Detection and Management of Delirium in the Neonatal Unit: A Case Series

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abstract

Delirium is increasingly recognized as a common syndrome in critically ill children, but in our experience, it is rarely considered in the NICU. Delirium is independently associated with prolonged length of stay and adverse long-term outcomes in children. We report the cases of 3 infants cared for in our NICU at corrected gestational ages of 4, 11, and 17 weeks who presented with classic symptoms of delirium. All 3 children had complex medical problems and were receiving multiple analgesic and sedative medications. All 3 children exhibited agitation that was unresponsive to increasing doses of medications, and they all appeared to improve after treatment with quetiapine, allowing weaning of other medications. It is possible that with increased vigilance, delirium will be increasingly recognized in newborns, thus allowing tailored intervention. Further research is needed to investigate the prevalence and associated risk factors for developing delirium in the NICU and to explore possible treatment options.

Delirium is increasingly recognized as a common syndrome in critically ill children, with prevalence rates >20% in the PICU.[1] Delirium is defined as an acute and fluctuating change in awareness and cognition, and occurs in the setting of serious medical illness.[2] This condition represents global brain dysfunction and may lead to adverse short- and long-term outcomes, as well as prolonged hospitalization.[1,3]

Although neonates are likely at risk,[1] delirium is not recognized as a common complication of the NICU stay, and few neonatologists consider the diagnosis. However, neonatologists are frequently confronted with infants who are "impossible to sedate"; that is, infants who are agitated, breathing against the ventilator, or receiving escalating doses of medication. Refractory agitation in young children is often the presentation of delirium.[4–6] We present 3 infants diagnosed with delirium in the NICU.

CASE SERIES

Case 1

An infant girl was born prematurely with cardiac disease requiring multiple surgeries. At corrected gestational age 17 weeks, she required 40% oxygen and nitric oxide via continuous positive airway pressure 2 weeks postoperatively. She was increasingly agitated and frequently inconsolable. She was kept in a quiet environment, and with careful swaddling, but was not fed enterally due to concerns regarding respiratory compromise. In an attempt to prevent episodes of desaturation associated with agitation, the infant received increasing sedation with morphine (20 μg/kg/h), midazolam (70 μg/kg/h), and dexmedetomidine (0.8 μg/kg/h). Concern regarding her agitation, as well as the inability to wean her from respiratory support, led to a consultation with PICU and child psychiatry. Carers noted that the infant was hyperactive and frequently inconsolable, with poor attention

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and an altered sleep–wake cycle. On examination, she was crying continuously and was unable to orient toward parent's face or voice (which she had previously done regularly). A diagnosis of delirium was made.

The infant's parents were counseled regarding the morbidity of ongoing delirium and its associated disruption in care. The care team decided to try pharmacologic management with quetiapine, an atypical antipsychotic agent that has been used successfully to treat delirium in critically ill adults.[7] The patient was started on quetiapine 0.5 mg/kg 8 hourly by nasogastric tube. Her electrocardiogram (ECG) was checked at baseline, and again after 48 hours, excluding prolonged QTc interval. No other changes were made in her care. After 48 hours, the infant's condition had improved. She still cried frequently, but she was more consolable and had some periods when she was quietly awake and responsive to her father's face and voice. Her sedation doses were decreased, allowing for weaning of her respiratory support. After 5 days of treatment, the infant's condition continued to improve, enteral feedings were restarted, and midazolam was successfully discontinued. She had breakthrough episodes of agitation for which the frequency of her quetiapine dosing was increased to 6 hourly. Opiates were discontinued 16 days after commencing quetiapine; dexmedetomidine was discontinued after 18 days. The infant was now calm, feeding, and breathing easily without support. Quetiapine was tapered off over the next 2 weeks.

Case 2

An infant girl was born prematurely with cardiac disease and infectious complications; she required surgical intervention in the neonatal period. At corrected gestational age 11 weeks, the infant had increasing oxygen requirements on continuous positive airway pressure and stridor requiring racemic epinephrine at 24 hours after extubation. She was fully enterally fed and receiving intravenous sedation with fentanyl (1 μg/kg/h) and dexmedetomidine (0.3 μg/kg/h). She had received no benzodiazepines in the previous 7 days. The infant was difficult to console, had increased spontaneous and purposeless movements, and was not sleeping. She experienced episodes of agitation that showed minimal or no response to fentanyl boluses. On examination, the infant was frequently writhing, with no spontaneous eye opening. The attending physician and bedside nurse assessed her level of arousal and cognition collaboratively, and she received a score of 16 on the Cornell Assessment of Pediatric Delirium (CAPD) (Appendix 1).[8] PICU and child psychiatry were consulted, and a diagnosis of delirium was made.

