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Acute Brain Dysfunction During Critical Illness



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- Delirium (acute brain dysfunction) can be a complication of critical illness.
- Brain organ dysfunction can manifest as a continuum of psychomotor behaviors that are categorised as hyperactive or hypoactive.
- Delirium can be diagnosed using validated and reliable bedside tools.
- Implementation of delirium monitoring can be enhanced by scheduled in-depth discussions about brain organ dysfunction via multidisciplinary rounds with the medical team.
- Delirium may be managed with use of non-pharmacologic and, if necessary, pharmacologic interventions thereafter.

Acute brain dysfunction is common in the critical care setting, presenting as delirium or coma. Delirium is a clinical syndrome of brain dysfunction characterised by an acute change or fluctuating course of altered mental status, inattention, and a disturbance of consciousness, cognition, or perception, such that a patient's ability to receive, process, store, and recall information is impaired (American Psychiatric Association 2013).

Prevalence

The prevalence of delirium among adults varies among different adult ICU populations: 20-30% in the cardiac ICU (McPherson et al. 2013; Pauley et al. 2015; Zhang et al. 2015), and 50%-80% in mechanically ventilated medical, surgical, trauma ICU (Bryczkowski et al. 2014; Pandharipande et al. 2008) and burn ICU (Agarwal et al. 2010) patients. The clinical presentation of delirium is expressed as a continuum of psychomotor behavior. Hypoactive delirium is characterised by apathy and decreased responsiveness (Meagher et al. 2007; Pandharipande et al. 2007). Conversely, patients with hyperactive delirium may exhibit mild restlessness to severe agitation. Among critically ill adults, hypoactive delirium (43.5%) is extremely prevalent versus the less common hyperactive subtype (1.6%) (Pandharipande et al. 2007), and unless routine monitoring is used, delirium will be missed.

Delirium does occur in critically ill children, although the true epidemiology has yet to be well described. Small case series report paediatric delirium rates of between 10-30% (Smith et al. 2011; Traube et al. 2014; Schieveld et al. 2007). Most recently, Smith and colleagues reported delirium prevalence of 36% in critically ill infants and young children, with rates as high as 46% in patients between 6 months and 2 years of age (Smith et al. 2014). Critically ill children are more likely to present with the hypoactive delirium subtype (81%) than hyperactive delirium (19%) (Goben et al. 2014).

Measurements

Delirium in the adult ICU can be diagnosed by using the validated [Confusion Assessment Method for the ICU \(CAM-ICU\)](#) (Ely et al. 2001a) or the Intensive Care Delirium Screening Checklist (ICDSC) (Bergeron et al. 2001). Given the fluctuating course of delirium, it is recommended that patients be screened at least once per shift to increase the chance of detection (Pun et al. 2013). The use of screening tools is superior to subjective assessment by providers and ideally should be part of routine modern ICU practice.

The first step in delirium diagnosis is assessment of level of arousal. Only patients who are responsive to voice can be evaluated for delirium, while those who are unresponsive are considered comatose. The [Society of Critical Care Medicine \(SCCM\) guidelines](#) recommend the use of either the [Richmond Agitation-Sedation scale](#) or the Sedation Agitation Scale for the assessment of the level of arousal (Barr et al. 2013). Patients who are arousable by voice can then be assessed for delirium with the CAM-ICU or the ICDSC, as shown in Figure 1 and Table 1. Delirium monitoring in paediatric patients is equally as important, especially during critical illness. Similarly to adult patients with delirium, paediatric patients demonstrate the core features of delirium, such as alteration of mental status, fluctuation and inattention. Additionally, infants and children with delirium may exhibit more subtle neuropsychiatric symptoms, such as inconsolability, purposeless actions, autonomic dysregulation, unexplained lethargy and even regression of previously attained developmental skills (Leentjens et al. 2008; Turkel et al. 2006).

