Assessment and Management of Delirium in Pediatric Patients

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LESSONS LEARNED AT THE INTERFACE OF MEDICINE AND PSYCHIATRY

The Psychiatric Consultation Service at Massachusetts General Hospital sees medical and surgical inpatients with comorbid psychiatric symptoms and conditions. During their twice-weekly rounds, Dr Stern and other members of the Consultation Service discuss diagnosis and management of hospitalized patients with complex medical or surgical problems who also demonstrate psychiatric symptoms or conditions. These discussions have given rise to rounds reports that will prove useful for clinicians practicing at the interface of medicine and psychiatry.

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Have you ever been uncertain about how to assess an altered mental status in children and adolescents? Have you been unsure about how delirium can present in pediatric patients? Have you worried about missing a life-threatening cause of an altered mental status in younger patients? Have you wondered about whether and how you can prevent and treat delirium in children and adolescents? If you have, then the following case vignette and discussion should prove useful.

CASE VIGNETTE

An 8-year-old boy with a history of asthma was brought to his pediatrician's office by his parents with an asthma exacerbation that had started after he had contracted a viral upper respiratory infection. On physical examination, he was wheezing upon both inhalation and expiration, and he was using his accessory muscles to breathe. The pediatrician sent him to the emergency department (ED), where he was started on a nebulizer (albuterol 0.15 mg/kg every 20 minutes and dexamethasone 0.6 mg/kg IV), but his breathing continued to worsen, and he became cyanotic. His oxygen saturation continued to decline to 83%, and he was intubated and admitted to the hospital with respiratory failure.

Two days later, he was extubated. However, his parents noted that he was now anxious and was not acting like he usually did. When he awakened, he needed to be reminded that he was in the hospital. The nurses noted that he had been sleeping during the day, was awake most of the night, and was having nightmares. His medication regimen in the hospital included Ativan 2 mg every 8 hours for anxiety.

DISCUSSION

How Can the Mental Status Examination of Children and Adolescents Be Assessed?

Mental status and neurologic examinations vary according to the age and developmental milestones of children and adolescents. Their interpretation also depends on the child's baseline functioning and presence or absence of a developmental delay. Given this variability, the neurologic/mental status examination should be informed by an interview with the child's caregivers to determine the child's baseline as well as to gather the medical and family history of neurologic diseases or developmental delay.[1–3]

In neonates, periods of wakefulness typically alternate with active and quiet sleep. However, presence of lethargy or irritability is considered abnormal. Since older infants

Clinical Points

- Delirium, particularly hypoactive delirium, is frequently underdiagnosed; therefore, routine screening is recommended in pediatric patients.
- When delirium is detected in pediatric patients, management includes identifying the etiology as well as removing any contributing factors that can include environmental and iatrogenic sources.
- There are both short-term and long-term effects from delirium in children and adolescents, including reduced quality of life after discharge from the hospital and impaired cognition.

should be able to fixate on objects or people, watching how they respond to visual, verbal, and physical stimuli is critical in assessing mentation, as is watching how they eat.[1–3]

In toddlers and children up to 6 years old, most of the mental status examination can be completed by observing day-to-day behaviors. Watching how a child plays with a toy can provide evidence of the level of alertness, as well as motor function and coordination.[2]

Children aged 6 years and older (who are without a developmental delay) should be able to participate in conversations and describe their symptoms; this can provide evidence of their level of alertness, speech and language, motor behavior, and orientation. When evaluating cognition, screening questions may include counting to 20, reciting the alphabet, or pointing to various body parts (such as the chin, nose, or knees), but this does not substitute for a more formal cognitive evaluation.[3]

The assessment of the mental status of adolescents is like that of adults, with testing of language, reading, writing, math, fund of knowledge, abstraction, judgment, insight, and memory. However, their educational level or the presence of a neurodevelopmental delay may affect the assessment.[1,2]

What Can Cause an Altered Mental Status in Children and Adolescents?

Common causes of an altered mental status in children and adolescents include seizures, trauma, shock, exposure to toxic agents, electrolyte abnormalities (including hyperglycemia or hypoglycemia), and encephalitis. In infants and toddlers, additional age-specific etiologies including brief resolved unexplained events, breath-holding spells, inborn errors of metabolism, nonaccidental trauma, sepsis, and intussusception should be considered. In children and adolescents, a brain mass, syncope, migraine headaches, or infectious etiologies (like shigellosis) should be ruled out. Additional age-specific etiologies in adolescents include a variety of psychiatric conditions and posterior reversible encephalopathy syndrome. A prolonged alteration in mentation after an episode of loss of consciousness with accompanying tongue biting can suggest a seizure as opposed to syncope.[4] Delirium has also been reported in adolescents with coronavirus disease 2019 (COVID-19), but further study is needed to determine prevalence.[5]

