Enfermería Intensiva 32 (2021) 57–61

SEEIUC
Sociedad Española de Enfermería Intensiva y Unidades Coronarias

Enfermería *Intensiva*

www.elsevier.es/ei

EDITORIAL

Future lines of research on pain care, sedation, restraints and delirium in the critically ill patient☆

Futuras líneas de investigación en cuidados sobre dolor, sedación, contenciones y delirium en el paciente crítico

The assessment and management of pain–analgesia, agitation–sedation, mechanical restraints (MR) and delirium in the critically ill patient has evolved in recent years, as stated in the recommendations of the clinical practice guidelines (CPG).[1] However, questions remain pending, which nurses may research, highlighting the effect that care may have on nursing-practice-sensitive health outcomes. Below is a proposal of twelve research lines in care for guiding future projects on pain, sedation, MR and delirium.

Pain assessment and management

1. - Pain assessment and management in specific population groups

The most valid and reliable scales for assessing pain in critically ill non-communicative patients are the Behavioural Pain Scale (BPS) and the Critical-Care Pain Observation Tool (CPOT).[1] In Spain, since the year 2010, the Behavioural Indicators of Pain Scale (ESCID for its initials in Spanish), have proven to be a valid and reliable tool for pain assessment of critically ill, non-communicative patients, whose motor functions are preserved and who have been subjected to mechanical ventilation (MV).[2] However, the psychometric properties of these tools in the assessment of pain in groups of specific patients, such as the patient with brain damage and a low level of awareness have not been widely researched. Recently, López-López et al.[3] showed that the ESCID scale detects pain behaviour patterns and is capable of discriminating between different types of stimulation in patients with brain damage, who are non-communicative and with MV. Notwithstanding, they also observed behavioural patterns which did not include any behaviour scale and whose level of awareness had a direct impact on the ESCID scale score. Another limitation of these tools is that they are inadequate for assessing pain in patients without behavioural indicators (RASS of $\leq$-4, or with muscle relaxation). In these patients the use of objective indicators of pain assessment is suggested, such as variation in the value of the Biespectral index (BIS), the (AlgiScan®) pupilometry, the Analgesia Nociception Index or the near infrared spectroscopy (NIRS). Pain assessment and management in these population groups are two current research lines where on the one hand, further validation studies are required in the use of behavioural scales in neurocritical patients and on the other, diagnostic test studies or randomised clinical trials (RCT) are required which evaluate whether the physiological variables in response to nociceptive stimuli are valid and reliable tests for pain assessment in patients without any behavioural indicators.[4]

2.- Assessment of the emotional experience of pain prior to painful procedures

The painful experience encompasses the objective assessment of the intensity of pain, and also the emotional experience derived from the discomfort which pain produces. Patients remember the pain caused by procedures, such as the introduction of arterial catheters, wound curing, secretion aspiration, extubation or the removal of drainage. The Behavioural Pain Assessment Tool (BPAT)[5] which has been validated in 28 countries, assesses both the intensity and the discomfort of painful procedures. Future studies should research the sensitivity and specificity of this tool in the assessment of pain in different cohorts of critically ill patients and to different painful procedures, as well as exploring from a qualitative focus what the emotional expe-

DOI of original article: https://doi.org/10.1016/j.enfi.2021.04.001

☆ Please cite this article as: Via-Clavero G, Frade-Mera MJ, Alonso-Crespo D, Castanera-Duro A, Gil-Castillejos D, Vallés-Fructuoso O, et al. Futuras líneas de investigación en cuidados sobre dolor, sedación, contenciones y delirium en el paciente crítico. Enferm Intensiva. 2021;32:57–61.

rience of procedural pain is and its consequences in critically ill patients.

