

Infants with Delirium: A Primer On Prevention, Recognition, And Management

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Delirium is a serious neuropsychiatric condition that emerges acutely in all age groups, including infants, children, and adolescents. Delirium as a psychiatric emergency is often unrecognized and undermanaged because healthcare providers tend to underestimate the impact of delirium on patients, and lack knowledge on recognition and risk factors (Basset, 2010; Schieveld & Leentjens, 2005). Prevention, recognition, and management of infants with delirium is often especially challenging due to their pre-verbal status and immature cognitive development. Pediatric nurses are in a key role to prevent, recognize, and ameliorate delirium in the pediatric intensive care unit (PICU) and other healthcare settings. As proximal care providers, pediatric nurses play perhaps the most critical role in pre-

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vention and early recognition of delirium in infants. Through the provision of essential nursing care, pediatric nurses may also contribute to amelioration of diagnosed delirium in infants.

This article presents an overview of delirium in infants, offers details regarding the presentation of delirium in infants, discusses the challenges to screening and identification of infants with delirium, and provides suggestions for pediatric nurses to optimize nursing care for infants at risk for or exhibiting delirium.

Background

Delirium is a neurobehavioral syndrome that represents acute brain dysfunction precipitated by medical conditions and iatrogenic factors (Maldonado, 2008, 2013; Smith, Fuchs, Pandharipande, Barr, & Ely, 2011). Delirium as part of critical illness may indicate organ failure of the brain, with a cascade of underlying pathophysiological mechanisms contributing to the negative clinical presentation. Many etiologies for delirium have been suggested, but the precise mechanism of delirium pathophysiology is yet unknown. The occurrence of delirium may originate in any number of pathways associated with systemic illness or iatrogenic intervention, including oxygen deprivation, in-

flammatory cytokine release, increased hypothalamic-pituitary-adrenal axis activity, or disruption of intracellular systems (Maldonado, 2013; Smith, Fuchs et al., 2011). Severe illness and physiologic stress may modify blood-brain barrier permeability and produce abnormalities of thyroid hormone concentrations, circumstances that can contribute to neurotransmitter synthesis changes and release of cytokines in the brain, potentially leading to delirium (Maldonado, 2008). Research into conditions, such as epilepsy, meningitis, and traumatic brain injury, shows that the still-developing brain of the child, when deprived of oxygen and experiencing cytokine-release effects, responds differently than the adult brain (Potts et al., 2006). Underlying medical conditions coupled with common PICU interventions, including polypharmacy, aggravate delirium, which is further exacerbated by multiple medical conditions, the severity of illness, age (with the youngest and the oldest patients most often affected by delirium), and stress.

Delirium serves as an urgent signal of distress that a child's brain is in trouble. Morbidity and mortality in children with delirium is higher than for children without delirium (Schieveld et al., 2008). Patients with prolonged hospital stays (particularly in a PICU) and more severe illness are at greater

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risk for the development of delirium (Holly, Porter, Echevarria, Dreker, & Ruzeheji, peer review; Schievelde et al., 2008; Smeets et al., 2010; Turkel & Tavare, 2003).

The exact incidence of delirium in children is unknown, with estimates ranging from 13% to 28%, although this is likely an underestimate, especially in very young children where the diagnosis of delirium is more challenging (Colville, 2008; Daoud, Duff & Joffe, 2014). Age-specific prevalence for delirium in very young children aged 0 to 3 years was 3% in one study and 19.5% for young children aged 0 to 2 years in another (Schievelde et al., 2007; Traube, Silver et al., 2014). Schievelde et al. (2007) considered only children who were referred to child psychiatry and likely only included those very young children with overt signs of delirium, so the 3% figure may be an underestimate. In addition, almost one-third of older children (ages seven to 17 years) report memories of upsetting delusions from their PICU stay (Colville, Kerry, & Pierce, 2008). For very young children, a determination of post-discharge memories of delusions in the PICU is difficult.