Delirium develops acutely and can be described as a fluctuation in cognition due to an underlying medical condition (such as the etiologies listed previously) (Table 1). Risk factors for delirium include infectious or inflammatory diagnoses, age < 2 years, receiving mechanical ventilation, and using benzodiazepines, narcotics, corticosteroids, or anticholinergic medications. Use of physical restraints and exposure to vasopressors or antiepileptics are also associated with delirium. Children are at higher risk for developing delirium if they have a developmental delay or if they have been in a coma or deeply sedated, and longitudinal studies[6–9] have shown that a diagnosis of delirium is most frequently associated with respiratory failure and postsurgical status.

How Can Delirium in Children and Adolescents Be Diagnosed?

Delirium can be detected and subsequently monitored by using validated assessment tools and scales. Multiple scales, including the Pediatric Anesthesia Emergence Delirium Scale (PAED),[10] the Cornell Assessment of Pediatric Delirium (CAP-D),[11] and the Confusion Assessment Method for the Intensive Care Unit for both pediatric and preschool populations[12] (PCAM-ICU and PSCAM-ICU, respectively) have been shown to have a high sensitivity and specificity for delirium (Table 2). These screenings are intended for use at bedside in the pediatric intensive care unit (PICU). The CAP-D and PAED are primarily observational screenings for delirium. The CAP-D can be performed on children of all ages, whereas the PAED specifically screens for the emergence of delirium or delirium that occurs after being under anesthesia. The PCAM-ICU (for children aged > 5 years) and the PSCAM-ICU (for children aged 6 months to 5 years) rely on both observations of the child and interviews to assess attention, orientation, and thought processes.[13]

The PSCAM-ICU has even been shown to be a valid screening tool in infants aged 6 months and younger.[12] The CAP-D has demonstrated a high interrater reliability, with utilization of anchor points for normal development at 8 weeks and 1 year. Limitations in screening specificity may be seen in patients with significant developmental delay; however, incorporation of the Richmond Agitation Sedation Scale[14] has been shown to improve this specificity.[11,15] Compared to the other tools, the PAED possesses a lower sensitivity for the diagnosis of hypoactive delirium.[13]

How Common Is Pediatric Delirium and Why Is It Often Overlooked?

Delirium develops in about 25% of children who are admitted to a PICU, with a 38% incidence seen in children who have been admitted for 6 days or more.[7] Hypoactive delirium is more common than hyperactive and mixed delirium, with delirium occurring in up to 34% of those admitted to ICUs. However, hypoactive delirium does not attract the same attention as hyperactive delirium and mixed (hyperactive and hypoactive) delirium with aggression and irritability, which often results in a longer time to diagnosis. Frequent shift changes of nursing staff throughout the day

Table 1. Manifestations of Delirium at Various Life Stages

Life Stage	Hypoactive Delirium	Hyperactive Delirium
Infants	Unable to fixate on faces Primitive reflexes only Lethargy Little movement when awake, with movement being non-purposeful Not crying when hungry	Unable to fixate on faces Primitive reflexes only Irritability Non-purposeful movements, shaking head Inconsolable, restless Minimal calm awake time
Children	Unable to communicate needs Confusion Decreased coordination Unable to participate in play Non-purposeful actions Not answering questions quickly or appropriately Lethargy Averting eyes or staring Increased effort to sit up and walk around	Unable to communicate needs Confusion Unable to participate in play Non-purposeful actions Not answering questions quickly or appropriately Irritability Inconsolable, restless Unable to make eye contact In hospital, attempting to remove intravenous and monitoring lines
Adolescents/adults	Disoriented Inattentive Impairment of sleep-wake cycle Emotional disturbance Falling asleep inappropriately	Disoriented Inattentive Impairment of sleep-wake cycle Emotional disturbance Irritable, agitated

Table 2. Pediatric Delirium Screening Tools

Screening Tool	Age Range for Applicability	Length of Time to Administer	Domains of Assessment
Pediatric Anesthesia Emergence Delirium Scale[10]	Emergence delirium in all ages	Less than 2 minutes	Primarily observational
Cornell Assessment of Pediatric Delirium[11]	All ages, with anchor points at 8 weeks and 1 year	Less than 2 minutes	Primarily observational
Preschool Confusion Assessment Method for the ICU[12]	Children 6 months to 5 years old	Less than 2 minutes	Observation with structured assessment of attention, orientation, and thought process
Pediatric Confusion Assessment Method for the ICU[12]	Children over 5 years old	Less than 2 minutes	Observational with structured assessment of attention, orientation, and thought process

and brief examinations by treatment teams contribute to low rates of detection of delirium. As a result, routine screening is recommended in the ICU.[16,17] Delirium in the non-ICU setting has been reported in adults, but little is known about the incidence of pediatric delirium in non-ICU admissions, further complicating its detection and treatment.

