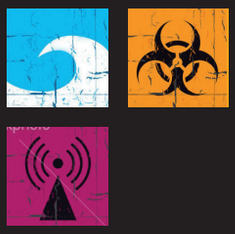

Chapter 10

Analgesia and Mass Casualty Incidents

By Daniel Kollek, MD, CCFP(EM)
Brian Goldman, MD, FACEP, MCFP(EM)

Preface

Because of the nature of the injuries involved, pain management is a key component to the management of mass casualty incidents (MCIs). Although various agents have been assessed for their risks and benefits related to specific individual clinical scenarios, there is no good evidence for generalized use of any specific analgesic agent over any other in MCIs. The present practice of using morphine for all significant field analgesia in MCI situations has not been proven to be either the best or safest practice and further research into other agents is warranted.

Contents

Pain Management

The classical definition of pain is "an unpleasant and sensory emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[1]

Pain management is a key component of the medical response to mass casualty situations, yet the evidence regarding optimal pain management in mass casualty situations is extremely limited. A review of both the PUBMED and OVID databases using the terms "disaster, pain, analgesia, and mass casualty incident" gleaned a total of 147 articles. Of these, only 4 satisfied the criteria of relevance, availability in English or French, and recentness (defined as published within the past 10 years).

Part of the reason for this lack of information is that mass casualty situations tend to occur unpredictably. Overall, in mass gatherings, the incidence of trauma

requiring any significant intervention is 0.032%.[2] Thus, it is not surprising that there is little research done on the topic.

Although there is variability in the pathology that occurs in mass casualty events, there is a characteristic pattern to the nature and distribution of the injuries. A review of mass casualty terrorist bombings by Arnold et al. found that 7461 of 8364 casualties survived their initial injuries.[3] The review was completed in 2002 and thus did not include the more lethal subsequent suicide bombings on buses. That said, the data do point out that depending on the type of the event (structural collapse, closed space, open air, etc.), there have been 75%–90% survival rates. There is a pattern of injuries in the survivors, the most common being penetrating soft tissue (48%–63%), fractures (29%–45%), intracranial injuries (8%–10%), and crush injuries (13%).[2] The Trauma Care under Combat Conditions guidelines teach that the distribution of the injuries across the body tend to be 21% to the upper extremity, 35% to the lower extremity, 13% to the chest, and 17% to the head and neck, with abdomen and other body parts sustaining the other 14%.[4] Thus, on the basis of past review, it is possible, at least in situations involving explosions and structural collapse, to predict what type of injuries will occur, what their distribution will be across the body, and also what percentage of the population affected will require hospitalization. Following from this, it should be possible to make some reasonable assumptions to the type of analgesic agents that will be useful.

Research into battlefield medicine has also focused on pain management and some of the comments that follow are collected from that literature.

Finally, some clinical experience can also be extrapolated from the research into management of pain in the wilderness, which is similar to MCI situations in that it may involve dealing with pain in the field with minimal diagnostic, therapeutic, and monitoring resources.[5] According to Wedmore et al., the ideal pain medication for wilderness and operation would be light and compact, something that can be carried without concerns such as environment or temperature; has a very high therapeutic index, particularly with regard to ensuring that airway reflexes are protected; does not require an IV or other equipment to administer; and can be used regardless of patient's level of stability. In the urban setting, there are other issues also that need to be addressed such as the control of trafficable narcotics and providing safety for the crews responding to the scene. In some settings, cost may be an important factor as well.

General Concepts

Pain is a concept well known to everyone, yet it is difficult to standardize its definition or allow direct comparison of pains. The International Association for the Study of Pain (IASP) has defined as mentioned earlier.

