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Delirium Monitoring in the Intensive Care Unit

Delirium is an acute confusional state associated with increased mortality in the Intensive Care Unit (ICU) and long-term global and neurologic 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 (CNS) dysfunction. Epidemiologic data shows that beyond patient's non-modifiable risk factors, there are modifiable clinical and environmental aspects that should be assessed to reduce the occurrence and severity of delirium. Recent studies demonstrate that interventions aiming to reduce sedative exposure and to improve patients' orientation and to implement early mobility are associated with reduced delirium rates. In a patient safety perspective delirium should be seen as a preventable adverse event and a low incidence of delirium should be targeted and considered as a measure of quality of care in the ICU.

Introduction

Delirium is an acute confusional state that encompasses a wide array of clinical manifestations (Pandharipande et al. 2005). Delirium prevalence in ICU ranges from 28% to 83% (Janz et al. 2010; Morandi et al. 2009; Ely et al. 2001b). Such variation can be attributed to heterogeneity in the evaluated population (e.g. severity of illness, ventilated versus non-ventilated) as well as in the definition and instrument chosen for delirium detection (Morandi et al. 2008; Salluh et al. 2009). Despite its elevated prevalence, delirium remains largely unrecognized (Salluh et al. 2009). There is current evidence demonstrating that delirium is associated with worse outcomes for critically ill patients including increased duration of mechanical ventilation, hospital length of stay and mortality (Ely et al. 2001a; Pandharipande et al. 2005; Ely et al. 2004). Furthermore, ICU patients that present delirium are at increased risk of impaired global functional recovery and long-term neurocognitive sequelae (Girard et al. 2010; Van Rompaey et al. 2009b). Therefore, understanding delirium epidemiology and risk factors is the key to implement effective monitoring and preventive strategies.

Risk Factors and Non-pharmacologic Prevention

Risk factors for delirium are divided in modifiable and non-modifiable (Van Rompaey et al. 2009a). Among non-modifiable factors are patient's characteristics such as:
• Age;
• Gender;
• Personal habits (e.g.-smoking, alcohol abuse);
• Comorbidities;
• Prior nervous system deficits;
• Genetic characteristics (e.g. APO-E4 mutation) (Ely et al. 2007); and
• Dementia (Pandharipande et al. 2008; Inouye 1999).

ICU physicians should focus on modifiable risk factors, especially in patients at high risk of developing delirium. The typical ICU environment represents a risk factor for delirium, due to the patient isolation and absence of natural daylight and clocks. Minor interventions, as allowing natural light through windows, access to visual and hearing aids and minimising sleep deprivation may humanise the ICU (Inouye et al. 1999). Additionally, invasive life support, tubes, drains and catheters are risk factors for delirium and should be removed as soon as possible. In a landmark study, Inouye et al. (Inouye et al. 1999) evaluated 852 hospitalised, non-ICU patients and instituted a multicomponent intervention consisting of reorientation of the patients, a nonpharmacologic sleep protocol, early mobilisation and early removal of catheters and restraints, use of eyeglasses and hearing aids and early correction of dehydration and electrolytes. The intervention significantly reduced the incidence of delirium (15.0% in the usual care versus 9.9% in the intervention group; OR = 0.60, 95% CI = 0.39 to 0.92). These results were subsequently confirmed in the postoperative setting (Marcantonio et al. 2001). Recently, early physical and occupational therapy has been shown to reduce delirium in ICU patients (Schweickert et al. 2009).

Another risk factor for delirium is sleep deprivation. ICU patients experience reduced sleep, sleep disturbance and fragmentation (Salas and Gamaldo, 2008). In healthy subjects, sleep deprivation causes inattention, fluctuating mental status and cognitive dysfunction (Dinges et al. 1997), characteristics that are present in delirious patients. Moreover, neurohormonal changes and anatomical sites are equally involved in delirium and sleep disturbances. Also, risk factors for delirium and sleep disturbances overlap, including benzodiazepines, that diminish slow-wave and REM sleep leading to serious sleep fragmentation (Bourne and Mills, 2004). Therefore, it is plausible that delirium may be precipitated by sleep deprivation and non-pharmacologic interventions to avoid it should be introduced (Weinhouse et al. 2009).

Sedation also plays a role in the development of delirium. Avoidance of oversedation is beneficial for a wide range of clinical outcomes (Kollef et al. 1998), including ICU-acquired infections (Nseir et al. 2010), duration of mechanical ventilation and length of ICU stay (Kollef et al. 1998). Interestingly, not only sedative exposure, but also the type of sedative may influence the development of delirium. There is increasing evidence that the use of benzodiazepines is strongly associated with the occurrence of delirium (Pandharipande et al. 2007; Pandharipande et al. 2008). In a cohort of trauma and surgical patients, more than 70% presented delirium during ICU stay, and the strongest predictive factor was midazolam exposure (Pandharipande et al. 2008). Similarly, lorazepam was shown to be an independent risk factor for transitioning to delirium in

mechanically ventilated patients (Pandharipande et al. 2006).

