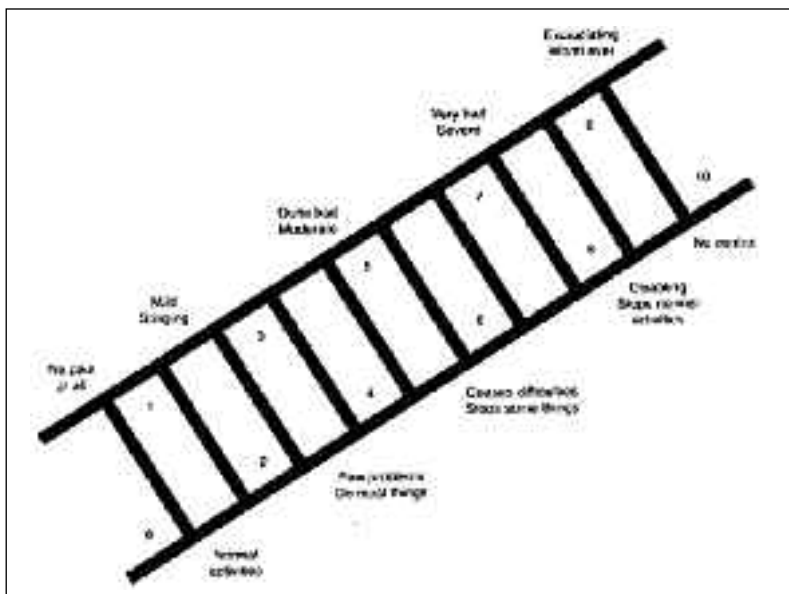


Fig 2. The pain ruler. The pain ruler includes a verbal descriptor ('mild stinging'), a visual analogue (the numbered ruler) and a pain behaviour ('disabling') scale to assess pain. Reproduced from reference 23.

post-operative analgesia but few which address pre-hospital or emergency department care. Nonetheless, systematic review of post-operative pain relief trials provides a reasonable evidence base from which recommendations can be derived (24). A comprehensive and up to date citation database of systematic reviews of acute pain relief can be found at The Oxford Pain Internet Site (25). These resources allow us to create an analgesic formulary based on the drugs that are likely to be most effective for different intensities of pain (Box 1).

Box 1. A simple analgesic formulary for acute pain in adults.

Drug and preparation	Dose
Paracetamol tablet 500 mg suppository 500 mg	0.5 to 1 g every 4 to 6 hours <i>max. 4g daily</i>
Co-codamol 30/500 tablet (codeine phosphate 30 mg and paracetamol 500 mg)	1 to 2 tablets every 4 to 6 hours <i>max. 8 tablets daily</i>
Ibuprofen tablet 400 mg	1.2 to 1.8 g daily in 3 to 4 divided doses, preferably after food <i>max. 2.4 g daily</i>
Diclofenac suppository 100 mg injection 25 mg/ml (1 ml)	75 mg by deep IM injection <i>max. twice daily for 2 days</i> 75 to 150 mg rectally in divided doses <i>max. 150 mg daily by any route</i>
Codeine phosphate tablets 30 and 60 mg injection 60 mg/ml (1 ml)	30 to 60 mg every 4 to 6 hours <i>max. 240 mg daily</i>
Morphine sulphate injection 10 mg/ml (1 ml)	10 to 15 mg IM 2 to 4 hourly 2 to 5 mg IV followed by 1 mg increments titrated against pain
Ketamine injection 10 mg/ml (20 ml) and 100 mg/ml (10 ml)	1 to 4 mg/kg IM 0.25 to 0.5 mg/kg IV <i>note that these are analgesic doses</i>

Mild to moderate pain

Mild to moderate pain from injuries and wounds can be difficult to manage unless the practitioner has a clear strategy. Figure 3 provides an approach to analgesia for these casualties. A key management decision is whether the oral route of administration is available. This decision clearly depends on the severity of the pain, the urgency of the situation, the need to restrict oral intake and the availability of suitable drugs. In civilian practice, it is normal to ensure that casualties remain nil-by-mouth prior to arrival at hospital and this negates the use of oral agents. However, if there is delay in getting to treatment or the injuries are such that it is not necessary for the casualty to remain nil-by-mouth, effective pain relief can be achieved with oral drugs. This is particularly relevant in the wilderness or military setting. Oral agents may also be appropriate once severe pain has been controlled or local analgesics employed in the casualty whose evacuation is delayed. Even if casualties do take drugs orally with water prior to evacuation and transfer to hospital, subsequent general anaesthesia is unlikely to

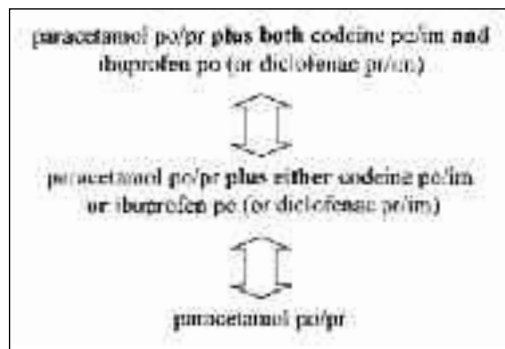


Fig 3. The drug management of mild to moderate pain with stepwise progression through analgesics of increasing efficacy and utilising combinations of oral (po), rectal (pr) and intramuscular (im) routes of administration.

be delayed. In elective surgery, there is evidence to suggest that a small drink two to three hours prior to induction has no deleterious effects on either gastric volume or acidity (26).

If the oral route is not possible due to injury or nausea and vomiting, rectal or intramuscular (IM) administration may be required (along with a suitable anti-emetic). There is, however, no evidence that either route provides better or faster analgesia than the same drug at the same dose given by mouth (17,25). Service personnel injured in the course of operational duties are likely to have immediate access only to IM morphine. It is worth noting however that systematic reviews of oral analgesics vs. placebo in post operative pain show that some non-steroidal anti-inflammatory drugs (NSAIDs) are at least as effective as 10 mg IM morphine over 4 to 6 hours. (15-17,24,25). Thus the oral route is viable for casualties with mild to moderate pain.

The common mode of action of NSAIDs is to block the production of chemical mediators of inflammation by inhibition of cyclo-oxygenase. Despite this common action, there are important differences between different drugs. Paracetamol (acetaminophen), although broadly classed as an NSAID, is a central cyclo-oxygenase inhibitor and has a very different pattern of activity. It is one of the safest and most effective drugs in the management of mild to moderate pain. Despite its ubiquitous use and availability, paracetamol is often neglected as a first line oral analgesic. Paracetamol alone (in doses of 1g four times a day) should be regarded as the first choice (17). It can be given orally or rectally. Although paracetamol is significantly less effective than 10 mg IM morphine, the combination of full dose paracetamol with a full dose of codeine (60 mg four times a day) has greater efficacy than paracetamol alone and is at least as effective as 10 mg IM morphine. (17,27,28). The paracetamol and codeine can be given separately or together as co-codamol 30/500. Codeine can also be given as an IM injection. Codeine may be associated with opioid side effects

(drowsiness, pruritis, respiratory depression, nausea and vomiting).

The more typical NSAIDs that have been shown to be most effective are ibuprofen and diclofenac (17,25). These are peripheral cyclo-oxygenase inhibitors and potent anti-inflammatory drugs. Ibuprofen has the lowest incidence of side effects of all the NSAIDs and is one of the most effective (29). It can only be given orally (or topically in musculo-skeletal injuries), whereas diclofenac can be given orally, rectally and by deep IM injection. Where the option exists, ibuprofen is safer and at least equally as effective as diclofenac (29).

