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COMMENTS TO RESEARCH ARTICLES

Clinical Practice Guidelines of the American College of Critical Care Medicine for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients☆

Guía de práctica clínica del American College of Critical Care Medicine sobre prevención y manejo del dolor, agitación/sedación, contenciones mecánicas, delirio, inmovilidad y alteraciones del sueño del paciente adulto

Devlin JW, Skrobik Y, Gélinas C, Needham DM, Slooter AJC, Pandharipande PP, et al. Clinical Practice Guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. Crit Care Med. 2018;46(9):e825–e873. doi: 10.1097/CCM.0000000000003299.

Abstract

Objective: To update and expand the 2013 Clinical Practice Guidelines for the management of pain, agitation, and delirium in adult patients in the ICU.

Design: Thirty-two international experts, four methodologists, and four critical illness survivors met virtually at least monthly. All section groups gathered face-to-face at annual Society of Critical Care Medicine congresses; virtual connections included those unable to attend. A formal conflict of interest policy was developed a priori and enforced throughout the process. Teleconferences and electronic discussions among subgroups and whole panel were part of the guidelines' development. A general content review was completed face-to-face by all panel members in January 2017.

Methods: Content experts, methodologists, and ICU survivors were represented in each of the five sections of the guidelines: Pain, Agitation/sedation, Delirium, Immobility (mobilisation/rehabilitation), and Sleep (disruption). Each section created Population, Intervention, Comparison, and Outcome, and nonactionable, descriptive questions based on perceived clinical relevance. The guideline group then voted their ranking, and patients prioritised their importance. For each Population, Intervention, Comparison, and Outcome question, sections searched the best available evidence, determined its quality, and formulated recommendations as ''strong,'' ''conditional,'' or ''good'' practice statements based on Grading of Recommendations Assessment, Development and Evaluation principles. In addition, evidence gaps and clinical caveats were explicitly identified.

Results: The Pain, Agitation/sedation, Delirium, Immobility (mobilisation/rehabilitation), and Sleep (disruption) panel issued 37 recommendations (three strong and 34 conditional), two good practice statements, and 32 ungraded, nonactionable statements. Three questions from the patient-centred prioritised question list remained without recommendation.

Conclusions: We found substantial agreement among a large, interdisciplinary cohort of international experts regarding evidence supporting recommendations, and the remaining literature gaps in the assessment, prevention, and treatment of Pain, Agitation/sedation, Delirium, Immobility (mobilisation/rehabilitation), and

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Sleep (disruption) in critically ill adults. Highlighting this evidence and the research needs will improve Pain, Agitation/sedation, Delirium, Immobility (mobilisation/rehabilitation), and Sleep (disruption) management and provide the foundation for improved outcomes and science in this vulnerable population.

Pain

Pain is a cause of great concern among Intensive Care professionals. However, critically-ill patients are still experiencing pain despite attempts to effectively control the physical and emotional aspects that accompany it.

Current guidelines, compared to those published earlier (2013), highlight the most painful procedures and how pain caused by the procedures is influenced by initial pain at rest. Hence their emphasis on the importance of regular and systematic, protocolised assessment before procedures are carried out using appropriate tools to ensure optimal pain management. To that end, they continue to recommend the Behavioral Pain Scale (BPS) and the Critical-Care Pain Observation Tool (CPOT) as the most valid and reliable tools for assessing the behaviour of intubated patients who are unable to communicate verbally. The current guidelines now include the Behavioral Pain Scale-Nonintubated (BPS-NI) for non-intubated patients who are unable to communicate verbally. The verbal or visual numerical rating scale (NRS/VRS) 0–10 is still recommended for patients who are able to communicate. These guidelines have not included the *Escala de Conductas Indicadoras de dolor* (ESCID) (Behavioural Indicators of Pain Scale), which is a tool created and validated in Spain, and which has good psychometric properties for assessing pain in mechanically ventilated patients unable to self report.[1,2] However, more evidence is necessary to support the use of this scale.

These guidelines describe the use of pain assessment tools for other populations, such as patients with brain injuries. The results, although these are studies with small samples, suggest that the expression of pain behaviours is related to level of consciousness.

Furthermore, the guidelines recommend possessing all the necessary information on risk factors at rest and during procedures. They highlight anxiety, depression and socio-demographic factors, being young and having undergone previous surgery, as predictors of more pain at rest, as well as sex (being female) and ethnicity (being Caucasian) as factors associated with more pain during procedures.

According to the authors, future research studies should continue to explore the socio-demographic variables and biomarkers that are associated with inadequate analgesic responses, the effect of non-pharmacological measures such as massage, cold, music therapy or relaxation, and the development of new objective measures such as pupillometry.

