

Pain measurement techniques: spotlight on mechanically ventilated patients

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Background: Procedural pain is a frequent problem in intensive care units (ICUs). For that, pain assessment has been increasingly introduced to the ICU professional's routine, and studies have been developed to show the relevance of measuring pain in critically ill patients.

Objective: This review aimed to describe pain measurement techniques for mechanically ventilated adult patients based on evidence and already published.

Method: Systematic literature search was performed on PubMed and Google Scholar. Keywords "pain", "pain measurement", "intensive care units" and "respiration, artificial" were combined to the Boolean operator AND. No language or publication year was limited in this search. The purpose and method of all papers were analyzed and only studies which described pain assessment in mechanically ventilated patients were included in this review.

Results: Objective methods were found in the literature to assess pain in mechanically ventilated adults. Behavioral scales were the most used method for pain measurement in noncommunicative patients. Vital signs were used, but the reliability of this method was questioned. Pupillometry, bispectral index and skin conductance were found and described as pain assessment methods.

Conclusion: This review showed that objective measures, as behavioral scales, are the gold standard tools to measure pain intensity in noncommunicative subjects. These data contribute to professionals' knowledge about ICU pain measurement and emphasize its importance and consequences for adequate pain management.

Keywords: pain, pain measurement, intensive care units, respiration, artificial

Introduction

Intensive care, or critical care, is a health specialty dedicated to multidisciplinary management of patients with acute organ dysfunction.¹ The main objective of intensive care is to prevent further physiologic deterioration by the treatment and solution of acute and/or severe diseases and to save life during a life-threatening condition.¹ For that, intensive care unit (ICU) is the environment organized to meet the needs of these critically ill and mechanically ventilated patients, once their care involves a specific physical space, with support, monitoring technology, and specialized human resources.²

In ICUs, three important concepts are commonly used: pain, agitation and delirium.³ Pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".^{3,4} Agitation and anxiety commonly occur in ICUs and are associated with adverse clinical outcomes, such as hypoxemia, hypotension, and/or withdrawal from alcohol and other substances.³ Lastly, delirium is known as "an acute onset of brain dysfunction, characterized by level of

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consciousness disturbance and cognition changes (memory deficit, disorientation, language disturbance)".³ Despite pain, delirium and agitation are interconnected, pain is the most neglected sign in ICUs.

Analgesics and sedatives are medicines commonly used in ICUs with the objective to maintain comfort, relieve anxiety, facilitate care and adapt patients to ventilatory support.⁵ Some sedation protocols emphasize lighter use of sedatives for mechanically ventilated patients, daily sedation interruption and analgesia based on sedation protocols, which means that analgesic administration occurs and then adding sedation if required.⁶⁻¹² Currently, clinicians observed that the primary goal in ICUs should be pain and discomfort control, and then, if necessary, sedation should be performed. To achieve this goal, analgo-sedation protocols have been developed and applied in ICU patients.¹² Analgo-sedation protocols that have been introduced into practice decrease duration of invasive mechanical ventilation (IMV), ventilator-associated pneumonia incidence and improve the probability of successful extubation.¹³⁻¹⁵

Despite the fact that pain in critically ill and mechanically ventilated patients has been studied over the last 20 years, this sign is present in about 50% of this population.³ One of the main causes of pain in the ICU is the medical procedures, unavoidable and necessary actions that are responsible for changes in pain intensity compared to rest.¹⁶ A study performed in Europe (The Europain® Study) observed the increase on pain intensity during 12 procedures, such as chest tube removal, peripheral intravenous insertion, wound care, mobilization, positioning, respiratory exercises and others.¹⁶ Among these routine activities, tracheal suctioning was considered the most painful, responsible for certain behaviors (grimace, facial responses and clenched fists) and changes on physiological parameters.^{16,17}

Inadequate procedural pain treatment is a problem in the ICU, and inadequate treatment of this sign remains as a lack in the clinical setting.³ Barriers on pain management are associated to difficulties on assessment, since pain has a subjective nature and it is understood as a variable that can be measured only when reported by the person experiencing it.³ The majority of patients undergoing intensive care are unable to self-report their pain because of low consciousness levels, sedatives or neuromuscular blocking agents use and IMV.^{3,18}

From the observation of these subjects unable to self-report, the International Association for the Study of Pain (IASP) registered that "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".⁴ For that, pain assessment has been increasingly introduced to the ICU professional's routine and studies have been developed to show the relevance of measuring this sign in critically ill patients.

