Chapter 4

Acute Pain Management in Intensive Care Patients: Facts and Figures

Nissar Shaikh, Saher Tahseen, Qazi Zeesan Ul Haq, Gamal Al-Ameri, Adel Ganaw, Arshed Chanda, Muhammed Zubair Labathkhan and Tariq Kazi

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.78708

Abstract

Pain is an unpleasant experience for all patients including intensive care patients; if it is not treated properly, it has deleterious effects on patients' acute and chronic well-beings. In ICU patients, it causes sympathetic stimulation leading to adverse hemodynamic effects and after discharge, these patients are at the higher risk for developing chronic pain and post-traumatic stress disorders. Apart from racial and regional factors, sleep deprivation, anxiety, and delirium increase the pain perceptions. Pain assessment is a prerequisite for adequate pain management. The ICU patients are sedated and ventilated, and assessment scales differ depending on whether the patient is able to communicate. There are different pain assessment scales for both groups of patients. The preferred mode of delivery of analgesic medication is intravenous route as intramuscular and subcutaneous route are not reliable for drug delivery in these patients. Patient and nurse controlled analgesia gives better sense of pain control. In the treatment of pain, opioids are the commonly used medications, but paracetamol, dexmedetomidine, and gabapentin are increasingly used. Newer trends are multimodal analgesia, where the combinations of analgesic medications with different mechanism of action are used. Another trend is increasing use of analgosedation; they not only control the pain but also relieve anxiety.

Keywords: pain, intensive care, pain scale, analgosedation, multimodal analgesia, opioid, paracetamol, gabapentin

1. Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage [1]. Although relieving pain is a

fundamental right, still majority of the intensive care patients will experience pain sometime during their ICU stay particularly during dressing, the change of position and even at rest, and it is a great source of stress. The majority of intensive care patients may be unable to self-report their pain both verbally or with other signs because of an altered level of consciousness, the use of mechanical ventilation, or high doses of sedative agents or muscle relaxant. The incidence of significant pain is still 50% or higher in both medical and surgical ICU patients [2]. In addition to experiencing pain at rest, pain related to surgery, trauma, burns, and cancer, these patients experience procedural pain. It is ubiquitous, and inadequate treatment of procedural pain remains a significant problem for ICU patients. Nursing care procedures such as bathing, massage of back and pressure points, sheets change and repositioning are the most common painful procedures in ICU patients [2]. Vazquez et al. [3] analyzed pain intensity during 330 turnings in 96 medical surgical patients and reported significantly increased pain score between rest and turning. The bolus of analgesic was used in less than 15% of the turnings.

The adverse psychological and physiologic effects of inadequate pain control in critically ill patients are long lasting and significant. The critically ill patients have identified pain as a traumatic experience and discomforting. Recently, it is realized that more than 80% of the ICU-discharged hospitalized patients had painful memories and discomfort associated with the endotracheal tube, and 38% patients remembers pain as their worst intensive care memory even 6 months later. Granja and colleagues [4] found that 17% of patients recollect experiencing severe pain 6 months after discharge and 18% were at the risk for developing posttraumatic stress disorder (PTSD). Schelling and colleagues [5] in their follow-up study found that the patients with acute respiratory distress syndrome compared the non-ARDS patients who experience pain and other traumatic situations when they are in the intensive care unit and had a higher occurrence of chronic pain and posttraumatic stress disorders and inferior quality of life.

The stress response due to pain has serious adverse effects in intensive care patients. It increases the circulating catecholamine levels and causes arteriolar vasoconstriction, impair tissue perfusion, and reduce tissue-oxygen partial pressure [6]. Other responses triggered by pain include catabolic hypermetabolism resulting in hyperglycemia, lipolysis and breakdown of muscle to provide protein substrate [7]. These changes will impair wound healing and increase the risk of wound infection. Pain also suppresses natural killer cell activity [8, 9] and results in a decrease in the number of cytotoxic T cells, leading to a reduced neutrophil phagocytic activity [10]. Acute pain in ICU patients is a greatest risk factor for developing debilitating chronic, persistent, and neuropathic pain [11].