What Are the Consequences of Misdiagnosis and Mistreatment of Delirium in Children and Adolescents?

Delirium in children and adolescents has been linked with a higher mortality rate (odds ratio = 4.4).[9] Delirium is also associated with a longer length of stay in the PICU (up to twice as long compared to that of patients without delirium) and more time spent receiving mechanical ventilation.[9] A diagnosis of delirium has also been associated with costlier hospitalizations (up to an 85% increase in cost).[18] For these reasons, early diagnosis and treatment of delirium is crucial.

How Can Delirium in Pediatric Patients Be Managed?

The approach to delirium in pediatric patients involves identifying the underlying illness and minimizing environmental and iatrogenic contributors. Timely evaluation is essential, as myriad medical conditions (involving deoxygenation, hypoperfusion of the central nervous system, drug withdrawal, infections, seizures, toxidromes, metabolic and electrolyte abnormalities, immunologic disorders, and neurologic diseases) can become lethal if left undiagnosed and untreated.[9]

Management of delirium is best accomplished by treating the precipitating problem as specifically as possible. In addition, environmental interventions can reduce delirium's behavioral accompaniments. A normal sleep-wake cycle can be promoted by implementation of daytime and nighttime routines and by use of melatonin or ramelteon at bedtime. In addition, lightening exogenous sedation, increasing mobility, reorienting frequently, and maintaining a low-stimulus environment can be soothing. Reducing or eliminating iatrogenic triggers is highly recommended (eg, discontinuing anticholinergic medications, opioids, corticosteroids, and benzodiazepines).[19,20]

To address the agitation, irritability, and restlessness seen with hyperactive delirium, use of atypical antipsychotics (including risperidone, olanzapine, and quetiapine) or first-generation antipsychotics (eg, haloperidol) has led to positive outcomes (Table 3).[19,21–23] Choosing an antipsychotic often depends on the formulation available; for

Table 3. Antipsychotics Used in Delirium

Medication	Routes of Administration	Dose Range	Potential Side Effects
Risperidone	PO (as tablet, ODT, liquid)	Infants: 0.05–0.1 mg/d at bedtime Children < 5 years old: 0.1–0.2 mg/d at bedtime Children > 5 years old to adolescents: 0.2–2.5 mg/d in divided doses	Sedation, metabolic side effects with long-term use Less risk for EPS compared to first-generation antipsychotics, neuroleptic malignant syndrome
Olanzapine	PO (as tablet, ODT)	Children > 3 years old to adolescents: 1.25–5 mg/d at bedtime	Sedation, metabolic side effects with long-term use Less risk for EPS or neuroleptic malignant syndrome compared to first-generation antipsychotics
Quetiapine	PO	Minimal literature, previous reports of dosing at 1.3 mg/kg/d[21]	Sedation Metabolic side effects with long-term use Less risk for EPS or neuroleptic malignant syndrome compared to first-generation antipsychotics
Haloperidol	PO, IV	Infants under 10 kg: 0.025 mg/kg/d IV has been reported[19]; expert opinion recommended Children/adolescents over 10 kg: 0.05–0.15 mg/kg/d either PO or IV divided into every 12 hours, oral formulation preferred; urgent 1-time dosing of 0.5–1 mg PO in children has also been reportedly tolerated[22,23]	PO formulation has higher risk for EPS including dystonia IV formulation has higher risk for QTc prolongation and arrhythmia Neuroleptic malignant syndrome and hyperpyrexia have been reported

Abbreviations: EPS = extrapyramidal symptoms, IV = intravenous, ODT = orally disintegrating tablets, PO = by mouth, QTc = corrected QT interval.