Agitation/sedation

Sedation is routine practice in ICU and enables the alleviation of anxiety and stress for critical patients, facilitating care and the use of vital support measures. However it is not free from complications that can increase morbidity. Therefore, it is compulsory to monitor levels of sedation and how they adapt to the clinical situation of the patient.[3–5]

These new clinical guidelines basically cover three aspects:

1. The recommendation for light sedation (LS) compared to deep sedation for critically-ill adult patients undergoing mechanical ventilation, although the quality of available evidence is low[6,7] due to the lack of consensus on the definition of LS. Although what a deeply sedated patient is and in which situations this level of sedation is indicated seem to be clear, there is no consensus as to the different levels of sedation. This discrepancy might have a negative impact when promoting LS for most critically-ill patients, as recommended in these guidelines.
2. The use of daily sedation interruption (DSI) or nurse-led protocols as safe practices with no differences between them, to achieve and manage a level of LS. Both appear to be associated with better clinical outcomes, as they facilitate weaning and early mobilisation. Here, the nurse, being at the bedside, is crucial in evaluating and managing sedation. However, DSI seems to be associated with a greater workload.[8] Therefore it is likely that the work model, the organisation and the nurse/patient ratio in our ICUs would adapt better to nurse-led analgesia and sedation protocols.
3. The use of the Bispectral Index (BIS) to monitor patients under deep sedation or neuromuscular block. This instrument enables us to be aware of brain activity below the deepest level of sedation indicated by the scales. However, for patients who are awake it does not discriminate between different levels of agitation. Therefore, it cannot substitute the use of scales for these types of patients.

The current scientific literature reflects the great variability in sedation management. Therefore further research studies are required that examine the impact of levels of sedation on patient outcomes, as well as the effect that stimulation performed during assessment by the scales and the different pathologies (neurocritical patients) could have on the real objectivity of the assessment tools.

Mechanical restraints

These recommendations set out explicitly and for the first time, a critical review of the use of mechanical restraints (MR) for critically-ill patients and correlate it with aspects such as pain, agitation and delirium. Acknowledging the high prevalence of MC used for patients who are critically ill and the wide variability of their use between countries, the authors highlight that, although ICU professionals generally justify the use of MC for reasons of safety, such as preventing self-removal of devices, there is currently a notable lack of evidence in this regard. Particularly striking is the absence of studies that demonstrate the effectiveness and safety of the use of MC, which might even increase self-extubation, increase agitation, delirium or length of stay in ICU.[9,10]

In an age of patient-focussed care, the use of MR seems increasingly controversial from the perspective of care excellence and the effects of their use; which might not be restricted to admission alone but extend beyond discharge, giving rise to strong emotional responses in patients who have been subjected to MR.

The authors conclude that, given the high prevalence and unintentional consequences of their use and the perceptions of patients who have been subjected to MR, ICU professionals should carefully weigh up the advantages and disadvantages of their use in each case. We also highlight that some countries have MR-free ICUs possibly due to better drug management and/or accompaniment of the patient at the bedside.

We suggest future research lines that highlight the assessment of the effectiveness of various interventions to reduce the use of MR or recommend the use of randomised clinical trials to assess relevant outcome indicators in relation to the use of MR.

Delirium

The current guidelines show that delirium in critically-ill adults is NOT associated with posttraumatic stress disorder[11] or anxiety after discharge from ICU (2 B). Although it is a distressing experience for patients, their families and staff, the guidelines suggest using strategies to improve information/training on delirium, its aetiology and consequences in order to alleviate it.

Monitoring and early detection can lead to prompt identification and correction of the aetiology thus improving patient safety. Therefore, it is advised that the risk of developing delirium in the ICU in the 24 h after admission is established using a scale such as PRE-DELIRIC[12] or similar (level of evidence 2 B). The authors make specific grade B recommendations for daily monitoring of the condition:

The CAM-ICU and ICDSC are still the recommended instruments. Despite the complexity and great variability of studies, the systematic use of the CAM-ICU is significantly associated with a shorter duration of delirium, over fewer nursing shifts therefore, compared to unstructured evaluations.

They suggest the use of the ICDSC to detect subsyndromal delirium since a critical patient who develops this type of subsyndromal delirium, compared to one who develops neither delirium nor a subsyndrome, is more likely to die in ICU, be hospitalised for longer and be transferred to a rehabilitation centre.

Moreover, the severity of delirium is associated with poorer outcomes for patients and they suggest a new validated tool (UCI-7)[13] that enables it to be documented opening future lines of research.

There is 2 B level of evidence on the risk factors of delirium, which indicates that:

The use of benzodiazepines and blood transfusions are the only modifiable factors associated with delirium.