A large number of instruments can be used for pain assessment of unconscious and mechanically ventilated patients. It is based on behaviors, observation, physiological parameters, and other body signs that can indicate nociception.¹⁹ From that, this review aimed to describe pain measurement techniques for mechanically ventilated adult patients based on evidences and perspectives already published about this subject.

This narrative review was based on a systematic literature search performed on PubMed and Google Scholar. The same results were obtained in both databases. Keywords "pain", "pain measurement", "intensive care units" and "respiration, artificial" were combined to the Boolean operator AND. No language or publication year was limited on this search and all available papers were analyzed. If full text was unavailable, corresponding authors were contacted by email. The purpose and method of all papers were analyzed and only studies which described pain assessment in critically ill patients were included in this review.

Pain assessment in ICUs

In the last two decades, the American Pain Society has established "Pain as the fifth vital sign" initiative. This proposal consists of professional's awareness about the introduction of pain assessment in addition to other vital signs measurement, such as blood pressure, pulse, temperature, and respiration.²⁰ This pain assessment task is indicated for all health professionals that directly care for critically ill patients. Nurses, clinicians, physical therapists, and other caregivers must use structured, valid, reliable, and feasible tools to assess pain in the ICU, in a routine and repetitive manner.³

The importance of this routine on critically ill patient's outcomes is proven by studies that report its impact in ICUs. It is evidenced that the establishment of pain assessment protocols is responsible for better pain management, more efficient use of analgesics and/or sedatives, decrease in IMV duration, increased odds for weaning from IMV, lower risk of ventilator-associated pneumonia, central catheter-related infections, urinary tract infections, and bacteremia development, shorter duration of ICU stay and decrease in agitation events and mortality rate.²¹⁻²³ Based on those positive outcomes, pain assessment is considered a strategy for a better ICU care. Behavior analysis and vital sign records are the most used methods for this practice. These and other pain measurement instruments will be described below.

Behavioral scales

Mechanically ventilated patients who are unconscious and unable to self-report, require instruments that detect behavior details associated to pain perception and expression. Facial expressions observation is the main method for pain assessment in ventilated subjects.²⁴ It is known that during painful procedures, there is an increase in facial movements – eyes closed, brow lowered, lid tightened, cheeks raised and lips parted.²⁵ In addition to that, body movements, muscle rigidity, compliance with mechanical ventilator and/or sounds are other behavior indicators of pain intensity in ICU patients.²⁴

Based on these pain indicators, behavior assessment scales were developed and validated to mechanically ventilated patients. These instruments can be either unidimensional or multidimensional, depending on the topics considered. Unidimensional scales are composed of a single dimension (behavior responses, for example) and can consider one (facial expressions, for example) or multiple domains (facial expressions, body movements and sounds).²⁶ Alternatively, multidimensional scales evaluate two or more pain dimensions (behaviors, physiological responses) and have several domains within each dimension.²⁶

From nine scales validated for critically ill adults, six are unidimensional and three multidimensional.^{26–28} Behavior assessment is the characteristic considered in most of these instruments, once it is the recommended method for pain measurement in subjects unable to self-report.²⁴ The other multidimensional scales are composed of behavior and vital signs data, also based on clinical judgement of nurses or other health professionals.²⁷

Previous scores were determined for each of these scales, with minimum, maximum and cut-off values that indicate the presence or absence of pain. It is important to notice that behavior pain scores based on patient observation should be interpreted differently from self-report. Although both of these measures represent pain scores, observation is associated with behavioral responses exhibited by patients to express their pain, while self-report relates to the sensory dimension of pain which refers to the perception of this sign by the person who is experiencing it.²⁴ It is known that pain intensity scores and behavioral responses are directly proportional, but they are not equivalent.²⁷ For that, only validated and specific instruments must be used for pain assessment in ICUs.

