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Pain in the ICU: A Psychiatric Perspective

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Abstract

Pain is abundant in the intensive care unit (ICU). Successful analgesia demands a comprehensive appreciation for the etiologies of pain, vigilant clinical assessment, and personalized treatments. For the critically ill, frequent threats to mental and bodily integrity magnify the experience of pain, challenging clinicians to respond swiftly and thoughtfully. Because pain is difficult to predict and physiologic correlates are not specific, self-report remains the gold standard assessment. When communication is limited by intubation or cognitive deficits, behavioral pain scales prove useful. Patient-tailored analgesia aspires to mitigate suffering while optimizing alertness and cognitive capacity. Mindfulness of the neuropsychiatric features of pain helps the ICU clinician to clarify limits of traditional analgesia and identify alternative approaches to care. Armed with empirical data and clinical practice recommendations to better conceptualize, identify, and treat pain and its neuropsychiatric comorbidities, the authors (psychiatric consultants, by trade) reinforce holistic approaches to pain management in the ICU. After all, without attempts to understand and relieve suffering on all fronts, pain will remain undertreated.

Keywords

pain, analgesia, delirium, anxiety, intensive care, psychiatry

Introduction

Omnipresent to the critical care setting, yet elusive, pain poses unique challenges for the intensive care unit (ICU) clinician as it increases the burden of suffering for patients and their families.[1]

Requisites for successful pain management include knowledge of nociceptive physiology, dependable tools for characterizing pain, and proficiency in analgesic treatment.[2] The last 50 years have seen encouraging advances in these arenas. Nociceptive pathways have been clarified[3]; graduate pain fellowships have gained accreditation[4]; pain assessments have been developed and analgesic formularies reinforced. Yet coinciding data suggest little improvement to rates of unresolved pain in the hospital setting, and failures of pain control persist.[5,6] In a survey of more than 5000 medically hospitalized patients across the United States, roughly half described pain[7]; 14.9% reported extreme pain or a predominance of moderate pain, and an equal percentage was dissatisfied with pain management.

At the heart of this deficit lie challenges inherent to critical care: an abundance of painful disease states and treatment requirements, along with barriers to patient–provider communication. These are compounded by potentially reversible factors: logistical hurdles to timely analgesic administration (eg, increased nursing burdens), excessive fears on the part of treatment providers (eg, precipitating opiate addiction with therapeutic analgesia), and subconscious reactions to "drug-seeking" behavior.[6,8] An historical underemphasis on multidisciplinary approaches to pain during medical education has left nuances of analgesia untaught to clinical trainees.[9,10] This may be magnified in the ICU, where rapid stabilization of medical and surgical conditions demands primary attention, leaving pain potentially forgotten.

In an effort to reinforce comprehensive approaches to pain management during critical illness, this review will visit physiologic mechanisms of nociception, present a larger framework of suffering in the ICU, survey pain assessment strategies, and offer considerations for analgesic management. Neuropsychiatric conditions that accompany acute pain will also be discussed. Unless germane, technical details that have received exhaustive review elsewhere (eg, opioid dosing practices) will be forgone.

Mechanisms of Pain in the ICU

Acute pain is a perceptual expression of nociception, the afferent signaling of activated nerve endings (nociceptors) in the presence of threatened or actual tissue injury.[2,6] The site of

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nociceptive signal transduction influences the subjective experience of pain. Originating in peripheral tissues, *somatic* nociception is typically experienced as a sharp stabbing pain or a dull focal ache; at the organ level, *visceral* nociception produces pain that is paroxysmal, cramping, and difficult to localize.[11,12] The transmission of impulses from peripheral nociceptors to dorsal horn neurons in the spinal cord follows synaptic release of endogenous neuropeptides, including glutamate and substance P. Binding of opioids at this juncture (among other afferent sites) attenuates neurotransmitter release and disrupts ascending pain pathways.[13] From the dorsal horn, axonal transmission along the spinothalamic tract terminates at various sites intracranially, including the somatosensory cortex, reticular activating system, and limbic network. Though incompletely mapped, the overlap of nociceptive tracts with networks of memory, emotion, and arousal forms a potential basis for the cognitive, affective, and behavioral experiences associated with pain.[11]