Although NSAIDs have an important role in maintenance of analgesia, their use is associated with some risks. Inhibition of prostaglandin synthesis in the kidney may precipitate acute renal failure in those who have lost > 10% of blood volume. Inhibition of thromboxane production in platelets prolongs the bleeding time and carries a theoretical risk of haemorrhage (15). NSAID associated peptic ulceration and bleeding can also be problematic (regardless of route of administration). In serious injury, it is therefore regarded as inappropriate to give NSAIDs before the casualty is adequately resuscitated or within the first 24 hours (15). In contrast, when NSAIDs are used postoperatively, they can considerably reduce opioid requirements - the opioid sparing effect - and thus the risk of opioid side effects (30). Anxieties concerning NSAID induced exacerbation of asthma and drug interactions are less relevant to the military population who should all be medically fit prior to deployment. However, provision of pre-hospital care to unselected civilian populations may temper the use of NSAIDs.

There are of course many other NSAIDs and their comparative efficacy is only currently being defined (25). IM ketoprofen has been used successfully in battle casualties with minor shrapnel injuries while awaiting treatment and IV ketorolac was recently recommended for military use (6). Ketorolac can be given intravenously (IV) or IM. However, current data from systematic reviews indicates that oral ibuprofen is as effective as IM ketorolac and rectal diclofenac is as effective as IV ketorolac. These comparisons do not suggest that ketorolac is an ineffective analgesic, rather that it is not necessary to use it when equally effective, safer and more widely available alternatives exist (15,17). Thus in the treatment of mild to moderate pain the evidence supports the use of combinations of oral paracetamol, paracetamol supplemented with codeine, ibuprofen supplemented with paracetamol or all three (fig 3). Where the oral route is not available, combinations of rectal paracetamol, IM codeine and IM or rectal diclofenac provide equivalent safe and effective alternatives. If acute pain is not

controlled, the possibility of a missed diagnosis should be considered and the presence of complications such as arterial injury or compartment syndrome should be excluded before progressing to further analgesia.

Severe pain

Intravenous analgesia is recommended for the first line treatment of severe acute pain (1,2,4-6,15-17). The options are opioids or ketamine or combinations of the two. Although there is no trial data to compare the two, IV opioids are widely regarded as the most effective analgesic agents available and of these, morphine and diamorphine are the most appropriate agents for pre-hospital use (1-6,31,32). The use of ketamine as an analgesic is considered in the discussion on sedation below.

The term opioid is used for all opioid receptor specific substances. Opioids reduce inflammation at the site of injury and act at the dorsal horn to impede transmission of nociceptive stimuli. They also act centrally to activate inhibitory pathways that descend to the spinal segment (3,32). There are a number of opioid receptors; the three broad classes of importance for analgesia being: μ (mu), κ (kappa) and σ (sigma). Morphine is the standard opioid against which others are judged (32). It is a pure agonist at μ receptors (responsible for analgesia, euphoria and respiratory depression). The usual dose is 0.1 to 0.2 mg/kg commencing with a bolus of between 2 and 5 mg followed by 1 mg increments titrated against pain intensity. This is best achieved by making up a 10 ml syringe with 1mg/ml solution. The full effect is within 15 – 20 minutes. Diamorphine is a semisynthetic morphine derivative which is much more lipid soluble and therefore more potent than morphine. It has a more rapid onset but shorter duration of action. The usual dose is 0.1 mg/kg titrated to effect as above. Because morphine and diamorphine cause nausea and vomiting it is common to administer an anti-emetic. In general, phenothiazines (e.g. prochlorperazine 12.5mg IM 8 hourly) and metoclopramide (10 mg IM/IV 8 hourly) are effective in drug induced nausea but an antihistamine may be better if motion sickness complicates evacuation (e.g. cyclizine 25 to 50 mg IM/IV 6 hourly). Fixed preparations of anti-emetic and opioid should be avoided (e.g. Cyclimorph®) because the opioid should be titrated to effect whereas a full dose of anti-emetic should be given. The widely held belief that diamorphine is associated with less hypotension and nausea than morphine (and a greater sense of euphoria) is currently the subject of a controlled trial (33).

Pethidine has been used widely in pre-hospital and emergency care. There is no evidence that pethidine has any specific advantages over other opioids (32,34).

Morphine, diamorphine and codeine have active metabolites. The problem of their accumulation is prevented by titration to effect (rather than administration of fixed doses). Pethidine, however, has a toxic metabolite, norpethidine, which accumulates with multiple dosing and in renal impairment (34). This may lead to twitching, tremor, agitation and convulsions. Thus in the absence of any specific advantage of pethidine, there seems little justification in exposing the casualty to these risks. The belief that pethidine provides better analgesia for colicky pain than other opioids has not been substantiated (17).

Recent studies of pre-hospital analgesia have helped to refute arguments that morphine and diamorphine are associated with a high incidence of dangerous side effects (8,31). Ambulance services that routinely use opioids in the UK (Cumbria) and USA have experienced little difficulty with the safe and effective field administration of both morphine and the more potent diamorphine (14,35,36). Nevertheless, the pre-hospital practitioner must be able to recognise and deal with the three most important side effects: respiratory depression (decrease in minute volume and sensitivity to carbon dioxide), cardiovascular depression (systemic vasodilatation following histamine release) and nausea and vomiting. In all cases, facilities for airway and ventilatory support and the μ antagonist naloxone must be available. Doses of opioids greater than that required to control pain will cause respiratory depression. This is prevented by careful and deliberate titration to effect. If respiratory depression does occur, it is easily reversed by naloxone 0.1 mg titrated at 1 min intervals against respiratory rate and pain (to a maximum of 10 mg - best achieved by making up a 0.1 mg/ml solution). Naloxone has a short duration of action and may itself cause nausea, vomiting, tachycardia and hypotension. Large doses may completely reverse analgesia and expose the patient to a sudden severe exacerbation of their pain. In patients with head injuries, chest injuries and abdominal pain, the decision on whether to use opioids should depend on whether the patient is expressing pain. The maxim that there is a safe analgesic for all those who are able to express a need for pain relief applies to opioids as well as other analgesics (31). They are often avoided in head injured patients because of anxiety over masking pupillary responses. Opioids cause constriction of the pupils by stimulation of the third cranial nerve nucleus but do not prevent pupil dilatation caused by compression of the third cranial nerve by an expanding haematoma or herniation (a late sign in head injury and unlikely to be present in an alert patient). Similarly, in abdominal pain, withholding analgesia in case it masked

the signs necessary for diagnosis has been shown to be unfounded (17).

Morphine and diamorphine are safe, effective and well understood analgesics. Despite the principle of titration to effect, the rapid reversibility of adverse effects with naloxone and the lack of evidence to suggest that therapeutic use in treating acute pain leads to addiction (37), medical and political anxieties have resulted in stringent controlled drug regulations concerning their storage and use (38). These have been the driving forces for the development of synthetic alternatives. The two alternative drugs most commonly used in pre-hospital care in the UK are nalbuphine and tramadol. These partial agonists at the μ receptor do not produce better analgesia than morphine but may cause fewer side effects and are not as addictive (and thus free from controlled drug legislation) (3,16,17,32).

Nalbuphine is used extensively by the ambulance service (14,39). It is an agonist at the spinal kappa κ receptor (causing analgesia, sedation and respiratory depression) and an antagonist at the μ receptor. It is thought that at doses above 10 mg, μ receptor antagonism predominates so a ceiling limit to both respiratory depression and analgesia may occur (14,32). Recent studies have raised questions about the use of nalbuphine in trauma. Although equally as effective as morphine (30 mg nalbuphine is equivalent to 10 mg morphine) and found to be effective at the scene (39), many patients require further analgesia in the resuscitation room (40). In cases where further opioid analgesia is required, there is a theoretical risk and some clinical evidence that nalbuphine may oppose the analgesic effect of morphine and thus result in a higher morphine requirement for the patient (41,42). There is currently debate on the evidence for this effect (43-45). Some suggest using further doses of nalbuphine to prevent this problem occurring (46) but the ceiling effect of nalbuphine (and tramadol) may result in inadequate relief of severe pain. The usual dose of nalbuphine is 10 to 20 mg which can be increased by increments up to a total of 40 to 60 mg.

