Analgesia for the critically ill patient

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CLINICAL NARRATIVE

You are the ICU fellow on call overnight at a tertiary care hospital. At approximately 2 AM, you receive a call from the emergency department (ED) with a consult. The ED resident gives you the following details: Mrs P is a 67 year old woman who presented recently with acute dyspnea and severe pain focused around an area of extensive erythema on her left arm. She has a pulse rate of 115, respiratory rate 45 breaths per minute, temperature 39°C, blood pressure 95/65 mm Hg, and O2 saturation 68% on room air. The resident also notes areas of dark and yellowish tissue surrounding her left elbow, which are suspected to be necrotic. She is currently receiving 100% O2 via a high flow mask and fluid resuscitation via two peripheral IVs. She is experiencing severe pain, which she rates as 10/10, but is otherwise stable. You agree to have this patient transferred to your care. While she is on the way up you remind yourself of the key components of pain management in the critically ill patient.

PAIN IN THE CRITICALLY ILL PATIENT

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.”¹ Pain-related issues are a major cause of presentation to the ED, with estimates as high as 70% of patients.² A majority of patients will experience pain at some point during their stay in an intensive care unit (ICU) and identify pain as a major source of stress.¹

The complications associated with poorly controlled pain in ICU patients must not be underestimated. Studies have shown that 82% of cardiac surgery ICU patients report pain as the most traumatic memory of their ICU stay.³ Other studies have reported that 18% of ICU patients are at high risk for developing posttraumatic stress disorder 6 months after their stay due to memories associated with pain.⁴ Poorly controlled pain has deleterious physiologic consequences; additionally, increased catecholamines associated with the stress response can impair tissue perfusion.⁵ Pain has also been shown to suppress critical immune-related processes such as natural killer cell, neutrophil, and T-cell activity.^{6,7} Therefore, appropriate pain management in all ICU patients must be considered an essential aspect of their care.

ASSESSMENT OF PAIN IN THE ICU

Assessment of the patient’s level of pain is a foundational element of treatment.¹ Numerous pain rating scales exist, such as the ubiquitous 1-10 rating scale often used in the ED, as well as in other settings.⁸ Assessing pain in the ICU presents additional challenges, as many patients will be hindered in their ability to self-report. Critically ill patients may have altered levels of

consciousness, be mechanically ventilated, or be administered high doses of sedatives.⁹ However, the International Association for the Study of Pain notes that “the inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of pain-relieving treatment”.¹⁰

Objective and reproducible assessment of pain should be the goal in all patients experiencing pain. Patient self-reported pain is considered the gold standard.¹ In patients who are not able to verbalize their responses, the use of visual scales has been shown to be the next best alternative,¹¹ though implementation is limited to patients with a suitable level of consciousness. Numerous scales based on observed patient behaviour have been devised, and their use has been shown to improve clinical outcomes and pain management when used consistently.¹² Most importantly, the assessment of pain must be carried out consistently throughout a patient’s stay in the ICU to ensure the most appropriate management.

TREATING PAIN IN THE ICU

Analgesic medications may be broadly classified as either opioid or non-opioid medications. Opioid medications (eg fentanyl, hydromorphone, morphine, methadone) are considered first-line medications for pain management in critically ill patients.¹ Choosing between the numerous opioid medications depends upon patient and medication characteristics. Patient factors include previous exposure to opioids, co-morbidities such as renal or hepatic disease, and hemodynamic stability. The rate of onset and elimination half-life of each medication also varies significantly and are important considerations. These properties are shown for select opioid medications in Table 1.

Non-opioid analgesics may be used as adjuncts in some circumstances.¹ They may be used to decrease the required dose of opioids, or to decrease opioid-related side effects (refer to Table 1). These have not been well studied in the ICU setting. Other non-pharmacological interventions have been proposed, including music and relaxation therapy. These interventions may reduce the required dose of opioids and are relatively low cost, safe, and easy to provide in appropriate patients. While limited evidence exists to support the effectiveness of these interventions, focus groups conducted with ICU patients and their caregivers have indicated that certain non-pharmacological interventions were found to be useful.¹³

What is the initial strategy with regards to pain management in the ED? What considerations must be taken into account in this case?

You ask the emergency physician whether any analgesia has already been provided and learn that a 0.5 xg/kg IV dose of fentanyl was given approximately 15 minutes ago. This is an excellent choice,

given that fentanyl has a rapid onset and has a relatively long half-life. Although morphine acts similarly, the patient is hypotensive, which could be exacerbated by morphine.

Upon arrival in your unit, what are your first steps in addressing this patient's pain?

After Mrs P is transferred into your care in the ICU, reassessment of her pain should occur promptly. You reassess her pain, and she indicates “a 6 or 7”, suggesting that the initial dose of fentanyl has had an effect. At this point, it has been nearly 45 minutes since Mrs P received fentanyl, and so you must decide whether to push another dose or start her on an infusion. Your working diagnosis is necrotizing fasciitis of the elbow, with resulting septic shock. The plastic surgery and infectious disease teams are consulted.

What agent will you choose for ongoing analgesia? What information would you want to make this decision?