Detailed discussion with the child's parents was limited by complex social circumstances. In an effort to use less deliriogenic sedation, dexmedetomidine was increased to 0.6 μg/kg/h, but the infant's agitation worsened. She was started on quetiapine 0.5 mg/kg every 8 hours via a nasogastric tube. Her ECG was checked at baseline and again after 48 hours, excluding prolonged QTc interval. After 48 hours, her sleep pattern and irritability had improved. With the infant's decreased agitation, rapid weaning from fentanyl and then dexmedetomidine dosing was possible. After 5 days of treatment, the infant's CAPD scores had decreased from 15–18 to 7–9, and she was successfully weaned off fentanyl. She continued on acetaminophen for analgesia, and dexmedetomidine was stopped 7 days after commencing quetiapine. She continued on quetiapine for 2 months with no ECG changes or apparent adverse events; she was then transferred for further cardiac surgical review.

Case 3

An infant boy was born prematurely with a complex congenital disorder requiring abdominal surgery and placement of a gastrostomy tube. At a corrected gestational age of 4 weeks, he was intubated and ventilated, fully enterally fed, and was receiving intravenous sedation with midazolam (50 μg/kg/h) and frequent doses of morphine (100 μg/kg as needed). Staff noted that the child experienced frequent periods of agitation and restlessness, with minimal response to morphine bolus. On examination, he was irritable with facial "scrunching" and frequent flailing of arms and legs. Six hourly assessments made by using the CAPD produced scores of 12-14. Psychiatry was consulted, and delirium was diagnosed.

After discussion with the patient's parents, he was given quetiapine 0.5 mg/kg 8 hourly by gastrostomy tube. The ECG was checked at baseline and again after 48 hours, excluding prolonged QTc interval. After 72 hours, his condition had improved, with increased sleep and less agitation. He was noted to be soothed by sucking on a pacifier and would track objects placed in front of his face. His CAPD scores had fallen to 3 to 7. Over the next 7 days, the infant was weaned off midazolam and morphine, and he continued on quetiapine for the next 5 weeks, with no ECG changes or apparent adverse events. The infant was then transferred to a rehabilitation center.

DISCUSSION

Delirium may be a frequent complication of neonatal critical illness. It is the result of the underlying medical condition, the adverse effects of medication used, and the medicalized environment in the NICU, which is highly unnatural

for a neonate.[1,9] Although it is rational that neonates, as with older children and adults, will experience delirium at times, consideration of this important diagnosis in the NICU is not yet standard of care. To our knowledge, these are the first reports of detection and treatment of delirium in the NICU, with infants at corrected gestational ages of 4, 11, and 17 weeks and weighing 2.5 to 4.0 kg. These infants presented with classic symptoms of delirium, and they exhibited an apparent response to therapy. Environmental measures included clustering care to the greatest extent possible and improving darkness and quiet during sleep times, and light and interaction during awake times. Support was provided for staff and parents to consistently soothe the infant. When environmental measures were not sufficient, pharmacologic therapy was added with an atypical antipsychotic agent.

The diagnosis of delirium in very young children requires an understanding of normal development and illness behaviors.[10] Even in the first 6 to 8 weeks of life, neonates have predictable normal levels of consciousness (eg, alertness, eye contact, awareness of surroundings) and cognition (eg, attention, memory). With education and increased index of suspicion, we can begin to recognize delirium in the NICU. The CAPD is an observational screening tool designed to assess critically ill children of all ages for delirium.[11] It has never been formally tested in a NICU population but has been validated in infants.[8] The CAPD was used in 2 of the infants we present (4 and 11 weeks' corrected aged). Our nurses used the companion Developmental Anchor Points chart to help interpret the infants' behavior in the context of reasonable developmental expectations for a seriously ill infant (Appendix 2).[10]

As our cases suggest, considering delirium in the differential diagnosis for the agitated infant in the NICU can lead to increased patient comfort and a decrease in sedation (rather than an escalation in response to agitation). All medications have adverse effects, and there is growing concern regarding the impact of benzodiazepines and opiates in the developing brain.[12] Extensive literature examining the impact of benzodiazepines on the developing rat brain found long-term negative consequences, such as altered learning and social behaviors.[13,14] Similarly, studies have described alterations in the development of the central nervous system in rats exposed to postnatal opiates.[15]

Less is known about the potential effects of early exposure to antipsychotic agents, although there is extensive research on long-term exposure in children and adults and the development of the metabolic syndrome.[16] With short-term use, there have been theoretical concerns regarding QTc prolongation and neuroleptic malignant syndrome, as well as anticholinergic and hypotensive effects. Short-term use of quetiapine to treat delirium in critically ill children seems to be safe.[17] In the present case series, addition of quetiapine allowed for weaning of benzodiazepines and opiates, which are believed to be toxic.[18] Less agitation and sedation also allowed for improved oxygenation and rapid weaning of ventilator support.

It is increasingly appreciated in the pediatric and adult literature that routinely used medications have deliriogenic properties, and that delirium itself may have significant short- and long-term sequelae. These cases illustrate our nascent experience with recognizing and managing delirium in the NICU. It is possible that with increased vigilance by the neonatal team, delirium can be recognized in the NICU, allowing tailored intervention. With a decrease in duration of delirium, we may be able to improve the long-term health of vulnerable neonates. Further research is needed to investigate the prevalence and associated risk factors for developing delirium in the NICU and to explore possible treatment options.

ABBREVIATIONS

CAPD: Cornell Assessment of Pediatric Delirium
ECG: electrocardiogram

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