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The importance of delirium monitoring in the intensive care unit

Importância da monitorização do delirium na unidade de terapia intensiva

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ABSTRACT

Delirium is an acute confusional state associated with increased mortality in the intensive care unit and long-term impaired functional recovery. Despite its elevated incidence and major impact in the outcomes of critically ill patients, delirium remains underdiagnosed. Presently, there are validated instruments to diagnose and monitor delirium, allowing the detection of early organ dysfunction and treatment initiation. Beyond patient's non-modifiable risk factors, there are modifiable clinical and environmental aspects that should be accessed to reduce the occurrence and severity of delirium. As recent studies demonstrate that interventions aiming to reduce sedative exposure and to improve patients' orientation associated with early mobility have proved to reduce delirium, a low incidence of delirium should be targeted and considered as a measure of quality of care in the intensive care unit (ICU).

Keywords: Delirium; Confusion; Septic encephalopathy; Intensive care units

INTRODUCTION

Delirium is an acute confusional state, and represents an acute brain dysfunction encompassing a wide array of clinical manifestations.[1] The attentional deficit is the most salient feature, although other cognitive and behavioral disturbances such as memory loss, hallucinations and agitation can be observed. Delirium remains largely unrecognized despite its elevated prevalence in the intensive care unit (ICU).[2] There are reports of delirium prevalence in ICU ranging from 28% to 73%.[3,4] Such variation can be attributed to heterogeneity in the evaluated population (e.g. severity of illness, ventilated versus non-ventilated, elderly) as well as in the definition of delirium and the instrument chosen for delirium detection.[2,5] The clinical presentation varies from the somnolent hypoactive patient to the combativeness and hallucinations in the hyperactive form. The most frequent presentation of delirium is the hypoactive form, while the pure hyperactive form is relatively rare (<5%).[6] Elderly patients exhibit mainly the hypoactive or mixed presentation. There is current evidence demonstrating that delirium is associated with worse outcomes for critically ill patients including increased duration of mechanical ventilation, length of hospital stay and mortality.[1,7,8] Furthermore, despite an adequate life support, patients that presented delirium during hospital admission may experience impaired global functional recovery and long-

term neurocognitive sequelae[9,10] with significant impact in the quality of life. Therefore, understanding delirium epidemiology and risk factors are the key to implement effective preventive measures.

Risk factors, prevention and feasible interventions

Risk factors for delirium can be divided as modifiable and non-modifiable.[11] Among non-modifiable factors are patient's characteristics such as age, gender, personal habits (e.g.-smoking, alcohol abuse), comorbidities, prior nervous system diseases, genetic characteristics (eg-APO-E4 mutation-)[12] and dementia.[13,14]

Considering the current potential for intervention, ICU physicians should focus on modifiable risk factors, especially in those patients at increased risk of developing delirium. The typical ICU environment itself represents a risk factor for delirium, due to the absence of natural daylight and clocks coupled with patient isolation. Some minor interventions can turn the ICU environment less harmful allowing a better perception of the environment, such as night and day through windows and lights, access to visual and hearing aids and interventions to minimize sleep deprivation.[15] Additionally, the presence of invasive life support, tubes, drains and catheters are also considered risk factors and should be removed as soon as possible. In a landmark study, Inouye et al.[15] evaluated 852 hospitalized, non-ICU patients and assigned them to usual care or management with a multicomponent intervention consisting of reorientation of the patients, a nonpharmacologic sleep protocol, early mobilization and early removal of catheters and restraints,

use of eyeglasses and hearing aids and correction of dehydration and electrolytes. The intervention significantly reduced the incidence of delirium (15% in the usual care versus 9.9% in the intervention group; matched OR = 0.60, 95% CI = 0.39 to 0.92). These results were subsequently confirmed in the postoperative setting.[16]

Other clinical issues that are also risk factors and must always be checked and corrected are electrolyte abnormalities, infections, drugs withdrawn and pain control. Although the role of these issues in delirium prevention in the ICU remains to be tested, they should be addressed as they represent good clinical practice and are well-known risk factors for delirium. Sedation plays a key role in the development of delirium. Avoidance of oversedation is beneficial in a wide range of clinical outcomes,[17] including ICU-acquired infections[18] duration of mechanical ventilation and length of ICU stay,[17](Chart 1). Interestingly, not only the exposure to sedation, but the type of sedation may influence the development of delirium. There is increasing evidence demonstrating that benzodiazepines are associated with the occurrence of delirium.[13,19] In a cohort of trauma and surgical patients, more than 70% presented delirium during ICU stay, and the strongest independent predictive factor was midazolam exposure.[13] Similarly, lorazepam was shown to be an independent risk factor for transitioning to delirium in mechanically ventilated patients, while opioids were not significantly associated with increased delirium incidence.[20] However, there is a role for benzodiazepines in patients with chronic use who develop delirium upon withdrawn of a drug of this class.