Age and Underlying Diagnosis

Infants under 12 months of age exhibit delirium symptoms, but the recognition and diagnosis is often more nuanced and challenging, somewhat similar to the challenges of pain assessment and management in infants. Because of their essentially pre-verbal status and still-developing cognitive abilities, infants are unable to verbally respond to reorientation, answer screening questions, or describe hallucinations and delusions (Schievelde & Leentjens, 2005).

Published studies detail delirium in infants, including in those as young as six months of age (Schievelde et al., 2010; Silver, Kearney, Kutko, & Bartell, 2010; Turkel & Tavare, 2003). A limited number of published reports document the following underlying medical conditions in infants with delirium: hypoplastic left heart syndrome, neuroblastoma, post-surgical status, sepsis, trauma, excess anticholinergic medication, and Ellis-van Creveld syndrome; however, many other medical conditions are implicated as well (Jacobson & Turkel, 2013; Madden, Turkel, Jacobson,

Epstein, & Moromisato, 2011; Silver et al., 2010; Traube, Augenstein, Greenwald, LaQuaglia, & Silver, 2014; Turkel & Tavare, 2003). Agents with neurotoxic effects may exacerbate infant delirium. These agents include benzodiazepines, opioids, other sedatives and analgesics, and steroids (Silver et al., 2010).

More recently, Groves, Traube, and Silver (2016) reported on three infants with corrected gestational ages of 4, 11, and 17 weeks who exhibited delirium symptoms, including agitation, inconsolability, poor sleep, and restlessness. The three infants all had complex medical challenges, including preterm birth, cardiac disease, multiple surgeries, infectious complications, and gastrostomy tube placement. All three infants were treated with quetiapine.

Symptoms of Delirium In Infants

Clinical signs of delirium vary among patients and are often dependent on patient age, and in the case of infants and children, their developmental stage. Information from a limited number of published case reports describe the following behaviors in infants with delirium: arching, agitation, inattention, inconsolability, insomnia, lack of recognition of familiar people, restlessness, screaming, self-extubation and pulling out lines, sleep-wake cycle reversal, and wiggling (Jacobson & Turkel, 2013; Madden et al., 2011; Silver et al., 2010).

Infants with delirium have deficits in awareness, cognition, and arousal (Madden et al., 2011; Schievelde et al., 2010; Silver et al., 2010). Delirium in infants is manifested by impaired consciousness, attention difficulties, and disturbances in sleep and wake routines (Jacobson & Turkel, 2013). Attention and state dysregulation may be noted in infants with delirium (Turkel, Jacobson, & Tavare, 2013).

Three subtypes of delirium have been identified: hyperactive, hypoactive, and mixed. In children, acute delirium can present as any one of the subtypes. Because children with hypoactive delirium are quiet, lethargic, and inattentive, they are less likely to cause self-harm, and thus, less likely to elicit healthcare provider concern (Kelly & Frosch, 2012; Silver et al., 2010). By contrast, children with hyperactive delirium may cause a great deal of consternation for nurs-

es and other healthcare providers because these children may be very anxious and agitated resulting in autoextubation or intravenous connection disruption. Some children present with cognitive and/or attention difficulties, moaning, and restlessness related to severe anxiety, but without overt agitation or lethargy. This subtype has been referred to as mixed or "emerging" or "veiled" delirium (Holly, Cantwell & Jadotte, 2012; Schievelde et al., 2007). Agitation is the symptom most commonly reported for infants suspected of having delirium; however, the hypoactive delirium subtype where the very young child is withdrawn and quiet is believed to be especially underrecognized in infants (Kelly & Frosch, 2012). According to Schievelde et al. (2010), refractory agitation may be a marker for delirium in infants.

Recognizing Delirium In Infants

The need for attentive monitoring of infants at risk for delirium as part of usual PICU care is essential because symptoms in infants may be more subtle and developmentally variable (Schievelde & Leentjens, 2005). Early recognition of delirium is critical because delirium in children may represent ongoing damage to the vulnerable, developing brain, so prevention and timely detection are essential. Delirium symptoms that can be attributed to a number of other conditions place the infant with delirium at risk for unnecessary testing, poorer neurodevelopmental outcomes, and increased length of stay (Madden et al., 2011; Smeets et al., 2010). Early recognition of delirium may prevent unnecessary laboratory tests, imaging tests, and fear-inducing procedures searching for the seemingly elusive cause of agitation or other symptoms.