1.1. Pain causing organ dysfunction in the ICU patients

In the ICU, patients are in need of pain medicine for various reasons, including weaning off ventilatory support, pulmonary dysfunction and cardiac dysfunction.

1.1.1. Pulmonary complications and prolonged mechanical ventilation

Intensive care patients should be liberated from mechanical ventilation as early as possible to prevent the occurrence of ventilator-associated events. Mechanical ventilation is indirectly

responsible for other medical complications such as pressure ulcers, gastric ulcers, muscular weakness and renal failure. The inadequate pain management will inhibit weaning from ventilatory support [12].

Pulmonary dysfunction is a common complication of improper pain control in postoperative upper abdominal and thoracic surgery as well as patients with abdominal pathology such as pancreatitis and bowel ischemia, and so on, it causes abdominal muscle contractions and results in a decrease in lung volumes and functional capacity The cough reflex is compromised with the abovementioned pulmonary changes and leads to retained pulmonary secretions, which complicates in the occurrence of pneumonia. Pain may induce vasoconstriction, when it is coupled with venous stasis from immobility and can lead to thrombus formation and fatal pulmonary embolism [13].

1.1.2. Cardiovascular dysfunction

Analgesia in patients with myocardial infarction or acute coronary syndrome is essentially important. Hence, morphine or other opioid analgesics are one of the components of initial therapy in these patients. Morphine reduces oxygen consumption by decreasing sympathetic activity and increases blood delivery through its vasodilatory affects [14]. Hence, it is necessary to treat the underlying cause of chest pain, but at the same time, the use of proper and adequate analgesics is recommended.

1.2. Factors modulating the pain response

Apart from racial and regional factors, anxiety, delirium, sleep deprivation and psychosocial history make ICU patients more susceptible to pain, even with the smallest stimuli. It is essential to address and minimize the following cofounding factor for pain modulation.

1.2.1. Anxiety

It is a double-edged sword, a factor causing pain and a result of pain. The intubated patients in the intensive care atmosphere have a higher anxiety and stress as they are unable to communicate and express the pain. Heightened anxiety can lead to agitation and associated with uncontrolled pain in the ICU patients. In combination with all, it can lead to patient ventilator asynchrony and difficulty in wean from the ventilator [15].

1.2.2. Delirium

It is common finding in the ICU patients, caused by environment, metabolic, intracranial, endocrine, organ failure, medication-related and respiratory conditions [15]. The ICU environment is one of the important etiologies for delirium due to the high noon level of stimulation, continuous sleep deprivation and ever-changing medical and paramedical staff. It can be challenging to appropriately assess and treat pain for patients with delirium. Few physical changes in intensive therapy environmental may decrease the occurrence of delirium. It includes having more windows, readable calendars, recognizable clocks in the ICU and to provide continuity of care. It is equally important to have a repeated and clear communication

with the patient about treatments and invasive procedure plans even when patients are not able to verbally respond [15].

1.2.3. Sleep deprivation

It is an important contributing factor for increased pain response in ICU patients. In burns patients, it is a well-realized fact that if these patients do not have proper night sleep, the intensity of pain during the day time is higher [16]. Sleep deprivation in the ICU patients can result from psychological states, bright lighting, noise from ventilators and monitors, and disrupted circadian rhythms [14]. ICU patients' sleep will be improved by reducing exposure to bright light, reducing ambient noise, respecting circadian rhythms and using appropriate sedative hypnotics.

2. Pain assessment in ICU patients

It is of vital importance that the pain be assessed properly so as to manage it well. As the International Association for the Study of Pain also states, "the inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment" [17]. Hence, the ICU physicians must learn to reliably detect pain, using assessment methods adapted to a patient's diminished communication capabilities. The pain assessment tools are mainly divided depending on the patient's ability to communicate or not. In later circumstances, clinicians should consider patients' behavioral reactions as surrogate measures of pain, as long as their motor function is intact [18]. Detection, quantification, and management of pain in critically ill adults are the priorities and have been the subject of research for the last two decades [19].