Chart 1 - Trials comparing benzodiazepine sparing strategies and alternative sedation method, separated by year and outcomes improved

Trial	Year	RCT	Outcomes improved protocol
Brook et al.[42]	1999	Yes	Ventilator days, ICU length of stay
Kress et al.[43]	2000	Yes	Ventilator days, ICU length of stay
Brattebo et al.[44]	2002	No	Ventilator days
De Jonghe et al.[45]	2005	No	Ventilator days, time to awaken
Chanques et al.[46]	2006	No	Ventilator days, pain/agitation, infection
Quenot et al.[47]	2007	No	Ventilator days, extubation success, VAP
Arias-Rivera et al.[48]	2008	No	Extubation success
Bucknall et al.[49]	2008	Yes	None
Girard et al.[50]	2008	Yes	Ventilator days, Hospital length of stay, survival
Robinson et al.[51]	2008	No	Ventilator days, Hospital length of stay
Pandharipande et al.[13]	2008	Yes	Delirium and coma free days, target sedation

RCT - Randomized controlled trial; ICU- intensive care unit.

Therefore, the use of non-gaba (or benzodiazepine sparing) sedation strategies were tested in patients undergoing mechanical ventilation aiming at decreasing delirium rates. In the MENDS study, a prospective randomized controlled trial, Pandharipande et al. concluded that the use of dexmedetomidine was associated with more days without coma/delirium (median days, 7.0 vs 3.0; P = 0.01) when compared to lorazepam.[19] Subsequently, the SEDCOM trial,[21] demonstrated that dexmedetomidine-treated patients spent less time on the ventilator (3.7 days [95% CI, 3.1 to 4.0] vs 5.6 days [95% CI, 4.6 to 5.9]; P = .01) and experienced less delirium (54% vs 76.6% difference, 22.6% [95% CI, 14% to 33%]; P < .001), when compared to those sedated with midazolam. These two trials suggest that the use of benzodiazepine-sparing strategies may be associated with a lower risk of developing delirium among other relevant clinical benefits as mechanical ventilation free days and ICU length of stay. A sub-group analysis showed that these clinical benefits seem to be especially relevant in patients with sepsis.[19]

Pharmacologic prevention was tested yielding contradictory results. Prakanrattana et al.[22] evaluated the impact of a single dose of risperidone in 126 patients after cardiac surgery. This RCT showed a decreased incidence of delirium with risperidone when compared to placebo (11.1% vs. 31.7%, P=0.009, relative risk = 0.35, 95% confidence interval [CI] = 0.16-0.77).[22] Otherwise, Gamberini found no difference in delirium incidence when rivastigmine were compared to placebo in a similar population.[23] Prophylactic low-dose haloperidol was associated with less severe and shorter delirium episodes with decreased length of hospital stay in elderly patients with hip fracture.[24]

Another potential modifiable risk factor for delirium is sleep deprivation. Patients admitted to the ICU are prone to reduced sleeping, with sleep fragmentation and other disturbances.[25] In healthy subjects, sleep deprivation is known to cause inattention, fluctuating mental status and cognitive dysfunction,[26] characteristics that are also present in delirious patients. Moreover, neurohormonal changes and anatomical sites are equally involved in delirium and sleep disturbances. In fact, the ICDSC (Intensive Care Delirium Screening Checklist) uses altered sleep as one of the criteria to establish the diagnosis of delirium. Indeed, in the ICU setting, risk factors for delirium and sleep disturbances overlap, including drugs, such as benzodiazepines, that diminish slow-wave and REM sleep leading to serious sleep fragmentation.[27] Therefore, it is plausible that delirium may be precipitated by sleep deprivation,[28] making environmental modification in the ICU a major challenge.

How to diagnose and monitor delirium?

In 1991 Inouye et al. developed an easy to use confusion assessment method (CAM), based on non-ICU elderly population.[29] Ten years later, Ely et al. conducted a prospective single-center cohort study to evaluate the efficacy of Confusing Assessment Method modified for nonverbal patients (CAM-ICU) in patients admitted to a medical ICU.[30] The CAM-ICU was able to detect delirium in this population with high interrater reliability. In the same year, the authors validated the CAM-ICU method for mechanically ventilated patients and delirium was diagnosed in 83.3% patients.[31] A large-scale implementation of sedation scales and CAM-ICU by nurse staff is feasible as shown in two medical ICUs. Sixty-four nurses evaluated 711 patients and the overall agreement (kappa) between bedside nurses and reference raters using the Confusion Assessment Method for the ICU ranged from 0.75 to 0.92.[32]

Based on the definitions of Diseases and Statistics Manual of Mental Disorders IV (DSM-IV), Bergeron created an eight criteria checklist (Intensive Care Delirium Screening Checklist – ICDSC) to be implemented in ICU patients. During three months, consecutive subjects admitted to a mixed ICU were evaluated, with only 15 developing delirium. Of them, 93% presented with at least 4 altered items. It is important to emphasize that 15 patients (19%) presented with altered checklist without the confirmation of delirium by psychiatric evaluation (the gold-standard considered). Indeed, the ICDSC stands with a high sensibility (99%) and lower specificity (64%).[33] Plaschke et al. compared the ICDSC and CAM-ICU in surgical elective ICU patients, in a single center observational study of 174 subjects. There was a good agreement between the two method (kappa coefficient was 0.80; CI 95%: 0.78-0.84; p<0.001).[34]