Widespread delirium screening as a standard of care, along with careful observation and attendance to parent concerns about changes in their infant's behavior, including sleep concerns, may support early recognition of delirium (Silver et al., 2012). Screening with an appropriate delirium tool should optimally be performed each shift to capture delirium's acute onset and fluctuating nature, as well as behaviors that are often worse at night (Traube, Silver, Kearney, Patel, & Atkinson, 2014; Turkel & Tavare, 2003).

Delirium Screening Tools

The American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)* criteria as applied by a child psychiatrist is the "gold standard" for diagnosis of delirium (Traube, Augenstein et al., 2014). In a recent systematic review, Daoud et al. (2014) were unable to recommend a routine pediatric delirium screening tool but found the following tools to be most promising: the Cornell Assessment of Pediatric Delirium (CAPD), which is especially useful in exposing hypoactive delirium; and the Pediatric Confusion Assessment Method (p-CAM-ICU). The p-CAM-ICU is for use with children aged five years and older.

Recently, a developmentally informed delirium screening tool appropriate for use with critically ill infants under age one year has been developed. Developed with pediatric nurse input, the CAPD is a rapid and valid observational bedside nursing screen designed to identify critically ill infants and children at risk for delirium (Cornell University, 2012; Silver, Kearney, Traube, & Hertzog, 2015; Traube, Silver et al., 2014). For pediatric patients 0 to 21 years of age, the CAPD has excellent sensitivity (94.1%) and fair specificity (79.2%). For very young children less than two years of age, CAPD sensitivity (100%) is improved, and specificity (67.7%) is decreased. Test sensitivity is the ability of a test to correctly identify those with the disease (true positive rate), whereas test specificity is the ability of the test to correctly identify those without the disease (true negative rate) (Pewsner et al., 2004).

Foundational knowledge of child development and the use of this knowledge is important to ensure high quality care in all pediatric settings. CAPD uniquely grounds pediatric delirium assessment in the context of child development (using developmental anchor points). This is especially important for nuanced developmentally informed screening of critically ill infants at risk for delirium who may exhibit subtle, developmentally variable symptoms of distress (Silver, Kearney et al., 2015). Developmental anchor points beginning with the newborn and progressing through the age points (four weeks, six weeks, eight weeks, 28 weeks, one year, and two years) provide bedside users with developmen-

tal reference points (Silver, Kearney et al., 2015). CAPD uses the strengths of primary bedside nurses, including experience caring for children of all ages and relationships with individual pediatric patients and their families, to establish baseline data and reliably assess the child "over time and across many interactions" to identify delirium risk (Silver, Kearney et al., 2015, p. 5). If the infant screens positive with the CAPD, consultation with a child psychiatrist experienced in working with critically ill infants is extremely helpful to assist in diagnosis and management (Silver, Kearney et al., 2015).

Another potentially useful tool for delirium screening in infants is also available. Smith and other members of an interdisciplinary team are validating the psCAM-ICU for use with infants at least six months of age through age five years (M.H. Chestnut, personal communication, June 25, 2015; ICU Delirium and Cognitive Impairment Study Group, 2014). The psCAM-ICU provides an "in the moment" point in time delirium screen (M.H. Chestnut, personal communication, June 23, 2015). An interim analysis of the psCAM-ICU of 127 patients found excellent good sensitivity (85%) and good specificity (81%) (Smith et al., 2014). For children under age two years, good sensitivity was maintained (85%), and specificity improved (91%). Importantly, for children under age five years who were mechanically ventilated, the analysis found good sensitivity (85%) and excellent specificity (100%). Mechanical ventilation may increase risk for delirium.

Delirium Hygiene: Essential Nursing Care to Prevent And Treat Delirium in Infants

Unfortunately, because high-quality research evidence for nursing care of infants at risk for and with delirium is lacking, much of the suggested care that follows is extrapolated from research with adult and older adult patients with delirium (Holly, Cantwell, & Kamienski, 2013; Holly, Rittenmeyer, & Weeks, 2014; Peters, Cull, Kent, Phillips, & Mistarz, 2013). Although children are indeed not little adults, research comparing children with delirium to adults with delirium has found similar symptom

profiles and phenomenology between the two age cohorts (Grover et al., 2012; Leentjens et al., 2008). Table 1 summarizes recommended activities to build a culture of delirium hygiene.

