Sedation strategies in children with pediatric acute respiratory distress syndrome (PARDS)

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Abstract: In this review, we discuss the changing landscape of sedation in mechanically ventilated children with pediatric acute respiratory distress syndrome (PARDS). While previous approaches advocated for early and deep sedation with benzodiazepines, emerging literature has highlighted the benefits of light sedation and use of non-benzodiazepine sedating agents, such as dexmedetomidine. Recent studies have emphasized the importance of monitoring multiple factors including, but not limited to, sedation depth, analgesia efficacy, opiate withdrawal, and development of delirium. Through this approach, we hope to improve PARDS outcomes. Overall, more research is needed to further our understanding of the best sedation strategies in children with PARDS.

Keywords: PARDS; pediatric acute respiratory distress syndrome; sedation; analgesia; delirium

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Introduction

Acute respiratory distress syndrome (ARDS) was first described in adults in 1967 (1). The ARDS definition has since been modified to the current syndrome characterized by the Berlin Criteria (2). Historically, pediatric intensivists were limited to using these adult criteria and guidelines in the care of their patients. In 2015, pediatric acute respiratory distress syndrome (PARDS) was formally defined by members of the Pediatric Acute Lung Injury Consensus Conference (PALICC) as the presence of hypoxemia and radiographic changes in the context of a new lung infiltrate occurring within seven days of a known insult (3). This insult occurs with histological changes including infiltration of inflammatory markers, alveolar edema, and disruption of alveolar capillary barriers (4). As recognition of PARDS as a clinically entity grew, so did research (5). While much of the literature on sedation and care of the mechanically ventilated patient is still centered on adults, there is an emerging body of literature in the pediatric world.

In the past, the primary sedation strategy in mechanically ventilated adults with ARDS was deep sedation within the first 48 hours of intubation. This sedative-hypnotic approach was thought to be optimal to control both pain and psychological sequelae of mechanical ventilation (6,7). However, in 2012, numerous reviews emerged compiling data suggesting benefits of an analgo-sedative approach (8,9). In the Clinical Practice Guidelines for adult intensive care unit (ICU) in 2013, Barr et al. recommended light target levels of sedation with an analgesia-first approach to sedation, as a growing body of literature from adult ICUs demonstrated the negative outcomes associated with deep sedation (10-12). This review will focus on optimal sedation strategies for mechanically ventilated children. Given the close relationship between sedation and analgesia, paralysis, mobilization and delirium, we will briefly discuss these other important considerations.
Sedation

Depth of sedation

In the past, clinicians favored early deep sedation in mechanically ventilated patients, as it was thought to improve their oxygenation status, decrease pain, and minimize negative perception of experiences (6,13). However, as more literature emerged, a shift toward a “less is more” approach began. In 2013, adult guidelines suggested light sedation might be associated with improvement in outcomes without increasing negative sequelae of increased physiologic stress (12). The Pediatric Acute Lung Injury Consensus Conference group has since concurred, recommending “minimal yet effective targeted sedation” with continued “monitoring, titration, and weaning” (14,15). These goals were reiterated in the adult guidelines produced in 2018 (16). Both groups describe an “analgo-sedation” approach, using analgesics first and adding a sedative only when necessary (14,16).

Studies have shown a survival benefit associated with light sedation in ARDS. A 2014 multicenter prospective cohort study in 45 adult ICUs enrolled 322 mechanically ventilated and sedated patients. Results suggested increased hospital mortality with deep sedation (OR 2.36; 95% CI: 1.31 to 4.25), with more ventilator days (7 vs. 5 days, \( P=0.041 \)) and more tracheostomies performed (38.9% vs. 22%, \( P=0.001 \)) in the cohort with deep sedation (10). This is consistent with findings from a recent multicenter longitudinal cohort study of 42 ICUs around the world to assess 180-day survival in 703 mechanically ventilated adults. Results showed a stark dose-dependent relationship between sedation intensity and increased risk of death (HR 1.29, 95% CI: 1.15 to 1.46; \( P<0.001 \)), increased prevalence of delirium (HR 1.25, 95% CI: 1.10 to 1.43; \( P=0.001 \)), and decreased chance of early extubation (HR 0.73 to 0.87; \( P=0.001 \)) in the cohort with deep sedation (10).