Table 4. Preventive Strategies for Delirium

Behavioral interventions
- Provide reassurance and reorientation frequently
- Have family available to assist in reorientation
- Reduce nighttime alarms and extraneous physical examinations

Environmental interventions
- Adequately manage pain
- Encourage early mobilization
- If able, have patient's favorite toys or pictures of family available
- Promote sleep-wake cycles with melatonin or ramelteon

Medication interventions
- Minimize drugs that alter mental status, including anticholinergic medications, opioids, corticosteroids, and benzodiazepines
- May consider using dexmedetomidine if sedation is required

example, risperidone may be prescribed in liquid form or as an oral disintegrating tablet (making it ideal for children who cannot swallow pills). Dexmedetomidine has also been used in the PICU, as it provides sedation and anxiety reduction without increasing the risk for delirium. Dexmedetomidine can be transitioned to other α-agonists (eg, oral clonidine) for continued anxiolysis.[20–22]

Other medications, such as α_2 agonists (eg, guanfacine), can reduce the norepinephrine surge that accompanies hyperactive delirious states. Guanfacine, an α agonist that is typically used for the treatment of attention-deficit/hyperactivity disorder, has shown promise in adults with delirium and in adolescents with delirium secondary to COVID-19 infection.[5,24] Specifically for delirium that arises shortly after surgery, dexmedetomidine can be used for purposes of sedation in the PICU and then be transitioned to clonidine to decrease the incidence of delirium.[20] Use of ketamine for management of hyperactive delirium in the ED has also shown positive results.[25]

How Can Delirium in Pediatric Patients Be Prevented?

Prevention of delirium often focuses on manipulating behavioral components as well as on screening and reducing biomedical conditions (eg, hypotension, hypoxemia) (Table 4). Psychosocial and behavioral interventions include having the child be accompanied at the hospital by family members and placing images of family members, favorite objects or toys, and clocks in the room to keep the child oriented. Providing reassurance and reorientation when the child wakes up from anesthesia can also help to reduce anxiety, as well as maintaining proper sleep-wake cycles and minimizing things (including alarms and additional examinations) that could wake the child during the night.[20] Adequately managing pain, minimizing iatrogenic contributors, and encouraging early mobilization have decreased the rate of delirium.[16]

Currently, there are no widely accepted medications for delirium prevention. There is also minimal agreement on which antipsychotics or dosing strategies should be used for the prevention of delirium. In adults, use of antipsychotics to prevent delirium is not routinely recommended.[16,26]

What Are the Long-Term Consequences of Pediatric Delirium?

In a study,[27] delirium was associated with a decreased quality of life, as measured by the Infant-Toddler Quality of Life Questionnaire at 1 month and 3 months after hospital discharge. Psychological consequences of delirium include an increased risk for delusional memories, particularly if children were given benzodiazepines or opioids during their hospitalization.[28] Moreover, 5%–28% of children with delirium were later diagnosed with posttraumatic stress disorder (PTSD), and 35%–62% of children with delirium had symptoms of PTSD.[29]

Delirium, which has been associated with longer length of stays in the neonatal ICU (NICU) and PICU, may also adversely affect long-term cognition. Prolonged stays in the NICU have been associated with a bottom 10% scoring on the Bayley Scales of Infant and Toddler Development on the 9-month and 24-month mental and motor assessments.[30] In the PICU, mechanical ventilation and longer ICU length of stays were associated with higher rates of acquired global

functional and cognitive disabilities as evidenced by lower scores on the Pediatric Overall Performance Category Scale and the Pediatric Cerebral Performance Category Scale.[31] Children who were admitted to the PICU for at least 48 hours with a diagnosis of delirium were found to have a significant decrease in Pediatric Cerebral Performance Category Scale scores (from their preadmission testing to their hospital discharge), with more than a 3-point decline.[32] Further research is needed to determine whether delirium independently adversely influences long-term cognition after discharge, as knowing so could provide insight into whether children can benefit from routine cognitive screening or mental status examinations after being discharged from the hospital

What Happened to Our Patient?

Our patient was able to think more clearly after his as-needed benzodiazepines were discontinued, and his pain was adequately treated. He was started on a twice-daily dose of guanfacine for agitation and anxiety and nightly melatonin to improve his sleep-wake cycle. His parents were instructed to reorient him frequently and to keep him engaged throughout the day. With these interventions, he quickly returned to his baseline cognitive state and no longer complained of any nighttime disturbances or anxiety. He was discharged to his home shortly thereafter. Upon follow-up with his primary care doctor, he was screened for PTSD symptoms, during which he reported worsening nightmares since returning home from the hospital. His primary care doctor recommended that if these nightmares persisted or were accompanied by other symptoms of anxiety or PTSD he may benefit from trauma-focused therapy.

CONCLUSION

Delirium is a common and frequently overlooked complication in children who are admitted to the hospital. Contributing factors include worsening underlying medical problems, disruption of sleep-wake cycles, and use of medications that are deliriogenic. Management of delirium should focus on addressing underlying medical problems and managing pain. Management of delirium often includes use of medications, including antipsychotics; however, further study on this issue is needed. Continued monitoring after discharge of both cognitive function and development is indicated, since there may be long-term effects from prolonged NICU and PICU stays. Screening for the psychological impact of hospitalization may also be appropriate to facilitate outpatient follow-up.

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