Infants thrive in circumstances where expectations are expeditiously and predictably met (Benson & Haith, 2009). This includes efforts to maintain normal sleep/wake cycles, including limitations to noxious noise and light, and provision of a natural light source. This may require re-evaluation of typical PICU routines while still ensuring safety concerns are addressed. Sleep deprivation and delirium are often reciprocal in critically ill patients. Sleep in these patients is characterized by sleep fragmentation, an increase in light sleep, and a decrease of both slow wave sleep and rapid eye movement sleep, which can contribute to the development of delirium (Figueroa-Ramos, Arroyo-Novoa, Lee, Padilla, & Puntillo, 2009).

Restful sleep supports physiological and psychological healing. Tactics with the potential to support restful sleep in the PICU include noise and light limitations, natural light during daylight hours, use of safe ear protection (such as ear muffs), low-level white noise, support for usual nap and sleep routines, scheduled opportunities for uninterrupted sleep, clustered care, and comfort measures (Kudchadkar, Aljohani, & Punjabi, 2014). Ensuring that all unit personnel understand the importance of restful, healing sleep for PICU patients may also help support circumstances that promote adequate sleep. This may be a challenge in the PICU environment because it is an extremely artificial environment with environmental, pharmaceutical, and physical aspects all contributing to fragmented and disrupted sleep (Kudchadkar et al., 2014), and infants require a great deal of sleep. Newborns typically sleep 16 to 20 hours in a 24-hour period; while infants up to 12 months of age typically sleep 13 to 15 hours per day (Bhargava, 2011). Support for safe sleep practices are also important, especially for younger infants and infants not able to roll over on their own.

Although close one-on-one nursing observation and assessment is important, clustered care as a preventative measure for delirium allows for greater rest and healing down time. Clustered care organizes various care activities into time-sensitive group-

Table 1.
Building a Culture of Delirium Hygiene for Hospitalized Infants

Concepts	Specific Tactics
Interdisciplinary Approach	Educate all personnel (including housekeeping, dietary, and laboratory) and family. Address parent concerns. Include routine child psychiatry consultation for children at risk for or exhibiting delirium. Treat underlying medical conditions. Involve child life specialists and physical therapy early. Conduct ongoing delirium education.
Integral Role for Pediatric Nurse/ Pediatric Nursing	Provide leadership education and support. Use developmentally-appropriate delirium screening tool each shift. Provide essential nursing care including comfort care and pain assessment/management. Promote judicious use of concerning medications and awareness of adverse effects. Assess the environment daily.
Modification of Aggravating Factors	Review of unit policies to ensure safety, prevent delirium, decrease noise, and decrease excessive interruptions to sleep. Develop policies to encourage staffing consistency. Develop policies to discourage room and bed changes. Develop policies to encourage natural light to support diurnal cycles.

ings, so the infant may experience fewer disruptions to rest and sleep. Clustered care is simply doing all the ‘hands on’ care (e.g., diaper, feeding, bathing, suctioning, repositioning, holding) at one time, which allows the infant periods of uninterrupted sleep. Facilitation of routine bath times and other comfort caregiving activities to maintain proper hydration, avoid hunger, ensure oral hygiene, and maintain moistened lips can also be clustered.

Facilitation of familiar objects at the bedside, such as favorite toys and photographs of parents, siblings, and pets, may be reassuring to very young children (Schieveld & Leentjens, 2005). Especially important is support for a reassuring, active parent presence at the infant’s bedside (Schieveld & Leentjens, 2005). Nurses should confirm with parents their very young child’s preferred comfort measures, such as holding, music, pacifier use, and/or favorite toy. Nurses should also educate parents about the importance of providing frequent reorientation to the infant. Close attention to the parent’s comments and concerns may alert the nurse to behavioral changes, indicating delirium in the infant, including decreased interaction, not recognizing parents, inability to com-

fort with usual practices, and the inability of the infant to settle down. Parent concerns may be directly or indirectly expressed, so nurses need to be alert to differing communication styles (Raspa et al., 2015).