Timing of sedation

In a 2012 multicenter prospective longitudinal cohort study in 25 adult ICUs, Shehabi et al. explored the effect of early sedation on patient outcomes. They defined “early” as sedation within four hours of initiating mechanical ventilation. Because most randomized controlled trials randomize beyond the four-hour time period, this window is not often captured. Their results showed that early deep sedation both delays extubation and increases overall mortality. In their study, each Richmond Agitation Sedation Scale (RASS) assessment indicating deep sedation acted as a predictor for delayed extubation (HR 0.90, 95% CI: 0.87 to 0.94, \( P<0.001 \)), hospital death (HR 1.11, 95% CI: 1.02 to 1.20; \( P=0.01 \)), and 6-month mortality (HR 1.08, 95% CI: 1.01 to 1.16; \( P=0.026 \)) (11).

Route of administration

Administration of both sedatives and analgesics can be via continuous infusion or via intermittent dosing. Theoretical advantages to continuous infusion include titratability, decreased infection risk, and maintenance of steady-state levels. Unfortunately continuous infusions also increase the risk of over-sedation and tolerance (19,20). Despite this, a 2014 survey of pediatric ICUs showed markedly higher rates of utilization of continuous infusions for sedatives in the mechanically ventilated pediatric population as compared to intermittent dosing (20). Further research is needed to determine the benefits of intermittent vs. continuous sedative infusions in PARDS.

Daily sedation interruption (DSI)

