

Preventing Pediatric Iatrogenic Withdrawal Syndrome:

A Quality Improvement Project

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Abstract

Purpose: (1) Utilize an algorithmic/standardized approach to optimize sedation weaning for all children in the pediatric intensive care unit (PICU). (2) Decrease incidence of iatrogenic withdrawal for all patients admitted to the PICU.

Methodology: A standardized protocol for weaning sedation was implemented in the PICU for patients 0-18 years who were at risk for developing IWS. These patients were classified as “low,” “moderate,” or “high” risk, and followed algorithmic weaning paths tailored to their risk and Withdrawal Assessment Tool-1 (WAT-1) scores. Nursing education was provided to enhance and solidify understanding of WAT-1 assessment and algorithm. PICU pharmacists and intensivists instituted this protocol and relied on bedside nurses for feedback.

Results: Retrospective chart review performed with limited pre- and post- protocol sample ($n=9$ for both cohorts). Preliminary data collection revealed decreased hospital and PICU length of stay, shorter duration of sedation use, and improved management of withdrawal symptoms for opioids. This was not reflected for alpha adrenergic utilization, and limited data available for benzodiazepine management.

Implications for Practice: Protocolized sedation wean may improve outcomes for critically ill children and decrease incidence of withdrawal. Further research that evaluates protocolized sedation management in the PICU needs further investigation.

Keywords: pediatric sedation, iatrogenic withdrawal, WAT-1, sedation protocol

Preventing Pediatric Iatrogenic Withdrawal Syndrome

Problem Description

Children admitted to the Pediatric Intensive Care Unit (PICU) often require sedation titration in order to keep them safe and comfortable, especially in preventing dislodgment of lines, drains and tubes. Sedation administration is common practice and offers many benefits, however there are a number of risks associated with this intervention, per the literature. One of the greatest risks involves the phenomenon, iatrogenic withdrawal syndrome (IWS). In order to prevent IWS from occurring, a sedation plan is typically formulated, but are variable because they are typically provider dependent and driven in the majority of pediatric critical care units (Solodiuk et al., 2019). This results in unnecessary variations in opiate, benzodiazepine and dexmedetomidine titration and places critically ill children at higher risk for developing adverse effects, such as IWS (Solodiuk et al., 2019). Prior to February 2020, Randall Children's Hospital (RCH) implemented practices of provider led sedation weaning, similar to many pediatric critical care units across the country (Solodiuk et al., 2019). The RCH PICU also lacked gaps in understanding patterns of withdrawal and its dissemination in critically ill children. This ultimately guided their practice and institution of a standardized protocol for sedation management.

Available Knowledge

Although multimodal pharmaceutical management has improved outcomes for children in the PICU, there are a number of risks associated with sedation. The threshold from a body of research cites that utilizing sedation for five days and greater in the pediatric population, is associated with the following risks: iatrogenic withdrawal syndrome (IWS), dependence, higher tolerance, delirium, delays in long-term neurodevelopment, prolonged length of hospital stay,

and specifically for the PICU population, higher rates of morbidity (Walter et al., 2019; Lebet et al., 2017; Sanchez-Pinto et al., 2018). Based on the literature, the term “sedation” encompasses opioids and benzodiazepines in bolus or continuous sedation infusions and dexmedetomidine infusions. Current sedation weaning practices are typically provider driven, resulting in unnecessary variations in sedation titration and place children at higher risk for developing the aforementioned risks (Solodiuk et al., 2019). Analysis of academic manuscripts revealed that only a small number of PICUs have instituted a standardized protocol to aid with sedation weaning practices.

Sedation management of five days and greater complicates the pediatric patient’s hospital stay and management. One of the greatest risks associated with this duration of sedation exposure is the risk of developing iatrogenic withdrawal syndrome (IWS), which increases by 50% at the five-day mark (Walter et al., 2019). Iatrogenic withdrawal syndrome is a phenomenon experienced by individuals who are receiving sedation medications, and occurs when these drugs are weaned too quickly, or stopped abruptly (Franck et al., 2008). This can ultimately lead to adverse effects including nervous system hyperirritability, autonomic system dysregulation, gastrointestinal dysfunction, and motor abnormalities (Frank et al., 2008). As a result, children who undergo improper sedation weaning plans can cause increased length of hospital admission and distress to the patient and family (Walters et al., 2019; Franck et al., 2008). In order to assess the trajectory and status of weaning plans, Franck et al. (2008) developed a validated, efficient, and bedside nurse driven tool named the Withdrawal Assessment Tool -1 (WAT-1) (Walter et al., 2019, Lebet et al., 2017, Chiu et al., 2017). Although the WAT-1 assesses opioid withdrawal, there is less evidence supporting its utilization

for benzodiazepine withdrawal, and limited research regarding its efficacy in assessing dexmedetomidine weans (Walter et al., 2019, Sanchez-Pinto et al., 2018; Amirnovin et al., 2018).