Tramadol is a weak agonist at all three main opioid receptors and also has some non-opioid mechanisms of analgesia. It is used much less frequently than nalbuphine and is associated with an increased incidence of nausea and vomiting (47). Tramadol is usually given as an initial IV bolus of 100 mg (equivalent to 10 mg morphine) followed by further doses of 50 mg every 10 to 20 minutes up to a maximum of 250 mg in the first hour. Subsequent doses are 50 to 100 mg every 4 to 6 hours up to a daily maximum of 600 mg.

There are currently plans to conduct

controlled trials of nalbuphine, tramadol and other opioids (43,47). However, the Joint Royal Colleges Ambulance Liaison Committee (JCALC) have recently submitted an application to the Home Office to add morphine to the list of drugs which can be carried and given by ambulance service paramedics. With mountain rescue teams, midwives, ships masters and one ambulance service already using opioids (36,48), it seems likely that other ambulance services will follow suit provided the legal requirements for storage and documentation can be met (38). Questions about the value of alternative synthetic opioids may then be less important. Nonetheless, synthetic opioids may be the only permissible opioids in some services and countries and it is important to be aware of their use.

Although IV administration of opioids for severe pain is preferable, the IM route may be all that is available – particularly in the military setting where personnel are issued with pre-filled morphine autojets (49). Practitioners should be aware that service personnel are likely to have received IM morphine before arrival of a medical team (or arrival at a field medical facility). Although the IM (and subcutaneous) route provides effective analgesia (50), the absorption is unpredictable and onset may be delayed in hypothermic or hypovolaemic casualties (51). Nonetheless, it may be the only method available, particularly for multiple casualties, expectant treatment of the severely injured (e.g. the casualty with burns) and where medical skills are limited. The principles of titration to effect still apply and have been clearly described for intermittent IM use in the military setting (6,21,49).

Local anaesthetics (local analgesics)

Local anaesthetic techniques can be very sophisticated with the use of peripheral nerve stimulators and indwelling catheters. However, in pre-hospital care, the options are limited to wound management (infiltration and field blocks), simple regional nerve blockade and haematoma blocks. These techniques are described in detail in standard works (1,2,52-54) and are best learnt under direct supervision in the anaesthetic room or emergency department. Local anaesthetics are underutilised for control of acute pain. The judicious use of regional nerve blockade and haematoma blocks can completely abolish pain due to serious injury (1,2,15-17). This has the additional advantage of avoiding or reducing side effects from other analgesics. There are three local anaesthetic agents in common use: lidocaine (lignocaine), prilocaine and bupivacaine .

Box 2. Local anaesthetic formulary.

Drug and preparation	Dose, onset & duration of action
<i>Box 2.</i>	
Lidocaine (lignocaine) 0.5, 1 and 2% solutions	3 mg/kg – onset < 5 mins, lasts 60 mins <i>max. 200 mg</i>
Prilocaine 0.5, 1, 2 and 4% solutions	6 mg/kg – onset < 5 mins, lasts 90 mins <i>max. 400 mg</i>
Bupivacaine 0.25 and 0.5% solutions	2 mg/kg – onset 20 mins, lasts 7 to 24 hrs <i>max. 150 mg</i>

All can be safely used in the pre-hospital setting. Prilocaine is similar to lidocaine but can be given in larger volumes. It is only routinely used in the UK for intravenous regional anaesthesia (Bier's block) despite the fact that it acts just as quickly, has at least an equal duration of action and can be used in twice the volume of lidocaine. Bupivacaine, although the most toxic of the three, has the advantage of a long duration of action. These three drugs act by causing a reversible block to conduction along nerve fibres in a dose dependent manner. The minimal effective doses block pain and temperature sensation selectively. With increasing doses, autonomic, touch and motor fibres are also blocked. The local anaesthetic agents discussed here are all available with added epinephrine (adrenaline). The epinephrine causes local vasoconstriction to counter the vasodilating effect of the anaesthetic. This prolongs its action and decreases the risk of toxicity by limiting systemic absorption. However, the risk of inadvertent IV injection and rapid systemic absorption is greater in the pre-hospital setting and there is little justification for using solutions with added epinephrine out of hospital. A longer acting local anaesthetic without epinephrine can achieve a longer duration of block more safely.

The principles of safe local anaesthetic administration are a thorough understanding of dose calculations and maximum safe doses, an awareness of toxic effects and complications and a good understanding of the specific techniques available. Dose calculations often cause the greatest anxiety. The percentage concentration of the solution is based on the number of grams dissolved in 100 ml. Thus 1% lidocaine is 1 g lidocaine dissolved in 100 ml (or 1000 mg dissolved in 100 ml) to give a 10 mg/ml solution. A simple rule of thumb is to multiply the percentage solution by ten to obtain the quantity of local anaesthetic in milligrams per millilitre. For example, a 1% solution contains 10 mg/ml of active drug whereas a 0.5% solution contains 5 mg/ml. A 60 kg casualty can safely have 120 mg of bupivacaine (2 mg/kg). This could be administered as 48 mls of 0.25% solution or 24 mls of 0.5% solution depending on the technique being used and the volume of local anaesthetic desired. Small volume, high

concentration local anaesthetics may be used for well localised nerve blockade where it is desirable to minimise tissue distortion and pressure. Dose calculations should always be completed and checked prior to administration of local anaesthetics as significant errors in dose can easily occur.

All local anaesthetic drugs are potentially toxic. Toxic effects are more likely to occur if the drug is injected accidentally into a vessel (or rapidly absorbed in an area of acute inflammation) or if an overdose is given by using either too large a volume or too high a concentration. Casualties may experience a feeling of inebriation, warmth, drowsiness and lightheadedness followed by anxiety, tinnitus and circumoral tingling. Depression of the central nervous system may progress to unconsciousness with twitching and possibly convulsions. There may also be hypotension secondary to direct myocardial depression. These effects may be very rapid on IV injection but more commonly occur during maximum arterial plasma concentrations some 10 to 25 minutes after administration. Rarely, true allergic reactions can occur. Toxic effects can be minimised by using the most dilute solution. Blood levels (which reflect systemic absorption) tend to be higher when more concentrated solutions are used; for example, 5ml of a 20 mg/ml (2%) solution will produce higher blood levels than 10 ml of a 10 mg/ml (1%) solution. Using dilute solutions also allows larger volumes to be used that in turn make precise anatomical placement less critical. Treatment of toxic side effects is primarily supportive and symptomatic. Anaesthetic injection should be stopped, resuscitation commenced and, if necessary, hypotension, convulsions and bradycardia treated conventionally.