DSI is the practice of discontinuing sedation once daily to allow the patient to “emerge”; sedation is resumed thereafter. Theoretically, this can minimize over-sedation and improve patient outcomes (21). While DSI has been largely used in the adult ICU patient population, it is not without its drawbacks. Though it was originally suggested for minimization of negative sedative effects, a randomized controlled trial in 2012 suggests that, when compared to protocolized sedation, there was no difference in duration of mechanical ventilation or ICU stay with DSI versus non-DSI in adults (22). Further, research shows there may be more hemodynamic changes in children being awakened from sedation, and DSI therefore must be used with
found significant heterogeneity
conducted a randomized clinical trial to assess for
-agonist use, including an association with decreased
-agonist. This
will be necessary to assess the effect of protocolized analgo-
and targeted light sedation levels (25,26). Further research
PICU studies showed clinical benefits to nurse-driven
there were potentially beneficial secondary outcomes; patients on a sedation protocol in this study had fewer
doctors of concomitant opioid use, overall fewer sedative class
exposures, increased time awake during intubation, and fewer pressure ulcers (6). In contrast, two single-center
PICU studies showed clinical benefits to nurse-driven
Protocolized sedation
Sedation protocols have been widely discussed in recent
literature. In the adult population, Devlin et al. supported
nursing-protocolized strategies to try and achieve light
sedation levels, but this is still up for debate in children (16).
In 2011, Deeter et al. successfully implemented a sedation
protocol in a pediatric ICU (PICU) allowing for decreased
use of benzodiazepines and opioids (26). However, in a
2014 survey, only 27% of pediatric intensivists utilized a
treatment algorithm when working with sedated patients,
and 52% of those protocols were physician-driven as
opposed to nursing-led (20). The efficacy of protocolized
sedation itself in children is uncertain. In 2015, Curley
et al. conducted a randomized clinical trial to assess for
efficacy of protocolized sedation (using a benzodiazepine-
based sedation algorithm) in pediatric patients and found
no difference in number of mechanical ventilation days,
and found that patients on the sedation protocol had
more days with higher pain scores and agitation. Of note,
there were potentially beneficial secondary outcomes;
patients on a sedation protocol in this study had fewer
days of concomitant opioid use, overall fewer sedative class
exposures, increased time awake during intubation, and fewer pressure ulcers (6). In contrast, two single-center
PICU studies showed clinical benefits to nurse-driven
Protocolized sedation—rather than deeper sedation with daily interruption) (24-26).
Sedative choice
In the past, benzodiazepines were the most common class
of sedative used in mechanically ventilated children. In
2014, Kudchadkar et al. found significant heterogeneity
in choice of sedative agents in pediatric ICUs, with a
majority using midazolam for sedation, most commonly via
continuous infusion. At that time, many hospitals restricted
dexmedetomidine use, and less than 1% of respondents
reported using dexmedetomidine alone for sedation (20).
However, emerging pediatric literature suggests the benefits
of α₂-agonist use, including an association with decreased
use of opioids and benzodiazepines, and improvement in
pediatric ICU outcomes (27-31). Here we will discuss the
possible benefits and drawbacks of dexmedetomidine versus
benzodiazepines.
Dexmedetomidine
Recent literature suggests numerous possible benefits of
dexmedetomidine and other α₂-agonists. In a randomized
clinical trial in 2009, Riker et al. found a significant decrease
in negative outcomes such as duration of mechanical
ventilation and delirium rates (32). In a landmark
randomized controlled trial, Pandharipande et al. compared
dexmedetomidine to lorazepam in critically ill adults, and
multiple outcomes all favored the use of the α₂-agonist. This
study showed dexmedetomidine was significantly easier
to control in achieving sedation goals, and was associated
with lower delirium rates. There were also trends toward
decreased mortality when comparing dexmedetomidine
to lorazepam (33). The ease of sedation control was
further validated in 2014 when Tanaka et al. showed that
dexmedetomidine use alone was unlikely to result in
over-sedation, when compared to use of midazolam and
fentanyl (10). Additionally, the sleep profile of
dexmedetomidine has been shown to be superior to other
sedative analgesics, with preservation of stage II sleep in
a pediatric cohort (34). Finally, multiple studies have also
reported on the opiate-sparing effects of dexmedetomidine,
with decreases in opioid consumption when being co-
administered with an α₂-agonist (27-31).
Possible adverse effects associated with dexmedetomidine
have been noted in case reports, including adrenal
insufficiency, and acute discontinuation syndrome.
Tachycardia, hypertension, and withdrawal are commonly
reported side effects, although generally not clinically
significant (31,35-37). Another significant barrier to use
of dexmedetomidine is the cost; however, it is important to note that improved PICU outcomes such as decreased length of stay and decreased incidence of delirium likely results in significant cost-savings with the use of dexmedetomidine as first-line sedative (33,38).

Lack of pediatric evidence
As dexmedetomidine has only recently been adopted for use in mechanically ventilated children, there is limited clinical research that has been published to date. In 2007, Tobias et al. conducted a literature review and found that dexmedetomidine had been used in a large number of pediatric patients with positive sedative and analgesic effects and limited negative effects (39). A single-center retrospective study from 2014 included 98 children and showed no significant hemodynamic effects that would limit long-term use in the PICU (31). Secondary analysis of data from a sedation titration trial showed that time at target sedation level was increased with use of dexmedetomidine (28% to 50%), and cumulative opiate exposure was decreased (40). Hayden et al. conducted a review in 2016 to compile all the literature on α2-agonist efficacy in pediatric sedation. The findings were equivocal, as the paucity of research in this area led to lack of necessary power to draw statistical conclusions (41).

The SLEEPS Study (Safety profile, Efficacy and Equivalence in Paediatric intensive care Sedation study) enrolled 129 children in ten PICUs across England, and compared intravenous clonidine to midazolam for sedation in children on invasive mechanical ventilation. Although underpowered, this study was able to demonstrate non-inferiority of clonidine (42). As such, while results for alpha agonist use in adults and children look promising, there is a need for more research to determine effect on pediatric outcomes.

