Delirium in Pediatric Critical Care

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KEYWORDS

• Delirium • Pediatric critical care • Pediatrics • Pain • Agitation • Sedation

KEY POINTS

- Delirium is a frequent and serious complication of pediatric critical illness.
- Pediatric delirium is associated with increased morbidity, including longer duration of mechanical ventilation, increased hospital length of stay, and higher resource utilization.
- Benzodiazepines likely increase the risk for development of pediatric delirium.
- Delirium in children is both treatable and preventable.

DELIRIUM IN PEDIATRIC CRITICAL ILLNESS

Introduction

As critical care medicine has matured over the decades, from a specialty fighting mortality from a myriad of diseases to one promoting recovery with as few disabilities as possible, mitigating complications of critical illness has become one of the intensivist's most important goals.[1] The sudden onset of unexplained deterioration of consciousness can be particularly worrisome. In critical illnesses such a deterioration of sensorium may represent delirium, which is characterized by an acute onset and fluctuating course with disturbances in awareness and cognition.[2] In adults, delirium occurs frequently and represents global cerebral dysfunction due to the direct physiologic effects of an underlying medical illness or its treatment.[2,3] Although delirium is generally a temporary state, it is strongly associated with poor outcomes, including increased mortality, and long-term cognitive impairment in survivors.[4,5] Because of the extensive research highlighting the morbidity associated with delirium, the Society of Critical Care Medicine (SCCM) released guidelines in 2013 that recommended routine

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monitoring for delirium in critically ill adults as standard of care.[3] A recent body of pediatric literature suggests that this recommendation should apply to children as well.[6,7]

Pathophysiology

The cause of delirium is complex, with many possible pathophysiologic pathways. Most researchers think that delirium results from a combination of predisposing and precipitating factors. Predisposing factors are patient related (for example, age, genetic susceptibility, or underlying disease). Precipitating factors include treatment effects (particularly sedative medications) and the intensive care unit (ICU) environment.[3,8,9] Here the authors highlight 3 processes that are thought to play important roles in the evolution of pediatric delirium.

The *neuroinflammatory* hypothesis suggests that systemic inflammation (commonly seen during critical illnesses, such as respiratory failure, sepsis, and others) leads to either compromise in the integrity of the blood-brain barrier or de novo production of inflammatory products within the brain.[10] Inflammation leads to endothelial activation, enhanced cytokine activity, and infiltration of leukocytes and cytokines into the central nervous system (CNS), producing local ischemia and neuronal apoptosis.[11] Several studies have demonstrated elevated levels of proinflammatory cytokines in delirious patients (such as C-reactive protein, tumor necrosis factor-alpha, and interleukin-6) compared with nondelirious patients, even after controlling for age and cognitive impairment.[12–14]

The *neurotransmitter* hypothesis was generated from clinical observations that delirium often followed the use of medications that change neurotransmitter function.[10] Studies show that impaired cholinergic function, coupled with an excess of dopaminergic transmission, leads to the development of delirium.[15–17] Notably, anticholinergic medications are tightly associated with development of delirium in the geriatric population, as the elderly have an age-related reduction in acetylcholine synthesis.[18,19] (Intriguingly, a similar phenomenon may exist in children less than 2 years of age, whereby functional MRIs have demonstrated sparse connectivity between control structures related to executive function. This sparse connectivity results in dependence on the cholinergic system to modulate attention and orientation. Like the elderly, these young children may be at particular risk of delirium with exposure to anticholinergic medication.)[20,21] In addition to dopamine and acetylcholine, dysregulation of melatonin, glutamate, norepinephrine, serotonin, histamine, and gamma-aminobutyric acid has also been suggested to contribute to delirium development.[10]