Of note, the majority of the research surrounding pediatric sedation studies PICU populations and weaning opiates. There are some resources available regarding benzodiazepines including weaning plans, however there is little to no information about delineating major differences between opiate and benzodiazepine withdrawal. Manuscripts evaluating alpha-2 adrenergic medications, dexmedetomidine and clonidine, are scarce in quantity. Currently, the only validated tool to assess for opiate and benzodiazepine withdrawal in pediatric patients is the Withdrawal Assessment Tool – Version 1 (WAT-1), with limited research available to support its efficacy in assessing dexmedetomidine withdrawal (Walter et al., 2019, Sanchez-Pinto et al., 2018; Amirnovin et al., 2018). Protocolized sedation plans are a relatively new protocol for pediatric intensive care units to utilize, and typically provide guidelines for opiates and benzodiazepine weans (Sanchez-Pinto et al., 2018; Amirnovin et al., 2018). The PICU at Randall Children’s Hospital is most familiar with administration of opioid and alpha-adrenergic medications as intravenous infusions and standing medications, but sparingly utilizes benzodiazepine infusions.

Rationale

This quality improvement project will be implemented in a PICU located in the Pacific Northwest and will be based on Institute for Healthcare Improvement’s Plan-Do-Study-Act (PDSA) cycle. The PDSA tool allows for testing change via creating a plan to test the change (plan), instituting the test (do), observing and adapting from the outcomes (study), and implementing changes made to the test (act) (IHI, 2020b). This model intends to guide and accelerate improvement, but does not replace the current change model an organization is

currently using (IHI, 2020b). The “Plan” cycle for improvement consisted of creating a protocolized sedation weaning toolkit with the stakeholder and key players of the unit, review of current literature providing evidence-based support for sedation protocols, and creating an educational plan for the nurses who share a significant role to the success of this quality improvement project. The protocol was modified several times to reflect changes from current literature and the educational plan stressed the significance the Withdrawal Assessment Tool Version-1, one of the major metrics used to evaluate how efficacy of the project. The “Do” cycle includes roll out and implementation of this project and providing education for nursing staff. The “Study” and “Act” portions of the IWS quality improvement project will be explained later on, as they reflect the measures and outcomes of the project.

Specific Aims

Aims of this project were driven towards improving outcomes for critically ill children. In order to do so, this quality improvement project utilized an algorithmic and standardized approach to optimize sedation weaning for patients in the PICU. This protocol intends to decrease rates of iatrogenic withdrawal syndrome for all PICU patients. In summary, aims of this project are to (1) implement an algorithmic and standardized approach to optimize sedation weaning, and (2) to decrease incidence of iatrogenic withdrawal for PICU patients.

Methods

Context

A sedation algorithmic protocol was instituted at the Randall Children’s Hospital PICU in February 2020 in order to mitigate complications related to withdrawal and sedation weaning. RCH PICU is located in Portland, OR and consists of a 24-bed unit which averages approximately 1200 patient admissions per year (Legacy Health, 2020). This unit is staffed by

nine providers, eight being attending intensivists along with one physician's assistant, one dedicated pharmacist, fifty registered nurses, and a team resource or float pool nurses typically rotate through the unit. Inclusion criteria consists of patients ages zero to eighteen years of age receiving continuous sedation infusions and who are at risk for developing IWS. Burn patients are excluded from the protocol.

Intervention

Delivery of the sedation protocol involved collaboration amongst the multidisciplinary PICU team. Initial steps to delivering interventions instituted for this project consisted of creating and implementing a standardized algorithmic approach to guide sedation weaning practices. Protocolized weaning strategies were created and managed primarily by the dedicated PICU pharmacist. Intensivists were liable for the intravenous infusion and sedation discharge prescriptions. Withdrawal assessment and rescue medication administration relied on bedside nursing evaluation. Nurses also received education pertaining to the protocol and reinforced education on performing a withdrawal assessment. Education was delivered via online competencies, presentations, and administered to both PICU and float pool registered nurses. At minimum, daily discussions pertaining to sedation management were carried out by the PICU multidisciplinary team during bedside rounds.