Scale development and validation is a meticulous and rigorous phase of psychometric properties evaluation. The most important of these properties are validity and reliability, which means, respectively, the “conclusions that can be

drawn from the results of a test or scale” and the “overall reproducibility of measures obtained from an assessment tool or scale that can be evaluated”.²⁷ The confirmation of those psychometric properties are necessary once assessment tools are only valid for a specific purpose, in a determined group of respondents and in a given context.²⁴ Because of that, most of the ICU pain scales were tested in different populations and languages, in order to prove their validity and applicability in general situations.²⁴ Description of each scale, population and languages used for validation are shown in Table 1.

Critical-care pain observational tool (CPOT)

CPOT is the most used behavior scale for pain assessment in patients unable to self-report. It was first validated in 2006 by Gélinas et al²⁹ in cardiac surgery patients from Canada.²⁹ This tool includes four behaviors, ie, facial expressions, movements, muscle tension, and ventilator compliance, and can be applied in intubated or non-intubated subjects.²⁹ CPOT was tested and validated in many populations^{30–46} and languages^{47–61} (Table 1), it has many psychometric properties already tested.

Interrater reliability (French version: weighted Kappa 0.52–0.88²⁹; English version: intraclass coefficient [ICC] 0.80–0.93⁵⁰; Spanish version: kappa 0.79 and 1.00,⁶¹ Swedish version: ICC 0.84,⁵⁷ internal consistency (Cronbach α coefficients from 0.31–0.81⁵⁷, sensitivity (67–86% in two different ICU samples,^{33,50} specificity (78–83% in two different ICU samples,^{33,50} feasibility (ICU nurses agreed that it was feasible and quick to use, simple to understand and easy to complete),⁶² criterion and discriminant validity were supported by different studies that confirm the effectiveness of this scale for ICU pain assessment.²⁷

A previous study that performed CPOT implementation as a pain measurement routine in an ICU evidenced a positive influence on pain management (use of analgesics and sedatives) after pain assessment phase.⁶³ In this study, French version of CPOT was applied by nurses for 12 months in ICU population, composed by medical and trauma patients (n=30).⁶³ Medical files were retrospectively analyzed to collect pain measurement and pain management data at three different times: pre-implementation, three months post-implementation and 12 months post-implementation. An increase on reports of pain assessment and on behaviors indicative of the presence of pain was evidenced. Alternatively, there was a decrease in the number of analgesics, propofol and morphine bolus administered after CPOT implementation.⁶³

