

Increasing Premedication for Neonatal Intubation: A Quality Improvement Initiative

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Abstract

Introduction: Endotracheal intubation is frequent in the neonatal intensive care unit (NICU) but may result in neonatal distress and instability. Premedication reduces adverse effects, such as hypoxia, bradycardia, and pain. The Specific, Measurable, Achievable, Relevant and Time-Bound aim for this project was to increase premedication use for nonemergent neonatal intubation in a specific NICU from 22% to 80% from March 2021 to May 2023. **Methods:** We use quality improvement methodology to explain our theory for improvement. Our key driver diagram depicts this initiative's aims, key drivers, and interventions to increase premedication use for neonatal intubation. We defined exclusion criteria and medications, and one author collected demographic data retrospectively after the procedure. The stakeholders summarized the baseline data, performed plan-do-study-act cycles, and showed outcome measures in a statistical process control chart. Statistical analysis used Fisher's exact test to compare categorical variables. **Results:** Between 2021 and 2023, 333 infants underwent endotracheal intubation; 130 infants were included. The most common indication for intubation was hypoxemic respiratory failure—52% (68/130). Premedication use increased from 22% to 52%. Among the exclusion criteria, the most common indication for nonpremedication was intubation in the delivery room, 38.4% (78/203). In the premedication group, intubation on the first attempt occurred in 77.6% (52/67) of the cases, versus the nonpremedication group, 66.7% (32/48) ($P = 0.3$). **Conclusions:** Premedication for neonatal intubation increased by 30%, although we did not reach the desired 80% goal. Establishing a premedication bundle, alongside a unit-specific protocol and effective teamwork, marks the initial stride toward enhancing analgesia/sedation practices in the NICU. (*Pediatr Qual Saf* 2025;10:e778; doi: 10.1097/pq9.0000000000000778; Published online December 24, 2024.)

INTRODUCTION AND BACKGROUND

Endotracheal intubation is common in the neonatal intensive care unit (NICU). Many planned

intubations or nonemergent ones should undergo sedation/analgesia/paralysis. Premedication decreases the neonatal risks of intubation and increases its success. Risks associated with intubation include hypoxia, bradycardia, intracranial hypertension, and airway injury.^{1–3} Premedication also reduces the pain and discomfort associated with the procedure. Attention to pain control is vital in neonates due to profound long-term neurodevelopmental implications related to inadequate analgesia.^{2,4}

Shared concerns in the medical community about premedication side effects and long-term sequela, related to the evidence of neuronal apoptosis mediated by narcotics and benzodiazepines, led to its infrequent use in the NICU.^{5–7} Furthermore, some providers consider premedication unnecessary, arguing that it delays the intubation as medications are not promptly available.^{8,9} Premedication may include a vagolytic such as atropine, narcotics for analgesia, a sedative, and muscle relaxants.¹ Fentanyl has a rapid onset and a short duration of action¹ and maintains hemodynamic stability due to less histamine release.^{9,10} Midazolam has an onset of hypnotic activity within 2 minutes.^{2,11} Providers should avoid using sedatives alone without analgesic agents, as the goal is to facilitate intubation and decrease pain.⁹ Among the nondepolarizing neuromuscular blockers, rocuronium has a shorter onset and duration of action.²

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The International Evidence-Based Group for Neonatal Pain stated that “tracheal intubation without the use of analgesia or sedation should be performed only for resuscitation in the delivery room or for life-threatening situations.” However, using a standardized protocol/guideline for procedural premedication is lacking despite evidence of benefit to neonatal patients.¹² The American Academy of Pediatrics recommends that every healthcare facility for neonates implement pharmacological and nonpharmacological therapies to prevent pain associated with procedures.^{13,14} NICUs must develop protocols with premedications and optimize logistics to ensure the safe and timely administration of required agents.² This unit created a premedication bundle for neonatal intubation using quality improvement (QI) methodology.