Pain assessments should include location, characteristics, severity, onset, progression, duration, quality, radiation, alleviating and exacerbating factors, and effects of previous therapies. Pain should be assessed by self-reporting scales in patients able to communicate, or by behavioral pain scores in patients unable to communicate. There are many self-report pain scales and behavioral pain scales developed for use in intensive care unit adult patients, which unfortunately are not always routinely used in the ICU. This self-reporting of their pain is the gold standard of pain assessment and provides the valid measurement of pain [20]. The commonly used pain intensity scales are the Numeric Rating Scale (NRS) and Visual Analogue Scale (VAS) while Behavioral Pain Scale (BPS) is considered to be an alternative tool for assessing pain in sedated and mechanically ventilated patients. The BPS assesses pain through the evaluation of facial expression, upper limb movements and compliance with mechanical ventilation. Another behavioral scale called the Critical-Care Pain Observation Tool (CPOT) may also be used.

There has been reluctance to use surrogates or individuals who make medical decisions when patients cannot do, to report patients' pain, due to their emotional attachment to these patients. They have a potential for overestimating pain. In SUPPORT study, it is concluded that surrogates can identify the patient's pain 73% of the time and accurately estimate its severity of pain 53% of the times [21].

The following pain scales will be useful in awake and cooperative patients:

2.1. Visual analogue scale (VAS)

In this, the patient can see and describe the severity of pain on a scale of 0–10. Zero for no pain and 10 for maximum pain (**Figure 1**).

2.2. Numerical rating scale (NRS)

Patients rate pain by writing on a 10-point scale (**Figure 2**) (0, no pain; and 10, most severe pain).

2.3. Verbal rating scale (VRS)

In this scale, the patient can verbalize the pain in four grades. Grade 1 indicates the absence of pain, whereas severe pain is indicated by grade 4.

Pain scales and tools are used for patients unable to communicate.

2.4. Behavioral pain scale (BPS)

It is a clinical observational score depending upon the patient's facial expressions, upper limbs posturing, and tolerance of the controlled mechanical ventilation (**Table 1**). This score ranges from 3 to 12, and a score of >6 require pain management [22].

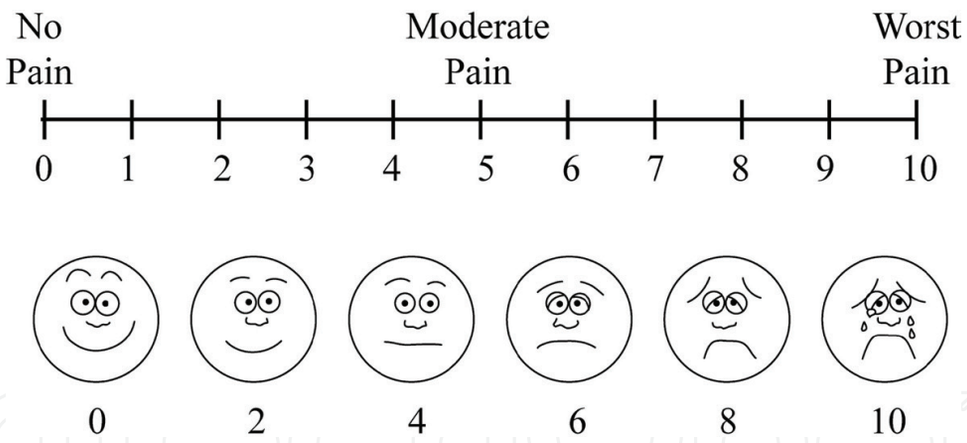

Figure 1. Visual analogue scale with its component.