Projections to the hypothalamus and pituitary gland contribute to autonomic and neuroendocrine-mediated reactions to nociception.[14] Sympathetic stress responses include tachycardia, elevated blood pressure, diaphoresis, and skeletal muscle hypertonia.[2,6] Untoward metabolic and neuroendocrine complications include glycemic dysregulation, elevated myocardial oxygen demand, immune suppression, hypoxemia, renal impairment, and coagulopathy.[5,15,16]

Pain in the ICU reflects acute nociception from disease processes aggravated by invasive therapies (eg, endotracheal intubation) and obligatory bedside care (eg, turning). These experiences are compounded further in the presence of chronic pain, believed to afflict over 70 million Americans.[16] Still, a comprehensive model of pain requires more than the physiologic mechanisms of nociception and neuropathy. Recognizing the additional impact of psychic distress, the International Association for the Study of Pain (IASP) define pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[17] Cognitive and emotional dilemmas described by ICU patients include fear of death, alarm at the sudden loss of bodily function, and perceptions of powerlessness, humiliation, and loneliness.[1,18] Whether or not these phenomena alter nociception directly is irrelevant to the patient's experience. Psychic distress impacts the perception of nociception as *pain* and the interpretation and expression of pain as *suffering*.

Assessment of Pain

With rare exception, pain *is* as the patient describes it. This may seem daunting to the ICU clinician faced with a suffering patient in spite of what would seem to be sizeable opioid doses. In fact, medical providers tend to underestimate the presence and severity of pain[19-21]; and while surrogates often successfully mediate patient–provider interactions, they frequently misgauge pain levels.[22] Consequently, accurate assessment hinges on direct communication with the patient. Questioning the onset, location, duration, intensity, and quality of pain allows the clinician to differentiate possible etiologies and consider further interventions. Helping the patient to identify exacerbating and relieving factors permits fine-tuning of analgesic care; and if even briefly, acknowledging fears related to the patient's experience of pain helps the physician to solidify a therapeutic alliance.

Taking a few moments to gather pertinent historical information provides the practitioner with clinical pearls from which to tailor pain assessment. Chart review should clarify the presence of an underlying pain syndrome or other chronic condition that can influence the experience of acute pain (eg, diabetes mellitus interfering with postoperative wound healing). When asked, the patient or family member may recount a history of critical illness and related pain experiences; this allows the clinician to identify pain-related behaviors and complications (eg, extreme anxiety) that may reemerge during the current ICU course. Information about prior beneficial, ineffective, or adverse responses to analgesics helps steer medication choices, and a history of long-term opioid use or misuse should raise suspicion for physiologic tolerance. Communicating this information via team rounds and written documentation helps to standardize analgesic approaches across ICU providers, thereby saving time.

The rapidly evolving nature of critical illness warrants frequent pain evaluation in the ICU. Pain should be assessed during routine nursing and physician visits, before and after movement or invasive procedures, and reassessed within 30 minutes of intravenous (IV) analgesic administration. When the critically ill patient is able to interact but unable to vocalize, questions should be simple, directive but nonleading, and adjusted to permit response by head movements, hand gestures, or writing. Because self-report in the ICU is often limited by intubation and sedation, the Society of Critical Care Medicine (SCCM) recommends tailoring pain assessment accordingly.[23]

The Communicative Patient

For the communicative patient, subjective pain scales help to clarify the patient's experience and standardize communication. While multidimensional assessments are preferred for chronic pain in the ambulatory setting,[24] the required monitoring frequency and functional limitations of critical illness make unidimensional pain assessments more practical. The Visual Analog Pain scale (VAS) and Numeric Rating scale (NRS) have been studied extensively among various age groups in medical, surgical, and emergency settings.[25,26] While scientific analysis of these scales during critical illness remains in infancy, the VAS and NRS are commonly used in the ICU.[27,28]