The sedation protocol algorithm was classified into categories of the respective sedation medication. This PICU commonly uses fentanyl or hydromorphone for opioid infusions, dexmedetomidine is the primary infusion medication for the alpha₂-adrenergic pharmacologic class, and benzodiazepines are rarely utilized. Patients followed a sedation algorithm based on their pharmacologic class of opioid, alpha-adrenergic, and benzodiazepine. By following the respective algorithm, patients were classified based on their level of risk of "low," "moderate,"

or “high” risk, depending on the number of days of sedation infusion or total dosage. Risk was determined 48 hours prior to planned extubation, while an initial baseline WAT-1 score was assessed the 24 hours before extubation. Patients who were categorized as “low” risk would not receive a scheduled dose titration. Those who followed the “moderate” or “high” risk trajectory pursued a scheduled dose titration, as recommended by the pharmacist. WAT-1 scores were performed every 12 hours, at minimum, and as needed, should the patient present with escalated withdrawal symptoms, per nursing discretion. Scores continued until 48 hours after their last scheduled dose of sedation wean. Although patients followed their assigned algorithmic track, reassessment of their status and plan were reassessed during the PICU team’s bedside rounds or provider notification.

Study of Intervention

The iatrogenic withdrawal sedation weaning protocol was implemented February 2020, and was instituted via the PDSA Cycle (IHI, 2020a). The “Plan” section of this quality improvement project consisted of formulation of an algorithmic approach to sedation management by the PICU pharmacist and education provided to the PICU and resource pool registered nurses. As patients progressed to the “Do” section of the PDSA cycle, the trajectory of their sedation weaning was determined by risk classification. The metrics used to “Study” the effects of this quality improvement project involved retrospective data mining and analysis. The key metrics to assess the trajectory of this QI project involve chart review of the patient's hospital and PICU length of stay, sedation data, and also WAT-1 scores that are greater than or equal to 4 (Figure 1). Refining changes via the “Act” portion of the PDSA cycle are discussed in the summary and conclusions sections of this manuscript.

Measures

In order to assess the aims of this quality improvement project a sedation algorithm and determine its impact on withdrawal, the following measures were collected. Descriptive metrics included patient demographics: age, gender, a general category of patient diagnoses, and Patient Index of Mortality (PIM) 2 and 3 scores, which reflect acuity (Qiu et al., 2017). Hospital and PICU length of stay (LOS), sedation length and exposure, and rescue doses will aid in the evaluation of whether or not incidence of IWS improved in the post-protocol sample. Administration of rescue doses were based on withdrawal scores greater than or equal to 4, prompting the need for intervention to relieve symptoms. The nurse driven WAT-1 assessment tool, in particular, is the key component in understanding how well patients were tolerating the sedation wean.

Analysis

A retrospective chart review was performed to evaluate the pre- and post- intervention data. Descriptive analysis of demographic data was performed. A statistical analysis of the following measures was performed: duration of opioid and alpha2-adrenergic sedation medication, rescue doses administered, and patient hospital and PICU LOS.

Ethical Considerations

Ethical considerations applied to this quality improvement project involved understanding the sample included was a vulnerable population, being critically ill children. Patient sensitive data was also considered. This project was deemed exempt by the Institutional Review Board for Oregon Health & Science University and Randall Children's Hospital. There are no conflicts of interest.

Results

The RCH PICU implemented their standardized protocol in February 2020. A retrospective chart review was performed, collecting data for patients who received opioid and alpha2-adrenergic continuous intravenous infusions and were transitioned to enteral weaning medications. The patients included in the pre-protocol sample were patients who were hospitalized between February 2019 to May 2019, and met inclusion criteria of the protocol. While post-protocol patients were those who met inclusion criteria and hospitalized between February 2020 to May 2020. Chart review yielded small samples ($n=9$) for both the pre- and post- protocol cohorts. Randall Children's Hospital PICU traditionally veers away from the utilization of benzodiazepine continuous infusions for sedation management, thus this pharmacologic classification was not included in the data analysis.

Demographic data analyzed patient characteristics of gender, age in partial months, and generalized diagnoses of respiratory, cardiac, and neurological divisions, represented as a percentage per pre-protocol and post-protocol samples (Table 1). The majority of patients included in the sample were male infants aged one to twelve months who were admitted due to respiratory related disease processes. There lacked representations of adolescent and neonatal aged children in both pre-intervention and post-intervention cohorts. Limited data was extrapolated from children outside of the infantile ages in the pre-protocol sample. There was also limited representations of patients who were diagnosed with cardiac, neurological, and other related disease processes for both cohorts.