Recently, there has been progress in the development and validation of paediatric-specific delirium tools. The paediatric confusion assessment method for the ICU (pCAM-ICU) was the first valid and reliable delirium tool created for use in critically ill children over 5 years of age, including those on mechanical ventilation, demonstrating a specificity of 99% and sensitivity of 83% for delirium diagnosis (Smith et al. 2011). Children under 5 years of age pose challenges for delirium diagnosis due to vast changes in their cognitive and developmental skills from infancy to early childhood. The [Cornell Assessment for Pediatric Delirium \(CAPD\)](#) is largely an observational delirium screening tool with a reported

specificity of 79% and sensitivity of 94% (Traube et al. 2014). Unlike DSM-5 criteria (ed American Psychiatric Association 2013), the CAPD does not require inattention to be present for delirium diagnosis. More recently, the [preschool CAM-ICU \(psCAM-ICU\)](#) was created and validated for use in critically ill infants and preschool-aged children. The psCAM-ICU is a largely objective and interactive, developmentally-targeted, 'in the moment' delirium assessment tool for children under 5 years of age. In preliminary validation study reports, the psCAM-ICU demonstrated a specificity of 91% and sensitivity of 84%, with excellent reliability (Smith et al. 2014).

Risk Factors

Critically ill adult patients are predisposed to multiple risk factors, and it has been shown that the presence of more risk factors is associated with increased delirium (Francis et al. 1990; Inouye et al. 1996). The SCCM guidelines state that the most consistent risk factors are preexisting dementia; history of hypertension and/or alcoholism; and a high severity of illness at admission (Barr et al. 2013). Other risk factors are sedative and analgesic medications (Bryczkowski et al. 2014; Pandharipande et al. 2008), mechanical ventilation (Pandharipande et al. 2005), restraint use (Bryczkowski et al. 2014; Mehta et al. 2015), age (Pandharipande et al. 2005) and specific medical conditions necessitating ICU care, e.g. sepsis (Agarwal et al. 2013; Lin et al. 2008).

Much work has been done on identifying modifiable risk factors of delirium. One of the most important is the use of analgesic and sedative drugs, drugs that are commonly prescribed to adults in the ICU. For example, patients receiving lorazepam have an increased risk for transitioning to delirium (Pandharipande et al. 2006). Follow-up studies have confirmed that the use of non-benzodiazepine drugs for sedation is associated with improved outcomes including delirium (Pauley et al. 2015; Riker et al. 2009). In the most recent sedation guidelines published by the SCCM there is a recommendation to use non-benzodiazepine sedatives and to consider dexmedetomidine in patients with delirium to potentially reduce the duration of delirium. (Barr et al. 2013).

Sedation protocols are now commonplace within modern adult ICU practice. Whilst there is conflicting evidence of the overall benefit of protocols (Sevransky et al. 2015), there is evidence that the use of sedation protocols leads to improved patient outcomes by reducing over sedation (Brook et al. 1999; Sessler et al. 2011). Other studies have included spontaneous awakening trials with sedation protocols, and showed decreased overall sedative use and decreased incidence of acute brain dysfunction (Girard et al. 2008; Khan et al. 2014). With the growing use of spontaneous awakening trials, it has also come to light that a small subset of patients will have rapidly reversible sedation-associated delirium. While seen in less than 10% of patients with sedative-associated delirium, these patients tend to portend better outcomes than those with more persistent forms of delirium associated with sedation (Patel et al. 2014). Protocols which optimise sedation and then have physical therapy added to the management practice significantly reduce the duration of delirium in critically ill patients (Schweickert et al. 2009).

Risk factors for the development of paediatric delirium have not been thoroughly studied. A recently published small cohort study demonstrated that developmental delay, need for mechanical ventilation and age were associated with delirium (Silver et al. 2015). The exposure to benzodiazepine administration has been associated with the development of delusional memories and subsequent development of post-traumatic stress disorder in children who survive critical illness (Colville et al. 2008). Future studies will help describe those risk factors that may be modifiable in the future for children during critical illness.

Outcomes

It is important to diagnose delirium in the critically ill adult patient, as the presence of delirium is associated with poorer patient outcomes, both short and long term. In the short term there is higher mortality (Ely et al. 2004), especially in patients with >2 days of delirium (Klein Klouwenberg et al. 2014), increased time of mechanical ventilation (Lat et al. 2009), increased ICU and hospital length of stays (Ely et al. 2001b) and increased cost of care. Pandharipande et al. (2013) found that longer durations of ICU delirium were associated with decreased cognitive function after one year and that the level of impairment was similar to that of a moderate traumatic brain injury in almost a third of survivors.