Visual analog pain scale. The VAS (Figure 1) consists of a 10-cm horizontal line with opposing descriptors of pain intensity at each pole (eg, "no pain" and "worst pain imaginable").[24,29] The patient is asked to point to or make a mark along the line that best represents pain severity. In clinical use

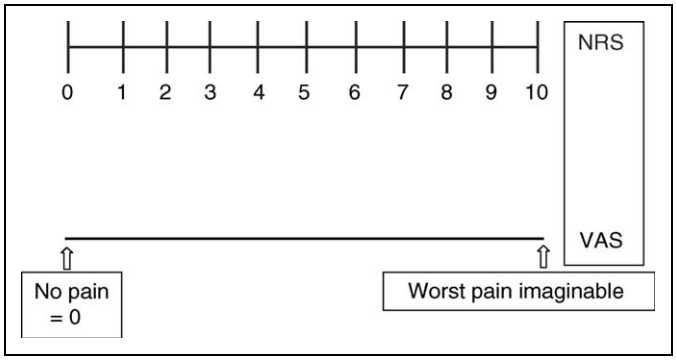

Figure 1. Visual Analog scale (VAS) and Numerical Rating scale (NRS). Adapted from Breivik et al,[24] with permission.

for over three decades, the VAS has demonstrated validity for pain assessment in the ICU.[28] Critics argue that patients may have difficulty understanding the task,[30] while tedious scoring and lack of readily identifiable indicators of progress may diminish feasibility.[29]

Numerical rating pain scale. The NRS permits patients to rate pain on a numeric axis from 0 (*no pain*) to 10 (*worst pain imaginable*).[29] While often administered verbally, use of a visual adaptation (Figure 1) has been described.[24,31] Both versions appear to be valid tools for detection of pain in the ICU, permitting consistently successful pain measure.[26] In a comparison of 5 self-report scales, a visual NRS was rated the most accurate and easy-to-use by patients.[28] Its adaptability permits consistent use of one scale across different levels of communication and makes the NRS an attractive choice for the ICU.

When asked to verbally rate pain on a numeric scale, the suffering patient may be tempted to respond with numbers greater than the upper limit (eg, "12 out of 10"). Whether this reflects the perception of being unheard or an association with nonnociceptive features of pain has not been studied formally, to the authors' knowledge. While such responses naturally elicit frustration in the questioning clinician (after all, how can anyone have more of something than the most allowed?), they signal the need to optimize analgesic pharmacotherapy while probing for psychological underpinnings of pain. Asking for a description of experiences that "tip the scales" encourages patients to retain an active role in assessing and managing pain; it also helps to ensure that pain-exacerbating clinical phenomena go unmissed.

The Noncommunicative Patient

When a patient presents with limited communication, the American Society for Pain Management Nursing (ASPMN) recommends identification and treatment of contributing pathology followed by observation for pain-related behaviors.[32] Behavioral pain indicators include muscle tension, posturing (eg, grabbing at a site), facial expression (eg, wincing), psychomotor agitation (eg, restlessness), and compliance with ventilation (eg, "bucking").[33,34] While the objectivity of autonomic signs makes them appealing pain markers in the ICU, physiologic features lack specificity for pain.[34] Accordingly, popular scales used to assess pain in nonverbal ICU patients rely heavily on behavioral measures.

Behavioral Pain Scale. The Behavioral Pain scale (BPS; Table 1) allows for identification of pain using evaluation of facial expression, upper limb movements, and ventilation compliance.[35] The BPS has been shown to assess pain accurately among sedated, mechanically ventilated patients in trauma-surgical, general medical, and mixed ICUs[35-37]; two of these studies also describe high inter-rater reliability.[35,36] Ahlers and colleagues[38] report valid pain assessment in 80 ICU patients during conscious ventilation. In this sample, BPS scores exceeded subjective pain measure in 16% of observations and underrated pain in only 12% during a nociceptive procedure.[38] Reliance of the BPS on mechanical ventilation precludes its use in nonintubated (NI) patients.