METHODS

Context, Setting, and Study Period

We conducted this QI project for approximately two years in an urban, academic, quaternary referral center, level-IV NICU. This hospital has an average of 3,400 deliveries and 600 NICU admissions annually. Baseline data were collected from July 2020 to March 2021. The institutional review board and the Albert Einstein College of Medicine ethics committee approved the project design. They waived informed written parental consent as this QI initiative focused on systems changes.¹⁵

Study Population

We included neonates admitted to the NICU who required intubation during their admission. The exclusion criteria were predefined as intubation in the delivery room, known allergies or specific contraindications to any of the drugs, the less invasive surfactant administration (LISA)^{16,17} and intubation-surfactant-extubation (INSURE)^{18,19} techniques, intubation due to apnea and no response to positive pressure ventilation or contraindication to positive pressure ventilation, airway malformations and cardiac arrest. As rocuronium should not be used for LISA and INSURE procedures as you aim for spontaneous breathing, these procedures were part of the exclusion criteria for the analysis, even though the provider could use morphine or fentanyl to decrease pain and discomfort.

Study Measures

The SMART goal was to increase the use of premedication for nonemergent neonatal intubation from 22% to 80% in this NICU from March 2021 to May 2023. Secondary aims included reducing intubation attempts and complications associated with intubation. The balancing measures were the use of antidotes for fentanyl and rocuronium side effects (chest wall rigidity or excessive neuromuscular blockade). Demographic data were collected retrospectively from the electronic medical record (EMR) on all infants, including gestational age, postnatal and postmenstrual age (PMA) at

the time of intubation, birth weight, sex, number of intubation attempts, and indications for the intubation. Complications were also collected retrospectively from procedure notes and vital signs flowsheet and ranged from desaturations ($\text{satO}_2 < 80\%$), bradycardia, and emesis to oral bleeding. We de-identified and stored the data in a password-protected database. For analysis, the premedication definition was fentanyl and rocuronium with or without midazolam. If a medication dose differed from the suggested ones in the protocol but was within the recommended doses per pharmaceutical guidelines, or if midazolam was administered to an infant < 37 weeks PMA, we still included these patients in the analysis.

Planning and Studying the Interventions

Using the Model for Improvement by the Institute for Healthcare Improvement, we assembled a team.¹⁵ It included a neonatology faculty, a neonatal-perinatal fellow, a registered nurse (RN), and the NICU pharmacist. This multidisciplinary group focused on standardizing the care of patients undergoing nonemergent endotracheal intubation in this NICU for two years. The team monitored premedication use, complications, number of intubation attempts, and balancing measures during the study period. A key driver diagram depicted the aims, key drivers (multidisciplinary involvement, information technology, nursing empowerment, and providers' mindset change), and interventions for this initiative (Fig. 1). Through multiple plan-do-study-act (PDSA) cycles, we evaluated the proposed protocol implementation and determined if new interventions or modifications were necessary.²⁰

PDSA Cycle 1: Protocol Tool

The team determined the medications, their doses, antidotes, and workflow. Other integral points were making the drugs readily available in the unit and educating the NICU team. We developed a tool with all chosen medications and their antidotes, contraindications for using the premedication set, and an algorithm for drug administration posted in all NICU patient care areas (Fig. 2). Pharmaceutical guidelines were the references for medications and doses in the protocol.^{21,22} The protocol included an opioid analgesic (fentanyl) and a muscle relaxant (rocuronium). A sedative (midazolam) was an option if 2 doses of fentanyl did not provide enough sedation, but only if PMA was 37 weeks or more, as it can decrease cerebral flow velocity in premature babies with a risk for intraventricular hemorrhage and periventricular leukomalacia, besides the evidence of neuroapoptosis. There were multiple versions of the education tool. We modified it with suggestions from the providers and nurses until the flowchart was clear with doses (the first version did not display the doses easily), and the team understood the exclusion criteria.