Untreated pain can cause many problems, both emotional and psychological. On the psychologic aspect, the cardiovascular system responds to stress by activating the sympathetic nervous system increasing heart rate and blood pressure, as well as cardiac work load and oxygen demand. At the endovascular level, it decreases fibrinolysis and can induce a hypercoagulable. From the respiratory viewpoint, pain can cause high pressure, small tidal volume, high respiratory rate, and lead to pneumonia and atelectasis. In addition to this, pain has an effect on the endocrine system and the immune system.[6,7,8]

The target of a caregiver should be tolerable pain as opposed to no pain at all. Although no pain at all may be an ideal situation, the potential risk from some analgesics does make it sometimes difficult to achieve without exposing the patient to risk. Thus, it is the responsible of the caregiver to titrate to an acceptable balance of mild pain versus adverse affects.[9]

Pain can be measured through various scales, all of which, by pain's very nature, are subjective. Similarly, the World Health Organization has described a pain ladder that allows for progression between management of mild, moderate, and severe pain. The model outlines the steps in provision of analgesia and, while based on cancer pain, does use principles that are equally applicable to MCIs.

The first step in the pain ladder is for the mildest of pains and would involve a nonopioid such as a nonsteroidal, anti-inflammatory drug (NSAID) or Tylenol. This level could also include so-called adjuvant treatments such as antidepressants or anticonvulsants. Some would also include local anesthetics at this level.

At the next step on the pain ladder, a weak opioid with or without a nonopioid with or without an adjuvant would be considered.

The next step on the pain ladder would be a strong opioid, again with or without a nonopioid or an adjuvant.

The general concept is one of stepped care in the provision of analgesia and the scale provides a framework for caregivers when considering what medications to use.[10]

Although the mainstay of analgesia remains chemical, it is important to remember the nonpharmaceutical approaches to analgesia. These are easy to administer, safe, and cost nothing making them ideal for deployment in any situation. The Battlefield Advanced Training Life Support (BATLS) defines these as management of airway breathing and circulation, correcting of hypoxia, hypercarbic, hypervolemia, reassuring the casualty to relieve emotional distress, splitting of fractures, and cooling of burns.[11]

Having covered the basic concepts of pain management in a battlefield or mass casualty situation and the nonpharmacologic interventions, the rest of this chapter deals specifically with various pharmacological agents. The analgesic efficacy of these agents is summarized in Table 10-1.

Table 10-1: Abridged Version of the 2007 Oxford League Table of Analgesic Efficacy[12]

Analgesic	Number of Patients in Comparison	Percent with At Least 50% Pain Relief	NNT
Ibuprofen 600/800	165	86	1.7
Ketroolac 20	59	57	1.8
Paracetamol 1000 + Codeine 60	197	57	2.2

Table 10-1: Abridged Version of the 2007 Oxford League Table of Analgesic Efficacy[12]

Analgesic	Number of Patients in Comparison	Percent with At Least 50% Pain Relief	NNT
Ibuprofen 400	5456	55	2.5
Ketorolac 10	790	50	2.6
Paracetamol 650 + Tramadol 75	679	43	2.6
Diclofenac 50	1296	57	2.7
Ibuprofen 200	3248	48	2.7
Pethidine 100 (IM)	364	54	2.9
Tramadol 150	561	48	2.9
Morphine 10 (IM)	946	50	2.9
Paracetamol 1000	2759	46	3.8
Tramadol 100	882	30	4.8
Codeine 60	1305	15	16.7

Abbreviations: NNT, number needed to treat; IM, intramuscular.
Number needed to treat are for 50% pain relief over 4–6 hours compared with placebo in randomized double-blind single-dose studies in patients with moderate to severe pain. The lower the NNT, the more efficacious the analgesic. Oral administration unless otherwise stated.[12]

Acetaminophen and Paracetamol

Acetaminophen is effective for mild to moderate nociceptive pain or as an adjunct to opioid analgesics for severe pain.[13] It is believed to act by inhibiting cyclooxygenase-3 (COX3). A single dose of 1000 mg of acetaminophen has a number needed to treat (NNT) of 3.8 for at least 50% of postoperative pain for 4–6 hours.[14] The maximum dose for short-term use (up to 10 days) is 4000 mg per day.