Critical-Care Pain Observation Tool. The Critical-Care Pain Observation Tool (CPOT; Table 2) comprises 4 subscales that assess facial expression, body movements, muscle tension, and either compliance with the ventilator or vocalization[39]; the last option permits CPOT use in spontaneously breathing patients. Studies support its accurate and reliable assessment of pain at various stages of ventilation and consciousness after cardiac surgery[39,40] and in the general medical-surgical ICU.[41,42] In a sample of postcardiotomy patients (n = 99), Gélinas and colleagues[43] report maximal psychometric success for identification of pain with a cutoff score greater than 2 during a nociceptive procedure (sensitivity 86% and specificity 78%). More recent studies demonstrate moderate correlation of CPOT scores with self-report in healthy individuals exposed to noxious stimuli[44] and reveal limitations of the CPOT (among other behavioral indicators) in a burn population.[45]

Behavioral Pain scale – Non-Intubated. Responding to the paucity of pain scales for spontaneously breathing patients who cannot self-report, Chanques and colleagues[46] designed a modified version of the BPS for nonintubated patients (BPS-NI; Table 3). In this scale, the ventilation compliance section of the BPS is replaced with an assessment of vocalization. The BPS-NI demonstrated construct validity and inter-rater reliability in one study of 30 critically ill patients, the majority of whom could not self-report due to delirium.[46]

General considerations. While studies of behavioral pain assessment are limited, a growing body of evidence supports use of the BPS or CPOT in mechanically ventilated ICU patients and the CPOT in spontaneously-breathing patients who cannot communicate. The BPS-NI is a promising tool for detection of pain in the non-intubated patient whose communication is limited by cognitive impairment (eg, delirium);

Table 1. Behavioral Pain Scale.[a]

Item	Description	Score
Facial expression	Relaxed	1
	Partially tightened (eg, brow lowering)	2
	Fully tightened (eg, eyelid closing)	3
	Grimacing	4
Upper limbs	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with ventilation	Tolerating movement	1
	Coughing but tolerating ventilation most of time	2
	Fighting ventilator	3
	Unable to control ventilation	4
Total score		3-12

[a] Adapted from Payen et al,[35] with permission.

Table 2. Critical Care Pain Observation Tool.[a]

Indicator	Description and Score
Facial expression	No muscular tension observed. Relaxed, neutral: 0 Presence of frowning, brow-lowering, orbit tightening, and levator contraction. Tense: 1 All of the above facial movements plus eyelids tightly closed. Grimacing: 2
Body movement	Does not move at all (does not necessarily mean the absence of pain). Absence of movements: 0 Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements. Protection: 1 Pulling at tube, attempting to sit up, moving limbs or thrashing, not following commands, striking at staff, trying to climb out of bed. Restlessness: 2
Muscle tension (evaluated by passive arm flexion and extension)	No resistance to passive movements. Relaxed: 0 Resistance to passive movements. Tense, rigid: 1 Strong resistance to passive movements, inability to complete them. Very tense or rigid: 2
Ventilator compliance (if intubated) or vocalization (if not intubated)	Alarms not activated, easy ventilation. Tolerating ventilation or movement: 0 Alarms stop spontaneously. Coughing but tolerating ventilator: 1 Asynchrony: blocking ventilation, alarms frequently activated. Fighting ventilator: 2 Talking in normal tone or no sound: 0 Sighing, moaning: 1 Crying out, sobbing: 2
Total score	0-8

[a] Adapted from Gélinas et al,[39] with permission.

further studies should clarify its role as a bridge from the BPS during sedated ventilation to eventual self-report. Effective use of behavioral pain markers in specialized ICU populations (eg, transplantation, burns) also warrants further investigation.