The Patient Index of Mortality (PIM) Scores and Patient Length of Stay were represented as mean numbers from the pre-protocol and post-protocol samples (Tables 2 and 3). Acuity in the post-protocol group was higher compared to pre-protocol patients (Table 2). Overall, children in the post-protocol group had a shorter length of stay in both PICU and hospital admissions

(Table 3). Post-protocol groups experienced a reduction by 0.8 partial days in the PICU, and 1.4 partial days for hospitalization.

Sedation medication was evaluated by mean dosages of sedation administered per patient and represented as partial days and mean number of rescue doses administered per patient (Table 4). Intravenous (IV) opioid management consisted of fentanyl or hydromorphone infusions, while rescue medications used to manage WAT-1 Scores ≥ 4 were either morphine or oxycodone in both respective cohorts. Alpha2-adrenergic intravenous medication used was a dexmedetomidine infusion, while clonidine served as the respective scheduled withdrawal and rescue medication. Data analysis demonstrated that the length of opioid IV drips were reduced by 6.6 days (~47.1% reduction) and a drop in total length of opioid utilization by 6.2 days (~22.7% reduction) for the post-protocol sample. There were also 1.7 less opioid rescue doses administered per patient (~63% reduction), post-intervention. Analysis of alpha-adrenergic sample groups demonstrated variability in outcomes. Although there was a reduction in the length of dexmedetomidine infusion by 1.1 days (~11.6% reduction), the length of clonidine wean nearly doubled in duration in the post-protocol sample, resulting in a longer duration of total alpha2-adrenergic usage. Of note the mean acuity of the post-protocol sample was higher than the pre-protocol group, which may have resulted in longer alpha2-adrenergic usage.

Discussion

Summary

This quality improvement project evaluated protocolized sedation management in a pediatric critical care setting. The project was implemented via a PDSA cycle, which aimed to implement a standardized algorithmic approach to optimize sedation weaning and to reduce rates of iatrogenic withdrawal for PICU patients. Strengths of this project include contribution to the

limited amount of publications that evaluate protocolized sedation management (Amirnovin et al., 2018; Sanchez-Pinto et al., 2018) and the implementation of the intervention via a multidisciplinary and collaborative strategy. Preliminary data analysis revealed that the post-intervention group was able to see these benefits: (1) decreased hospital and PICU LOS, (2) decreased rates of overall opioid administration, and (3) improved management of withdrawal symptoms assessed via rescue dose administration.

Interpretation

The positive outcomes delineated from the IWS sedation protocol may be attributed to the interventions implemented. The Randall Children's Hospital PICU intended for multidisciplinary collaboration in order to promote success and evaluation of the sedation protocol. This was a pharmacy driven protocol, which involved sharing sedation management orders of sedation management by the PICU designated pharmacist and PICU intensivists, and heavily relied on nursing assessment from the WAT-1 tools. The protocol and patient status were closely monitored by nurses and an interdisciplinary consensus for the patient's sedation plan of care was discussed during daily rounds, at minimum. Educational seminars delivered to PICU and resource pool nurses prior to implementation of the protocol also solidified bedside RNs' knowledge of WAT-1 assessments, and optimized understanding of the sedation algorithm. Institution of this quality improvement project resulted in a reflecting on the systemic gaps in sedation management at the RCH PICU. There were minimal additional costs due to the education provided for staff members, such as the registered nurses and pharmacists.

This project's outcomes were similar to the recent publications in regards to sedation protocol interventions in the PICU. Similar to this project, Amirnovin et al. (2018) instituted an opioid and benzodiazepine weaning protocol in a cardiac PICU which resulted in decreased

usage of opioids and benzodiazepine, reduced withdrawal symptoms, and also shortened hospital length of stay. Sanchez-Pinto et al. (2018) demonstrated that implementing a risk-stratified opioid weaning protocol in a medical surgical PICU reduced opioid exposure without increasing rates of withdrawal symptoms. However, Sanchez-Pinto et al. (2018) did not attain a statistically significant decreased length of hospital stay.