The *oxidative stress* hypothesis suggests that reduced oxygen delivery in critical illness, coupled with increased cerebral metabolism, leads to the production of reactive oxygen species that cause global CNS dysfunction.[10] Hypoxia has clearly been associated with delirium development.[22–24] For instance, a study of patients undergoing cardiac surgery found that intraoperative desaturation was an independent risk factor for postoperative delirium.[23] Demonstrating that overlapping sources of pathophysiology contribute to delirium, hypoxia also results in an excess of dopamine due to the failure of the oxygen-dependent conversion of dopamine to norepinephrine. The enzyme responsible for dopamine degradation, catechol-o-methyl transferase, is inhibited by toxic metabolites produced during oxidative stress.[22] An excess of dopamine has been evidenced in multiple studies to underlie the pathogenesis of hyperactive delirium.[10]

Regardless of the exact pathophysiology that triggers an episode of delirium, the end result is the same: altered neurotransmission that leads to a failure of integration and processing of sensory information and motor response. This final common pathway leads to the behaviors that we recognize as delirium.[25]

Clinical Presentation

There are 3 major subtypes of delirium recognized by the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition: hyperactive, hypoactive, and mixed-type delirium, with each having specific characteristics. Hyperactive delirium is characterized by agitation, restlessness, hypervigilance, and combative behavior. In contrast, hypoactive delirium is notable for lethargy, inattention, and decreased responsiveness. Mixed-type delirium exhibits aspects of both hyperactive and hypoactive delirium.[2,3] Importantly, hypoactive delirium can be easily misdiagnosed as oversedation or clinical depression without appropriate screening and diagnostic tools for assessment.[26–28] Unfortunately, hypoactive delirium has been associated with poorest prognosis and greatest frequency, emphasizing the need for diligent screening for delirium in patients with critical illnesses.[29,30] In a longitudinal study of pediatric delirium and its subtypes, involving 1547 children and more than 7500 patient days, hypoactive and mixed-type delirium were most common (46% and 45%, respectively), whereas the hyperactive subtype was only found in 8% of patients.[7] This profile of delirium is consistent with observations of adults with critical illnesses.

Delirium in children is often marked by changes in psychomotor activity, ranging from delayed responsiveness to constant, agitated movements. Emotional lability is also common, evidenced by inconsolableness or, alternatively, inappropriate calmness. Some pediatric patients (particularly adolescents) experience auditory and visual hallucinations. Disordered sleep is nearly always present in delirious children.[8,9,31,32]

Preliminary evidence suggests that delirium often occurs early in the ICU course of children with critical illnesses, with a median time to development of delirium of 1 to 3 days in pediatric studies.[7,33–35] Furthermore, the few studies that have been conducted to assess the duration of delirium suggest it is a relatively brief condition, with a median of 2 days.[7,33,34] A substantial portion (approximately one-third) of patients with early onset delirium will demonstrate recurrent episodes during their ICU stay.[7,33]

Regardless of its duration or timing, delirium has measurable effects on a variety of outcomes. In a recent study of postoperative delirium in children, 2 patterns of delirium were described. For approximately half of the children, delirium was diagnosed early in the course of their illness (within 24 hours), was of short duration (less than 24 hours), and was characterized by relatively low scores on the Cornell Assessment of Pediatric Delirium (CAPD). Within this series, these children were categorized as having mild delirium. In contrast, another cohort of children experienced delirium throughout the study period (5 days) and were categorized as having severe delirium. Compared with children who were never delirious, those with mild delirium had increased time on mechanical ventilation and longer hospital length of stay (LOS), whereas those with severe delirium had even longer hospitalizations, took longer to emerge from sedation, had longer time to extubation, and had higher resource utilization.[34]

Epidemiology

Delirium in adults is a well-known problem, with many hospitals implementing delirium scoring plans, because more than 30% of all critically ill adults develop delirium during their ICU stay.[3,36] Delirium research in pediatrics lagged behind because of the lack of validated screening tools and a decreased awareness of this condition among clinicians.