Analgesic Modalities in the ICU

Successful analgesia starts with identifying and managing conditions that contribute to pain, well before the use of any medications. Insomnia, anxiety, and delirium can amplify the pain experience and also require prompt treatment. Normalizing the sleep–wake cycle begins with maximizing daytime light and reducing disruptive nocturnal stimuli, including noise and unnecessary procedures.[47] Insomnia that does not respond to behavioral approaches (and is not attributable to untreated pain or delirium) prompts the addition of a pro re nata (PRN) sleep aid. Trazodone (typical start dose: 50-100 mg) and zolpidem (typical start dose: 5-10 mg) may be used in the critical care setting, although both

Table 3. Behavioral Pain Scale—Nonintubated.[a]

Item	Description	Score
Facial expression	Relaxed	1
	Partially tightened (eg, brow lowering)	2
	Fully tightened (eg, eyelid closing)	3
	Grimacing	4
Upper limbs	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Vocalization	No pain vocalization	1
	Moaning infrequently ($\leq$3$\times$/min) and not prolonged ($\leq$3 seconds)	2
	Moaning frequently (>3$\times$/min) or prolonged (>3 seconds)	3
	Howling or verbal complaints including Ow! Ouch! Or breath-holding	4
Total score		3-12

[a] Adapted from Chanques et al,[46] with permission.

have been associated with delirium. Recent studies support use of melatonin (typical start dose: 1-5 mg) for insomnia in the ICU[48,49]; modest evidence also suggests that melatonin may help to prevent postoperative delirium in elderly patients.[50,51]

Nonpharmacologic Treatment

Nonpharmacologic interventions are safe, versatile, and can be implemented at the bedside. Peripheral therapies, including heat or cold application, are believed to curb nociception by modulating local responses to noxious stimuli.[52] Interventions that promote serenity, including music and relaxation therapies, have been shown to decrease pain intensity after major surgery and may be used adjunctively in the ICU.[53-56] While cognitive–behavior therapy is rarely feasible in this setting, helping patients to quickly identify and correct cognitive misinterpretations can attenuate discomfort associated with common physiologic experiences (eg, fear of asphyxiation with mechanical ventilation).[57] Albeit simple acts, minimizing unnecessary exposure to noxious stimuli (eg, line/tube traction) and warning patients before nociceptive maneuvers (eg, dressing changes) can go a long way in maximizing pain relief.[52]

Opioid Medications

Opioid medicines constitute the mainstay of pain management during critical illness, with morphine, fentanyl, and hydromorphone commonly prescribed in the ICU. Most commercially available opiates act similarly at the mu opioid receptor, differing in potency, available routes of administration, metabolism, and lipid solubility.[58] Consistent bioavailability dictates preference for IV opioid delivery. Erratic absorption patterns after enteral, intramuscular, and subcutaneous opioid administration, and the delayed availability of transdermal formulations make these routes less favorable for management of acute pain in the ICU.[59] Successful analgesic selection and dosing require consideration of volume status, end-organ function, historical response to opioids, and clinical prognosis.

In the ICU, opioids are frequently administered by continuous infusion or intermittent injection along with sedative-hypnotic agents. The practice of *analgo-sedation* seeks to maximize comfort and improve tolerance of mechanical ventilation.[60] Sedated individuals are capable of experiencing pain, and most sedative agents do not confer analgesia. Analgesic treatment should therefore precede sedative administration, and sedation algorithms typically require concurrent management of pain.[27,61]

Side effects. Adverse effects common to opioids include nausea, constipation, sedation, respiratory depression, and urinary retention.[62] Decreased bowel motility reflects action at local opiate receptors in the gut[63] and is particularly uncomfortable for the ICU patient. Peripherally acting mu opioid-receptor antagonists (eg, methylnaltrexone, alvimopan) appear to counteract bowel dysfunction while preserving central analgesia.[64,65] Use of these agents has principally targeted constipation during palliative care and postoperative ileus,[66,67] though Woo and colleagues[68] report IV administration of methylnaltrexone in a critically ill burn patient with successful promotion of enteral motility and nutrition. Further studies are expected to clarify the effectiveness, safety, and feasibility of peripheral mu antagonists in the general ICU setting.