While the associations between delirium and outcomes have yet to be well defined in children, critical illness has been shown to have long term ramifications. Decreases in spatial and verbal memory, inattention (Fiser 1992), significantly longer school absences (Rees et al. 2004) and development of executive dysfunction months after discharge have been demonstrated among critically ill children who survive to home. Thus there may be elements of critical illness or management factors that exacerbate delirium development and predispose patients to long standing cognitive impairment after discharge.

Prevention and Treatment

Given the impact of delirium on outcomes, focus on prevention and management has become vital. Unfortunately the pathophysiology of delirium has not been fully elucidated and therefore directed therapies are not currently available. In both adults and children with delirium the prompt identification and treatment of underlying causes such as sepsis, hypoxia, poor oxygen delivery or drug withdrawal should be undertaken, leading to symptom resolution. There are other situations in which the source of delirium cannot be acutely reversed, and rather the focus becomes decreasing factors that may exacerbate or prolong acute brain dysfunction. Non-pharmacological strategies may help maintain orientation and support normal function of brain systems, thus improving outcomes (Inouye et al. 1999). Promotion of the sleepwake cycle is crucial and can usually be achieved by non-pharmacological means. Additionally the ongoing assessment of need for and goal of weaning psychoactive medications should be considered, including the necessary goal for level of consciousness and monitoring and treatment of pain. Non-pharmacological strategies that have been shown to be effective in reducing the incidence and duration of delirium in adults include early mobilisation (Schweickert et al. 2009) and sleep hygiene protocols (Kamdar et al. 2015). One such framework for good sedation and delirium practices is the ABCDE approach, which incorporates Assessment and management of pain; Both spontaneous awakening and breathing trials; Choosing the right sedative; Delirium monitoring and management; and Early exercise has been shown to be effective in reducing delirium (Balas et al. 2013).

Current pharmacological interventions are focused on treatment of the behavioural expression of delirium, both hyperactive and hypoactive, ranging from excessive agitation or combativeness to withdrawal and apathy (Balas et al. 2013; Smith et al. 2013). There are currently no U.S. Food and Drug Administration-approved medications for treatment of delirium in either adult or paediatric populations. However, both typical and atypical antipsychotics have been used successfully to modify delirium symptoms in both adults and children (Schieveld et al. 2007; Silver et al. 2010). A recent study investigated the use of haloperidol prophylaxis for adult patients with >50% predicated chance of developing delirium. Patients in the treatment group had decreased incidence of delirium and more delirium-coma free days, with the effect most pronounced in those with the highest baseline risk (van den Boogaard et al. 2013). This is consistent with other small studies that have had positive results with the use of antipsychotics for reducing delirium in adults (Skrobik et al. 2004; Devlin et al. 2010; Devlin et al. 2011). In contrast the HalOPERidol Effectiveness in ICU delirium (HOPE-ICU) trial, which randomised patients to haloperidol or placebo, showed no benefit in adult ICU patients receiving haloperidol prophylaxis (Page et al. 2013), nor did the Modifying the INcidence of Delirium (MIND) study comparing typical to atypical antipsychotics to placebo (Girard et al. 2010). The current adult SCCM guidelines thus do not recommend the routine use of any pharmacological prevention strategy for delirium including antipsychotics, but do acknowledge that atypical antipsychotics may reduce the duration of delirium (Devlin et al. 2011).

Conclusion

Delirium is a major contributor to both in-hospital and outpatient morbidity and mortality. Delirium monitoring and management may help decrease development and duration of delirium in both adults and children. Clearly, institution of a consistent monitoring plan for sedation, pain, and delirium may benefit critically ill patients. Though risk factor and outcome data in adults are better elucidated, further understanding and future studies are required in the paediatric population.

See Also: [Sedation in Acute Brain Injury: Less is More?](#)

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