Recent reports have found that pediatric delirium is quite frequent, with prevalence rates between 12% and 65% in pediatric medical, surgical, and cardiac ICUs.[6] In one of the earliest series in the field, a prevalence of 12.3% was reported; but this cohort

included only children older than 5 years and only 6% of the children were mechanically ventilated (MV).[37] In another cohort of children (0–21 years of age, 25% on MV), a delirium prevalence rate of 22% was observed. In this study, delirium was associated with age less than 5 years and preexisting developmental delay.[38] In a study of children with heart disease cared for in a cardiac ICU, a delirium prevalence of 49% was observed, largely comparable with adults with heart disease.[33] In the surgical population, a prevalence rate of 27% was described, with an overall delirium incidence of 65% in children within 5 days after surgery. (In this study, many subjects were infants after cardiac bypass procedures).[34] Another cohort study that included children within a limited age range (6 months to 5 years) found an overall prevalence of 47%; the highest rate (56%) was found in children younger than 2 years of age.[35] A large-scale, longitudinal study of delirium in all patients admitted to a single pediatric ICU (PICU) over a 1-year period of time, including more than 1500 patients, demonstrated a delirium rate of 17%.[7] It should be noted that this unit was an early adopter of delirium screening and had systematically changed its approach to sedation and management to minimize delirium risk. So it is likely that this 17% incidence is lower than rates in other institutions that have not been leaders in delirium screening.[7] In the largest multi-institutional pediatric delirium study to date, 994 children were assessed for delirium in 25 different PICUs. Delirium prevalence overall was 25%.[39]

Risk Factors

It is useful to separate risk factors for pediatric delirium into 2 categories: modifiable and nonmodifiable (**Table 1**). Independent risk factors for delirium development in critically ill adults include high severity-of-illness score on admission, elderly age, hypertension, dementia, alcoholism, and cigarette use. Hospital-related risk factors for delirium development in adults include depth of sedation, receipt of benzodiazepines, and use of restraints.[3]

Demographic risk factors for development of delirium in children include age less than 5 years and preexisting diagnosis of neurodevelopmental delay. It is not surprising that both the immature and abnormal brains, respectively, are more prone to development of delirium; this is similar to the finding of increased delirium in the elderly, and in those with underlying dementia.[7,25,33,35,39]

Children with higher severity-of-illness scores on admission are more likely to develop delirium. Delirium, in turn, then contributes to multiple organ dysfunction syndrome, as delirium itself is an indication of end-organ (brain) dysfunction.[7,33,34,40]

Duration of ICU stay likely contributes to delirium development, but this relationship is difficult to understand as a prolonged LOS likely exposes children to increased

Table 1
Risk factors for development of delirium

Predisposing Risk Factors	Precipitating Risk Factors
Age <2 y	Anticholinergic medications
Developmental delay	Benzodiazepines
High severity of illness	Cardiac bypass surgery
Low albumin	Immobilization
Mechanical ventilation	Prolonged ICU length of stay
Preexisting medical condition	Restraints

Risk factors for delirium can be separated into predisposing and precipitating risk factors. It is important to recognize that several risk factors are modifiable.

factors associated with delirium – and delirium also causes increased LOS.[7,25,33,34] To attempt to understand this relationship, an international study showed an increase in delirium rates after 5 days in the ICU (20% in children with LOS ≤5 days vs 38% in children with LOS >5 days, $P<.001$).[39]

Risk factors particular to children with congenital heart disease have been identified as well. Specifically, cardiac bypass surgery is thought to be a unique exposure, marked by a significant inflammatory response to the cardiotomy and bypass circuit, or possibly subclinical evidence of emboli during bypass.[41,42] Incidence of pediatric delirium after cardiotomy was strongly and independently associated with longer bypass times and greater complexity of the surgical repair. Children with cyanotic lesions were at increased risk for delirium, supporting several theories of delirium development, including those associated with hypoxia and oxidant stress. Poor nutritional status (using a preoperative albumin level <3 mg/dL as a surrogate marker for adequacy of nutrition) also strongly predicted delirium.[33]