Benzodiazepines
Despite their wide use in adults and children in the past, benzodiazepines have been associated with a number of negative effects. In December 2016, the Federal Drug Administration (FDA) released a warning regarding use of specific sedative agents in children under three years old, including lorazepam and midazolam, with a new black-box warning (43). This was based on numerous animal and human studies that demonstrated neuronal loss, and effects on long-term cognitive outcomes (44-49). However many experts believe that this FDA announcement was premature; a perspective in the New England Journal of Medicine detailed how evidence from the FDA warning was incomplete, and that many relevant clinical studies were under way at the time of the release (50).

In support of the FDA warning, there is mounting clinical evidence that favors avoidance of benzodiazepines in the PICU setting. Benzodiazepines have been shown to frequently reach a deeper sedation than the initial target (when compared to dexmedetomidine), and deep sedation has been linked to poor outcomes (33). A 2012 prospective cohort study noted that midazolam exposure was associated with delayed extubation (11). Benzodiazepine exposure has also been linked to lower likelihood of ICU discharge in children (51). A further issue with benzodiazepines is their effect on sleep, with decreased REM and slow wave sleep (20,52-54).

In the pediatric world specifically, recent studies have elucidated the relationship between benzodiazepine use and development of delirium. In a prospective longitudinal cohort study, benzodiazepine administration was an independent predictor of delirium development in 1,547 critically ill children (adjusted OR 5.2, 95% CI: 3.7 to 7.5; P<0.001) (55). A cohort study assessing the risk factors for delirium in 994 pediatric oncology patients found that receipt of benzodiazepines was associated with a near-quadrupling of delirium risk (OR 3.71; P<0.001) (56). An international point prevalence study assessing the risk factors for delirium in 994 pediatric patients also showed benzodiazepine administration was an independent risk factor for development of delirium (adjusted OR 2.2, 95% CI: 1.5 to 3.3; P<0.001) (57). Mody et al. took the association one additional step when they identified a temporal relationship and a dose response between benzodiazepine administration and development of delirium, citing a 43% increase in risk for subsequent delirium for every one log increase in benzodiazepine administration (58). Alvarez et al. further established this relationship as significant in an observational study in the pediatric cardiac intensive care unit (CICU) (59).

Monitoring of sedation
When working with sedated patients, it is highly important to both determine a goal sedation level and be able to monitor the sedation level frequently (Figure 1). In adult clinical guidelines, the Richmond Agitation-Sedation Scale (RASS) and Sedation-Agitation Scale (SAS) are considered the most valid and reliable tools for monitoring sedation levels in critically ill patients (12). Unfortunately,
when surveyed in 2014, only 42% of pediatric intensivists reported routinely using sedation scoring mechanisms in their PICUs (20). Since that time, the RASS was validated for use in a pediatric population, providing a quick and easy way to monitor sedation levels in all PICU patients (60). There has not been data since that time on the frequency of sedation scoring protocols, but given the shift in paradigm toward light sedation, this review would urge the use of monitoring to ensure the desired level is met. This is consistent with ESPNIC recommendations to use validated sedation assessment tools in critically ill children to avoid negative outcomes (61).

Figure 1 Our review of the literature urges the use of goal directed care. In order to optimize sedation in PARDS we need to monitor pain, sedation, and delirium prospectively and adjust our interventions accordingly. By setting measurable goals, using validated tools, and titrating to those goals, clinicians will be able to decrease their use of sedatives and analgesics and decrease the prevalence of delirium. PARDS, pediatric acute respiratory distress syndrome.