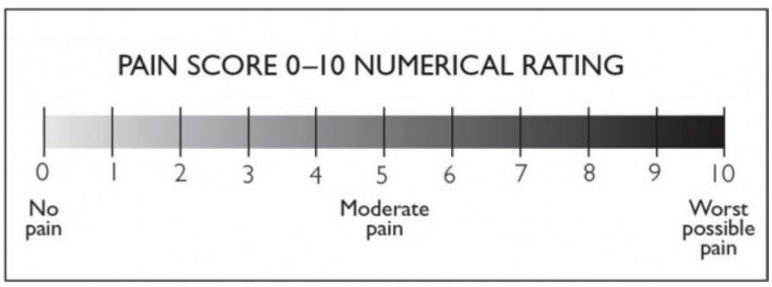

Figure 2. Numerical rating scale and its description of pain.

Facial expressions	Relaxed	1
	Partially tightened	2
	Fully tight	3
	Grimacing	4
Upper limbs	No movements	1
	Partially bent	2
	Fully bent with fingers flexion	3
	Permanently retracted	4
Compliance with mechanical ventilation	Tolerating movements	1
	Coughing but tolerating ventilation most of the time	2
	Fighting with ventilator	3
	Unable to control the ventilation	4

Table 1. Behavioral pain scale and its components.

2.5. Critical care pain observation tool (CPOT)

This pain assessment tool has four clinical components, facial expressions, body movements and muscle tension and compliance with the invasive mechanical ventilation. CPOT score ranges from 2 to 8. A score of more than 2 requires pain management.

3. Mode of analgesia administration in ICU patients

The mode of analgesic medication administration is an important factor for the pharmacologic management of pain in the ICU. Intravenous (IV) administration is more commonly the route of choice in critically ill patients because of altered GI tract function that could lead to unpredictable absorption of medication. Intravenous route is generally preferred over subcutaneous or intramuscular routes given potentially inadequate absorption due to regional hypoperfusion due to shock, subcutaneous oedema. The Fentanyl patch can be used for chronic pain relief in stable patients but not in ICUs or for acute pain relief because of the 12–24 h delay in peak serum levels.

The choice of intermittent versus continuous infusion administration depends on factors such as the frequency and severity of pain and the pharmacokinetics of the analgesic medication. The administration in bolus is associated with the variation in the peak plasma concentration, since the infusion maintains a more stable concentration but can lead to accumulation of medication in patients with renal or liver failure.

3.1. Patient-controlled analgesia (PCA)

It is an effective method for administering analgesic medication and gives patients a sense of control over their pain. Patients have autonomy on when and how much medication

they receive. However, this technique requires awake and orientated patients which make use of PCA limited in ICU patients. In combination with intravenous paracetamol and pro-paracetamol, the opioid consumption is significantly less [23].

3.2. Nurse-controlled analgesia (NCA)

It is inferior to the PCA but still can be useful, as nurses can administer the analgesia quickly when required or during the procedures.

3.3. Regional (nerve blocks) and neuraxial (spinal or epidural)

Analgesia techniques are used in ICU-selected trauma patients and surgical procedures. Epidural analgesia is probably the most commonly used regional anesthetic technique in the ICU. It is more useful in critically ill postoperative thoracic, abdominal, major vascular surgery, orthopedic surgery and trauma patients. Positioning patients during catheter insertion is a challenge for using regional anesthesia in ICUs. The main disadvantages of epidural and regional analgesia are the rare but catastrophic complications such as infection, epidural hematoma formation and nerve damage, which can occur in ICU patients who have a high risk of developing these complications [24].

The combination of intravenous opioid PCA, paracetamol and regional anesthesia techniques is multimodal analgesia which decreases the total opioid analgesia consumption and hence decreasing the side effects and better patient comfort. The NCA proved to not be superior to PCA and increases the rapid response team activation.

4. Analgesic medications used in ICU patients

Opioids are the main medications used for analgesia in ICU patients due to potency, concomitant mild sedative and anxiolytic effects. It can be administered by multiple routes. The commonly use opioids include Fentanyl, Remifentanil, and Morphine. The choice of opioid and the dosing should be individualized based on potency, pharmacokinetics and pharmacodynamics, adverse effect, patient comorbidities and organ dysfunction [25].