Table 1 Characteristics of pain assessment tools used in the intensive care unit

Instrument	Score	Population	Language
Critical-care pain observational tool (CPOT) ²⁹	Each domain: 0–2 Total score: 0 (no pain) to 8 (most pain) ²⁹	Cardiac surgery ^{29,30,33,34,38,40,41,43} Non-agitated patients ³¹ Neurosurgery ^{32,45} Brain injury ^{35,36,39} Delirium ^{37,44} Surgical wards ⁴² Burned ⁴⁶	French ²⁹ English ⁵⁰ Turkish ⁴⁷ Chinese ^{48,51,55,56} Polish ^{52,53} Korean ⁵⁴ Swedish ⁵⁷ Finnish ⁵⁸ Dutch ⁵⁹ Italian ⁶⁰ Danish ⁴⁹ Spanish
Behavioral pain scale (BPS) ⁶⁴	Each domain: 1–4 Total score: 3 (no pain) to 12 (most pain) ⁶⁴	Non-intubated ⁷⁵ Traumatic brain injury ^{35,76–78}	French ⁶⁴ English ^{65,74} Chinese ^{68,69} Swedish ⁷⁰ Polish ⁵³ Finnish ⁵⁸ Dutch ⁷³ Portuguese ^{66,67,71} Spanish ⁷²
Behavioral pain assessment tool (BPAT) ⁸³	Eight dichotomized behavior items: present or absent ⁸³	ICU patients of 28 countries ⁸³	12 different languages ⁸³
Escala de conductas indicadoras de dolor (ESCID) ²⁸	Each domain: 0–2 Total score: 0 (no pain); 1–3: mild-moderate pain; 4–6: moderate-severe pain; >6: very intense pain ²⁸	Traumatic brain injury ⁸⁵ Severe trauma ^{84,86}	Spanish ^{28,84–86}
Nonverbal pain assessment tool (NPAT) ⁸⁷	Each domain: 0–2 Total score: 0 (no pain) – 10 (most pain) ⁸⁷	Cardiothoracic surgery, cardiology, medical and surgical patients ⁸⁷	English ⁸⁷
Nonverbal pain scale (NVPS) ⁸⁸	Each domain: 0–2 Total score: 0 (no pain) to 10 (most pain) ⁸⁸	Trauma ^{45,88,90–92} Surgery ^{80,88,90,92} Burned ⁸⁸ Cardiac surgery ⁴¹ Neurological ^{91,92} Surgical ^{93,94}	English ⁸⁸ Iranian ⁹² Finnish ⁵⁸
Behavioral pain rating scale (BPRS) ⁹³	Each domain: 0–3 Total score: 0 (no pain) to 12 (most pain) ⁹³	Surgical ^{93,94}	English ⁹³
Pain assessment and intervention notation (PAIN) algorithm ⁹⁵	Total score: 0 (no pain) to 10 (most pain) ⁹⁵	Surgical ⁹⁵	English ⁹⁵
Face, legs, activity, cry, consolability (FLACC) ⁹⁷	Each item: 0–2 Total score: 0 (no pain) to 10 (most pain) ⁹⁷	Surgical ^{97,98} Neurological ^{97,98} Cardiac surgery ⁴¹	English ⁹⁷
Multidimensional objective pain assessment tool (MOPAT) ^{100,101}	Behavioral dimension: 0 (none) to 3 (severe) Physiologic dimension: 0 (no change) or 1 (change) ^{100,101}	Medical patients ¹⁰¹	English ¹⁰¹

Despite its advantages, CPOT also has limitations. It is highlighted that traumatic brain injured patients present different facial expressions compared to other patients when exposed to nociceptive procedures; because of that, more studies are required to validate its use in this ICU population.²⁷ In addition, the complex interpretation of the scores and the training to use this instrument is also reported as difficult. Despite these limitations, CPOT is considered a well-designed behavioral tool for use with nonverbal critically ill subjects.

Behavioral pain scale (BPS)

BPS is the second most used pain scale in ICUs. It evaluates three behavioral domains (facial expressions, movement of upper limbs, and compliance with ventilation)⁶⁴ and it is valid in different languages^{53,58,64–74} and samples^{35,75–78} (Table 1). Psychometric properties, as internal consistency (Cronbach α coefficient ranged from 0.63 to 0.72,^{65,74,79,80}) interrater reliability (Kappa coefficient ranged from 0.67–0.83^{64,79,81} and ICC of 0.95,⁶⁵) sensitivity, specificity, criterion and

discriminant validity (significant increases of 2–3 points in BPS scores following nociceptive procedures^{64,65,69,74,79,80}) were supported previously and confirm the advantages of BPS use, including frequency of pain assessments and patient's positive outcomes.^{64,65,74,82}

BPS implementation in ICUs resulted in improvements for pain management and patients outcomes. Some items can be interpreted in a different way by users, which consists as a limitation in the practice.²⁷ As an example of confounders, the items “movement of upper limbs” can be confused with muscle tension, and “compliance with ventilator” is defined by professionals as the less clear item described in this scale.²⁶

Behavioral pain assessment tool (BPAT)

BPAT is a new instrument created in 2017 by Gélinas et al and validated in 28 countries.⁸³ While other scales as CPOT requires interpretation of scores that is more complex than identifying when behaviors are present or absent, BPAT was created for use in a multinational study of procedural pain in ICU patients.⁸³ It is an eight-item scale composed of names and descriptions of facial expressions (accompanied by a picture), verbal responses (moaning and verbal complaints of pain) and body muscle responses (rigidity and clenched fists). These behavior items are dichotomized, that is, “present” or “absent” are possible answers to provide an easy and viable use for clinicians.⁸³