There are other methods for detecting delirium, as cited by Luetz recently. At a University Germany Hospital, the author prospectively evaluated three instruments: CAM-ICU, Nursing Delirium Screening Scale (DDS) and the Delirium Detection Score, using ICDSC as the gold standard. Once more, CAM-ICU was able to diagnose delirium with high inter-observer agreement. DDS was the less sensitive tool (30%).[35]

In the other hand, a few questions about the pos-

sibility of overtreatment or excessive antipsychotic use were raised when delirium is routinely monitored. For this reason, van den Boogaard et al.[36] evaluated 1742 subjects during three years testing the effect of implementation of delirium monitoring in haloperidol use. ICU staff reached a good compliance (92%), and delirium was diagnosed almost twice as much than before the implementation (10% in 2006, 13% in 2007 and 23% in 2008 p<0.001). Haloperidol was prescribed for more patients, but in lower dose and for a shorter duration. Treatment with haloperidol decreased from five to three days after the implementation of the CAM-ICU (p = 0.02). And median haloperidol dose prescribed decreased from 18 mg to 6 mg (p = 0.01).[36]

Why we must monitor delirium: a patient safety issue?

There are reports from 32 to 66% of unrecognized delirium, probably due to several confounding factors.[37] First of all, the appropriate terminology and definition were only proposed recently.[5] As the most frequent presentation is the hypoactive form, and usual clinical evaluation may not detect delirium in calm, somnolent delirious patients, the largest proportion of these subjects are still not diagnosed. However, despite this knowledge, the use of clinical evaluation as opposed to the implementation of validated tools seems to be frequent among ICU physicians.[2,38] Considering that delirium has a major impact on clinical outcomes and subsequent quality of life of ICU survivors this represents a major gap between the current knowledge and its translation into practice. Clearly, the hyperactive form with agitation and hallucinations are a major source of concern about patient safety. Accidental extubation, catheter removal and other self-inflicted injuries can lead to severe consequences and worst outcomes.[39] In addition, patients with hypoactive delirium have up to threefold higher chance to be reintubated, and also a threefold increase in 6-month mortality.[8]

Delirium should be monitored routinely to allow the early diagnosis and to provide accurate data on its frequency in the ICU.[40] Monitoring delirium at the ICU is important not only as a surrogate of an early organ dysfunction, but also to prevent accidental injuries, promoting safe care and allowing the institution of preventive and therapeutic measures to provide adequate rehabilitation and potentially diminish losses in quality of life. As previously mentioned, environmental changes are feasible, and when allied to attention on clinical aspects the earliest liberation from mechanical ventilation and ICU discharge can be optimized. Recently, Phandaripande et al. introduced the concept of "liberation and animation" meaning that patients should be as early as possible awake, liberated from mechanical ventilation and perform physical and occupational therapy. In this short but lovely commentary, the ABCD bundle was purposed (**A**wakening and **B**reathing **C**oordination of Daily sedation and ventilator removal trials; Choice of sedative or analgesic exposure; **D**elirium monitoring and Management; and **E**arly mobility and exercise), as a strategy to stimulate clinicians to adopt these practices in daily care.[41]

Low delirium incidence should be a quality improvement goal in the ICU, and could represent the achievement of better process of care and optimal patient-centered outcomes.

CONCLUSION

Delirium is a common acute manifestation of brain dysfunction in critically ill patients that is now recognized as a major source of short and long term morbidity. Routine monitoring of delirium using a validated tool should be implemented. The institution of pharmacologic and non-pharmacologic preventive measures is a feasible and efficient way to reduce delirium incidence. Delirium is preventable and, possibly, it should never occur. The full adherence to process of care measures and trends in delirium prevalence should be introduced and used as quality indicator in the ICU.

RESUMO

O delirium é um estado confusional agudo associado a maior mortalidade na unidade de terapia intensiva e comprometimento da recuperação funcional em longo prazo. Apesar de sua elevada incidência e relevante impacto nos desfechos de pacientes criticamente enfermos, o delirium continua sendo sub-diagnosticado. Atualmente existem instrumentos validados para diagnosticar e monitorar o delirium, permitindo a detecção precoce dessa disfunção orgânica e início precoce do tratamento. Além dos fatores de risco não modificáveis do paciente, existem aspectos clínicos e ambientais modificáveis que devem ser avaliados para reduzir a ocorrência e gravidade do delirium. Conforme demonstrado por estudos recentes, intervenções para reduzir a exposição a sedatição excessiva e melhorar a orientação do paciente podem estar associadas a redução da incidência de delirium. Baixa incidência de delirium deve ser almejada e considerada como uma medida da qualidade nas unidades de terapia intensiva.

Descritores: Delirium; Confusão; Encefalopatia séptica; Unidades de terapia intensiva

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