Daily environmental assessments may help ensure circumstances that support the prevention of delirium. The pediatric nurse wants to ensure a quiet, mildly stimulating environment with familiar and comforting people and objects present (Gover, Malhotra, Bharadwaj, Bn, & Kumar, 2009). In the event agitation and motor activity result from delirium, the nurse needs to make sure opportunities for self-injury are limited and minimal disruption of lifesaving devices occurs.

Adequate management of pain is also an essential tactic in preventing or reducing the effects of acute delirium in the infant. Pain is frequent in critically ill patients with an incidence of up to 50% in medical and surgical patients at rest, and increasing up to 80% during common care procedures, often heightened by immobilization (Chanques, 2007). Moving patients for nursing care procedures is reported as one of the most painful routine care procedures (Puntillo, 2004); routine preemptive

analgesics in these circumstances need to be considered. Frequent pain assessment using a developmentally appropriate pain scale for non-verbal children is a first step in pain management in infants that may improve pain management. The Faces, Legs, Activity, Cry, Consolability (FLACC) behavioral scale is an observer rated pain assessment tool appropriate for use in pre-verbal children (Voepel-Lewis, Zanotti, Dammeyer, & Merkel, 2010). The use of medications in pain management should be closely monitored. The pediatric nurse should understand the potential impact of opiates and other analgesics on the infant’s mental status. Use of these drugs and overall polypharmacy increases delirium risk, which may be of even more of a concern with infants and very young children who may exhibit more sensitivity to certain drugs and also more severe adverse effects.

Delirium behaviors may occur outside the PICU (Jones, Fiser, & Livingston, 1992). Pediatric delirium-related behaviors may persist after discharge from the PICU and after discharge from the hospital to home. Children may return home with their days and nights reversed and exhibiting regressed development. Pediatric nurses need to incorporate such knowledge into discharge teaching activities and communicate this to their community-based primary care and home health service colleagues because PICU-related delusional memories may impact the development of post-traumatic stress disorder (Silver, Kearney et al., 2010). Early telephone follow up with the family after discharge by the primary bedside nurse may also be helpful in reinforcing discharge education objectives. Delirium should also be documented on the final diagnoses list (Kelly & Frosch, 2012).

Medications Used To Manage Delirium In Infants

Haloperidol is widely used to manage infants with delirium (Jacobson & Turkel, 2013). Other medications that may also improve infant delirium include aripiprazole, chlorpromazine, olanzapine, quetiapine, risperidone, and ziprasidone (Silver et al., 2010). None of these, however, are approved by the Food

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and Drug Administration (FDA) for use in infants (Turkel et al., 2013).

The pediatric nurse needs to be alert for less-known adverse effects with the use of antipsychotics in the management of delirium in infants. Antipsychotics may be indicated, but their use in infants and young children is often concerning to healthcare professionals because they may induce extrapyramidal effects (Madden et al., 2011). Extrapyramidal effects may present as continuous spasms and muscle contractions; irregular, jerky movements; motor restlessness; rigidity; and bradykinesia, but are usually less severe with atypical antipsychotics (Rasimas & Liebelt, 2012). However, children are often more sensitive than adults to these adverse neuromotor effects (Rasimas & Liebelt, 2012). The nurse should also be alert for tongue contractions or protrusion, extraocular movements, and torticollis. Laryngeal spasm may manifest as throat pain, stridor, or dysphonia (Rasimas & Liebelt, 2012).

Cardiac effects, including an abnormal ECG, are of concern with antipsychotic medications, including prolonged QT interval and significant cardiac arrhythmias, such as Torsades de Pointes, a potentially fatal ventricular dysrhythmia (Rasimas & Liebelt, 2012; Smith, Fuchs et al., 2011). Neuroleptic malignant syndrome may manifest as an adverse effect

with altered mental status, hyperthermia, muscular rigidity, and autonomic nervous system dysregulation. Other adverse effects of all antipsychotics include metabolic effects, such as glucose and lipid dysregulation; and anticholinergic effects such as constipation, urinary retention, and dry mouth (Pandharipande, Jackson, & Ely, 2005). All antipsychotics may induce photosensitivity, skin pigmentation changes, and leucopenia (Rasimas & Liebelt, 2012).