In this validation study, interrater reliability (Kappa coefficients from 0.43–0.60), discriminant, criterion and convergent validity, sensitivity and specificity (61.8–75.1%) were assessed.⁸³ Unlike other scales such as BPS and CPOT, BPAT does not have an item related to compliance with mechanical ventilation, which can be considered an advantage, once this is a confounder item. Authors who developed this instrument describe the necessity of further tests for different ICU patients groups for further validation in daily ICU practice.⁸³

Escala de conductas indicadoras de dolor (ESCID) Behavioural Indicators of Pain Scale

ESCID is a Spanish instrument created and validated to assess pain in critically ill, nonverbal and mechanically ventilated patients.²⁸ Four items are considered in this scale: facial muscles (“*musculatura facial*”/“*facial expression*”), tranquility (“*tranquilidad*”/“*calmness*”), muscle tone (“*tono muscular*”/“*muscle tone*”), adaptation to mechanical ventilation (“*adaptación a ventilación mecánica*”/“*compliance with mechanical ventilation*”) and comfort (“*confortabilidad*”/“*Consolability*”), scored from 0–2.²⁸

Reliability (Cronbach α ranged from 0.70 to 0.80) and validity (good correlation between BPS and ESCID scores – Pearson correlation from 0.94–0.97) were tested first in a general ICU²⁸ and later in different sample, as severe trauma and brain injury patients.^{84–86} ESCID is a valid and applicable instrument,²⁸ it is available only in Spanish, which is a limitation for clinicians in other countries with different languages. In addition to that limitation, authors recommend that ESCID should be tested in other situations such as painful and nonpainful procedures.²⁸

Nonverbal pain assessment tool (NPAT)

NPAT was developed by Klein et al in 2010, based on behaviors commonly observed in ICU daily practice.⁸⁷ Five categories are assessed by this tool: emotion (affective response to a situation), movement (change in the placement and positioning of the body and extremities when not engaged in any care activities), verbal cues (sound cues or vocalizations from the patient other than speech), facial cues (facial expressions) and positioning/guarding (body responses that imply a protection of the body from contact with external touch).⁸⁷

Some limitations are reported about this three-phase study conducted to validate this scale: (1) no information was provided about the occasions when pain was assessed; (2) the third study phase was conducted with a different sample; and (3) low correlation coefficients were found between NPAT scores and self-reports of pain intensity.²⁷ These limitations suggest that more studies are necessary to prove NPAT validity and its applicability in ICUs.

Nonverbal pain scale (NVPS)

NVPS is a multidimensional instrument, initially modified from face, legs, activity, cry, consolability (FLACC) scale (NVPS-I) by Odhner et al in 2003⁸⁸ and later revised (NVPS-R).²⁷ It is composed of three behavioral (face, activity/movement, and guarding) and two physiological indicators (Physiologic I – blood pressure, heart rate, respiratory rate and Physiologic II – skin temperature, pupil dilation, perspiration, flushing, pallor).⁸⁸

Interrater agreement and discriminant validity of NVPS were supported in previous studies.^{80,89,90} It is also known that after NVPS implementation in a critical care setting, patients' ratings of their pain experiences, documentation by nurses, and nurses' increased confidence in assessing pain in nonverbal patients were improved.⁹¹ Good applicability and validity (Cronbach α coefficients ranged from 0.36–0.75 and ICC ranged from 0.60–0.76) in different samples^{41,45,48,80,88,90,91} and languages^{58,88,92} encourages use of NVPS in clinical practice.