3. - The use of assessment algorithms and pain management

Pain should be prevented and treated with multimodal analgesia,[1,6] which is the combination of two or more drugs or analgesic techniques, aimed at reducing the complications derived from the administrating of opioids, such as delirium, respiratory depression, ileums, immunosuppression, opioids detoxification syndrome or opioids-induced hyperalgesia. The use of evidence-based algorithms for increasing pain assessment and management by nurses is an alternative which may help to systematise their evaluation and reduce their use of analgesics. Future studies should assess nurses' adherence to these algorithms,[7] their reliability, what their qualitative perception and assessment is, their association with the use of drugs and their effectiveness in the incidence of agitation, delirium, early mobility and the appearance of post-traumatic stress from systematic reviews.

4. - Non-pharmacological measures for the treatment of procedural and non-procedural pain

The 2018 guide for pain management, agitation/sedation, delirium, immobility and sleep or the English PADIS guidelines for Pain, Agitation/sedation, Delirium, Immobility (rehabilitation/mobilization), and Sleep (disruption) suggest the use of non-pharmacological measures such as massage, cold therapy or music therapy to relieve both procedural and non-procedural pain.[1] However, for these actions a conditional recommendation is obtained with low evidence quality, and future lines of investigation should aim at evaluating the effectiveness and real impact of these measures in pain management, with an intervention study design and RCT.

Sedation assessment and management

5. - Impact of early, mild sedation

The latest CPG recommend the use of mild and dynamic sedation, appropriate for the medical condition of the patient, to reduce anxiety, allow rest and keep the patient in a calm, comfortable and cooperative state.[1–9] Deep sedation is reserved for patients in severe respiratory distress, with intracranial hypertension, active epileptic status or neuromuscular block. However, there is no clear consensus regarding what is considered mild sedation due to the high variety in the scales of sedation level measurement. The most highly recommended scale and with the best psychometric properties for assessing sedation-agitation in critically ill patients is the Richmond Agitation Sedation Scale (RASS). The American guidelines define mild sedation as a RASS $\geq$-2 score, but acknowledge that a RASS of -2 may be a deeper level of sedation than required for the management of an adult ventilated patient.[1] For their part German[8] and Spanish [9] recommendations consider mild sedation as a RASS of -1 and 0. Early mild sedation seems to be associated with the best outcomes in critically ill patients as it facilitates ventilator removal and shortens MV times, as well as early mobilization and rehabilitation. These result in a reduction in ICU and hospital stay [1,10]. However, its beneficial effect on delirium, depression and post-traumatic stress syndrome is still unclear. Few studies with a high level of evidence probe into these issues.

6. - Effects of the practice of non sedation

In order to avoid over-sedation and minimise the undesirable effects of sedatives, in the year 2010, Strøm et al. [11] demonstrated that a practice of non sedation and its replacement by the intervention of a nurse in the control of anxiety had major benefits on the duration of the MV and ICU and hospital stay. Furthermore, a recent study related the strategy of non sedation with a lower rate and duration of delirium, with no changes in the cognitive patient outcomes 3 months after discharge, with respect to patient who had received sedation.[12] Notwithstanding, Olsen et al.[13] have now studied the impact of non sedation compared with mild sedation, and have found there to be no conclusive benefits. As a result, the effect of non sedation in clinical outcomes of patient both during hospital stay and on discharge requires further investigation. More studies are also required to probe into the conceptualisation of nurses regarding early mild sedation or the practice of non sedation and what factors promote or limit the application of these strategies from a qualitative focus.

7. - Optimum sedation strategies: daily sedation interruption versus the use of nurse-guided algorithms

Recommendation for administrating appropriate sedation is supported in the implementation of protocols which normalise the monitoring of the objective and the level of sedation–agitation, through the use of validated tools, and also the titration of sedative doses. Adjustment of sedative doses for reaching the prescribed objective may be made using two strategies: the application of nurse-guided algorithms, or daily sedation interruption (DSI). Existing evidence has found no difference between them and indicates that both are useful for reaching and maintaining a mild sedation level in the critically ill adult, although the DSI means a higher burden of work for nurses.[1,14] Variables such as type of patients, unit characteristics, MV management, nursing ability and autonomy, and nurse:patient ratio may impact the outcomes in the application of these strategies in a determining fashion. The results pending from the systematic review registered as the PROSPERO CRD42016037480[15] study, in which different sedation strategies are compared for the critically ill patient, may possibly clarify this matter.