Apart from toxicity, the greatest dangers with use of local anaesthetics are peripheral nerve damage and the adverse effects of any other systemic analgesia (such as opioids) once the painful stimulus is removed. Casualties receiving intermittent doses of opioid analgesia (either IM or IV) without respiratory depression who then receive successful nerve block must have their opioid dose reduced (55). Nerve damage is minimised by good technique and avoidance of regional nerve blocks in anaesthetised or unconscious casualties. The bevel of the needle being used should, ideally, be aligned along the direction of the nerve fibres rather than across them to reduce damage if the nerve is actually punctured. Some practitioners deliberately blunt needles prior to use. If a patient reports pain or paraesthesia on insertion of the needle or injection, the needle should be withdrawn 2 to 3 mm before continuing with injection. The needle should be re-positioned if there is persistent resistance to injection. Other unwanted effects may be pain on injection, complete

anaesthesia of the limb (which renders it susceptible to other injuries and may make the casualty more anxious), and unwanted additional nerve blocks. Again, good technique and a sound anatomical knowledge reduce these effects. There is good evidence from clinical studies that warming and buffering the local anaesthetic agent can dramatically reduce pain due to local anaesthetic administration (53). Buffering with sodium bicarbonate is not practical in the pre-hospital setting but it takes little effort to warm the ampoule before administration.

Perhaps the most valuable techniques are femoral nerve block, digital nerve block, haematoma block, intercostal nerve block and blocks around the ankle and wrist. The following comments concern specific features worth re-emphasising for some of these techniques. Femoral nerve block is one of the most valuable techniques. Excellent analgesia to the anterior of the thigh and the periosteum of the middle third of the femur is produced and it is ideal for the patient with a femoral shaft fracture. The femoral nerve runs deep to the inguinal ligament and lateral to the femoral artery. The nerve is best blocked immediately below the inguinal ligament. While palpating the femoral artery, a needle should be inserted perpendicular to the skin to a depth of 3 to 4 cm immediately lateral to the artery (the abdominal wall should be retracted if the casualty is sitting). The sensation of penetration of the femoral fascia helps judge the depth. After aspirating to ensure that the femoral artery has not been punctured, local anaesthetic (usually 1% lidocaine for rapid effect or a mixture of lidocaine and bupivacaine) is injected in a fan like manner to cover an area up to 3 cm lateral to the entry point. If the artery is punctured, the needle should be withdrawn and the artery compressed for at least 5 minutes. A more extensive block (the 'three-in-one' block) can be achieved if pressure is applied with the palm of the hand to the femoral sheath distal to the block during and after injection and volumes of 20 to 30 ml are used. The local anaesthetic will track up the femoral sheath to anaesthetise the obturator nerve and the lateral cutaneous nerve of the thigh as well as the femoral nerve. This provides analgesia for the hip as well as the anterior and lateral aspects of the thigh and femur (2).

Haematoma blocks involve identifying a fracture haematoma and injecting anaesthetic directly into the haematoma. This is the only injection technique where the practitioner deliberately injects after aspirating blood. Correct anatomical placement is thus important and the risk of rapid systemic absorption is relatively high. There is also the risk of introducing infection into the fracture site. To reduce this risk, an aseptic technique, and exclusion of fractures

which are over 24 hours old is important. Sufficient time must be allowed for the block to take good effect, particularly if the fracture is to be manipulated.

Digital nerve blocks are generally considered for finger injuries including entrapment, crush injuries and amputations. Digital nerves can also be blocked at the level of the metacarpals in the hand. The danger with digital nerve blocks is that following injection, the pressure within the digit may become high enough to impede venous return and cause increased pain and swelling in the digit. A metacarpal digital nerve block reduces this problem but provides equally adequate analgesia. The landmark for a metacarpal block is the distal palmar skin crease. Local anaesthetic can be injected through the palm either side of the metacarpal (3 to 5 ml). Epinephrine (adrenaline) must never be used for nerve blocks or local anaesthesia of digits or of any other appendage.

Intercostal nerve blocks are valuable in managing the patient with rib fractures, a flail segment or intercostal drains. These blocks involve injecting local anaesthetic around the neurovascular bundle on the inferior aspect of several ribs (at the angle of the rib). There is thus a risk of causing a pneumothorax. However, if the blocks are placed when a chest drain is in situ, the consequences of inducing a pneumothorax are less relevant. The other important risk associated with intercostal nerve blocks is rapid systemic absorption of local anaesthetic from the chest wall.

Nitrous oxide

Nitrous oxide is discussed alone because a mixture of nitrous oxide and oxygen containing 50% of each gas (e.g. Entonox®) is a simple and effective analgesic which can be used with immediate effect to help gain rapid control of acute pain (1,2,4). It produces analgesia equivalent to 10 mg IV morphine (1) without loss of consciousness. The onset of action is very rapid (2 to 5 minutes for full effect) but reversal is equally rapid when the gas is no longer being inhaled. The response to nitrous oxide is very variable. Some casualties achieve good analgesia, others do not. Similarly, some casualties enjoy the sensation they experience when breathing nitrous oxide whilst others experience nausea and light headedness. The main role of nitrous oxide is in providing rapid initial pain relief that may facilitate movement, medical interventions and administration of other analgesics.

Nitrous oxide is normally administered by the casualty via a demand valve. Gas can only be released by holding the facemask against the face and breathing in deeply. Slow, large volume breaths are required. A mouthpiece can be used for those with facial injuries and for children. The casualty must therefore be

conscious, co-operative and have sufficient respiratory excursion to operate the demand valve. It is sometimes desirable to over-ride the demand valve and deliver continuous 50% nitrous oxide in oxygen. Casualties with upper limb injuries and those with difficulty using the apparatus may benefit from this. However, over-riding the demand valve negates the failsafe of a conscious casualty regulating his or her own analgesic needs. There is a risk that sufficient nitrous oxide will be inhaled to render the patient unconscious. This should be regarded as a general anaesthetic.

The only absolute contraindication to nitrous oxide is nitrogen decompression sickness (the 'bends' or 'Caisson disease'). However, care must be taken when administering nitrous oxide to casualties who may have an air-containing closed space since nitrous oxide may diffuse into the space and possibly increase the pressure. Actual or potential pneumothorax and basal skull fractures which extend into the nasopharynx are the two injuries most likely to be complicated by nitrous oxide administration. Another problem with nitrous oxide / oxygen mixtures is liquefaction of the nitrous oxide component in cylinders at temperatures below minus 7°C. When liquefied, the two gases separate out, resulting in pure oxygen being administered first followed by pure nitrous oxide. At these temperatures, it is not sufficient to simply agitate the cylinder to provide the correct mixture. The data sheet for Entonox[®] requires the cylinder to be rewarmed at 10°C for 2 hours then agitated, or more rapidly warmed by immersion in water at 37°C for 10 minutes and then agitated. Neither of these options is practical for field use and the logistic and safety problems associated with compressed gas cylinders in a tactical environment have resulted in nitrous oxide being used less often in military practice. In contrast it has become the mainstay of analgesia in civilian pre-hospital care and has stood the test of time (despite little systematic review evidence) (14,17,25,56).

Sedation

The injured casualty is likely to be frightened, anxious, distressed and restless. The contribution of these feelings to the perception of pain has already been emphasized (fig 1). Sedative and anxiolytic agents may thus be useful adjuncts to analgesia in the management of such casualties. However, anxiety must not be confused with restlessness due to hypoxia, hypovolaemia or other complication of injury. Once these have been excluded, it is also important to reassess pain control before considering sedatives. In those cases where anxiety and agitation are still problematic despite adequate analgesia, or where medical interventions require sedation as well as

analgesia (e.g. reduction of fractures or dislocations), then a sedative agent should be used (57-59).

Sedation can be described as either conscious or deep. Conscious sedation can be defined as a pharmacologically induced, minimally depressed level of consciousness that retains the casualty's ability to maintain a patent airway independently and continuously, and respond appropriately to physical stimulation and/or verbal command. In contrast, deep sedation is a state of depressed consciousness from which the casualty is not easily aroused. The casualty is not able to respond purposefully to physical stimulation or verbal command. Deep sedation may be accompanied by a partial loss of protective reflexes, including the ability to maintain a patent airway. It therefore has risks to the casualty equivalent to those of general anaesthesia. In considering sedating a casualty, the drugs, doses, and techniques used should carry a margin of safety wide enough to minimise the risk of unintended deep sedation. Opioids have a sedative effect but they are unpredictable for planned sedation (10 fold variation in dose requirement). The most appropriate agents for pre-hospital use are midazolam and ketamine (1,2,4,5).