Paracetamol is the UK equivalent to North American's acetaminophen (Tylenol). By itself, it is a weak analgesic; however, it does enhance the effect of other NSAIDs, weak opioids, and morphine when used concurrently.[15–17]

Both Tylenol and paracetamol have a remarkable lack of side effects and toxicity. They should be given regularly to all patients. IV paracetamol formulations do exist and may have significant advantages over oral forms. However, they are not as yet found in the North American market.[18]

NSAIDs and Coxibs

Anti-inflammatory drugs are effective for nociceptive pain. Ibuprofen 400 mg has a NNT of 2.4 (range 2.3–2.6) for postoperative pain.[19] Diclofenac has a NNT of 2.3 (range 2.0–2.7), whereas naproxen has a NNT of 2.6 (range 2.2–3.2).[20,21] According to Wedmore et al., ibuprofen (known colloquially as "Ranger Candy") is used frequently in the operational setting.[22] Likewise, ketorolac, an injectable NSAID, has often been selected by the military as the intramuscular analgesic of choice for moderate or severe pain.[23] A single dose of IM ketorolac 30 mg has a NNT of 3.4 for at least 50% pain relief over 4–6 hours with few side effects when administered as a single dose.[24]

Unfortunately, NSAIDs have several potential risks associated with their use. The first concern is the risk of NSAID gastropathy. Taking an NSAID for 2 months or more carries a 1 in 5 risk of an endoscopically proven ulcer and a 1 in 150 risk of a bleeding ulcer.[25] The risk for NSAID gastropathy rises with age and a previous history of peptic ulcer disease.

Renal impairment is a second risk associated with NSAIDs. In younger patients, the risk of NSAID-induced renal impairment is small. The incidence of hospitalization for acute renal failure in individuals under the age of 64 is 0.6 per 100,000 person years of NSAID use.[26] Military casualties tend to be younger. Many of the victims of terrorist bombings may be older. The use of NSAIDs in this patient population may result in a greater risk of acute renal failure, especially if the victims suffer from dehydration.

NSAIDs increase the risk of hypertension and can precipitate acute congestive heart failure. Recently, concerns have been raised that some NSAIDs may increase the risk of cardiovascular events, including myocardial infarction and cerebrovascular disease.[27]

Platelet dysfunction is the fourth adverse effect of NSAIDs. The resulting prolongation of bleeding time could result in increased bleeding from severe injuries associated with mass casualty situations. Concerns regarding this adverse effect led the Committee on Tactical Combat Casualty Care consensus panel to recommend that coxibs be used instead of NSAIDs as the analgesic of choice in combat operations.[28]

Celecoxib 200 mg has a NNT of 4.5 (3.3–7.2).[29,30] Coxibs have roughly half the risk of gastrointestinal perforations, ulcers, and bleeds compared to NSAIDs.[31] However, rofecoxib (marketed as Vioxx®) use was found to double the risk of myocardial infarction and stroke, a finding that resulted in rofecoxib being withdrawn from the market. There are concerns that the risk of cardiovascular events is a class-based effect.[32] More recently, valdecoxib (marketed as Bextra®) was withdrawn from the market due to an increased risk of cardiovascular events as well as an increased risk of serious skin reactions.[33]

Coxibs are not routinely used in emergency departments (EDs) or battlefield situations; hence, little data exist to extrapolate to MCIs.

Opioid Analgesics

Opioid analgesics are a mainstay of the management of severe pain. Opioids work by binding to μ receptors in the central nervous system and also have peripheral antinociceptive effects. There is tremendous variation in the effective

dosage of opioids due to genetically mediated interindividual differences in opioid efficacy and toxicity. Morphine is often regarded as the "gold standard" for opioid analgesia.[34] However, morphine should be considered as part of an opioid armamentarium that also includes hydromorphone, fentanyl, and oxycodone.

Opioids can be administered intramuscularly, intravenously, or by mouth. This flexibility makes them applicable to multiple scenarios.