8. - Use of inhalation sedation

The administration of inhaled sedatives in the critically ill patient, such as sevoflurane and isoflurane in the MV equipment, including the AnaConDa® (Sedana Medical, Uppsala, Sweden) system and the Mirus® (Pall Medical, Dreieich, Germany) system are being introduced as an alternative to intravenous sedation. These inhalation agents lead to deep sedation with no risk of accumulation and with a rapid reversal, which may be associated with an improvement in patient outcomes.[16] However, further studies are still required to probe into the safety and efficacy in the administration of these agents, together with their levels of exposure to professionals, strategies to minimize them and their effects on health.

Mechanical restraints and delirium

9.- Detection of predisposing factors for the use of MR

The use of MR in critically ill patients is a common practice to prevent the self-removal of life supports and to manage agitation, despite international guidelines recommending that they be reserved as a last resort.[1] This usage has been associated with a higher risk of unscheduled extubation, agitation, use of psychoactive drugs and an independent factor in the development of delirium.[14] Differences in nurse:patient ratios; being intubated; the presence of delirium; the use of benzodiazepines and propofol; professional knowledge and attitudes, and the organisational culture of each unit has been correlated with their use. On the contrary, preventative administration of analgesia or tracheotomy has been associated with a probability of lower usage.[17] Several studies report that the treatment the patient receives in the UCI is a better predictor of MR than the actual patient characteristics (age, severity of disease, tobacco habit) or those of the unit.[17,18] However, a much more profound examination is required into the relationship between the use of MR and the different subtypes of delirium, the use of dexmedetomidine, and organisational factors such as the nurse:patient ratio, care omitted, taking of shared decisions or quality criteria in the use of MR when they are deemed necessary.

10.- Improvement in the detection and stratification of delirium

In delirium, lack of attention, alteration and fluctuation of awareness and disorganised thinking coexist. Three subtypes are distinguished (hyperactive, hypoactive and mixed), the classification of which is related to psychomotor activity and DSM-5 classification. Delirium is a multifactorial syndrome which encompasses physiopathological processes such as oxidative stress, neuroinflammation, changes in the behaviour of neurotransmitters, sensory privation and metabolic disorders, among others. New research lines have now begun which are aimed at classifying new phenotypes to improve knowledge of their cause and effect from study models which may combine precipitant elements, their neurophysiopathology or their psychiatric symptoms.[19]

11.- Design of new tools of detection adapted to the patient type, aetiology and physiopathology of the delirium

For the detection of delirium, international guidelines recommend the use of the Confusion Assessment Method for Intensive Care Units (CAM-ICU) scale or the Intensive Care Delirium Screening Checklist (ICDSD).[1] These tools only provide a binary result that identifies the presence or absence of delirium and in this result is influenced by the degree of sedation and measurement tool.[20] Several authors try to improve their detection and stratification with diagnostic tools using numerical scores, such as the Neelon and Champagne Confusion Scale (NEECHAM) or the Stanford Delirium representative factor test of (S-PTD). In line with this same proposal an App has been developed for smart phones, the Del-App-ICU which discriminates the presence and severity of delirium by means of the Edinburgh Delirium Test Box (EDTB-ICU), in which after an initial assessment (behaviour, excitation and visual tracing) the patients are asked to carry out simple orders and to complete tasks with require concentration, all on three different levels. This EDTB-ICU has been shown to have high sensitivity (100%) and specificity (92%).[21]

Regarding stratification, the predictive models PRE-DELIRIC and E-PRE-DELIRIC stratify the risk of presenting with delirium[22] and therefore prevent its appearance in a more precise fashion or cut short its duration reducing the morbimortality associated with this syndrome. Together with a proactive monitoring of the possible analytical, hemodynamic, inflammatory or stressful causes, there are studies which propose new technical resources such as the use of actigraphs for assessing activity and circadian rhythms.[23] These resources have not yet been meticulously validated by means of the corresponding correlation with polysomnography (Gold Standard) due to the complexity surrounding the critically ill patient. However, once the problems of appliances and validity have been overcome, they could become an important tool in delirium control studies.