4.1. Morphine

It is the most frequently used medication in cancer patients. It is the standard by which other opioids are compared. Morphine is directly extracted from opium poppies; it stimulates the release of histamine which produces allergic and vasodilation-induced cardiovascular instability. Initial bolus intravenous (IV) morphine 2 mg dose administered slowly over 4–5 min then can be titrated with 1–2 mg every 10–15 min till adequate analgesia is achieved. Continuous IV morphine can be administered with an initial 2–5 mg bolus dose followed by 1 mg/h. Morphine is primarily metabolized in the liver and it is excreted through kidneys. It has active metabolites; morphine-3-glucuronide and morphine-6-gluconoride. Accumulation of these metabolites in renal insufficiency can produce opioid toxicity and adverse effects such as nausea, sedation, respiratory depression myoclonus and seizures (**Table 2**) [25].

Analgesic medications	Dosage	Half-life	Main adverse effects
Morphine	2–5 mg bolus, 1–10 mg/h infusion	2–4 h	Purities, hypotension and metabolites accumulation in renal in impairment
Fentanyl	25–100 μg bolus 25–200 μg/h	2–5 h	Muscle rigidity, accumulation in hepatic impairment
Remifentanil	0.5–2 mg bolus 0.5–15 μg/kg/h	3–10 min	Bradycardia and hypotension
Dexmedetomidine	02–1.4 μg/kg/h	6 min to 3 h	Cardiac asystole, bradycardia and hypotension
Paracetamol	1 g every 6 h	2–3 h	Hypotension, liver and kidney injury

Table 2. Various opioids and non-opioid analgesic, their dosage, half-life and side effects.

4.1.1. Fentanyl

Fetany is a synthetic opioid that is 100 times more potent than morphine. It has far more lipid-soluble property than morphine and is easily taken into the CNS. Compared to morphine, it does not cause histamine release and hence no vasodilation and hypotension, making Fentanyl the preferred choice for hemodynamically unstable patients. Its intravenous onset is immediate with a short duration of 30 min to 1 h, and it is extracted though liver. Fentanyl is given IV in 25–100 μg boluses for 1–2 min and then is repeated every 10–15 min till pain is controlled. Moderate–severe pain: a loading dose of 50–200 μg intravenously followed by 25–50 μg/hr. is typically administered. Its administration for more than 5 days causes accumulation in fatty tissue, which is mobilized after the drug is stopped and may cause prolonged sedation [25].

4.1.2. Remifentanil

It is a fast-acting and an equally fast recovery drug. It is 200 times more potent than morphine. Its metabolism does not depend on the liver. Analgesia-based sedation with remifentanil is a useful option for mechanically ventilated patients, and it can be used in patients that need frequent neurological assessment. Hence, it is a drug of choice in analgosedation in ICU. It has shown a shorter duration of mechanical ventilation and quicker ICU discharge with Remifentanil compared with other opioids. It offers precise control of analgesia for painful procedures in ICU patients and has a highly predictable onset and offset, with a stable context sensitive half-time (3–10 min). Initial dose adjustment is not required for patients with impaired renal and hepatic functions. Remifentanil can be administrated in higher doses than are normally used with other opioids without concerns about accumulation and the possibility of unpredictable and/or delayed recovery. Frequently, ICU patients are managed without bolus doses, and it is recommended that remifentanil infusions should be started at 6–9 μg/kg/h and then titrated in the range dose of 0.5–15 μg/kg/h. The major adverse effects are hypotension and bradycardia (**Table 2**) [24].

4.1.3. Tramadol

It is a centrally acting opioid-like medication, acts by binding to the μ opiate receptor; it is a pure agonist and inhibits adrenaline and serotonin reuptake. The most common adverse

effect includes nausea, vomiting, dizziness drowsiness, dry mouth and headache. Tramadol causes less respiratory and cardiovascular depression, euphoria and constipation. Initial bolus dosage is 100 mg. After 90 min following the initial bolus, further doses of 50 mg may be given every 30 min up to a total dose of 250 mg. Subsequent doses should be 50 or 100 mg for 4–6 h up to a total daily dose of 400 mg [24].