Limitations

Even though outcomes manifested by the protocolized sedation weaning practices at RCH were beneficial, there were also limitations to this project. One of which included the process of data collection, which was obtained via a retrospective chart review of pre-interventional and post-interventional cohorts. Since this quality improvement project was implemented at a single facility, it may decrease generalizability of the benefits of a protocolized sedation wean in other institutions. Benzodiazepine analysis was not included due to the limitations of intravenous drips utilized by the RCH PICU. To add, this project yielded a small preliminary sample size which was affected by the recent pandemic, COVID-19. Limitations of a small sample size include potential for bias, limited reliability of data analysis, and inability to determine the validity of this quality improvement project.

Conclusions

Overall, the benefits noted from standardized or algorithmic approaches to PICU sedation weaning yielded similar results for the RCH PICU as demonstrated in the literature review. This quality improvement project supports the positive outcomes disseminated in protocolized sedation management, as it may decrease hospital LOS, decrease usage of opioids in critically ill children, and also reduce incidence of withdrawal. In order to fully optimize and assess outcomes

for standardized sedation management in the PICU, a larger sample size should be analyzed, and the intervention needs to be studied in more institutions.

Table 1*Patient Demographics as Percentages of Cohort*

Patient Demographics as Percentages of Cohort		
Characteristic	Pre-Protocol (n= 9)	Post Protocol (n = 9)
Gender		
Female	44.4%	33.3%
Male	55.6%	66.7%
Age (months)		
Infancy (1-12)	77.8%	44.4%
Toddler (13-24)	11.1%	22.2%
Childhood (25-132)	11.1%	22.2%
Adolescence (≥ 133)	-	11.1%
General Diagnosis		
Respiratory	66.7%	77.8%
Cardiac	22.2%	11.1%
Neurological	11.1%	-
Other	-	11.1%

Table 2*Mean Patient Index of Mortality Scores*

Mean Patient Index of Mortality (PIM) Scores		
Characteristic	Pre-protocol (n=9)	Post-protocol (n=9)
PIM 2	2.4	3.4
PIM 3	2.3	2.7

Table 3*Mean Patient Length of Stay*

Mean Patient Length of Stay (LOS)		
Characteristic	Pre-protocol (n=9)	Post-protocol (n=9)
PICU LOS (partial days)	11.6	10.8
Hospital LOS (partial days)	17.3	15.9

Table 4***Mean Dosages of Sedation Administered per Patient***

Mean Dosages of Sedation Administered per Patient		
Characteristic	Pre-protocol (n=9)	Post-protocol (n=9)
<u>Opioid</u>		
Length of IV drip (partial days)	14	7.4
Length of methadone Wean (partial days)	8.4	8.8
Total length (partial days)	22.4	16.2
Rescue doses administered (dose per patient)	2.7	1.0
<u>Alpha Adrenergic</u>		
Length of IV dexmedetomidine drip (partial days)	9.5	8.4
Length of clonidine (partial days)	3.5	6.5
Total length (partial days)	13	14.9
Rescue doses administered (dose per patient)	-	-

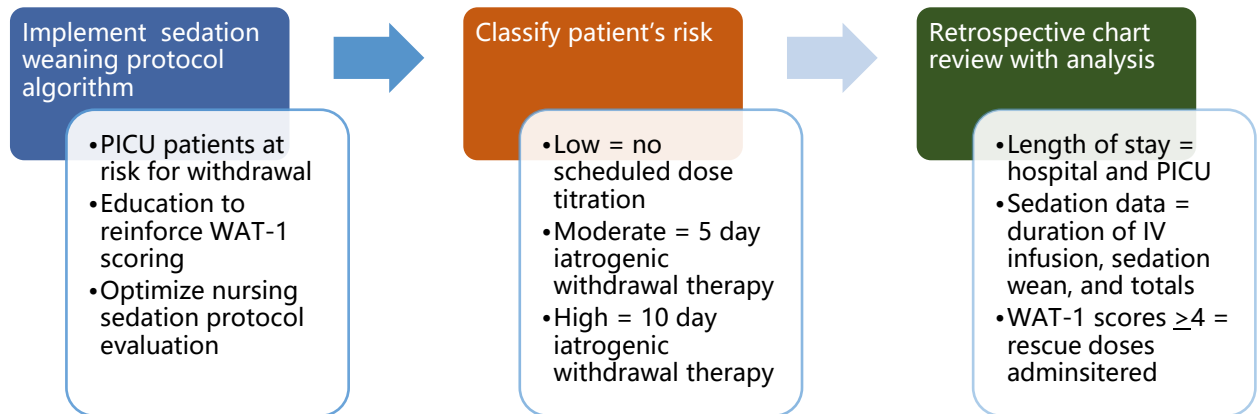


Figure 1. Study of Intervention and PDSA Cycle

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