Adverse neuropsychiatric effects of opioids include affective dysregulation, sedation, cognitive slowing, visual hallucinations, and delirium. Myoclonus and seizures are infrequent complications of opioid toxicity and are most notably associated with high-dose parenteral meperidine used in the setting of renal impairment, malignancy, or a preexisting seizure disorder.[11,69] Daeninck and Bruera[70] describe risk factors for opioid-induced neuropsychiatric toxicities that include prolonged or high-dose opioid administration, advanced age,

preexisting encephalopathy, dehydration, and renal failure. Management of neuropsychiatric complications includes symptomatic treatment (eg, antipsychotic agents for agitated delirium), supportive care (eg, hydration), and opioid rotation or dose reduction.[70]

Tolerance and withdrawal. Repeated exposure to an opioid agent may lead to tolerance, the reduction in effect of a particular dose.[71] Any apparent weakening of analgesia with a previously beneficial opioid regimen should prompt consideration of tolerance, in addition to evaluation for new or evolving nociceptive conditions and psychological contributions.[52]

Acute withdrawal has been described in ICU patients during weaning of high-dose opioids administered for as little as 7 days.[72,73] Clinical features of opioid withdrawal are nonspecific and include fever, hypertension, tachycardia, piloerection, mydriasis, diaphoresis, and restlessness.[74] Gradual opioid taper should minimize this complication. Empirical methadone conversion has also been used to prevent withdrawal in ICU patients who require opioids for longer than 1 week.[75] If cardiac or hepatic dysfunction does not limit its use, methadone is particularly helpful when prolonged nociceptive conditions or treatments are anticipated (eg, burn management).

Nonopioid Medications

Use of nonopioids in the ICU is limited by potential for drug–drug interactions, side effects complicating critical illness, severity of pain states, and limited routes of administration. Alpha-adrenergic agents, nonsteroidal anti-inflammatory drugs (NSAIDs), and anticonvulsants may assist with analgesia during select clinical scenarios.

Postoperatively, the addition of an NSAID has been shown to reduce opioid requirements by 25% to 66%.[76] A meta-analysis by Marret and colleagues[77] demonstrates reduction of postoperative nausea and vomiting by 30% and sedation by 29% when NSAIDs are used alongside morphine PCA; other side effects, including respiratory depression, were not significantly reduced. Risks of gastrointestinal and renal injury should be weighed against any potential benefit of NSAID use, particularly during critical illness.

For patients with preexisting pain conditions, continuation of a previously effective nonopioid should be considered when the patient's clinical condition tolerates, as long as the medication does not interact adversely with other required agents.[52] While primarily used for chronic neuropathic pain, gabapentin and pregabalin have demonstrated adjunctive benefit for acute postoperative pain at doses of 300 to 1800 mg and 150 to 600mg, respectively[78]; still, these agents have been studied minimally in the ICU. Caution is especially advised with use of tricyclic antidepressants, given associations with impaired cardiac conduction and anticholinergic effects.

Special Considerations for the Chemically Dependent Patient

Managing pain of the chemically dependent patient presents conflicting challenges for the ICU physician.[79] An obligation to alleviate suffering is often met with suspicion of exaggerated pain behaviors for the purpose of procuring drugs and fears of propagating addiction. Stereotypes of the opioid-dependent patient as needy, drug seeking, or malingering can interfere with the physician's management of acute pain and engender animosity between providers and patients. Appreciation for the needs of the chemically dependent patient optimizes medical care and minimizes frustration on all fronts.

Opioid-dependent patients present with altered physiologic and psychological responses to pain.[80] Evidence to guide analgesia in the critically ill opioid-dependent patient is limited, in part, by difficulty of data collection and interpretation. Information is therefore gleaned from studies of individuals who receive opioid agonist therapies (OATs), such as methadone, for management of addiction.

Opioid agonist therapy-maintained patients frequently develop cross-tolerance to other opioid agents; additionally, repeated exposure promotes altered nociceptive sensitivity, rendering the OAT-maintained patient hyperalgesic.[81] These phenomena have been reported to occur as early as 1 month into OAT.[82] Doverty and colleagues[83] report lower tolerance for painful stimuli among opioid-dependent patients in chronic methadone treatment, when compared to controls. In a study by the same group,[84] morphine was administered after a painful stimulus to methadone-maintained individuals who also intermittently used heroin. Compared to controls, these individuals achieved less robust and shorter responses to morphine; moreover, they experienced minimal antinociceptive effects despite serum morphine levels that are typically therapeutic postoperatively.[84] Compton and colleagues[85] report comparable degrees of pain intolerance in dependent patients maintained on buprenorphine.