Importantly, recent research has identified potentially modifiable risk factors for delirium development. A prospective observational study (n = 1540 children) used a multivariable model to demonstrate a 5-fold risk of delirium in children who were ever prescribed benzodiazepines (after controlling for severity of illness, developmental delay, mechanical ventilation, and other important confounders).[7] However, an assessment of the relationship between benzodiazepine use and delirium can be confounded by the fact that a child with hyperactive delirium could be prescribed benzodiazepines as a treatment of agitation. Therefore, it is important to assess the clinical context in much more detail. This was done in a longitudinal study that followed every child in a PICU throughout hospitalization. Each child was prospectively assigned a daily cognitive status of (1) delirium, (2) coma/deep sedation, or (3) delirium free/coma free. In this circumstance, and only considering children who developed next-day delirium (ie, a child who developed delirium after scoring delirium free/coma free the previous day), benzodiazepines remained independently associated with delirium (odds ratio [OR] 3.14, confidence interval 2.08–4.74, $P<.001$) after controlling for multiple covariates. In addition, an analysis of benzodiazepine doses administered to 539 critically ill children showed a dose-response effect, with delirium rates of 79% in those who received greater than 0.82 mg/kg/d of midazolam equivalents as compared with a 27% delirium rate in children given less than 0.82 mg/kg/d ($P<.001$).[7]

A multi-institutional point prevalence study demonstrated that odds of delirium quadrupled in patients who were physically restrained. Although this analysis was controlled for mechanical ventilation and use of sedating medications, temporality was not assessed (and it is possible that children were restrained after developing delirium).[39] However, it is consistent with a large body of adult literature that shows a clear relationship between use of physical restraints and subsequent development of delirium.[3,36,43,44]

Outcomes

Delirium that develops in adults with critical illnesses has been associated with poor outcomes, including a 3-fold increased risk of mortality, increased ICU and hospital LOS, longer time on mechanical ventilation, long-term cognitive impairment, and post–intensive care syndrome.[3–5,45,46] Additionally, delirium has been linked to increased rates of auto-extubation and inadvertent removal of catheters.[3]

Preliminary studies strongly suggest a similar pattern in children with critical illnesses. Pediatric delirium has been linked to short-term morbidity, including increased duration of mechanical ventilation in children with delirium (median 4 vs 1 day, $P<.001$).[7]

Several studies have shown that delirium is associated with increased length of hospital stay. In fact, in a cardiac ICU cohort, delirium was independently associated with an increase in LOS of 60%.[33] In a general PICU, adjusted relative LOS was 2.3 in children with delirium, after controlling for mechanical ventilation and severity of illness on admission.[7] In yet another study, delirium predicted increased hospital LOS, increased duration of mechanical ventilation, and higher resource utilization; the extent of increases was directly related to duration of delirium.[34]

From a financial perspective, a diagnosis of delirium in children has been associated with increased health care costs. In a single-center study, daily PICU costs were 23% higher for an ICU day with delirium as compared with an ICU day without delirium. Incidence of delirium was associated with an overall 85% increase in hospital costs (relative costs 1.85 [1.51–2.26], $P<.001$), even after controlling for severity of illness, PICU LOS, and other important confounders. This increase translates into more than $500 million each year in US hospital costs alone.[47]

A prospective pediatric study has shown a strong and independent association between pediatric delirium and mortality, with an adjusted OR of 4.4 for in-hospital death in children who were diagnosed with delirium. In this cohort delirium was a stronger predictor of mortality than the Pediatric Index of Mortality 3 score (OR of 3.2 in patients in the highest severity-of-illness category). Delirium may be an important identifier of children who are most vulnerable to poor outcomes.[7] To date, there are no long-term studies published that describe the association between delirium and cognitive outcomes in children after discharge or the effect of delirium on the long-term psychological and emotional health of PICU survivors and their families.