The non-modifiable risk factors include increased age, dementia, prior coma, emergency surgery or trauma before ICU admission and increased APACHE and ASA scores.

Sex, the use of opiates and mechanical ventilation DO NOT ALTER the risk of delirium onset.

Multicomponent intervention studies,[14] focussing on the approach to cognitive impairment (reorientation, cognitive stimulation, music therapy, use of clocks, ...); sedation/sleep (reduced sedation minimising light and noise); immobility (early mobilisation); and hearing and sight disability (use of hearing aids and glasses) significantly reduced delirium with a level of evidence 1B/A.

Rehabilitation and mobilisation

Rehabilitation/mobilisation, understood in these guidelines as prompt and active intervention, has been the focus of numerous scientific studies in the last decade having been postulated as a safe and effective strategy to prevent ICU-acquired muscle weakness.

Compared with their former version (2013), the current guidelines have studied rehabilitation/mobilisation specifically and not as a subject linked to delirium management. To that end, studies have been included that compare rehabilitation/mobilisation (early and active) with conventional rehabilitation/mobilisation (passive and/or late), as well as interventions of less frequency or duration. The variables chosen to evaluate its efficacy were muscle strength on discharge from ICU, mechanical ventilation time, health-related quality of life, hospital mortality, and physical function.

Although it was not possible to make specific recommendations, due to the disparity between the types of intervention and/or the initiation periods studied, we detail below the conclusions on rehabilitation/mobilisation:

1. Rehabilitation/mobilisation is recommended for adult critically-ill patients (conditional recommendation, low quality evidence). In a total of 16 randomised controlled studies (RCS), rehabilitation/mobilisation was associated with significant improvement in muscle strength on discharge from ICU and a reduction in mechanical ventilation time, as well as moderate improvement (not significant) in health-related quality of life. By contrast, no significant effects were found on physical function short term or hospital mortality. It is important to stress, as flagged up by the authors, that due to the little benefit demonstrated and the low level of quality of evidence, the panel of experts made this recommendation weighing up the possible benefits of the intervention against its undesirable consequences. Furthermore, its implementation is influenced by aspects that determine its viability such as the availability of appropriate resources and/or staff.
2. Rehabilitation/mobilisation is rarely associated with major adverse events, defined as physiological change or damage that requires intervention (declaration without classification). Only 15 events were described for more than 12,000 sessions in 13 studies (5 RCS and 8 observational studies).
3. The opinion of the panel of experts established a set of specific safety criteria for starting or stopping rehabilitation/mobilisation (both in and out of bed) based on 17 studies including 2774 patients or 14 studies including 2617 patients, respectively. However, the authors declare (recommendation without classification) that the

main indicators of the safety of the intervention are cardiovascular, respiratory and neurological stability.

Sleep disturbances

Sleep in critically-ill patients is characterised as being fragmented, with increased light sleep stages (stages N1 + N2) and reduced deep sleep (stages N3 and REM). In general, although total sleep time and efficacy are occasionally normal in critical patients' daytime sleep time increases to the detriment of night-time sleep and perceived quality of sleep. Even assuming the lack of evidence in this regard, it seems that these effects worsen in patients undergoing mechanical ventilation or those with delirium.

The prevalence of patients with unusual or dissociative sleep patterns is very variable and can be determined, among other things, by the pattern and quality of their sleep prior to admission to ICU or the use of drugs to help them sleep at home. Moreover, issues such as pain, nursing care performed at night, psychological and respiratory factors, and specific drugs can affect the quality of sleep in ICU. Although studies suggest an association between sleep quality and delirium, a cause-effect relationship has not yet been established.

These guidelines do not recommend routine physiological monitoring of sleep, however, they do emphasise the need to systematically ask patients about their sleep quality or use tools such as the Richard-Campbell Sleep Questionnaire, validated for alert and orientated patients admitted to ICU. Moreover, the tendency for professionals at the bedside to overestimate patients' total sleep time is underlined.

The use of controlled ventilation modes during the night and the reduction of light and noise (masks and earplugs) are suggested among the non-pharmacological interventions to improve patients' sleep. However, aromatherapy, acupressure or music are not recommended during the night. The authors make no recommendation for using melatonin or dexmedetomidine as pharmacological strategies, but they do recommend that propofol should NOT be used as a strategy to promote sleep (conditional recommendation, low quality of evidence). In any case it is recommended that all means should be included in a protocol to promote sleep.[14]

The introduction of a section devoted to sleep is again a novelty in these guidelines, and although it is recognised that its importance has not yet been demonstrated through randomised clinical trials, it seems intuitive to assign it an important role, at least as a measure to promote comfort that could improve patients' quality of life.

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