Opioid-dependent patients receiving OAT seem to experience hyperalgesia and increased opioid requirements when compared to nondependent individuals. This seems to be true regardless of the mechanism of action, cross-tolerance profile, or presumed analgesic properties of the OAT agent. To what degree these phenomena can be attributed to direct outcomes of chronic OAT, to physiologic features or sequalae of the underlying addiction, or to psychological reactions is unclear. It seems likely that all of these factors intermingle to effect the opioid-dependent patient's hypersensitivity to and forbiddance of pain, which drives the request for more opioids.

Psychiatric Syndromes Associated With Acute Pain

Anxiety and delirium complicate the experience of acute pain and potentially confound its detection. In the ICU, subjective assessment of anxiety and delirium are limited by intubation and sedation, while objective indicators are often nonspecific.

Table 4. Features of Anxiety in the Intensive Care Unit (ICU).[15,86]

Cognitive	Behavioral	Physiologic
Apprehension	Agitation	Breathlessness
Catastrophization	Irritability	Diaphoresis
Fear of death	Restlessness	Pallor
Helplessness	Urgency to flee	Palpitations
Loss of control	Withdrawal (interpersonal)	Tachycardia
Sense of doom		Tremor

Anxiety, delirium, and pain are not mutually exclusive, and treatment of one may exacerbate the other (eg, excessive anxiolytic administration promoting delirium). For these reasons, understanding the relation of neuropsychiatric conditions to pain and to each other proves especially vital.

Anxiety

Forced into unfamiliar environs and dire clinical scenarios, the ICU patient will understandably experience intermittent anxiety. Like pain, anxiety presents with a combination of cognitive, behavioral, and physiologic attributes (Table 4) and is best assessed by self-report.[15,86] Anxiety can be triggered by pain, mechanical ventilation, withdrawal states, and underlying psychopathology (eg, panic disorder). Screening and monitoring tools validated in the ICU include the Hospital Anxiety and Depression scale and Faces Anxiety scale.[87-89]

The SUPPORT investigation demonstrates a direct correlation between anxiety and pain.[7] Among the study's critically ill participants (n = 5176), individuals with any degree of anxiety were twice as likely to experience a higher intensity of pain than anxiety-free patients, and anxious patients were more likely to be dissatisfied with pain management.

Mitigating anxiety permits the rallying of cognitive and emotional mechanisms to cope with pain. Treatment starts with identifying and managing sources of anxiety. Reconciling medications on admission ensures that previously beneficial psychotropics are continued (when appropriate) and prevents the experience of an iatrogenic withdrawal state. The latter is imperative for patients maintained on sedative-hypnotic agents but should also be considered for patients taking a serotonin reuptake inhibitor (SRI). Abrupt discontinuation of SRIs is associated with anxiety, headaches, GI upset, insomnia, irritability, and paresthesias,[90] potentially exacerbating the pain experience. In certain cases, risk for serotonin syndrome (eg, addition of linezolid), platelet dysfunction, and hyponatremia may prompt the adjustment or discontinuation of a serotonergic agent. Psychiatric consultants can assist with treatment planning in these situations.

Benzodiazepines (BZDs) constitute the mainstay of rapid anxiolytic therapy. Through enhanced effects of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), BZDs act on limbic networks that presumably underlie the experience of fear. Given the availability in intramuscular, IV, and enteral formulations, lorazepam is preferred for as needed [PRN] management of anxiety during critical illness (recommended starting dose: 0.5-1 mg every [Q] 4-6 hours PRN mild-moderate anxiety, 1-2 mg Q 4-6 hours PRN severe anxiety). Metabolism via glucoronidation makes lorazepam an especially useful agent in the setting of hepatic dysfunction. Caution is required when using the IV formulation, which includes a propylene glycol additive that can precipitate metabolic acidosis at high doses or with renal impairment.[91] Adverse effects of BZDs, including hypotension, respiratory compromise, prolonged sedation, and delirium, should be considered prior to use. When fear or agitation appears to be driven by delirium, use of an antipsychotic medication is preferred in lieu of BZDs.