Diagnosis

Until the advent of bedside screening tools, pediatric intensivists relied on consultation with pediatric psychiatrists to make the diagnosis of delirium. Not surprisingly, psychiatrists were usually only consulted in extreme cases, when delirium resulted in disruptive and aggressive behaviors that interfered with the medical team's management plans or the symptoms were so extreme as to require an expansion of the differential diagnosis to other possible neurologic conditions.[30,48,49] A psychiatric assessment, although reliable, is not available for point-of-care use in every child in the PICU.[50] As in adults, there was a need to establish delirium screens for nonpsychiatrists to use routinely at the patients' bedside.

It would not be possible to simply adopt delirium tools designed for adults, as diagnosing delirium in children is complicated by developmental variability. The behavior expected from a hospitalized 2-year-old child, as compared with a 16-year-old adolescent, are vastly different; appropriate developmental expectations are necessary.[51] As pediatric clinicians became aware of the significant burden of delirium in adult ICUs, it was clear that it was necessary to develop child-specific bedside screening tools.[8,9,52]

Two different versions of pediatric delirium screens were developed: the Pediatric Confusion Assessment Method for the ICU (pCAM-ICU or psCAM-ICU for preschool-age children) and the CAPD. Both have been proven to be valid and reliable for detection of delirium in critically ill children. Each requires that the child be arousable to verbal stimulation in order to be assessed. Both the pCAM-ICU and CAPD should take only minutes to complete.[6,35,37,38,53]

The pCAM-ICU/psCAM-ICU are interactive, cognitively oriented screens (**Fig. 1**). The pCAM-ICU is designed for patients older than 5 years, and the psCAM-ICU is designed for children aged 6 months to 5 years. These tools are point-in-time screens, designed to detect delirium that is present at the time of testing. The interactive nature of the tool should yield objective results (delirium present or absent).[35,37]

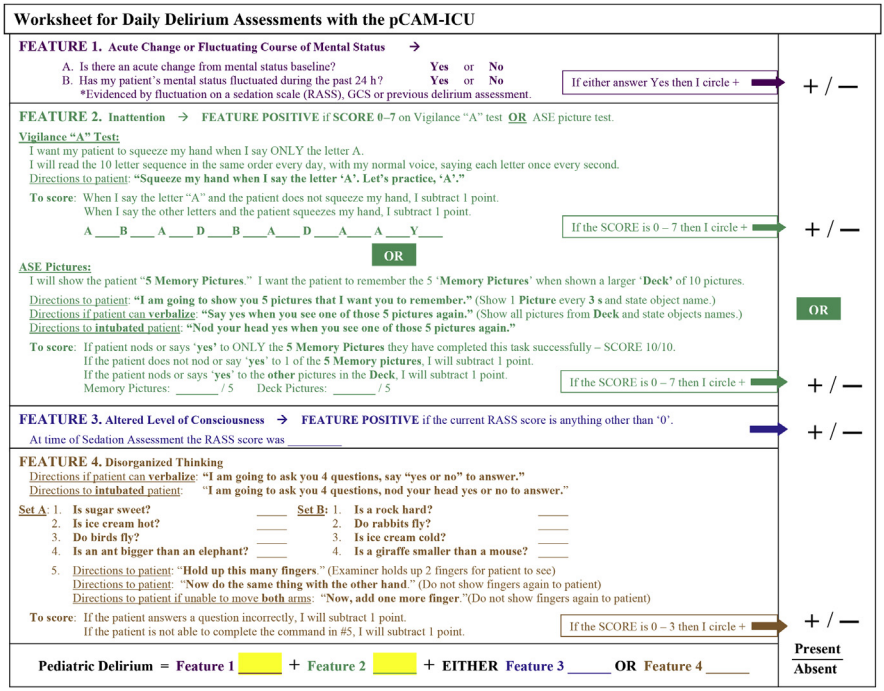

Fig. 1. pCAM-ICU. The pCAM-ICU is an interactive cognitively oriented tool validated in children from 5 to 18 years of age. (Available at: http://www.icudelirium.org/docs/ped_Instruction-Tool_pCAM-ICU_9-2016.pdf. Accessed July 10, 2017.)