Therefore, the use of non-GABA (or benzodiazepine- sparing) sedation strategies was tested in patients undergoing mechanical ventilation. Data from the MENDS study, demonstrated that the use of dexmedetomidine was associated with increased coma/delirium free-days (median days, 7.0 vs. 3.0; P=0.01) when compared to lorazepam (Pandharipande et al. 2007). Subsequently, the SEDCOM (Safety and Efficacy of Dexmedetomidine Compared with Midazolam) trial (Riker et al. 2009) 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), as compared to those sedated with midazolam. Results from these RCTs suggest that the use of benzodiazepine-sparing strategies may be associated with a lower risk of developing acute brain dysfunction among other relevant clinical benefits (Wunsch and Kress, 2009). A recent subgroup analysis showed that these clinical benefits are especially relevant in patients with sepsis (Pandharipande et al. 2010b).

How to Diagnose and Monitor Delirium?

In 2001, Ely et al. published a prospective study that evaluated the efficacy of the Confusion Assessment Method (CAM) modified for nonverbal patients (CAM-ICU) in the ICU (Ely et al. 2001c). The CAM-ICU was able to detect delirium in this population with high interrater reliability. In the same year the authors validated the CAMICU for mechanically ventilated patients and delirium was diagnosed in 83.3% patients, (Ely et al. 2001b). A large-scale implementation by nurse staff was proved to be feasible. Sixty-four nurses evaluated 711 patients and the overall agreement between bedside nurses and reference raters was excellent (Pun et al. 2005).

Based on the definitions of Diseases and Statistics Manual of Mental Disorders IV (DSM-IV), Bergeron et al. created an eight criteria checklist (Intensive Care Delirium Screening Checklist – ICDSC). In its validation study, the ICDSC presented high sensibility (99%) and lower specificity (64%) (Bergeron et al. 2001). In a single centre study of 174 subjects Plaschke et al. compared the ICDSC and CAM-ICU in surgical ICU patients and observed a good agreement between the methods (kappa=0.80; CI 95%0.78-0.84; p<0.001) (Plaschke et al. 2008).

There are also other methods for detecting delirium. Luetz et al. prospectively evaluated three instruments: CAM-ICU, Nursing Delirium Screening Scale and the Delirium Detection Score (DDS), using ICDSC as the gold-standard. Once again, the CAM-ICU was able to diagnose delirium with high inter- observer agreement. The DDS was the less sensitive tool (30%) (Luetz et al. 2010). Van den Boogaard et al. evaluated 1742 subjects testing the effect of implementation of delirium monitoring. ICU staff reached a good compliance (92%), and delirium was diagnosed almost twice as much than before the implementation (10% vs. 23%, p<0.001) (van den Boogaard et al. 2009).

Why We Must Monitor Delirium: A Patient Safety Issue

There are reports demonstrating that 32- 66% of delirium cases remain unrecognised, probably due to several confounding factors (Ely et al. 2001d). First of all, the appropriate terminology and definition were only proposed recently (Morandi et al. 2008). 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 (Patel et al. 2009, Salluh et al. 2009). 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 (Garrouste Orgeas et al. 2008). In addition, patients with hypoactive delirium have up to threefold higher chance to be reintubated, and also a threefold increase in 6-month mortality (Ely et al. 2004).

Delirium should be monitored routinely to allow the early diagnosis and to provide accurate data on its frequency in the ICU (Jacobi et al. 2002). 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. This may lead adequate rehabilitation potentially diminishing losses in quality of life (Schweickert et al. 2009). Recently, the ABCD bundle was purposed (Awakening and Breathing Coordination of Daily sedation and ventilator removal trials; Choice of sedative or analgesic exposure; Delirium monitoring and Management; and Early mobility and exercise), as a strategy to stimulate clinicians to adopt these practices in daily care (Pandharipande et al. 2010a).

The increasing knowledge in this relatively young medical field shows that a 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-centred outcomes.

Conclusion

Delirium is a common acute manifestation of brain dysfunction in critically ill patients that is now recognised as a major source of short and long term morbidity. Routine monitoring of delirium using a validated tool should be implemented to optimise diagnosis and allow early recognition. The institution of non-pharmacologic preventive measures is a feasible and efficient way to reduce delirium incidence. Monitoring the adherence to process of care measures and trends in delirium prevalence should be introduced and used as quality indicator in the ICU.

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