Pain assessment and intervention notation (PAIN) algorithm

PAIN algorithm is a multidimensional instrument developed to be tested by critical care nurses.⁹⁵ It is divided into three parts: (1) pain assessment (presence or absence of six behavioral domains – facial expression, movement, posture, vocal sounds, pallor and perspiration – and three physiologic indicators – heart rate, blood pressure, respiration); (2) assessment of patient's ability to tolerate opioids; and (3) guidelines for analgesic treatment decisions and documentation.^{26,95}

As a multidimensional instrument, PAIN algorithm appears to be more than a single pain scale; it can be considered as a pain management educational tool.²⁷ Despite psychometric properties as content and convergent validity were tested in this instrument, other properties were not previously reported, including internal consistency, interrater reliability and construct validity.^{26,27} Besides this weakness, the length of PAIN algorithm and the use of non-standardized assessment method based only on nurses' judgement and experience limits the use of this tool in clinical practice.^{26,27}

Face, legs, activity, cry, consolability (FLACC)

FLACC scale is a unidimensional instrument largely used in pediatric population with cognitive impairment, developed in 1997 by Merkel et al.⁹⁶ In critically ill adults, FLACC validity was tested by Voepel-Lewis et al in a recent study,⁹⁷ which showed a good interrater reliability (ICC ranged from 0.72 to 0.98), internal consistency (Cronbach $\alpha=0.882$), criterion and construct validity.⁹⁷ Previously, FLACC was used in comparison to other pain assessment instruments and was tested in different samples.^{41,98}

Each item named in this scale (Face, Legs, Activity, Cry, Consolability) is rated from 0 to 2, with a maximum possible score of 10 points.⁹⁶ In the ICU adult sample, the "cry" category presented poor correlation with other categories and consequently lowered the internal consistency of this tool,⁹⁷ suggesting that this item may not be relevant for adult patients.²⁷ From that, it is suggested that the "cry item" should be modified in this scale, as occurred in FLACC in pediatrics.⁹⁹ Despite the good results on psychometric analysis, further studies are necessary to establish FLACC reliability and validity for use in adult ICU patients.²⁷

Multidimensional objective pain assessment tool (MOPAT)

MOPAT is a multidimensional scale developed and firstly validated to nonresponsive hospice patients in 2011 by McGuire et al.¹⁰⁰ This instrument is composed of two

subscales or dimensions (behavioral and physiological). The behavioral dimension has four indicators of acute pain (restless, tense muscles, frowning/grimacing, patient sounds), which are rated from 0 (none) to 3 (severe). The physiologic dimension has also four indicators (blood pressure, heart rate, respirations and diaphoresis), which are rated as 0 (no change) or 1 (change), according to patients' usual values of these physiologic indicators.^{100,101}

Recently, MOPAT psychometric properties were tested in critically ill patients from a medical ICU.¹⁰¹ For reliability, internal consistency was considered moderate in this sample and interrater reliability agreement was reasonable for both dimensions and for total score.¹⁰¹ Validity results suggest that MOPAT is sensitive to measure acute pain in noncommunicative patients and that it is a quick and easy to use instrument.¹⁰¹

These results are based on a single study performed with a small sample. Due to that, studies with a larger ICU sample could improve psychometric properties' values and consolidate MOPAT use in practice.

Vital signs

The use of vital signs, blood pressure (BP), heart rate (HR) and respiratory rate (RR), by nurses in ICUs is a common practice due to the easy access through continuous monitoring.¹⁰² In a previous validity test of this pain assessment method for mechanically ventilated patients, a discriminant validity was supported, once there was higher HR and BP during a painful procedure (suctioning) than before and after this same or a non-nociceptive procedure.¹⁰³ However, this same study concluded that there was no significant correlation between patients' self-report of pain intensity and HR and BP values,¹⁰³ which instigates the research about the real validity of this method.

Vital signs validity as a pain assessment method is not supported by previous studies,^{3,102} since it is considered an unstable measure. It means that vital signs can increase, decrease or remain stable in ICU patients depending on their clinical condition.^{3,102} In addition, it is also proved that changes in physiological parameters can be caused by fear, anxiety and other psychological stressors¹⁰² or can be suppressed by analgesia.¹⁰⁴ Because of these multifactorial causes of change, this is not a reliable pain measure.

This validity weakness was evidenced in many ICU samples, such as cardiac,¹⁰⁵ brain¹⁰⁶ and general post-surgical¹⁰⁷ patients. In all these studies, vital signs were not recommended as a valid measure, once they do not predict the presence of pain. Considering this poor evidence about vital signs utility for pain assessment, it should be used with caution,¹⁰² associated with objective measures (behavioral

scales) for complete and reliable information about patient's pain intensity.