A qualitative systematic review found that a 10-mg intramuscular dose of morphine has an NNT of 2.9 for at least 50% pain relief over 4–6 hours compared with placebo in pain of moderate to severe intensity.[35] A similar review found that meperidine 100 mg IM also has a NNT of 2.9.[36] However, meperidine is not recommended for repeat dosing due to the risk of neurotoxicity and seizures associated with the accumulation of the toxic metabolite normeperidine.[37,38] A systematic review of hydromorphone in acute pain found analgesic efficacy comparable to that of other opioids.[39] However, heterogeneity of the studies precluded meta-analysis. As well, most studies that investigated hydromorphone involved small numbers of patients, making it difficult to determine real differences between hydromorphone and morphine.

Codeine, fentanyl (transmucosal), and oxycodone are available as orally administered analgesics. Acetaminophen 1000 mg with codeine 60 mg has a NNT of 2.2.[40] A systematic review found single-dose oxycodone, with or without acetaminophen, is of comparable efficacy to IM morphine and to NSAIDs.[41]

All opioids have adverse effects. These include nausea, vomiting, dizziness, and lightheadedness. Some opioids have active metabolites that are cleared by the kidneys. A recent review by Dean recommended that morphine and codeine be avoided in patients with renal failure and that hydromorphone or oxycodone be used with caution and close monitoring. However, fentanyl appears to be safe to use.[42]

The ideal route of administration for opioid analgesics is somewhat controversial. The oral route has the advantages of being the most practical and the most portable. However, there are significant limitations to the oral route of administration. Both the onset and the time to peak analgesic effect are significantly slower than with parenteral administration. As a consequence, oral titration is much more difficult than through the parenteral route.

In the ED, IV is the preferred route of administration for rapid titration of opioid analgesia. However, the IV route has been considered problematic in operational settings.[43,44]

Recently, oral transmucosal fentanyl citrate has been proposed for use in operational settings. Fentanyl citrate is a lipophilic synthetic phenylpiperidine derivative that has been used for years in the ED as an analgesic for painful procedures. It has also been used for years in epidural analgesia. Oral transmucosal fentanyl is a crystalline form of fentanyl citrate (marketed under the name Actiq®) that is incorporated into a flavored lozenge. The lozenge is intended to be administered over 15 minutes.

Oral transmucosal fentanyl appears to possess the characteristics of rapid onset of action and relatively long duration of action. Its rapid onset is because approximately 25% of the fentanyl contained in the lozenge is absorbed transmucosally. The transmucosal component has an onset of action of 5–10 minutes, which is comparable to the onset of intravenously administered opioid analgesics.

However, the remainder of the drug is swallowed and absorbed through the gastrointestinal tract, which accounts for the product's duration of action. There is a significant first-pass effect of the component of drug that is absorbed through the gastrointestinal tract.

A study by Kotwal et al. evaluated the use of oral transmucosal fentanyl administered by medical personnel during missions in support of Operation Iraqi Freedom over a 2-month period in 2003. A total of 22 patients met the study criteria. Twenty-one of 22 patients received a single dose of 1600 µg fentanyl. One patient received 2 doses of 1600 µg fentanyl. Three patients required IV analgesics in addition to the oral transmucosal fentanyl citrate. The results of this small study were impressive. Oral transmucosal fentanyl citrate reduced verbal pain scores by a mean of 5.77 and the benefits were sustained for an average of 5 hours.[45] Adverse effects included nausea (13.6%), emesis (9.1%), lightheadedness (9.1%), and pruritus (22.7%). One patient experienced an episode of hypopnea requiring the use of naloxone. Patients in the study were instructed to remove the lozenge from the mouth once adequate analgesia or significant side effects developed. This helped to prevent overmedication. The authors found taping the stick of the lozenge to the patient's index finger also helped reduced accidental overadministration, by ensuring patients had to remain alert enough actively self-administer the medication.