### Analgesia
Analgesia is a highly important component of successful sedation and positive ICU outcomes (23). Recent studies suggest that pain is under-recognized and undertreated in ICU settings (62). Getting control of acute pain is highly important, as delay in pain relief can later transition to chronic pain and cause significant psychological sequelae such as anxiety and post-traumatic stress disorder (PTSD) (63,64). It has been noted that over-sedation can lead to under-recognition of pain, with delay in treatment leading to suboptimal pain control (62). With an analgo-sedation approach, the patient will be more awake. With less sedative on board, the bedside providers will be more effective at recognizing and treating pain (Figure 2). Here we will discuss analgesic choice, route of administration, and monitoring strategies.

#### Analgesic choice

**Non-opioids**

Clinical guidelines in adults suggest multiple modalities to treat pain in mechanically ventilated critically ill adults, including but not limited to relaxation techniques, cold therapy, music therapy, massage, NSAIDs, neuropathic pain medication, ketamine, nefopam, and acetaminophen (12,13,16). Though potentially beneficial, ketamine has had deleterious neurologic effects in animal studies, urging caution when used for long-term sedation or analgesia in children (65).

**Opioids**

In 2014, Kudchadkar et al. found significant heterogeneity in choice of analgesic agents in pediatric ICUs, with most using fentanyl for opioid analgesia and most commonly on continuous infusion (20). Tanaka et al. found a similar pattern of use in adults, with 39.4% of participants using midazolam and fentanyl together, and 12.4% using fentanyl alone (10). While opioids have a number of unwanted side effects including gastrointestinal upset and motility issues, they provide excellent pain control and can be used effectively in a PICU setting (13). If using an opioid, it seems that morphine may have a more favorable profile than fentanyl, as it requires less up-titration when dosing (66). Further research, with attention to pharmacokinetics and pharmacogenomics, will be necessary to determine optimal analgesic choice in children with PARDS.
Route of administration

Like sedatives, administration of analgesics can also be via continuous infusion or via intermittent dosing. Advantages of continuous infusion include titratability and maintenance of steady-state levels; however, there is the risk of increasing tolerance (19,66). Of note, research suggests continuous infusions of opioids do not provide significant benefit over intermittent use in adults or children (67-69). Despite this evidence, Kudchadkar et al.’s review in 2014 suggested increased prevalence of continuous infusions for analgesics in the mechanically ventilated pediatric population (20). Further research may demonstrate benefit to an intermittent approach to opiate administration.

Monitoring of pain

Devlin et al. suggests that vital signs may not be a useful tool to monitor pain in mechanically ventilated patients. Instead, behavioral scales and self-reports are the most reliable measures (12,16). There are a number of validated assessment tools for children that have been recommended by the European Society of Pediatric and Neonatal Intensive Care (EPNIC), including the Premature Infant Pain Profile (PIPP), the COMFORT scale, the Multidimensional Assessment of Pain Scale (MAPS), and the Face, Legs, Activity, Cry, Consolability scale (FLACC) (Figure 1) (61,70-73).

An important consideration when using analgesics in any child is the possibility of tolerance, withdrawal, and dependency. Literature suggests the development of tolerance is unlikely with less than 72 hours of therapy, and that iatrogenic withdrawal syndrome (IWS) does not generally develop unless opiates are used for six or more days (61,74). After five days of exposure, it may be prudent to monitor for IWS when weaning medication. The Withdrawal Assessment Tool (WAT) can be used in mechanically ventilated children (75). In order to decrease the incidence of tolerance and withdrawal, Anand et al. recommend finding the minimum effective doses and avoiding long acting opioids if possible. The use of multiple drug classes in a rotation has been shown to be effective in adults, and may be considered for children who will be getting long-term opioid treatment (19,23). It is worth noting that neonates and infants may develop tolerance to opioids more quickly, though the pathophysiology behind this phenomenon is not completely understood (23,74). It is possible that these young children presented with delirium