12. - Effectiveness of the use of bundles and non-pharmacological strategies in the prevention of delirium and the use of MR

The preventative application of the ABCDEF package has obtained notable results in the reduction of the development of delirium, the use of MR, the duration of MV and hospital survival.[24] In a recent meta-analysis, early mobilization, family participation and multi-component interventions were associated with a reduction in delirium rates.[25] Further intervention studies are needed, together with more systematic reviews to analyse what the most effective and efficient combination of non-pharmacological measures are (reorientation, distraction, family accompaniment policy, early mobilisation and respect for sleep) in preventing delirium and reducing the use of MR, and also their long-term effect on the psychological well-being of patients and family members. Moreover, there is a need for further exploration into how families experience the presence of delirium in a patient who is in the ICU and what their experience is regarding their participation in the detection and management of delirium in their family member. At present multi-component non-pharmacological strategies with a multidisciplinary approach which include physiotherapists, psychiatrists, psychologists, occupational therapists, neurologists, geriatricians and biologists as well as nurses and intensive care doctors continue being the first line treatment of approach to delirium and aim at both controlling symptoms as well as emphasizing the functional recovery of the patient.

References

1. 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:e825–73, http://dx.doi.org/10.1097/CCM.0000000000003299.
2. Latorre-Marco I, Solís-Muñoz M, Falero-Ruiz T, Larrasquitu-Sánchez A, Romay-Pérez AB, Millán-Santos I. Validación de la Escala de Conductas Indicadoras de Dolor para valorar el dolor en pacientes críticos, no comunicativos y sometidos a ventilación mecánica: Resultados del proyecto ESCID. Enferm Intensiva. 2011;22:3–12, http://dx.doi.org/10.1016/j.enfi.2010.09.005.
3. López-López C, Arranz-Esteban A, Arias-Rivera S, Solís-Muñoz M, Pérez-Pérez T, Latorre-Marco I. Application of the behavioural indicators of pain scale in patients with traumatic brain injury. J Adv Nurs. 2020;76:1862–70, http://dx.doi.org/10.1111/jan.14400.