The CAPD is an observational screen that provides a longitudinal picture of a pediatric patient over the course of a nursing shift (usually 8–12 hours) (**Table 2**). It is suitable for use in children 0 to 21 years of age and was validated in both developmentally delayed and developmentally typical children. A score of 9 or higher is consistent with a delirium diagnosis; the CAPD score can be trended within an individual patient over time, allowing for assessment of trajectory and response to interventions.[38]

With availability of rapid, valid, and reliable bedside tools for use in children of all ages, delirium screening has become feasible for use as standard of care in PICUs. In fact, 3 years after the publication of the SCCM's guidelines for adults, the European Society for Pediatric and Neonatal Intensive Care released consensus guidelines in 2016 calling for "use of CAPD as an instrument to assess pediatric delirium (grade of recommendation = A)" once each shift in critically ill children[6]. Routine monitoring will allow providers to detect and treat delirium earlier and potentially improve outcomes.[3,6]

Differential diagnosis

In children with underlying developmental delay, there is a need to establish alteration from cognitive baseline before diagnosing delirium. In addition to a positive delirium screen, the clinician needs to confirm that there is an acute process (ie, not merely static encephalopathy) with a fluctuating level of awareness over the course of the day.[50,51]

The classification of sedation-related delirium is controversial.[54] This type is a specific form of delirium that rapidly resolves once sedation is lifted and was noted in a protocol

Table 2
Cornell Assessment for Pediatric Delirium

Please answer these questions based on your interactions with the patient over the course of your shift:

	Never 4	*Rarely 3*	*Sometimes 2*	*Often 1*	*Always 0*	*Score*
1. Does the child make eye contact with the caregiver?						
2. Are the child's actions purposeful?						
3. Is the child aware of his or her surroundings?						
4. Does the child communicate needs and wants?						
	Never 0	*Rarely 1*	*Sometimes 2*	*Often 3*	*Always 4*	
5. Is the child restless?						
6. Is the child inconsolable?						
7. Is the child underactive: very little movement while awake?						
8. Does it take the child a long time to respond to interactions?						
TOTAL						

The CAPD is an observational longitudinal tool validated in children from birth to 21 years of age. (Available at: http://www.icudelirium.org/docs/capd.pdf. Accessed July 10, 2017.)

whereby adults were kept sedated for most of the day, with scheduled sedation breaks to allow for a period of wakefulness. In the subset of patients with delirium limited to rapidly reversible sedation-related delirium, outcomes were similar to patients who did not experience delirium,[55] suggesting that this was merely residual sedation and not delirium. This finding has not been replicated in a recent pediatric study using the CAPD, wherein delirium could be clearly distinguished from sedation by analysis of individual test items, and even mild delirium of short duration was associated with poor outcomes.[34] In fact, in a multicenter pediatric study, daily sedation interruption was associated with an overall increase in exposure to narcotics and benzodiazepines, increased time on mechanical ventilation, and increased length of hospital stay.[56] This finding highlights the importance of judicious sedation management in children.[57]

Iatrogenic withdrawal syndrome (IWS) can result in both the physiologic signs of abstinence and the behavioral symptoms of agitation, confusion, and motor activity that are consistent with hyperactive delirium. It is critically important to recognize and treat the physiologic signs of withdrawal (ie, dilated pupils, diarrhea) with judicious narcotic replacement.[58]

Treatment

When a child is diagnosed with delirium, the key to effective treatment is identifying the underlying cause. Clinically, delirium can be thought of as a product of the underlying illness, iatrogenic effects of treatment, and the ICU environment[9,25,31] (**Fig. 2**). With a stepwise approach, one should investigate for an underlying medical problem that