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<tr>
<th>Analgesia</th>
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<tbody>
<tr>
<td>Choice: Judicious use of opioid and non-opioid analgesia</td>
<td>Choice: Inappropriate use of opiates</td>
</tr>
<tr>
<td>Administration: Intermittent when appropriate</td>
<td>Administration: Continuous infusion, with frequent dose escalation</td>
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<tr>
<td>Monitoring: Frequent use of a behavioral tool</td>
<td>Monitoring: Infrequent monitoring</td>
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<th>Sedation</th>
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<tr>
<td>Choice: Dexmedetomidine</td>
<td>Choice: Midazolam</td>
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<tr>
<td>Monitoring: Richmond Agitation Sedation Scale, performed hourly</td>
<td>Monitoring: Continuous infusion, with frequent dose escalation</td>
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<tr>
<th>Outcomes</th>
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<td>↓ Delirium</td>
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<td>↓ Length of stay (LOS)</td>
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<td>↑ Mobilization</td>
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Figure 2 This cartoon provides an example of an analgo-sedation approach (on left) as compared to a traditional benzodiazepine-based sedation regimen.
that was mis-diagnosed as “early tolerance” (as, without routine screening, delirium often goes undetected and mismanaged) (76).

**Paralysis/neuromuscular blockade (NMB)**

NMB can be a useful adjunct in a patient with severe PARDS. It can minimize ventilator-induced lung injury (VILI), prevent dyssynchrony, decrease trans-pulmonary pressures, and decrease oxygen consumption (77-83). However, NMB must be used sparingly, and with caution.

In 2009, a systematic review suggested NMB in ventilated adults might be a risk factor for later development of neuromuscular weakness. However, the authors noted that there was potential for many confounding factors in the studies reviewed, including co-administration of steroids (84). Papazian *et al.* conducted a seminal multicenter double blind trial in 2010 in mechanically ventilated adults with ARDS comparing use of cisatracurium besylate with placebo. This study showed that use of NMB for 48 hours resulted in decreased ventilator time, increased 90-day survival, and no increase in resulting neuromuscular weakness (80). This is consistent with numerous studies in the past decade that have shown no independent association between NMBs alone and muscular weakness; rather, studies only show an association when co-administrated with steroids (80,85-89). However, a follow-up study executed by the NIH Prevention and Early Treatment of Acute Lung Injury (PETAL) network, “ROSE: Reevaluation Of Systemic Early Neuromuscular Blockade”, was recently completed to assess the efficacy of NMBs in ARDS in adults. This large-scale randomized controlled trial (n=1,006) showed no benefit to the use of early paralytic agents for moderate-to-severe ARDS with respect to barotrauma or mortality (90). Experts have opined that this may be due to the deep sedation used in the first study (80), which may have increased the incidence of reverse triggering in the paralyzed cohort, and worsened VILI (91).

In 2016, Wilsterman *et al.* studied the short-term effects of NMBs in children and found improvement in the oxygenation index 15 minutes after administration. However, this study did not assess long-term outcomes such as VILI, barotrauma, or survival (92). There is inadequate research to conclude that NMBs are effective in pediatric respiratory failure. Further studies will be necessary to explore the potential benefit or harm of deeper sedation and/or paralysis in children with severe PARDS. As of now, PALICC recommends that only “if sedation alone is inadequate to achieve effective mechanical ventilation, neuromuscular blockade (NMB) should be considered” at the “minimal yet effective” dose (14,15).

**Delirium**

In the fifth edition of the Diagnostic and Statistics Manual (DSM-V), the American Psychiatric Association defines delirium as a fluctuating disturbance of consciousness or change in cognition developing over a short period of time (93). As described above, poor sedation strategies can lead to delirium, which is independently associated with pediatric morbidity and mortality. This relationship makes delirium an important topic to address when discussing sedation approaches.

**Delirium effect on outcome**

Delirium can be highly problematic in children, leading to prolonged mechanical ventilation, increase in PICU and hospital length of stay, higher number of sequelae post-discharge, and increased morbidity and mortality (12,51,55,59,94-97). Despite this, a 2014 review suggests the prevention, recognition, and treatment of delirium is inadequate in most pediatric intensive care units (20).