4.2. Non-opioid analgesic agent or adjuvants used in ICU patient

Non-opioid analgesics are use in the management of mild to moderate pain and moderate to severe pain with adjunctive opioid analgesics. The potential advantages of multimodal analgesia, which involves a combination of analgesics with different mechanisms of action, include improved analgesia with a lower opioid dose required and a decreased risk of opioid-related adverse effects [24].

4.2.1. Nonsteroidal anti-inflammatory drugs (NSAIDs)

NSAIDs have opioid-sparing effect but they are not sufficiently investigated in ICU patients. Their use in ICU patients is still controversial. The most worrying adverse effect includes gastrointestinal bleeding, renal dysfunction and inhibition of platelet function.

4.2.2. Paracetamol

It is commonly administered for the short-term treatment of mild to moderate pain and febrile critically ill patients with infection. It differs from the available opioids and NSAIDs, since paracetamol does not increase the incidence of nausea, vomiting and respiratory depression that can occur with opioids, or the platelet dysfunction, gastritis and renal toxicity that are associated with NSAIDs. It has a relatively good safety profile but there is limited information regarding IV use in critically ill patients. The study to date has described that paracetamol can cause transient abnormalities of liver function and may cause hypotension in critically ill patients. Acute liver failure is the most serious potential complication of the use of paracetamol. The key criteria for assessing potential hepatotoxicity with conventional doses of paracetamol may include hypoxic injury, altered pharmacokinetics, relative over-dosage, muscle glutathione depletion, malnutrition, dehydration, older age and alcoholism which are often seen in critically ill patients [24].

4.2.3. Prop-paracetamol

It is a prodrug form of paracetamol which is formed from the esterification of paracetamol and the carboxylic acid diethyl glycine. It has the advantage of making it more water-soluble. It is used in postoperative care and is delivered by intravenous route [23].

4.2.4. α2-agonists

The Clonidine and Dexmedetomidine are α2-adrenoceptor agonists, which provide both analgesia and sedation. Hence, they are also termed as analgosedation agents. Dexmedetomidine has eight times more affinity for α2-receptors compared with clonidine.

Dexmedetomidine infusion has been shown to reduce the prevalence and duration of confusion and delirium when compared with the use of morphine and midazolam [25].

α2-Agonists are used to improve the quality of analgesia and aid opioid rotation in opioid-tolerant individuals. The side-effect profile of both α2-agonists includes bradycardia, cardiac asystole and hypotension. Although rare, it can cause rebound hypertension and can cause withdrawal syndrome.

4.2.5. Ketamine

It is an N-methyl-aspartate antagonist, commonly used as analgosedative agent. Its use in combination with the opioid PCA reduces the opioid consumption and side effects. In combination with midazolam, ketamine provides effective analgesia in sickle cell crisis patients. Ketamine has an opioid-sparing effect and commonly used in lower dosage in burns patients. The main side effects of ketamine are tachycardia, hallucination, delirium ketotonia and increase intracranial pressure [25].

4.2.6. Magnesium

It acts through the NMDA receptors and acts as adjunct by reducing analgesic requirements without any major adverse effects, but there is no evidence that magnesium has any opioid-sparing effects in the critically ill patients [25].

4.2.7. Gabapentinoids

The Gabapentin and Pregabalin work by binding to the α2δ subunits of voltage-dependent calcium ion channels. They reduce the development of hyperalgesia and central sensitization and are useful adjuncts in the treatment of neuropathic pain.

Gabapentin compared with Carbamazepine or placebo reduces pain intensity in patients with GBS (Gillian Barrie syndrome) without increasing side effects. Gabapentinoids are used mainly in neuropathic and post-burn debridement pain. The extra advantage is that these medications are available in the enteric form and get absorbed in the duodenum; hence, one has to be careful when the patient is fed through a jeujenostomy tube. The major side effects of these medications are confusion, dizziness, ataxia and convulsions [25].