Midazolam is a water soluble benzodiazepine with a short half life (2 to 4 hours) and no active metabolites. It produces sedation with amnesia but has no analgesic properties. For sedation, 2 mg should be given IV over 30 seconds, followed by incremental doses of 0.5 to 1 mg after 2 minutes to achieve adequate sedation. The onset is rapid and the typical dose range in adults is 2 to 8 mg (approx. 0.1 mg/kg). If opioid analgesia has already been used, lower doses of midazolam are required. The effects (and side effects) of benzodiazepines and opioids are additive and include cardiovascular depression, hypotension and respiratory depression (58,59).

Adverse side effects from the administration of midazolam can be reversed by the administration of the benzodiazepine receptor antagonist flumazenil. The initial dose is 200 micrograms over 15 seconds then a further 100 micrograms at minute intervals up to a total of 1 mg. It is preferable to titrate the dose of midazolam to avoid over sedation rather than have to reverse the effects. Flumazenil is associated with significant side effects of its own, including nausea, flushing and convulsions. Furthermore, its half life is shorter than midazolam and there is a risk that casualties will become re-sedated. Flumazenil is not licensed for this indication. Nevertheless, for practitioners who plan to give IV midazolam (or any other benzodiazepine) flumazenil should be immediately available (2,4,57-59).

Ketamine

A valuable adjunct or alternative to opioids is the phencyclidine derivative ketamine. This produces profound analgesia at low doses (1 to 4 mg/kg IM or 0.25 to 0.5 mg/kg IV) which slides imperceptibly into dissociative general anaesthesia at higher doses (2-4 mg/kg IV). Ketamine is an effective analgesic either alone or in combination (e.g. with an opioid) (4,16,59-61). The characteristics of the dissociative state are unique. The sedated casualty is dissociated from normal consciousness and appears in a trance like or 'fugue' state with the eyes open. At higher doses, the casualty will have increased muscle tone and catalepsy (may move or be moved into a position which is self-maintaining). Analgesia and amnesia are often complete. There will also be occasional purposeless movements with clonus and nystagmus. Laryngeal and pharyngeal protective reflexes are maintained more than with any other sedative or anaesthetic agents (62), but they may still be partially suppressed. A combination of increased masseter tone, increased salivation and marginally suppressed cough and upper airway reflexes can result in a compromised airway. This suppression will be increased if any other sedative or analgesic agents have been used. Similarly, hypoxic and hypercarbic driving stimuli to respiration are minimally suppressed by ketamine so respiratory depression does not occur unless it is administered rapidly (IV) or concomitantly with other analgesics or sedatives.

Other effects of ketamine include an increase in mean arterial pressure, pulse rate and cardiac output secondary to an increase in sympathetic activity. Thus ketamine is contraindicated in casualties in whom an elevation of blood pressure would constitute a serious hazard. This explains why the use of ketamine in casualties with major head injuries and loss of cerebral autoregulation is generally discouraged (even though ketamine may have a direct neuroprotective effect related to blockade of N-methyl-D-aspartate type glutamate receptors). The main disadvantage of ketamine sedation is hallucination during the recovery phase. This can be readily blocked by concurrent use of a small dose of midazolam and by ensuring that the recovery environment is as free from visual and auditory stimuli as possible (63).

Ketamine has been extensively used as an analgesic and sedative agent in both civilian and military pre-hospital settings (1,2,60,64,65). For those who have the necessary anaesthetic experience, ketamine can also be used for emergency airway management, rapid sequence induction and resuscitative surgery in the field (66-69). In a study of ketamine analgesia in a field hospital, the average initial dose required to produce adequate analgesia without losing verbal contact was 20.5 mg (given as 5 mg

increments every 3 minutes) (65). However, in contrast to midazolam (which has no analgesic properties), analgesic doses of ketamine were considered to have no anxiolytic properties. Analgesic doses of ketamine were also less effective than opioids in removing the pain associated with visceral injuries (65).

The IV route provides more effective and predictable sedation than the IM route and should be used unless the casualty is trapped with no IV access (64,70). An initial dose of 2mg/kg produces deep sedation within 30 seconds for 5 to 10 minutes. This should be achieved by slow injection (over a minute) to avoid respiratory depression. Recovery is indicated by nystagmus, vocalization and movements in response to stimulation (as opposed to purposeless movements). This initial profound sedation may allow painful procedures to be carried out including extrication from entrapment (64,70), and manipulation of fractures. Facilities for airway management must be available although use of ketamine in this way (as opposed to prolonged procedures under general anaesthesia) has few risks in published series (71). If sedation has been performed in order to complete a painful or distressing procedure, it is generally considered that the casualty will be fit for further evacuation (with minimal observation) if they have stable vital signs, are able to walk unsupported (if appropriate) and have adequate analgesia.

Summary

Pre-hospital care covers a wide spectrum of medical activity from sophisticated peacetime emergency medical services to wilderness environments with minimal medical support and long lines of communication. It is difficult to provide guidance on safe and effective analgesia and sedation for all conceivable environments and operations. The experienced practitioner will make best use of scarce resources and choose a variety of agents in combination to combat pain and anxiety. However, the guidance in this article will help the inexperienced to provide analgesia in a logical and stepwise manner with a wide margin of safety (fig 4). The brief descriptions of the role of nitrous oxide, local anaesthetics, midazolam and ketamine will remind the experienced of the value of these agents in acute pain and give the inexperienced some insight into their use in the pre-hospital environment. There is, however, no substitute for practical experience of these drugs and techniques gained in a controlled environment such as an Accident and Emergency Department or an anaesthetic room. The drugs described are all on the essential drugs list of the World Health Organisation (72). It is therefore likely that the modest formulary described

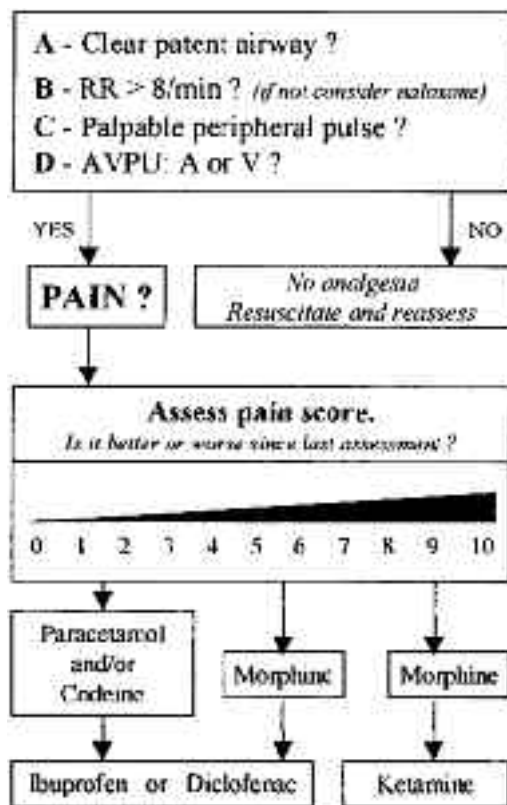


Fig 4. A simplified version of the analgesic protocol proposed by Hocking and De Mello (6) which summarises the key principles in the management of acute pain (assessment of life threatening conditions, assessing severity of pain and titrating analgesics against severity in a logical and stepwise manner). Nitrous oxide in oxygen can be used at any stage to give rapid pain relief. See text for details of routes and doses.

here will be equally accessible across different national medical services and countries. Time spent becoming familiar with their use during peacetime will not be wasted.