Bispectral index (BIS)

Brain activity in different cortical areas during pain and nociception integration can be measured by a specific technique named bispectral index (BIS).¹⁰⁸ It consists of a noninvasive technology that provides, by the use of electrodes placed on the frontal and temporal areas, a cortical activity value that ranges from 0 (no cortical activity) to 100 (completely awake).¹⁰⁹ This value (BIS) is calculated from a proprietary algorithm that interprets cortical activity (electroencephalography, EEG) and corrugator supercilii muscle activity (electromyography, EMG).¹⁰⁹

The use of BIS for pain assessment has been studied in ICUs and surgery rooms.¹⁰⁹ In mechanically ventilated patients, an increase in BIS value was evidenced during routine nociceptive procedures,^{110–113} such as endotracheal suctioning and mobilization, that can be reversed by opioids, neuromuscular blocking agents and sedative effects.^{110–112}

This method appears promising due to its precision and technological value. However, BIS index was not primarily developed to measure pain,²⁴ which implies in a lack of validated application method and standard values for ICU population. From that, it is suggested that further research with larger samples is needed to confirm BIS index clinical utility in ICUs.²⁴

Pupillary reflex/pupillometry

The pupillary dilatation reflex (PDR) is known as a sympathetic reflex that dilates the pupil in response to noxious stimuli.¹¹⁴ Due to the autonomic nervous system influence on pain, pupillary responses have been studied as a method to detect its sign.¹¹⁵ It has been proposed as an alternative instrument for pain assessment during anesthesia for surgery or out of the surgery room.^{112,116–118}

High sensitivity, specificity and positive correlation between pupillometry and pain scores were demonstrated in postoperative patients.¹¹⁶ Other studies show that PDR can predict quality of analgesia before procedural pain in ICU.¹¹⁷ However, PDR is not specific for pain and some conditions, as fear and anxiety, can confound results and should be considered during assessment.¹⁰² Future research is encouraged to describe specific conditions to use PDR with nonverbal ICU patients.¹⁰²

Skin conductance

Palmar sweat gland activation is known as a physiological response to an increase on sympathetic nervous system

activity due to emotional stress.¹¹⁹ This response also occurs when nociceptive stimulation is performed in the organism, resulting in an increased number of skin conductance fluctuations (NSCF).^{119,120}

In order to measure this ongoing palmar sweat gland activation in response to pain (or emotional stress), a monitor and electrodes placed on the palmar surface of patient's hand are used.¹²¹ In ICUs, this procedure is reported in a previous study¹²¹ as a pain assessment method. It was evidenced that in critically ill intubated patients NSCF values increased during painful stimulation.¹²¹ However, NSCF data were not associated with pain behaviors and facial expressions in these patients,¹²¹ which is a weakness on validity for this method.

A recent study performed in a postsurgical ICU evidenced that skin conductance analgesimeter index (SCAI) and hemodynamic variables (BP and HR) significantly increased during painful procedures.¹²² A negative and significant correlation between SCAI and sedation level (Ramsay scale scores), was also observed which means that the higher the sedation level, the lower is the ability to express painful behaviors.¹²² Based on these results, authors defined that skin conductance analgesimeter has good properties for detecting pain in critically ill subjects.¹²²

The fact that sympathetic nervous system can be altered by many factors limits the reliability of skin conductance as an isolated pain assessment method. While it is still a new assessment instrument, more evidence is needed to be well established in the clinical practice.

Discussion

This review emphasizes the use of validated and standardized instruments for pain assessment in mechanically ventilated patients. It is shown that behavioral scales are the most commonly used methods, followed by observation of vital signs. This last one is known as an unreliable procedure, as pain is not the only phenomena that can alter physiologic parameters.

In a recent perspective, new technological trends have been used for pain intensity measurement in ICUs that include pupillometry, BIS index and skin conductance analysis. Besides these advances, these instruments demand new research to confirm their validity and applicability in practice.