**Delirium risk factors**

There are numerous risk factors associated with delirium. Predisposing factors include young age and developmental disabilities (51,55,59,95). While these risk factors are not modifiable, environmental hospital factors—such as poor sleep quality due to light and sound pollution—often are. Sadly, as of 2014, only a very limited number of pediatric ICUs optimized these factors, with a study showing that only 16% and 9% addressed noise and light exposure, respectively (20). However, it is likely that the single most important modifiable risk factor for delirium in mechanically ventilated children is sedative choice. As discussed in the sedation section above, sedation depth and exposure to benzodiazepines are highly associated with increased delirium risk (12,51,55,57,58).

**Prevention of delirium**

Prevention begins with recognition of risk factors and...
implementation of monitoring tactics. To prevent delirium in adults, guidelines suggest “non-pharmacologic intervention focused on (but not limited to) reducing modifiable risk factors for delirium, improving cognition, and optimizing sleep, mobility, hearing, and vision in critically ill adults.” (12,16).

Regular assessment for delirium using a validated screening tool is highly important in the prevention, recognition, and treatment of delirium (16). In a 2014 survey, 71% of PICUs reported no routine delirium screening (20). That same year, the Cornell Assessment of Pediatric Delirium (CAPD) was developed and validated to assess for delirium in children of all ages. Importantly, the CAPD was specifically designed for ease of use in mechanically ventilated children (98). Another valid and reliable pediatric delirium screening tool is the Pediatric Confusion Assessment Method for the ICU (pCAM-ICU) for children older than five years old, with a preschool version available for children between six months and five years of age (99,100). The EPNIC has recommended use of the CAPD for delirium screening in all critically ill children, and the CAPD is now used as standard of care in many North American PICUs (61,101). In fact, studies have shown that simply implementing universal delirium screening can lead to a decrease in delirium rates (Figure 1) (25). Most relevant to PARDS, data show that less sedation will result in less delirium in mechanically ventilated children, and may lead to better short- and long-term outcomes (55).

Mobilization

Early mobilization (EM) is defined as “an interdisciplinary, goal-directed therapy used to facilitate movement” in patients with ARDS (102). Given that a commonly cited issue in the literature is the development of neuromuscular weakness following mechanical ventilation, intensivists began the routine use of mobilization to try and prevent its development (103).

Thus far, literature on the effects of mobilization has been overwhelmingly positive. Recent evidence suggests that EM in the ICU setting is not only safe, but also may improve functional outcomes (103). Clinical practice guidelines in adults suggest EM decreases both incidence and number of delirium days (12,16).

In the pediatric world, an observational quality improvement project entitled “PICU Up!” studied 200 critically ill children to assess the feasibility of EM in the pediatric ICU. Post-implementation results demonstrated an increase in median number of mobilizations (3 vs. 6; P<0.001), without any mobilization related adverse events. This study advocated for the feasibility and safety of EM in children (104). As far as effectiveness of EM, a 2017 pediatric study implemented an EM protocol in the PICU and showed a significant decrease in delirium prevalence (25). As it is necessary for a patient to be awake and cooperative in order to participate in EM, this provides further incentive to adopt a light approach to sedation in PARDS.

Conclusions

Overall, mortality from PARDS has decreased over the last decade. With increased survival (specifically in higher-income countries), research has demonstrated substantial morbidity after PARDS. It is possible that a paradigm shift in our approach to sedation may further optimize the care we provide. With an analgo-sedation approach—targeting as light a level of sedation as possible (and using alternatives to benzodiazepines when sedation is required)—we may be able to decrease over-sedation, optimize pain control, shorten duration of mechanical ventilation, decrease delirium rates, and increase EM. A change in our approach to sedation may directly improve short- and long-term outcomes in PARDS.

Acknowledgments

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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