In deciding what agent to choose going forward, you reassess the patient's blood pressure and find that it has increased to 105/75 mm Hg. She continues to receive fluid through peripheral IVs, and now has a central line inserted for invasive blood pressure monitoring. Considering that Mrs P is now in the more controlled ICU environment, you are comfortable that you will be able to closely monitor and appropriately manage any changes in blood pressure. Mrs P is still able to communicate, and indicates that she used opioids “for a few weeks after a knee operation” several years ago. She does not report any issues with addiction or dependence stemming from this use. At this point you decide to start Mrs P on a morphine infusion at a dose of 5 mg/h.

Mrs. P is treated with IV antibiotics and surgical debridement of her elbow. During the wound debridement, extensive tissue invasion was discovered and a substantial amount of necrotic muscle tissue was removed. She improves markedly with ongoing administration of fluids.

What are the essential steps in the ongoing management of this patient?

Mrs P must be regularly reassessed throughout her stay in the ICU, and have her morphine infusion titrated to achieve effective analgesia. Given that her management includes a surgical procedure to debride necrotic tissue, special care must be taken in the perioperative and postoperative periods to control her pain.

DISCHARGE AND FOLLOW UP

As Mrs P's condition improves, preparations for discharge from the ICU are undertaken. Pain management is an essential component of follow-up care, as more than half of ICU patients report ongoing problems with pain many years after their discharge.¹⁴ Appropriate referral to rehabilitation services and practitioners who can provide ongoing support should be made. In some centres, specialized patient navigators work with each patient and their caregivers to facilitate care in the year following discharge.¹⁵ It remains to be seen whether these programs will significantly impact patient outcomes.

Patients, caregivers, and practitioners may be concerned that opioids administered in the ICU will lead to dependence on the drugs. A follow up study of 2595 patients admitted to the ICU at a tertiary care hospital found that there was a decrease in opioid use at 48 months post-discharge, with only 1.8% of patients using opioids on most days, compared to 6.2% using opioids most days prior to admission.¹⁶ These findings suggest that post-ICU opioid dependence is rare.

Patients who remain on opioid medications post-discharge for chronic, non-cancer pain must be followed closely by an experienced practitioner. The 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain recommends a 5 to 10% dose reduction rate every 2 to 4 weeks for patients on high doses of morphine (>90 mg daily).¹⁷ Rotation between opioids as a potential strategy to taper dosage for gradual withdrawal was also suggested. This requires close monitoring, and regular follow-up visits must be scheduled. Each session should discuss functional goals, psychosocial support, and plans for withdrawal symptoms and re-emerging pain.

Table 1. Pharmacology of opioid and non-opioid analgesics.

Class	Analgesic	Route of Administration	Onset	Half-Life	Contraindications, Side Effects, and Other Information
Opioid	Fentanyl	IV	1-2 min	2-4 h	Contraindicated by hepatic impairment. Induces hypotension, though less dramatically than morphine
	Remifentanyl	IV	1-3 min	3-10 min	Can be used in patients presenting with hepatic or renal failure
	Morphine	IV	5-10 min	3-4 h	Contraindicated by hepatic or renal impairment
	Hydromorphone	IV	5-15 min	2-3 h	Contraindicated by hepatic or renal impairment. Consider usage for patients with morphine or fentanyl tolerance
	Methadone	IV	1-3 d	15-60 h	A potent analgesic itself, but it can also be used to slow the development of tolerance to opioids when there is an escalation of opioid dosing requirements. Unpredictable pharmacokinetics; unpredictable pharmacodynamics in opiate naive patients. Monitor QTc for arrhythmia
Non-Opioid	Ketamine	IV	30-40 s	2-3 h	May cause hallucinations and other psychological disturbances. Attenuates the development of acute tolerance to opioids
	Acetaminophen	IV	5-10 min	2 h	May be contraindicated by significant hepatic dysfunction
	Ketorolac	IV/IM	10 min	2.4-8.6 h	Contraindicated by renal dysfunction, gastrointestinal bleeding, platelet abnormalities, concomitant ACE inhibitors, congestive heart failure, cirrhosis, and asthma
	Ibuprofen	IV	N/A	2.2-2.4 h	See contraindications listed for Ketorolac
	Ibuprofen	PO	25 min	1.8-2.5 h	See contraindications listed for Ketorolac
	Acetaminophen	PO/PR	30-60 min	2-4 h	May be contraindicated by significant hepatic dysfunction
	Carbamazepine (immediate release)	PO	4-5 h	25-65 h initially, 12-17 h subsequently	Contraindicated by Stevens-Johnson syndrome or toxic epidermal necrolysis with HLA-B*1502. Multiple drug interactions involving hepatic enzymes. Common side effects include nystagmus, dizziness, diplopia, lightheadedness, and lethargy. Rare side effects include aplastic anemia and agranulocytosis
	Gabapentin	PO	N/A	5-7 h	Common side effects include sedation, confusion, dizziness, and ataxia. Adjust dosing in renal failure patients

Abbreviations: intravenous (IV), intramuscular (IM), PO (oral), PR (rectal). Adapted from Barr *et al* (2013).

CONCLUSION

Pain among patients admitted to the ICU is common, and must be treated appropriately to avoid long-term complications. Frequent and objective reassessment of patients' pain is the basis of appropriate care. Opioid therapy remains the standard of care in most cases, but non-opioid and non-pharmacological interventions may have some utility in selected cases. Patients who are discharged from the ICU should be referred to appropriate follow-up care, including ongoing pain management. In the long term, ongoing pain or traumatic memories associated with pain experienced during illness represent a significant burden on many patients, further emphasizing the importance of managing pain in all critically ill patients.

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