The effective management of pain in the pre-hospital environment may be the most important contribution to the survival and long term well being of a casualty that we can make. As our understanding of the consequences of unchecked pain develop further, the impact of effective analgesia will be better understood. General Patton said 'Pain is just like the enemy. You keep moving and the enemy cannot hit you. Same way with pain, the quicker you break away from the pain, the quicker you will drive the pain out of your system' (73). The pre-hospital practitioner has the first and perhaps only opportunity to break the pain cascade. Regardless of the drugs used, application of the following principles will ensure that this is achieved as quickly and effectively as possible:

- Look for and treat life threatening problems first.
- Assess pain routinely and treat it as early as possible.
- Use non-drug and drug interventions synergistically.
- Deliberately choose appropriate drugs, route and mode of delivery.
- Titrate analgesic and sedative drugs to effect.

- Reassess pain regularly and alter analgesia as necessary.
- Use combinations of systemic and local analgesics.
- Opt for simplicity and safety as far as possible.

This article was previously published in Journal of the Royal Army Medical Corps, Vol 146 No. 2 June 2000.

References

1. Basics Monograph on Immediate Care No 2: Pain Relief. (2nd ed.) British Association for Immediate Care, 1995.
2. Sherwood N. Analgesia and pain relief. In: Greaves I, Porter KM (eds). Pre-hospital medicine: The principles and practice of Immediate Care. London: Arnold, 1999.
3. Besson JM. The neurobiology of pain. *Lancet* 1999; **353**:1610-1615.
4. Mahoney PF, Haji-Michael PG, Wood PR. Pre-hospital analgesia. In: Greaves I, Ryan JM, Porter KM (eds). *Trauma*. London: Arnold, 1998: 29-40.
5. Mahoney PF, Haji-Michael PG. Therapeutics. In: Greaves I, Porter KM (eds). Pre-hospital medicine: The principles and practice of Immediate Care. London: Arnold, 1999:170-177.
6. Hocking G, De Mello F. Battlefield analgesia: An advanced approach. *J R Army Med Corps* 1999;**145**:116-118.
7. Chambers JA, Guly HR. The need for better pre-hospital analgesia. *Arch Emerg Med* 1993;**10**:187-192.
8. Ricard-Hibon A, Challet C, Saada S, Lovidant B, Marty J. A quality control program for acute pain management in out-of-hospital critical care medicine. *Ann Emerg Med* 1999;**34**:738-744.
9. Gray A, Johnson L, Goodacre S. Paramedic use of nalbuphine in major injury. *Eur J Emerg Med* 1997;**4**:136-139.
10. Selbst SM, Clark M. Analgesic use in the emergency department. *Ann Emerg Med* 1990;**19**:99-102.
11. Fung AS, Bentley TM. Pre-operative analgesia for acute surgical patients: no place for complacency. *Ann R Coll Surg Engl* 1994;**76**:11-12.
12. Morgan-Jones R. Pre-operative analgesia after injury. *Injury* 1996;**27**:539-541.
13. Commission on the Provision of Surgical Services. Report of the working party on pain after surgery. London: Royal College of Surgeons, 1990.
14. Clarke TNS, Ennis BP, Joicey P, Meehan C. Paramedic administered analgesia - an appraisal of current practice. *Pre-hospital Immediate Care* 1998;**2**:123-127.
15. Young Y, Fletcher SJ. Sedation and analgesia for the trauma patient. In: Parke GR, Sladen RN (eds). Sedation and analgesia in the critically ill. Oxford: Blackwell Science 1995.
16. Carr DB, Goudas LC. Acute pain. *Lancet* 1999;**353**:2051-2058.
17. McQuay H, Moore A, Justins D. Treating acute pain in hospital. *BMJ* 1997;**314**:1531-1535.
18. Beecher HK. Resuscitation and anaesthesia for wounded men: the management of traumatic shock. Springfield, Illinois, CC Thomas, 1949.
19. Beecher HK. Control of suffering in severe trauma. *JAMA* 1960;**173**:534.
20. Laurence DR, Bennett PN. Clinical Pharmacology (7th ed.) Edinburgh: Churchill Livingstone 1992.
21. Director General Army Medical Services. Battlefield Advanced Trauma Life Support (Army Code 63726). London: The Stationary Office, 1997.
22. Huskisson FC. Measurement of pain. *Lancet* 1974; **2**:1127-1131.
23. Manchester Triage Group. Emergency Triage. London; BMJ Publishing Group, 1997.
24. McQuay HJ, Moore RA. An evidence-based resource for pain relief. Oxford: Oxford University Press, 1998.