5. Few final recommending points

5.1. Hospital pain team

Consider referring complex ICU patients to the hospital pain team. It helps the patients on multimodal therapy but if still experiencing severe pain. Referral to the pain team can often lead to an increased level of support that would benefit the suffering patients, and once patients are discharged from the critical care unit, the pain team follows them to the ward [26].

5.2. Alternative therapy

The alternative medicine modalities of pain management like transcutaneous electrical nerve stimulation (TENS), acupuncture and aromatherapy have a very weak evidence base pain management in intensive care, but should be considered as the adverse-effect profile is low [25].

5.3. Reassessment

Patients must be evaluated hourly to ensure appropriate response to therapeutic interventions so that health-care providers can proactively act to relieve pain. If reassessment reveals inadequate pain control despite the initiation of therapeutic interventions, we should consider titration of medications, rotation of medications or changes in the route of administration [26].

5.4. Guidelines and protocols

These guidelines should be developed that combine a scientific basis and expert opinion. Wellness model from the World Health Organization's treatment of pain after cardiac surgery, we can see that guidelines and protocols lead to the effective management of post-cardiac surgery pain. If we look at the complexity of ICU pain, we need to have organized protocols to help us care for these patients. The examination of published literature reviews and evidence-based guidelines can facilitate the development of institution-specific guidelines.

5.5. Clinical pathways

It provides a consistent and repeatable time line for planning individualized patient care. The pathway details the precise course of the patient, including multidisciplinary elements. It includes history, examination, diagnostics and treatment and incorporates pre-emptive treatment for procedures as well as management of chronic pain issues [26].

5.6. Checklists

It is a way to verify that clinical pathways or tasks are completed and it is a good way to ensure that pathways or tasks are followed. It helps in errors prevention [26].

5.7. Daily goals

Daily goals highlighting by white board, electronic reminders to all members of the multidisciplinary team can access the plan and ensure that the patient is being treated from all perspectives [26].

6. Conclusions

Intensive care unit (ICU) patients are at the higher risk of pain and they are having pain even while resting. If pain is not adequately treated, it leads to adverse effect and increases the chances of chronic pain and posttraumatic stress disorders in these patients. In ICU patient, anxiety, delirium and sleep deprivation increase the sensitivity to pain. The organ dysfunctions in these patients will decrease the potency of analgesic medication and increase the toxicity. Pain assessment is the basic essential factor in adequate management of pain. The different pain scales are used depending on their abilities to communicate. The commonly used analgesic medication in ICU patients is opioids but there is an increased use of multimodal

analgesia and analgosedation approach obvious reasons. In the management of pain in ICU patients, the involvement of pain management teams, the use of clinical pathway, guidelines and protocols may have better impacts.

Author details

Nissar Shaikh[1]*, Saher Tahseen[1], Qazi Zeesan Ul Haq[1], Gamal Al-Ameri[1], Adel Ganaw[1], Arshed Chanda[1], Muhammed Zubair Labathkhan[1] and Tariq Kazi[2]

*Address all correspondence to: nissatfirdous99@gmail.com

1 Surgical Intensive Care Unit: Hamad Medical Corporation, Weill Cornell Medical Collage in Doha, Doha, Qatar

2 Medical Intensive Care Unit: Hamad Medical Corporation, Doha, Qatar

References

[1] Barr J, Puntillo K, Ely EW, Gélinas C, Dasta JF, et al. Clinical practice guidelines for the Management of Pain, agitation, and delirium in adult patients in the intensive care unit. Critical Care Medicine. 2013;**41**:264-306

[2] de Jong A, Molinari N, De Lattre S. Decreasing severe pain and serious adverse events while moving intensive care unit patients: A prospective interventional study (the NURSE-DO project). Critical Care. 2013;**17**:R74

[3] Vazquez M, Pardavila MI, Lucia M, Aguado Y, Margall MA, Asiain MC. Pain assessment in turning procedures for patients with invasive mechanical ventilation. Nursing in Critical Care. 2011;**16**:178-185