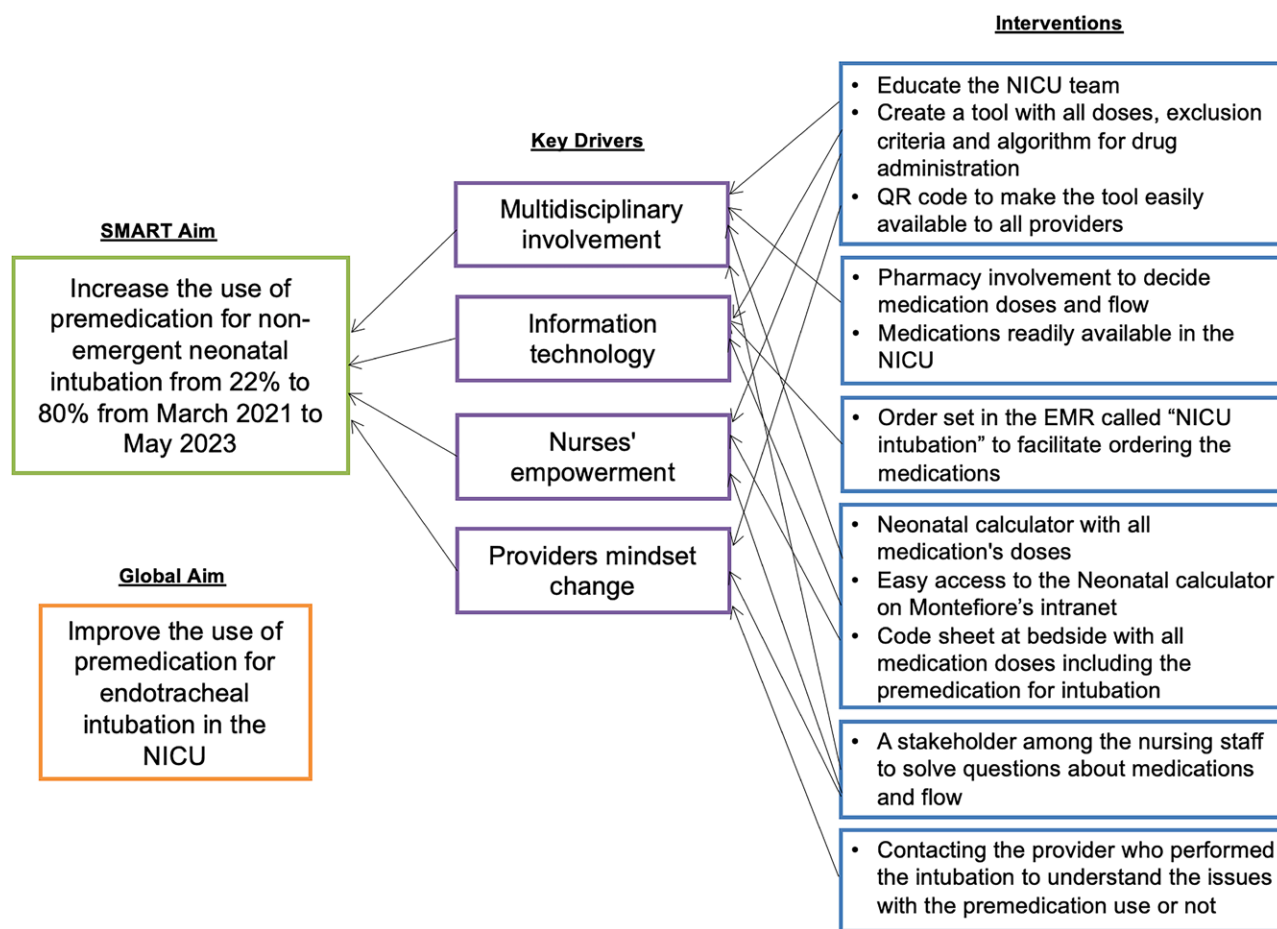


Fig. 1. Premedication for endotracheal intubation in the NICU—key driver diagram. SMART, Specific, Measurable, Achievable, Relevant and Time-Bound.