Previous reviews^{24,102,123} also describe these assessment methods as the best practice for pain evaluation in ICUs. Objective pain behavior scales, vital signs and BIS analysis were first cited in the last two decades¹²³ as good techniques for pain and sedation assessment, with further studies necessary to prove their efficacy. In recent reviews,^{24,102} these

instruments are well described, with details about psychometric properties, applicability, strengths and weaknesses of each item. This approach stimulates clinical use and knowledge application in the clinical practice, which is the aim of this review.

Specifically, reviews were previously published as a guide for clinicians and researchers with the main topics about behavioral scales.^{26,27,124–126} These studies reinforce the importance of their pain assessment tools and their use by nurses and other health professionals in ICUs. In addition to those reviews, a guideline written by Barr et al (2013)³ also demonstrates pain assessment and management strategies for critically ill patients, with emphasis on the clinical applicability and professionals' consciousness about pain measurement. Based on that, the present review also shows the importance of this review by the description of validated and standard tools.

An important point elucidated in this review is the low number of pain assessment methods for critically ill adults in comparison to other ICU population, such as neonatal and pediatric ventilated patients. Over 40 methods for assessing pain in infants are available,¹²⁷ while only 13 tools are known for adult subjects. Many studies with a summary of pain in neonatal and pediatric ICUs are published,^{128–131} while published data for adults is scarce.^{24,102}

This discrepancy can be justified by the high concern about pain in early life, once it is already evidenced that newborns and infants do not have descending inhibitory pathways developed, that is, endogenous pain control is not well established during childhood.¹³² Additionally, it is proved that infants are 30–50% more sensitive to pain than adults and have lower pain tolerance than older children.¹³³ Another fact that justifies the major attention to pain in this population consists in the cognitive inability to express pain, that is accentuated by a clinical condition, as mechanical ventilation, that limits body expressions. These facts can explain the reduced number of pain assessment tool for adults, but do not justify this lack in the literature.

The scarcity of studies about this theme in adults is accompanied by the difficulty to establish a pain assessment routine in ICU. A recently published qualitative study¹³⁴ analyzes the challenges faced by nurses when using pain assessment scales for patients unable to communicate. Difficulties reported in this study were “forgotten priority”, “organizational barriers”, “attitudinal barriers” and “barriers to knowledge”,¹³⁴ which represents internal (personal) and external (daily routine) reasons for a low quality pain evaluation.

Despite its widespread use, there are still some barriers for the use of behavioral scales in ICUs, such as the lack of

knowledge, skepticism regarding the evidence or benefit, a nonintuitive result or the perception that positive points observed in previous studies are not generalizable to local practice.¹³⁵ From this perspective, studies that summarize pain assessment techniques are useful to stimulate their use in the clinical setting. Because of that, reviews like this one are necessary to improve health professionals' knowledge and affinity with this theme.

Pain treatment is strongly associated to pain assessment. The measurement of pain signs (behaviors, hemodynamic parameters and others) is recommended to establish appropriate analgesia intervention.³ This is encouraged as a routine practice³ to be performed by all ICU professionals, particularly those who directly assist patients (clinicians, nurses, physical therapists).

Gold standard pain assessment tools (behavioral scales) and new trends for pain measurement in mechanically ventilated patients (pupillometry, skin conductance and BIS index) were identified and described in this study. This review encourages research to develop studies about pain measurement in mechanically ventilated patients to improve scientific evidence about this theme. Moreover, the present review aims to stimulate evidence-based practice in ICUs, promoting pain assessment as the fifth vital sign and, as consequence, improving analgo-sedation routine.

Conclusion

This review showed that objective measures, such as behavioral scales, are the most commonly used in adults unable to self-report their pain. Vital signs recording is not recommended as a reliable technique, since not only pain can change these parameters. Pupillometry, skin conductance and BIS index are new trends which have been studied for use in ICUs, which need to be established as valid and reliable methods. Data from this review emphasizes the importance of pain measurement in mechanically ventilated patients and its consequences for an adequate pain management in ICUs.

Disclosure

The authors report no conflicts of interest in this work.

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