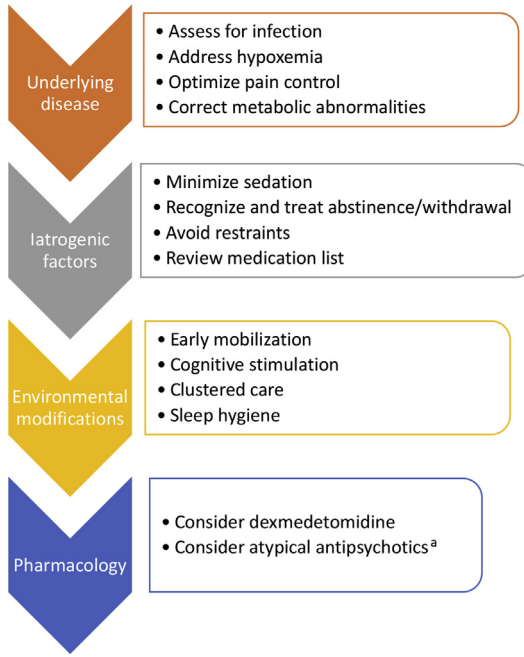

Fig. 2. Delirium treatment algorithm. With a systematic approach to targeting underlying triggers of delirium, most children will improve. If agitated behaviors persist, clinicians can consider pharmacologic treatment. [a] Note: This treatment is an off-label use of these drugs, as the Food and Drug Administration has not approved either dexmedetomidine or the atypical antipsychotics for treatment of pediatric delirium.

may have triggered the delirium episode. Delirium can be an early warning sign of an evolving infection or the result of hypoxia or acute metabolic derangements. A careful neurologic examination to exclude a primary CNS disease should be considered.[31,59,60]

After assessing for underlying illness, addressing iatrogenic causes of delirium is necessary. Optimizing pain control is essential, especially in preverbal children. Sedatives should be minimized, with consideration given to replacement of benzodiazepines with dexmedetomidine if possible, as several studies suggest that dexmedetomidine prevents and/or treats delirium.[61–65] (It is important to note that this is an off-label use, as the Food and Drug Administration has not approved dexmedetomidine for the treatment of pediatric delirium.) A careful review of the patients' medication list is warranted with consideration of discontinuing medications that might be associated with delirium, if possible (particularly sedatives, anticholinergics, and steroids).[3,9,25] Identification of IWS is necessary, with judicious narcotic replacement until the physiologic signs of withdrawal abate.[58] But after treating IWS, the agitated behavior of hyperactive delirium may persist and often requires environmental modifications (and sometimes pharmacologic alternatives) rather than a further increase in narcotics, which may just prolong the delirium.[66]

Careful attention to patients' environment is part of the process of treating delirium.[67] Repeated reorientation of patients, use of eye glasses or hearing aids when indicated, and minimization of excessive noise can be helpful. Keeping a child's favorite stuffed animal or blanket from home can normalize the ICU bed. Clustering

care can dramatically reduce the frequency of stimulation.[9,25,39] Creating an environment less disruptive to sleep is important – ensuring lights off at night and on during the day helps to promote normal circadian rhythms.[68] Early mobilization has been an effective intervention in adult ICUs, not only in reducing poor functional outcomes, but also in decreasing delirium rates.[69] Progressive increase in activity levels can be safely achieved, even in extremely young and MV children.[70]