PDSA Cycle 2: RN as a Stakeholder

The NICU team accepted the tool as an accessible resource, but the nursing staff needed more clarification on administration and charting. We identified a stakeholder to support nursing and advanced practice providers' education. This RN provided feedback on the protocol application and suggestions on the education tool that made it more straightforward for nurses, for example, adding how the medication would be administered (intravenous push or in the pump for 3–5 min). These changes made the education tool trustworthy as the source for medication doses and flow, intending to decrease the time for preparation.

PDSA Cycle 3: Discussion with the Provider

After PDSA cycle 2, the core team noticed that the medical team's decision was essential for premedication use. We reached every provider after the intubation. This initiative promoted an understanding of the barriers to premedication use, the number of intubation attempts, the success and failure factors in the tool, and the clinical presentation of the infant at the time of the procedure. It also created an opportunity to discuss premedication,

including muscle relaxation for all nonemergent intubations, changing the mindset from a choice to a routine in the NICU.

PDSA Cycle 4: Order Set in the EMR

An EMR order set for neonatal intubation was created and made available. This order set comprised analgesic/sedative/muscle relaxant drugs, antidotes, respiratory support, and chest radiography. The goal was to have these items in the order set with predefined doses so that the correct premedication dose could be obtained and administered. This order set was a valuable tool for the QI project, but its implementation took months, as the providers had to be informed and introduce it to their intubation routine.

PDSA Cycle 5: QR Code in the Protocol Tool

We updated the teaching/protocol tool and included a QR code (Fig. 2) that allowed users (trainees, RNs, respiratory therapists, and providers) to save the protocol on their smartphones. Two modifications were made to the protocol tool to clarify the QR code's function for quickly checking doses and flow.

Premedication for Endotracheal Intubation

(Order set in **Epic**: "NICU intubation")

Medications – do not dilute!

Doses in the Neonatal Calculator

Fentanyl 10 mcg/mL - IV PUMP over 3 min

Dose: 2 mcg/kg/dose

Rocuronium 10 mg/mL - IV PUSH

Doses: 0.45 mg/kg/dose for <37 wks PMA

0.6 mg/kg/dose for ≥37 wks PMA

Midazolam 1 mg/mL - IV PUMP over 5 min

To be used if ≥37 wks PMA

Dose: 0.1 mg/kg/dose

Used for **ALL** intubations in the NICU, **except**:

Known allergy or specific contraindication to any of the drugs

Emergency intubation due to apnea and no response to PPV

LISA (Less Invasive Surfactant Administration)

InSurE (Intubation-Surfactant-Extubation)

Intubation in the Delivery Room

Contraindication to PPV

Airway malformations

Cardiac arrest

Exclusion Criteria

Antidotes – do not dilute!

Doses in the Neonatal Calculator

If chest wall rigidity didn't improve after Rocuronium

→ Naloxone 0.4 mg/mL

Dose: 0.1 mg/kg/dose IV PUSH

If neuromuscular blockade was excessive

→ Neostigmine 0.5 mg/mL

Dose: 0.03 mg/kg/dose IV PUMP over 1 min

&

→ Atropine 0.1 mg/mL

Dose: 0.02 mg/kg/dose IV PUMP over 1 min

How to access the Neonatal Calculator:

