

Introductory Chapter: Pain in ICU

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1. Introduction

According to the International Association for the Study of Pain (IASP), pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage” [1]. This “pain distress” is usually augmented in the ICU where patients suffer the additional psychological distress of hospitalization, communication difficulty, and self-control loss [2]; and it is considered the main source of anxiety, agitation and sleep deprivation, and delirium in the ICU [3].

Apart from that, sustained pain leads to a state of persistent adrenergic activation and systemic inflammatory response syndrome encapsulating which are related to tachycardia, hypertension, increased myocardial oxygen consumption, and myocardial ischemia [4]; atelectasis, diaphragmatic dysfunction, respiratory impairment, increased catabolism, hyperglycemia, immunosuppression impaired wound healing and hypercoagulation [5–8].

The former result not only in a higher ICU length-of-stay, ICU morbidity, and mortality but also long-term consequences even after ICU discharge. The incidence of chronic pain (duration of more >3 months) after ICU varies from 28 to 77% and risk factors for chronification of pain involve pre-existing chronic pain, the intensity of acute pain, and the presence of acute pain at discharge from ICU [9, 10]. Chronic pain is a key element of Post Intensive Care Syndrome, a physical, cognitive, and psychological entity that may persist for years after ICU discharge [2].

Despite these facts, pain continues to be a commonly reported experience among ICU patients. More than half of critically ill patients report moderate to severe pain at rest and 80% experience pain during procedures with fewer than 25% receiving analgesics before painful procedures [11–15].

The rates of pain do not defer between medical and surgical ICUs [16]. Patients in ICU experience pain due to their illness or the diagnostic and therapeutic procedures carried out by medical and nursing staff. ICU-related procedures characterized as uncomfortable are repositioning, physiotherapy and mobilization, wound and burn dressing changes, tracheal suctioning, and mechanical ventilation but the care-related procedures described as most painful are arterial line insertion, chest tube removal, and wound drain removal [14].

2. Assessment of pain in ICU

Diagnosing and quantifying pain in ICU is a complex matter and a systematic and thoughtful approach is needed. It is essential to differentiate pain from other causes of distress, like delirium, hypoxemia, hypotension or withdrawal of alcohol and drugs,

and address the issue accordingly [1]. The approach should be systematic and protocolized. However, surveys have shown that only 50% of ICU professionals assess pain and they only do it infrequently [17]. Clinicians should assess critically ill patients for their level of pain regularly, that is every 2–3 hours and every time before a painful procedure or mobilization, using validated scales [3]. Vital signs associated with pain (hypertension, tachycardia, tachypnea) are poor indicators of pain because physiological parameters related to pain can be augmented or inhibited by several other factors in the ICU setting [1].

When patients in ICU can interact and communicate, either verbally or not, commonly used pain scales are very useful in the assessment of pain. The most valid and feasible among several pain intensity rating scales is a visually enlarged numeric rating scale (NRS) from 0 to 10, where 0 represents no pain and 10 represents severe pain [18]. Intubated patients can report their level of pain either by pointing on a large board that includes the numeric rating scale or by nodding as a provider holds up the board with the scale and points at the specific rating of their pain.

When patients in ICU are unable to communicate, scales that rest upon patient's behavior are implemented. Behavioral Pain Scale (BPS) and Critical-Care Pain Observation Tool (CPOT) are the most effective. Behavioral Pain Scale relies on the observation of the patient's expressions, upper limb movements, and synchrony with mechanical ventilation. It ranges between 3 and 12 and any value over 6 necessitates treatment of pain [19]. Critical-Care Pain Observation Tool is similar. It includes four components: facial expressions, body movements, muscle tension, and compliance with the ventilator for intubated or vocalization for extubated patients. This scale scores from 0 to 8 and a score over 2 indicates high levels of pain that need to be addressed [20]. Behavioral scales have been validated in critically ill patients [21, 22], but their correlation with self-reported scales is poor [23].

Despite the high availability of assessment tools for the diagnosis of pain in the ICU, existing literature suggests that as little as 19% of intensive care personnel adhere to the actual implementation of standardized diagnostic protocols [24]. Even then, adequate assessment must be partnered with an appropriate and adequate analgesic strategy to alleviate pain.

3. Treatment of pain in ICU

The pain must be treated before the administration of sedation, which should be initiated only if needed. It should rely on an algorithm-based approach using evidence-based protocols in response to pain scores [3, 16] and must be multimodal and holistic based on a variety of combined interventions to achieve the best analgesic effect with minimal side effects [15]. Furthermore, pain should, whenever possible, be treated preemptively, before the initiation of potentially painful procedures. Lastly, the specific analgesic pharmacological agents chosen to treat pain and the administered dosage must be tailored to each patient concerning the patient's specific needs.

Non-pharmacologic methods include massage therapy [25–27], cold therapy [28, 29], music and sound [30, 31], and relaxation therapy [32, 33]. They have been shown to decrease patient-reported and behavioral pain scores and the need for pharmacologic interventions [3] but are time-consuming requiring the engagement of the patient's family and should always be used in conjunction with pharmacologic therapy [16].