Most pediatric delirium will improve with management of underlying medical illness, minimizing iatrogenic triggers, and optimizing the PICU environment. However, if the delirium persists and the child has agitated behaviors that are distressful or interfering with the medical care plan, pharmacologic therapies are available. Most experts recommend use of the atypical antipsychotics because of their procognitive effects and favorable side effect profile.[3,71,72] This therapy is an off-label use, as this drug class is not approved for treatment of pediatric delirium. Nonetheless, a randomized controlled trial of quetiapine (an atypical antipsychotic) as treatment of adult delirium indicated a benefit; pediatric case series have suggested efficacy in children.[49,73–76] A retrospective safety study in 50 delirious children treated with quetiapine showed no serious adverse events.[77] Important when starting any form of antipsychotic is to monitor for QT prolongation, dysrhythmias, and extrapyramidal side effects.[72,78]

Prevention

Delirium can be conceptualized as a hospital-acquired complication that results in both short- and long-term adverse effects in survivors of pediatric critical illness. As such, prevention of delirium is an important goal.[3,6]

Anecdotally, the culture within critical care units, both adult and pediatric, seems to be changing. In years past, most critically ill children were sedated during their time in the ICU. They were often physically restrained, kept on strict bed rest, and exposed to noise and lights 24 hours a day. Although parents were allowed at the bedside, they were discouraged from physically interacting with their child. Cognitive stimulation was kept to a minimum. This practice was likely the result of the desire to spare children from a traumatic hospitalization and/or to allow them to rest. When children became agitated, they were labeled as difficult to sedate and sedating medications (usually benzodiazepines) were increased further.[53,54]

However, recent research on post-ICU outcomes (including myopathy and cognitive impairment) shows that neither the mind nor the body benefits from prolonged periods of inactivity.[3,79–81] In particular, use of deep sedation (specifically benzodiazepines) in children leads to increased delirium and decreased sleep and may be associated with delusional memories and posttraumatic stress disorder.[82–85]

The SCCM has endorsed an alternative approach in adult ICUs, termed *analgo-sedation*, that is now being adopted in PICUs as well (**Fig. 3**). For most patients, sedation is not necessary as first-line therapy. Rather, with an analgesic-first approach, the goal is to optimize pain control and minimize sedation. With less sedation on board, patients are less likely to develop iatrogenic delirium. They are better able to communicate pain, which in turn leads to better pain control. They are also more available to participate in early mobilization. Family members and child life specialists provide age-appropriate cognitive stimulation during the day, and the medical care team attempts to optimize the PICU environment for nighttime sleep.[3,83,86,87]

With heightened awareness as to the frequency and seriousness of pediatric delirium, implementation of an analgo-sedation approach, incorporation of early mobilization, and involvement of family members in daily care, we may be able to prevent delirium in at-risk children.

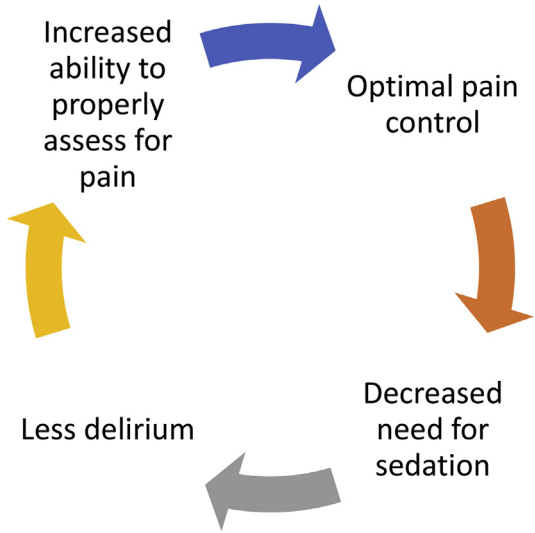

Fig. 3. Analgo-sedation. An analgesic-first approach avoids sedatives unless necessary. This approach decreases frequency of delirium.

SUMMARY

Delirium is a frequent complication of pediatric critical illness. Universal screening is feasible and necessary for early detection. This screening allows for targeted intervention and identification of children at risk for short-term morbidity and mortality. Further research is necessary to determine the long-term cognitive and psychological effects of pediatric delirium, and interventional studies are needed to establish best practices for treatment and prevention of delirium in critically ill children.

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