Delirium

Delirium affects 20% to 40% of critically ill patients and roughly 80% of patients during mechanical ventilation.[92,93] This is particularly concerning, given the associations of delirium with prolonged ICU stay and mortality.[94,95] Delirium is characterized by impaired consciousness, inattention and cognitive or perceptual disturbances; it develops acutely, fluctuates in course, and is typically reversible.[96] Arousal and kinesis present on a spectrum from stupor to combativeness, driving the classification of delirium as *hypoactive* or *hyperactive*. While the agitated patient may prompt quicker action to treatment than the "pleasantly" confused one, hypoactive features are equally distressing and associated with poorer outcomes.[27] Conditions that precipitate delirium are common in the ICU and include acute metabolic disturbances, infectious processes, postoperative states, and central nervous system (CNS)-acting medicines. A more comprehensive list of offending conditions can be found in reviews of delirium.[97-99]

While scientific data are sparse, delirium can be expected to worsen the experience of pain at both ends of the nociceptive pathway. At the tissue level: agitation can lead to movement against traction or to pulling of lines, catheters, and endotracheal tubes, while hypoactivity accelerates skin breakdown. At the CNS level: sensory disturbances can result in misinterpretation of noxious and innocuous stimuli, and cognitive impairment may drive refusal of ameliorative procedures. Just as delirium confounds the diagnosis of psychiatric conditions, it should be expected to influence the assessment of pain. Disturbed consciousness limits the patient's ability to report pain and the clinician's ability to monitor analgesic effects. Thoughtful opioid dosing takes into account evidence that both opioid overuse[100] and opioid underuse[101] increase the risk for delirium in the setting of pain.

During routine care, ICU clinicians must maintain a high index of suspicion for delirium and monitor for subtle indicators thereof. The patient who has trouble following commands or maintaining alertness, appears fearful or bewildered, or does not seem to understand his current condition deserves further evaluation for delirium. The Confusion Assessment Method (CAM-ICU) has demonstrated validity as an assessment for delirium in the ICU,[102,103] and its use appears to foster clinicians' understanding and detection of confusional states.[104]

Nursing notes, family input, and serial evaluation clarify the degree of cognitive deviation from baseline and help to identify fluctuations in course.

Resolution of delirium tends to follow treatment of underlying medical conditions and minimization of contributing factors. Proposed hypocholinergic and hyperdopaminergic neural mechanisms[97] drive the elimination of unnecessary anticholinergic medicines and, in some cases, use of a neuroleptic agent. The latter is particularly beneficial when features of delirium include psychosis, agitation, or fear. Among various antipsychotic options, haloperidol has established clinical efficacy with decades of use in the general hospital setting (recommended start dose: 2-5 mg IV Q 2 hours PRN agitation); lower start doses are recommended for older and neuroleptic naive individuals, with escalation based on clinical effect. Monitoring of electrocardiograph (EKG) for QT prolongation (QTP) is required with use of IV haloperidol, given the associated risk of polymorphic ventricular tachycardia.[105] Correction of other reversible risk factors for cardiac dysrhythmia (eg, hypomagnesemia) is prudent, and holding the neuroleptic for QTc exceeding 500 ms is recommended. When cardiac dysfunction precludes the use of haloperidol for agitated delirium, the psychiatrist's guidance may be solicited for alternate pharmacologic options.

Concluding Remarks

Just as medical or surgical complications drive speedy treatment in an effort to prevent negative outcomes, pain warrants an equal degree of clinical vigilance in the ICU. Efforts to improve pain management have targeted every level of care, from identification and monitoring to treatment and documentation. Quantifiable benefits follow implementation of systematic pain assessments and analgesic protocols,[31,106] as well as initiatives to increase bedside access to pain scales and standardize expectations for analgesic care among providers.[107] Ultimately, critical care improves and patients benefit when ICU clinicians practice thoughtful and systematic pain management. This includes sensitivity to the cognitive and emotional components of pain, knowledge of its neuropsychiatric comorbidities, and challenging of prejudices that interfere with the alleviation of suffering.

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