Pharmacologic therapy is based on the administration of numerous different classes of drugs that are often simultaneously used to block the various receptors and pathways of pain. Intravenous is the main route of administration but other options exist too. Regional analgesia, for example, and the use of local anesthetics can play a fundamental role in postoperative and post-trauma pain control in ICU. Central and peripheral neuraxial blocks have been shown to ensure adequate pain control with less opioid consumption and reduced stress response to surgery or trauma [34].

3.1 Opioids

Opioids are the mainstay for the treatment of acute non-neuropathic pain in the ICU. They are mostly administered intravenously by infusion following an initial bolus dose but can also be given by other routes like enteral (oxycodone, diamorphine, tramadol, codeine, morphine) or transcutaneous (fentanyl). Even when opioids are titrated to effect, prolonged use has been associated with several side effects: hemodynamic instability (bradycardia, hypotension), respiratory depression, gastrointestinal dysfunction (constipation, ileus, nausea, and vomiting), delirium and muscle rigidity, tolerance, dependency and iatrogenic withdrawal syndrome [35].

All opioids have the same analgesic efficacy, respecting the equianalgesic table. Except for meperidine which should be avoided in ICU, there is no evidence to favor the use of one opioid over another. Fentanyl is a highly lipid soluble short-acting potent drug with low impact on the hemodynamic status of the patient with safe renal and hepatic profile [36]. However, it accumulates displaying a prolonged duration of action, when given in high doses for long periods. Remifentanyl has quick onset and offset of action, and it is metabolized to inactive metabolites through hydrolysis by plasma esterase. Alfentanil also has quick onset and offset of action, but its clearance is prolonged in liver failure. Morphine still has a place in ICU pain management. Caution is warranted because morphine is metabolized by the liver to morphine-3-glucuronide and morphine-6-glucuronide which are cleared by the kidneys. The former metabolite can cause delirium and the latter is more potent than morphine itself. Thus, accumulation and toxicity are possible in hepatic and renal failure. Other opioids like oxycodone, diamorphine, codeine, and tramadol are less commonly used in ICU.

3.2 Non-opioids

Paracetamol can be given through many routes (oral, intravenous, and rectal). It is effective in the treatment of mild to moderate pain and can be used in combination with opioids for the management of severe pain [18]. It should be given with caution in patients with reduced glutathione stores (malnutrition, co-morbidity) because of the potential risk of liver injury [18, 36, 37].

Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit the regulation of cyclooxygenase enzymes COX-1 and/or COX-2. Their analgesic properties in critically ill patients have not been studied elaborately [36]. Their use can cause kidney injury and gastrointestinal bleeding and are to be used with great caution in patients with renal dysfunction, congestive heart failure, and coagulopathy [38]. Thus, they are generally avoided in critically ill patients.

Alpha (α_2)-adrenergic receptors agonists, clonidine and dexmedetomidine, are also implemented for the management of pain in the ICU. The latter has eight

times more affinity for α_2 -receptors than the former. They are both used in the ICU mostly for sedation. Even though they can have opioid-sparing properties they are not routinely used for reducing opioid administration in the ICU [18, 35–38]. They are mainly used to treat opioid, benzodiazepine, and alcohol withdrawal syndrome or improve analgesia quality in opioid-tolerant individuals. They can cause hypotension and bradycardia or, in case of abrupt cessation, rebound hypertension.

Ketamine is a sedative and analgesic agent that is reserved for special circumstances in ICU. It has an opioid-sparing effect for opioid-tolerant and dependent patients and has been shown to be effective in the management of pain in sickle cell crisis and after major abdominal surgery [39]. It reduces cough and stress response during tracheal suctioning attenuating intracranial pressure increase in head-injured and neurosurgical patients. It is also indicated in refractory status epilepticus and status asthmaticus.

Neuropathic pain is a disturbing condition resilient to the usual treatment regimens which call for special measures. Gabapentinoids are useful in the treatment of neuropathic pain. Gabapentin and pregabalin are brought into play for the management of pain in conditions like multiple sclerosis, spinal cord injuries [40], and demyelinating polyradiculoneuropathies such as Guillain-Barré syndrome [41] by reducing the central sensitization and hyperalgesia developed in these situations. They are only available in the enteral formulation and are excreted unchanged in the urine, so their dosage needs to be adjusted for renal impairment. Finally, useful adjuvants are tricyclic antidepressants (TCAs) with amitriptyline being the main representative.

4. Conclusion

Pain is a common issue in critically ill patients and remains poorly assessed and treated, despite its detrimental effects. Recognition of pain among ICU patients, whether they are communicative or not, is essential and is based on the regular assessment of pain with the use of validated tools. Effective treatment relies on a multimodal protocol-based analgesic strategy tailored to each patient that incorporates numerous pharmacologic agents.

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