The pediatric nurse also needs to be alert for less-known adverse effects with the use of antipsychotics in the management of delirium in infants. Jacobson and Turkel (2013) described an eight-month-old infant of Vietnamese descent with delirium and with significant congenital heart disease who exhibited elevated liver enzymes with no liver-related clinical symptoms during treatment with fluphenazine. Jacobson and Turkel (2013) suggest that the infant's Asian race and significant degree of heart disease (heart disease may negatively impact liver function) placed the infant at increased risk for liver effects from fluphenazine. Some individuals who are of Asian descent are poor metabolizers of certain medications and genotyping may provide additional information (Aronsohn & Jensen, 2011; Pharmgkb, 2015; Poolsup, Li Wan Po, & Knight, 2000).

Team Delirium Hygiene

Ideally, the approach to delirium prevention and management is interdisciplinary (Kelly & Frosch, 2012; Madden et al., 2011). Treatment of the underlying medical condition and modification of aggravating factors, especially judicious use of exacerbating medications, is essential. A review of unit policies to emphasize safety and delirium hygiene may be indicated. Limiting room and staff changes may also contribute to delirium prevention and amelioration. All personnel and family members should be aware of the importance of delirium hygiene for infant patients in the PICU and elsewhere in the hospital. Broad awareness is especially important to reduce overall noise levels and excessive interruptions to restful sleep (Kol, Aydin, & Dursun, 2015).

Consultation with a child psychiatrist may assist in the identification and treatment refinement of delirium in infants (Kelly & Frosch, 2012). Child psychiatrists with experience managing critically ill infants can provide psychiatric focus and a high level of suspicion when it comes to the potential diagnosis of delirium. Child psychiatrists will take a detailed symptom and medication history, perform thorough physical examination, and recommend personalized interventions for the infant suspected

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of or exhibiting delirium (Rasimas & Liebelt, 2012; Silver et al., 2010). Routine use of child life specialists and developmentally appropriate efforts to keep the child moving and mobile with early involvement of physical therapy may also facilitate delirium prevention and management (Madden et al., 2011).

Implications for Pediatric Nurses

Nurses are in closest proximity and are the healthcare providers spending the most time with patients; therefore, nurses are likely in the best position to prevent and provide early recognition of delirium in infants. Enabling a culture of delirium hygiene through efforts that promote a standard of nursing care to prevent delirium is critical. Widespread delirium screening as a standard of care, along with careful observation and attendance to parent concerns about changes in their infant's behavior, can support early identification of delirium in infants (Schieveld & Leentjens, 2005). Daily environmental assessments of the infant's bedside and care unit circumstances can help ensure conditions that support the prevention of delirium. Provision of essential pediatric nursing care, including comfort care, pain assessment and management, and developmentally appropriate delirium assessment, are vital to prevention, recognition, and optimal treatment of infant delirium.

Conclusion

Due to the severity of underlying medical conditions and comorbidities, as well as the routine use of exacerbating medications, such as benzodiazepines and opiates in the PICU setting, the prevention of delirium in infants is challenging. Total prevention of infant delirium may be impossible, but standardized efforts must be made to both prevent and mitigate

(Madden et al., 2011). Widespread screening using developmentally appropriate tools is a critical step in early identification of and timely intervention with infants experiencing delirium. Pediatric nurses have a key role in this important effort. In addition, the pediatric nursing research literature is relatively limited, making pediatric delirium and infant delirium an understudied phenomenon, and as such, delirium in infants and young children offers a significant research opportunity for pediatric nurses. Future research to explore the knowledge and awareness of delirium among pediatric nurses, the role of nurse-led prevention and recognition of pediatric delirium, comparison studies for delirium screening tools validated for infants, interventions to address pediatric delirium post-hospital discharge, and usefulness of family education materials concerning delirium are important potential research topics for pediatric nurse scientists to consider.

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