25. The Oxford Pain Internet Site - <http://www.jr2.ox.ac.uk/painres/painpag/index.html>
26. Agarwal A, Chari P, Singh H. Fluid deprivation before operation: the effect of a small drink. *Anaesthesia* 1989;44:632-634.
27. Moore A, Collins S, Carroll D, McQuay H. Paracetamol with and without codeine in acute pain: a quantitative systematic review. *Pain* 1997;20:193-201.
28. De Craen AJM, Di Giulio G, Lampe-Schoenmaeckers AJE, Kessels AGH, Kleijnen J. Analgesic efficacy and safety of paracetamol-codeine combinations versus paracetamol alone: A systematic review. *BMJ* 1996;313:321-325.
29. Collins SL, Moore A, McQuay HJ, Wiffen PJ. Oral ibuprofen and diclofenac in postoperative pain: a quantitative systematic review. *Eur J Pain* 1998;2:285-291.
30. Hodsman NBA, Burns J, Blyth A, Kenny GNC, McArdle CS, Rotman H. The morphine sparing effect of diclofenac sodium following abdominal surgery. *Anaesthesia* 1987;42:1005-1008.
31. Baskett PJF. Acute pain management in the field. *Ann Emerg Med* 1999;34:784-785.
32. McQuay H. Opioids in pain management. *Lancet* 1999;353:2229-2232.
33. Fong C. A double blind randomised crossover trial of intravenous diamorphine and morphine. NRR Project NO241041423. The National Research Register 1999 Issue 2.
34. Szeto HH, Inturrisi CE, Houde R, Saal S, Cheigh J, Reidenberg M. Accumulation of norperidine, an active metabolite of meperidine, in patients with renal failure or cancer. *Ann Intern Med* 1977;86:738-741.
35. Bruns BM, Dieckmann R, Shagoury C, et al. Safety of pre-hospital therapy with morphine sulphate. *Am J Emerg Med* 1992;10:53-57.
36. Robson RH, Gilbert A, Martin E, Hall M. Diamorphine administered by paramedics. *Pre-hospital Immediate Care* 1999;2:51-52.
37. Porter J, Jick H. Addiction rate in patients treated with narcotics. *New Engl J Med* 1980;302:123.
38. Merrills J, Fisher J. Pharmacy law and practice. Oxford: Blackwell Science, 1995.
39. Chambers J, Guly HR. Pre-hospital intravenous nalbuphine administered by paramedics. *Resuscitation* 1994;27:153-158.
40. Kelly AS, Guly HR. Nalbuphine – the optimal pre-hospital analgesic for lower limb fractures? *Pre-hospital Immediate Care* 1999;3:224-225.
41. Hyland-McGuire P, Guly HR. Effects on patient care of introducing prehospital intravenous nalbuphine hydrochloride. *J Accid Emerg Med* 1998;15:99-101.
42. Houlihan KPG, Mitchell RG, Flapan AD, Steedman DJ. Excessive morphine requirements after pre-hospital analgesia. *J Accid Emerg Med* 1999;16:29-31.
43. Robinson N, Burrows N. Excessive morphine requirements after pre-hospital nalbuphine analgesia. *J Accid Emerg Med* 1999;16:380-385.
44. Houlihan KPG, Laing J, Leonard PA. Pre-hospital nalbuphine administration and subsequent analgesia requirements in accident and emergency. *J Accid Emerg Med* 2000;17:70.
45. Volans AP. Effects of pre-hospital nalbuphine on emergency room analgesia. *J Accid Emerg Med* 2000;17:69.
46. Jones AG. Pre-hospital nalbuphine analgesia. *J Accid Emerg Med* 1999;16:462.
47. Ward ME, Radburn J, Morant S. Evaluation of intravenous tramadol for use in the prehospital situation by ambulance paramedics. *Prehospital and Disaster Medicine* 1997;12:158-162.
48. Hearn ST. First aid training and equipment in UK mountain rescue teams. *Pre-hospital Immediate Care* 1999;3:215-218.
49. Hocking G, De Mellow F. Battlefield analgesia: A basic approach. *J R Army Med Corps* 1996; 142:101-102.
50. McQuay HJ, Carroll D, Moore RA. Injected morphine in postoperative pain: a quantitative systematic review. *J Pain Symptom Management* 1999;17:164-174.
51. Greenblatt DJ, Koch-Weser J. Intramuscular injection of drugs. *N Engl J Med* 1976;295:542-546.
52. Illingworth KA, Simpson KH. Anaesthesia and Analgesia in Emergency Medicine. (2nd ed.) Oxford: Oxford Medical Publications, 1998.
53. Edlich RF, Rodeheaver GT, Thacker JG. Local and regional anesthesia for wound repair. In: Tintinalli JE, Ruiz E, Krome RL. Emergency medicine (4th ed). New York: McGraw-Hill, 1996.
54. Kloss T, Lenz G, Schwandt-Boden H, Bauer J, Stehle R. The role of regional anaesthesia under field conditions. *Prehospital and Disaster Medicine* 1990;5:349-352.
55. Hanks GW, Twycross RG, Lloyd JW. Unexpected complications of successful nerve block. *Anaesthesia* 1981;36:37-39.
56. Baskett PJF, Withnell A. Use of entonox in the ambulance service. *BMJ* 1970;ii:41-43.
57. Deo S, Knottenbelt JD. The use of midazolam in trauma resuscitation. *Eur J Emerg Med* 1994; 1:111-114.
58. Wright SW, Chudnofsky CR, Dronen SC, Wright MB, Borron SW. Midazolam use in the emergency department. *Am J Emerg Med* 1990;8:97-100.
59. Chudnofsky CR, Weber JE, Styanoff PJ, et al. A combination of midazolam and ketamine for procedural sedation and analgesia in adult emergency department patients. *Acad Emerg Med* 2000;7:228-235.
60. Austin TR, Tamlyn RSP. Ketamine. A revolutionary anaesthetic agent for the battle casualty. *J R Army Med Corps* 1972;118:15-23.
61. Austin TR. Ketamine hydrochloride: a potent analgesic. *BMJ* 1976;2:943.
62. Drummond G. Comparison of sedation with midazolam and ketamine: effects on airway muscle activity. *B J Anaesthesia* 1996;76:663-667.
63. Cartwright PD, Pingel SM. Midazolam and diazepam in ketamine anaesthesia. *Anaesthesia* 1984;39:439-442.
64. Cottingham R, Thomson K. Use of ketamine in prolonged entrapment. *J Accid Emerg Med* 1994; 11:189-191.
65. Bion JF. Infusion analgesia for acute war injuries: a comparison of pentazocine and ketamine. *Anaesthesia* 1984;39:560-564.
66. White PF. Comparative evaluation of intravenous agents for rapid sequence induction—thiopental, ketamine, and midazolam. *Anesthesiology* 1982; 57:279-284.
67. Gofrit ON, Leibovici D, Shemar J, Henig A, Sapira SC. Ketamine in the field: the use of ketamine for induction of anaesthesia before intubation in injured patients in the field. *Injury* 1997;28:41-43.
68. Kirby MG, Blackburn G (eds) Field surgery pocket book. London:HMSO, 1988.
69. Dufour D, Kroman Jensen S, Owen-Smith M, Salmela J, Stening GF, Zetterstrom B. Surgery for Victims of War. Geneva, International Committee of the Red Cross 1988.
70. Mackenzie R, Sutcliffe RC. Pre-hospital care: The trapped patient. *J R Army Med Corps* 2000;146:39-46.
71. Green SM, Rothrock SG, Lynch EL, Ho M, Harris T, Hestdalen R, Hopkins GA, Garrett W, Westcott K. Intramuscular ketamine for paediatric sedation in the emergency department: safety profile in 1,022 cases. *Ann Emerg Med* 1998;31:688-697.
72. World Health Organisation. Essential drugs. *WHO Drug Information* 1999;13:249-262.
73. Williamson PB. General Patton's principles for life and leadership. Tucson: Management and Systems Consultants 1988.

Analgesia And Sedation

Commentary

J Mauger, J Field

This comprehensive article on pre-hospital analgesia and sedation was originally published in 2000. While the principles discussed in the paper are equally applicable to military and civilian casualties, it is their application that remains constrained by the particular environments. There are a few areas which merit updating and others that we would like to re-enforce.

Analgesia

Pain is defined by The International Association for the Study of Pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”. This highlights two important issues: that pain relief can be augmented by attention to the emotional component, and that the complete elimination of the sensory component may conceal extension of the injury. In addition, a multimodal approach to analgesia can provide the combined benefits of more effective analgesia with reduced side effects.

For mild to moderate pain, the non-steroidal anti-inflammatory drugs (NSAIDs) have gained in popularity. These are most effective when given on a regular basis. Although the oral route for analgesics should be considered for mild to moderate pain, it should be remembered that patients in severe pain or who have received opioids, will have considerably delayed gastric emptying so that oral drugs may be very poorly absorbed and ineffective (1). Intravenous paracetamol has been available for several years in many parts of Europe and is now available in the UK. However, the relatively mild effect and requirement for a fifteen-minute infusion will make its use in pre-hospital care impractical for the majority of patients. Ketorolac and diclofenac were until recently the only intravenous NSAIDs commonly given in the UK. Ketorolac has recently undergone a change in licensing which specifically contra-indicates its use in the pre- or intra-operative period (due to inhibition of platelet aggregation) (2). This effectively precludes its use in the trauma patient. The selective COX-II inhibitors such as parecoxib, etoricoxib and valdecoxib are examples of a relatively new sub-group of NSAIDs that have developed rapidly over recent years. COX-II inhibitors have established themselves as oral analgesics,

not just for patients who may not be able to tolerate the more traditional non-selective NSAIDs, but because they may also be more effective (with lower values for “number needed to treat” - NNT - in clinical trials) (3). Parecoxib has the additional benefit that it can be given intravenously, and may therefore become a useful adjunct in pre-hospital care.

Control of pain in the pre-hospital civilian setting took a leap forward in the year 2000 when an act of parliament enabled civilian paramedics to administer morphine (4). Until this time many UK ambulance services had been using another opioid, nalbuphine. Nalbuphine had become rather unpopular in many immediate care areas as it was seen as a weaker alternative to morphine and, because of its partial agonist / antagonist activity, it prevented the subsequent administration of morphine from achieving its full effect. Diamorphine is now less widely used than morphine in pre-hospital practice, although it has more recently been shown to be very effective when administered intranasally in children (in a dose of 100 mg/kg for acute pain) (5). Tramadol usage seems also to have diminished since the introduction of morphine by ambulance services. A consequence of the more widespread use of morphine has been the requirement for anti-emetics to be available to paramedics. Currently, metoclopramide is the only anti-emetic that can be administered by paramedics in the UK, despite some evidence that it is of less use than ondansetron when administered with an opioid (6). Ondansetron, cyclizine or a combination of antiemetics are now more commonly used for post-operative nausea and vomiting (7), although the incidence of nausea in trauma may be reduced by the slow titration of smaller aliquots of morphine rather than large intravenous boluses.