[4] Granja C, Gomes E, Amaro A, et al. JMIP study group: Understanding posttraumatic stress disorder-related symptoms after critical care: The early illness amnesia hypothesis. Critical Care Medicine. 2008;**36**:2801-2809

[5] Schelling G, Stoll C, Haller M, et al. Health-related quality of life and posttraumatic stress disorder in survivors of the acute respiratory distress syndrome. Critical Care Medicine. 1998;**26**:651-659

[6] Akça O, Melischek M, Scheck T, et al. Postoperative pain and subcutaneous oxygen tension. Lancet. 1999;**354**:41-42

[7] Hedderich R, Ness TJ. Analgesia for trauma and burns. Critical Care Clinics. 1999; **15**:167-184

[8] Beilin B, Shavit Y, Hart J, et al. Effects of anesthesia based on large versus small doses of fentanyl on natural killer cell cytotoxicity in the perioperative period. Anesthesia and Analgesia. 1996;**82**:492-497

[9] Pollock RE, Lotzová E, Stanford SD. Mechanism of surgical stress impairment of human perioperative natural killer cell cytotoxicity. Archives of Surgery. 1991;**126**:338-342

[10] Peterson PK, Chao CC, Molitor T, et al. Stress and pathogenesis of infectious disease. Reviews of Infectious Diseases. 1991;**13**:710-720

[11] Puntillo KA, Miaskowski C, Summer G. Pain. In: Carrieri-Kohlman V, Lindsey AM, West CM, editors. Pathophysiological Phenomena in Nursing: Human Responses to Illness. 3rd ed. St. Louis, MO: Saunders; 2003. pp. 235-255

[12] Marino PL. Analgesia and sedation. In: Marino PL, Sutin KM, editors. The ICU Book. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007. pp. 885-907

[13] Desai PM. Pain management and pulmonary dysfunction. Critical Care Clinics. 1999; **15**:151-166

[14] American Heart Association. 2005 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care part 8: Stabilization of the patient with acute coronary syndrome. Circulation;**2005**(112):89-110

[15] Szokol JW, Verdin JS. Anxiety, delirium and pain in the intensive care unit. Critical Care Clinics. 2001;**17**:821-841

[16] Raymond I, Nielsen TA, Lavigne G, Manzini C, Choiniere M. Quality of sleep and its daily relationship to pain intensity in hospitalized adult burn patients. Pain. 2001;**92**:381-388

[17] International association for the study of pain. IASP taxonomy. Available at: http://www.iasp-pain.org/AM/Template.cfm?Section=Pain_Defi

[18] Anand KJ, Craig KD. New perspectives on the definition of pain. Pain. 1996;**67**:3-6 discussion 209

[19] Puntillo KA. Pain experiences of intensive care unit patients. Heart & Lung. 1990; **19**:526-533

[20] Hamill-Ruth RJ, Marohn ML. Evaluation of pain in critically ill patients. Critical Care Clinics. 1999;**15**:35-54

[21] Desbiens NA, Mueller-Rizner N. How well do surrogates assess the pain of seriously ill patients? Critical Care Medicine. 2000;**28**:1347-1352

[22] Payen J, Bru O, Bosson J, et al. Assessing pain in critically ill sedated patients by using a behavioural pain scale. Critical Care Medicine. 2001;**29**:2258-2263

[23] shaikh N, Kettern MA, Ahmed AHA, Louon A. Morphine sparing effect of Proparacetamol in surgical and trauma intensive care. The Middle East Journal of Emergency medicine. 2006;**6**:28-30

[24] Višnja Nesek A et al. Pain management in critically ill patients. Periodicum Biologorum. 2015;**57**:61

[25] Narayanan M, Venkataraju A, Jennings J. Analgesia in intensive care: part 1. BJA Education. 2016;**16**:72-78

[26] https://www.practicalpainmanagement.com/resources/managing-pain-intensive-care-units; downloaded on 17th Feb 2018

IntechOpen