4. Ledowski T. Objective monitoring of nociception: a review of current commercial solutions. Br J Anaesth. 2019;123:e312–21, http://dx.doi.org/10.1016/j.bja.2019.03.024.
5. Gélinas C, Puntillo KA, Levin P, Azoulay E. The behavior pain assessment tool for critically ill adults: a validation study in 28 countries. Pain. 2017;158:811–21, http://dx.doi.org/10.1097/j.pain.0000000000000834.
6. Hamrick KL, Beyer CA, Lee JA, Cocanour CS, Duby JJ. Multimodal analgesia and opioid use in critically ill trauma patients. J Am Coll Surg. 2019;228:769–75, http://dx.doi.org/10.1016/j.jamcollsurg.2019.01.020, e1.
7. Olsen BF, Rustøen T, Sandvik L, Miaskowski C, Jacobsen M, Valeberg BT. Implementation of a pain management algorithm in intensive care units and evaluation of nurses' level of adherence with the algorithm. Heart Lung. 2015;44:528–33, http://dx.doi.org/10.1016/j.hrtlng.2015.08.001.
8. DAS-Taskforce 2015, Baron R, Binder A, Biniek R, Braune S, Buerkle H, Dall P, et al. Evidence and consensus based guideline for the management of delirium, analgesia, and sedation in intensive care medicine. Revision 2015 (DAS-Guideline 2015) - short version. Ger Med Sci. 2015;13, http://dx.doi.org/10.3205/000223. Doc19.
9. Celis-Rodríguez E, Díaz Cortés JC, Cárdenas Bolívar YR, Carrizosa González JA, Pinilla DI, Ferrer Záccaro LE, et al. Guías de práctica clínica basadas en la evidencia para el manejo de la sedoanalgesia y delirium en el paciente adulto críticamente enfermo. Med Intensiva. 2020;44:171–84, http://dx.doi.org/10.1016/j.medin.2019.07.013.
10. Shehabi Y, Howe BD, Bellomo R, Arabi YM, Bailey M, Bass FE, et al. Early sedation with dexmedetomidine in critically ill patients. N Engl J Med. 2019;380:2506–17, http://dx.doi.org/10.1056/NEJMoa1904710.
11. Strøm T, Martinussen T, Toft P. A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial. Lancet. 2010;375:475–80, http://dx.doi.org/10.1016/S0140-6736(09)62072-9.
12. Nedergaard HK, Jensen HI, Stylsvig M, Olsen HT, Korkmaz S, et al. Effect on nonsedation on cognitive function in survivors of critical illness. Crit Care Med. 2020;48:1790–8, http://dx.doi.org/10.1097/CCM.0000000000004573.
13. Olsen HT, Nedergaard HK, Strøm T, Oxlund J, Wian KA, Ytrebø LM, et al. Nonsedation or light sedation in critically ill, mechanically ventilated patients. N Engl J Med. 2020;382:1103–11, http://dx.doi.org/10.1056/NEJMoa1906759.
14. Mehta S, Burry L, Cook D, Steinberg M, Granton J, Herridge M, et al. Daily sedation interruption in mechanically ventilated critically ill patients cared for with a sedation protocol: a randomized controlled trial. JAMA. 2012;308:1985–92, http://dx.doi.org/10.1001/jama.2012.13872.
15. Hutton B, Burry LD, Kanji S, Mehta S, Guenette M, Martin CM, et al. Comparison of sedation strategies for critically ill patients: a protocol for a systematic review incorporating network meta-analyses. Syst Rev. 2016;5:157, http://dx.doi.org/10.1186/s13643-016-0338-x.
16. Jerath A, Panckhurst J, Parotto M, Lightfoot N, Wasowicz M, Ferguson ND, et al. Safety and efficacy of volatile anesthetic agents compared with standard intravenous midazolam/propofol sedation in ventilated critical care patients: a meta-analysis and systematic review of prospective trials. Anesth Analg. 2017;124:1190–9, http://dx.doi.org/10.1213/ANE.0000000000001634.
17. Lawson TN, Tan A, Thrane SE, Happ MB, Mion LC, Tate J, et al. Predictors of new-onset physical restraint use in critically ill adults. Am J Crit Care. 2020;29:92–102, http://dx.doi.org/10.4037/ajcc2020361.
18. Luk E, Sneyers B, Rose L, Perreault MM, Williamson DR, Mehta S, et al. Predictors of physical restraint use in Canadian intensive care units. Crit Care. 2014;18(March (2)):R46, http://dx.doi.org/10.1186/cc13789.
19. Oldham MA, Flaherty JH, Maldonado JR. Refining delirium: a transtheoretical model of delirium disorder with preliminary neurophysiologic subtypes. Am J Geriatr Psychiatry. 2018;26:913–24, http://dx.doi.org/10.1016/j.jagp.2018.04.002.
20. van den Boogaard M, Wassenaar A, van Haren FMP, Slooter AJC, Jorens PG, van der Jagt M, et al. Influence of sedation on delirium recognition in critically ill patients: a multinational cohort study. Aust Crit Care. 2020;33:420–5, http://dx.doi.org/10.1016/j.aucc.2019.12.002.
21. Smit L, van der Jagt M. Delirium in the ICU—a structured review of promising diagnostic and therapeutic approaches: next steps in ICU delirium. Neth J Crit Care. 2020;28:126–33.
22. van den Boogaard M, Pickkers P, Spronk PE, Donders R, Schoonhoven L. Development and validation of PRE-DELIRIC (PREdiction of DELIRium in ICu patients) delirium prediction model for intensive care patients: observational multicentre study. BMJ. 2012;344:e420, http://dx.doi.org/10.1136/bmj.e420.
23. Gupta P, Martin JL, Needham DM, Vangala S, Colantuoni E, Kamdar BB. Use of actigraphy to characterize inactivity and activity in patients in a medical ICU. Heart Lung. 2020;49:398–406, http://dx.doi.org/10.1016/j.hrtlng.2020.02.002.
24. Pun BT, Balas MC, Barnes-Daly MA, Thompson JL, Aldrich JM, Barr J, et al. Caring for critically ill patients with the abcdef bundle: results of the ICU liberation collaborative in over 15,000 adults. Crit Care Med. 2019;47:3–14, http://dx.doi.org/10.1097/CCM.0000000000003482.
25. Liang S, Chun Chau JP, Hoi Shan Lo S, Zhao J, Chow Choi K. Effects of nonpharmacological delirium-prevention interventions on critically ill patient's clinical, psychological, and family outcomes: a systematic review and meta-analysis. Aust Crit Care. 2020, http://dx.doi.org/10.1016/j.aucc.2020.10.004.