Ketamine remains an extremely effective analgesic when used in small doses for pre-hospital care. However, we would caution against its use by the inexperienced. Although an excellent analgesic, it acts as an anaesthetic agent in larger doses or when used in combination with other agents, and it therefore behoves the practitioner to be experienced and skilled in the management of inadvertent overdosage. Ketamine is available in the UK as a racemic mixture of

J Mauger BSc MB BS
FRCA
Consultant Anaesthetist
Immediate Care
Practitioner, Suffolk
Accident Rescue
Service (SARS)
email:
Jeremy.Mauger@wsh.nhs.uk

J Field FFARCSI
Consultant Anaesthetist
Immediate Care
Practitioner, Suffolk
Accident Rescue
Service (SARS)

Department of
Anaesthetics,
West Suffolk Hospitals
NHS Trust
Hardwick Lane,
Bury St. Edmunds
Suffolk, IP33 2QZ

R(-)- and S(+)-ketamine. There is some evidence that the stereoselective (S)-ketamine enantiomer may have fewer emergence phenomena and is twice as potent as an analgesic than the racemic mixture (8), although this is not yet commonly available in the UK.

Local anaesthetics can be used to abolish peripheral pain when used appropriately in peripheral nerve blocks. The practitioner must be aware of the maximum safe dosage of each agent and be skilled in the recognition and treatment of inadvertent intravenous injection or toxicity. Bupivacaine is a longer acting local anaesthetic than lidocaine, and is available as a racemic mixture of dextro- and levo-bupivacaine. When given as a pure levo-bupivacaine solution there are fewer risks of cardiotoxic side effects than for the racemic mixture. Levo-bupivacaine is now available in the UK in the form of Chirocaine 0.25%, 0.5% and 0.75% solutions (Chirocaine®). Chirocaine and lidocaine can both be used in pre-hospital care but their effective use for nerve blockade may be limited by the need for detailed anatomical knowledge and clinical experience. The use of low current electrical nerve stimulators with insulated needles has dramatically improved the success of nerve blocks for orthopaedic procedures and analgesia for fractures in hospital practice. The use of local anaesthetic nerve blocks in pre-hospital care remains of limited value if nerve stimulators are not available.

There are three additional points that we would highlight when considering the administration of a local anaesthetic. Firstly, prior to nerve blockade careful neurological testing of the affected limb should be carried out and recorded. Secondly, if a local anaesthetic block for major long bone fractures is effective, compartment syndrome, particularly of the lower leg, may be missed with catastrophic results. Thirdly, simple application of local anaesthetics is often under-utilised. If children have topical anaesthesia applied in the field, blood tests or cannulation are less painful on arrival in hospital – this technique is already in use in some parts of the US.

Multimodal analgesia has become a mainstay of in-hospital analgesia. The multimodal concept was originally developed from the idea that many different receptors are involved in pain pathways and that rather than blocking one receptor group, better (and safer) analgesia could be achieved using drugs acting at different sites in combination. Post-operative analgesia is now most commonly managed using a combination of standard paracetamol, codeine and an NSAID. Stronger opioids and anti-emetics are given in addition as

required. This concept can be translated to the pre-hospital environment. Morphine is a good analgesic on its own but when combined with splinting or traction, reassurance and, where appropriate, Entonox®, its effects may be greatly enhanced. A correctly applied traction splint may provide better analgesia than a significant dose of morphine for femoral fractures, while the addition of very small doses of ketamine and / or midazolam to this analgesic cocktail can provide optimal analgesia in a wide variety of causes of severe pain. The multi-modal approach has the combined benefits of more effective analgesia and reduced analgesic doses. Attempts to achieve total abolition of pain with large doses of potent analgesics are often unnecessary and may result in obtunded patients. In an entrapment situation, for example, it is sometimes beneficial for the patient to be able to tell rescuers that a particular movement causes pain which could lead to a worsening of injury. In these situations the aim should be to administer enough analgesia, rather than too much analgesia.

Sedation

Sedation has always been a contentious issue in civilian immediate care and other out-of-hospital environments. Sedation should be administered in such a way that verbal contact can be maintained at all times with the patient. Any form of deeper sedation should be viewed as equivalent to pre-hospital anaesthesia. It should only be undertaken after appropriate training, with a full understanding and previous supervised experience. Full resuscitation facilities and skills should be immediately available and the practitioner must be fully competent in the recognition and management of a compromised airway. Minimal monitoring standards have been in place for several years in anaesthetic practice and these should be considered essential when sedation techniques are used in the pre-hospital phase. Hypovolaemic trauma patients are sensitive to sedative drugs and 'standard' dosage charts should be used with extreme caution. Midazolam and ketamine remain the sedatives more commonly used by doctors in pre-hospital care, but these will interact with, and be potentiated by, other sedative and analgesic agents that may have been administered.

Conclusion

There is a growing desire for the pre-hospital practitioner to be able to administer all forms of analgesia. In many cases the most desirable option is to administer the right dose of analgesic to the right patient at the right time – to paraphrase another popular pre-hospital quotation. Rendering a patient apnoeic

through the over-zealous use of potent analgesics by an inexperienced practitioner is a disaster that should be avoided at all costs. There are often simple methods which can and should be used together to achieve patient comfort without recourse to the stronger analgesics. The pre-hospital practitioner should, as the article concludes, opt for safety and simplicity as far as possible.

References

1. Carlin CB, Scanlon PH, Wagner DA, Borghesi L, Geiger JW, Long CL. Gastric emptying in trauma patients. *Dig Surg* 1999;**16**:192-6.
2. Knaggs R, Bennett MW. Change of datasheet for ketorolac. *Anaesthesia* 2004;**59**:305
3. The Oxford Pain Internet Site – <http://www.jr2.ox.ac.uk/bandolier/booth/painpag/>
4. Joint Royal Colleges Ambulance Liaison Committee and The Ambulance Service Association. *Clinical practice guidelines for use in UK ambulance services*. June 2004.
5. Wilson JA, Kendall JM, Cornelius P. Intranasal diamorphine for paediatric analgesia: assessment of safety and efficacy. *J Accid Emerg Med* 1997;**14**:70-72.
6. Chung, Lane R, Spraggs C, et al. Ondansetron is more effective than metoclopramide for the treatment of opioid-induced antiemesis in post-surgical adult patients. *Eur J Anaesthesiol* 1999;**16**:669-77.
7. Scholz J, Steinfath M, Tonner PH. Postoperative nausea and vomiting. *Curr Opin Anaesthesiol* 1999;**12**:657-661
8. Himmelseher S, Pfenninger E. The clinical use of S-(+)-ketamine – a determination of its place. *Anesthesiol Intensivmed Notfallmed Schmerzther*. 1998;**33**:764-70.
9. Eichhorn JH, Cooper JB, Cullen DJ, Maier WR, Philip JH, Seeman RG. Standards of patient monitoring during anesthesia at Harvard Medical School. *JAMA* 1986;**256**:1017-20.
10. The Association of Anaesthetists of Great Britain and Ireland. *Recommendations for standards of monitoring during anaesthesia and recovery* (3rd edition). December 2000.