Intranasal administration of analgesic agents is becoming more commonplace in the United Kingdom civilian emergency practice, but as of yet, it is not as common in Canada. Concerns had been expressed over the opportunity for abuse of these medications, if only because the method of delivery is so simple; however, opportunity for abuse in an operational environment is no greater for intranasal, oral, or buccal therapy than for existing injectable opioids. As long as the distribution and counting is carefully controlled and the penalty for misuse is appropriate, the opportunity for overdose could effectively be avoided if each nasal applicator is restricted to a single adult dose.[46]

Ketamine

Ketamine is a dissociative anesthetic that has been used extensively in the ED as an analgesic. Ketamine has been used for pain associated with burns and procedural sedation.[47,48] The drug has been used quite effectively for procedural sedation in children.[49] Ketamine has many of the characteristics of the ideal analgesic. It works quickly and provides effective analgesia without compromising airway or cardiovascular reflexes.

Ketamine has been used extensively in the prehospital setting, for extrications and entrapment situations. It is generally avoided in head-injured patients because of the increase in intracranial pressure. Because ketamine preserves airway reflexes, it is an attractive agent in the prehospital and mass casualty environment and has had extensive use in the Vietnam and Falklands wars. Some authorities would suggest providing it with a small dose of benzodiazepine in order to reduce dysphoria.

Ketamine has been used in operational settings.[50,51] The recommended dosage of ketamine used for analgesia is 0.44–1.0 mg/kg IM or 0.2–0.5 mg/kg IV. Some authors recommend a starting dose of 0.1 mg/kg titrated to effect.[52]

There are anecdotal reports of ketamine being used as an IV anesthetic to perform austere surgeries in Somalia and Uganda.[53]

As a result, ketamine, with the aforementioned qualifier of head injury, has been proposed as an ideal analgesic for mass casualty and disaster situation.[54]

For most indications, ketamine is administered IM or IV. Ketamine is also available in oral, rectal, and sublingual preparations. Intranasal ketamine has been studied for pain control in the operational setting. It has superior bioavailability to oral, rectal, and sublingual preparations.

There is growing clinical experience with intranasal ketamine. This modality provided statistically significant relief of breakthrough pain in patients with chronic noncancer pain. The onset of analgesia was within 10 minutes with duration of action of up to 60 minutes. There were no reports of auditory or visual hallucinations, phenomena both observed with IV or IM administration.[55] A randomized, prospective placebo-controlled trial of intranasal ketamine (administered through a metered-dose inhaler) demonstrated statistically significant relief of postoperative pain at 10 mg, 30 mg, and 50 mg doses. There were no serious adverse events including hallucinations or psychotomimetic effects.[56]

Compared to intramuscular morphine, intranasal ketamine offers several potential advantages. It maintains normal heart and respiratory rate and blood pressure. The onset of analgesia is within 10 minutes. It does not cause drowsiness or confusion. The drug is administered noninvasively. Finally, intranasal ketamine appears to have a wide margin of safety. There is little, if any, literature on the use of intranasal ketamine in austere settings. However, there are anecdotal reports this new modality is presently being used in combat situations.[57]

Other Medications

There are other medications used for analgesia that need to be considered; however, they have less acceptability in the mass casualty/disaster setting and these would include:

Alpha-2 receptor agonists such as clonidine, amitryptyline, and anticonvulsants such as gabapentin. In addition to the IM, IV, or PO methods of drug delivery mentioned earlier, there are also epidural infusions, local anesthesia by infiltration or infusion, nerve sheath catheters, and so forth. Although these may not be contraindicated medically in a battlefield situation, it becomes increasingly difficult to dedicate the time and provide the aseptic technique required for some of these. They are generally not recommended in the field and, if used at all, might first be applicable in the field hospital situation. At a receiving hospital level, the choice as to whether to use these procedures, considering that they are both equipment and human resource consumptive, will depend on the infrastructure available to the hospital. As mentioned earlier, the contraindications to these are not medical but operational.

Summary

This review demonstrated that although various agents have been assessed for their risks and benefits on individual cases, there is no good evidence for generalized use of any specific analgesic agent over any other in MCIs. The

present practice of using morphine for all significant field analgesia in MCI situations has not been proven to be either the best or the safest practice, and further research into other agents is warranted.

This chapter focused on the medications required for analgesia but not the delivery process. Delegating the administration of analgesia to RNs or EMTs or equivalent can hasten delivery of the medication. The process of defining the delegated act will depend on local legislation and facility bylaws.

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