G. Via-Clavero (PhD)[a,*], M.J. Frade-Mera (PhD)[b], D. Alonso-Crespo (RN)[c], A. Castanera-Duro (PhD)[d], D. Gil-Castillejos (PhD)[e], O. Vallés-Fructuoso (PhD candidate)[f], J.J. Rodríguez-Mondéjar (PhD)[g], C. López-López (PhD)[h], G. Robleda (PhD)[i], M. Acevedo-Nuevo (PhD)[j], Grupo de Trabajo de Analgesia Sedación Delirio y Contenciones

[a] *Enfermera Clínica, Área del Paciente Crítico, Hospital Universitari de Bellvitge, Profesora Asociada, Escuela de Enfermería, Facultad de Medicina y Ciencias de la Salud, Universitat de Barcelona, Grup de Recerca Infermera (GRIN-IDIBELL), Spain*

[b] *Enfermera Clínica, Área del Paciente Crítico, Hospital Universitario 12 de Octubre, Profesora Asociada, Facultad de Enfermería, Fisioterapia y Podología, Universidad Complutense de Madrid, Spain*

[c] *Enfermero, Unidad de Cuidados Intensivos, Área Sanitaria de Vigo, Hospital Álvaro Cunqueiro SERGAS-UVigo, Translational Neuroscience Group-CIBERSAM, Galicia Sur, Instituto de Investigación Sanitaria (IIS Galicia Sur), Spain*

[d] *Enfermero Clínico, Área del paciente crítico, Hospital Universitario de Girona Dr. Josep Trueta, Profesor Asociado departamento de Enfermería Universitat de Girona (UdG), Spain*

[e] *Enfermera Clínica, Área de Críticos, Servicio de Medicina Intensiva, Hospital Universitari Joan XXIII, Tarragona, Spain*

[f] *Enfermera, Unidad de Cuidados Intensivos, Hospital Vall d'Hebrón, Barcelona, Spain*
[g] *Enfermero en UME-2 Alcantarilla, Gerencia de Urgencias y Emergencias Sanitarias 061 Región de Murcia, Servicio Murciano de Salud, Profesor asociado en la Facultad de Enfermería de la Universidad de Murcia, Campus Mare Nostrum, Miembro del grupo de investigación ENFERAVAN en el IMIB-Arrixaca, Spain*
[h] *Enfermera, Departamento de Cuidados Intensivos, Hospital Universitario 12 de Octubre, Madrid, Investigadora, Grupo de Investigación en Cuidados (InveCuid), Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12), Madrid, Profesora Asociada, Facultad de Enfermería Fisioterapia y Podología, Universidad Complutense de Madrid, Spain*
[i] *Campus docente Fundación Privada Sant Joan de Déu, Escuela de Enfermería, Universidad de Barcelona, Centro Cochrane Iberoamericano, Spain*
[j] *Enfermera, Organización Nacional de Trasplantes, Grupo de Investigación en Enfermería y Cuidados de Salud – Instituto de Investigación Sanitaria Puerta de Hierro – Segovia de Arana (IDIPHISA), Spain*

[*] Corresponding author.
E-mail address: gviac@ub.edu (G. Via-Clavero).