Intranet → Resources → Clinical Resources →

Neonatal Calculator
NICU Only



Scan QR code to keep
this tool on your phone

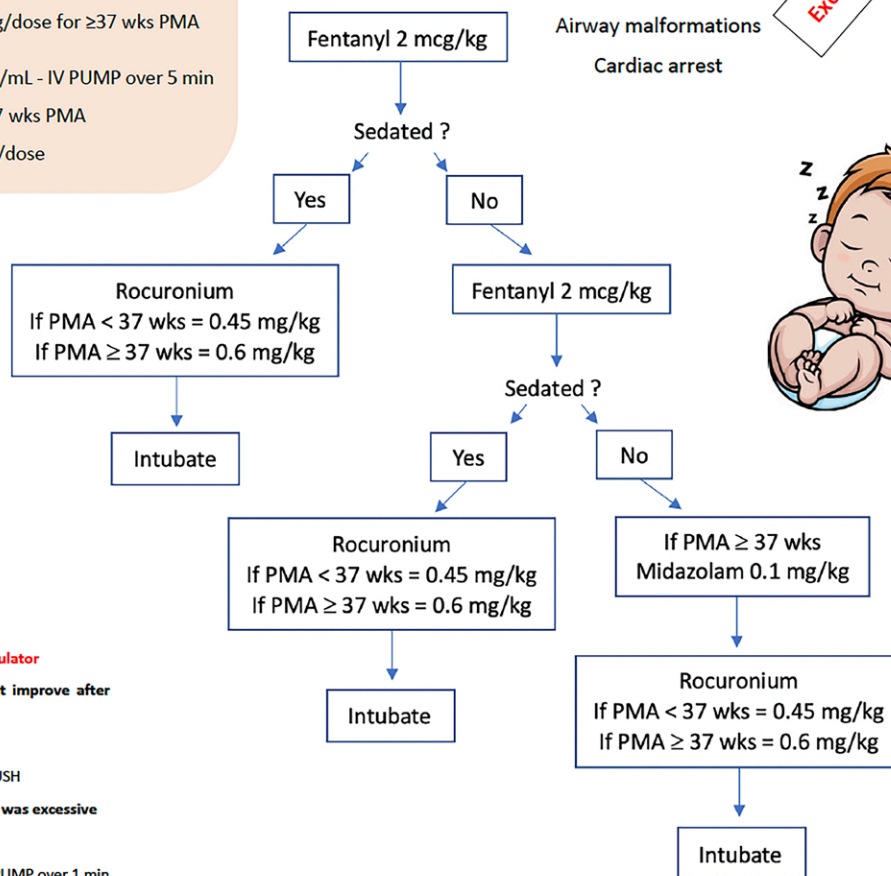


Fig. 2. Education/protocol tool. IV, intravenous; PPV, positive pressure ventilation.^{21,22}

PDSA Cycle 6: Neonatal Code Calculator ("Code sheet")

The core group developed another tool for posting at the patient's bedside: a neonatal drug calculator, also

known as a "code sheet." This tool included multiple emergency medication doses based on weight, including those for intubation. The nursing staff updated it weekly as it became available on the hospital intranet.

The calculator was specific to each patient, empowering the nurses to prepare the medications before they were ordered in the EMR. This extra tool became a routine in the NICU.

Data Analysis

We completed frequent run charts and statistical process control charts throughout the study, with partial outcome measures. We analyzed the data using QI Macros for Excel (KnowWare International Inc., Denver, CO.).²³ A final “NP chart” measured the number of items in each sample and two outcomes (“yes” or “no”) for the premedication use. A sustained special cause variation (SCV) was characterized by more than 8 values exceeding the baseline center line, representing a process modifier signal.^{20,23} Statistical analysis used Fisher’s exact test to compare categorical variables.

RESULTS

Three hundred thirty-three infants underwent intubation in the unit; 203 had predefined exclusion criteria, leaving 130 infants eligible for analysis. The mean birth weight was 1,212 (390–5,380) gm, and 56.9% were male. The mean gestational age was 27.6 (22–40) weeks. The mean PMA was 32.9 (23.3–50) weeks, and the mean postnatal age at intubation was 37 (0–182) days. Hypoxemic respiratory failure was the most common indication for intubation in 52% (68/130) of the cases, followed by hypercarbic respiratory failure in 19% (25/130), elective intubation for a procedure in 18% (24/130), and unplanned extubation 8% (11/130) (Fig. 3). Among the

exclusion criteria, the most common indication for non-premedication was intubation in the delivery room at 38.4% (78/203), followed by LISA at 17.7% (36/203) and INSURE at 16.3% (33/203).

From the baseline data to the initial PDSA cycle, the utilization of premedication with sedation/analgesia/paralysis for neonatal intubation escalated from 22% to 52%. An NP chart (Fig. 4) depicts this 30% increase with a shift in the centerline upon protocol implementation. Each data point on the *x*-axis represents every 10 intubations.

In the premedication group, successful intubation on the first attempt occurred at a rate of 77.6% (52/67) compared with the nonpremedication group, 66.7% (32/48) ($P = 0.3$). Complications, such as desaturations ($\text{satO}_2 < 80\%$), occurred in 27.7% (36/130) of infants. The lack of numbers deferred statistical analysis. One patient receiving premedication presented emesis, but bleeding due to trauma occurred once in the nonsedation/analgesia group. There was no use of antidotes, even though one case of chest rigidity was reported among 75 fentanyl administrations.

DISCUSSION

In this single-center QI project, we modified practice routines to include current recommendations. A multidisciplinary group created a protocol to decrease pain in the neonatal population during nonemergent intubation. We showed that premedication used for endotracheal intubation increased from the baseline data with this project, even though our optimistic 80% aim was distant. We believed we could reach 80% of intubations with premedication,

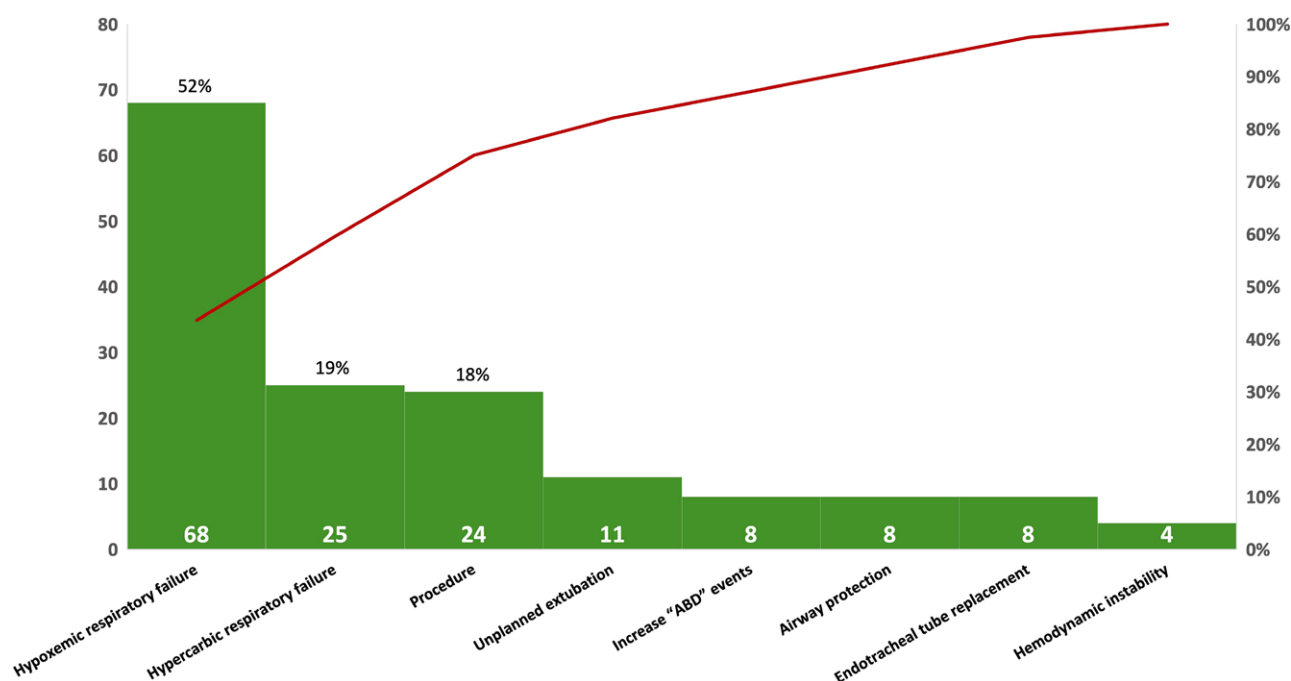


Fig. 3. Indications for intubation—Pareto chart. ABD, apnea, bradycardia, and/or desaturations.

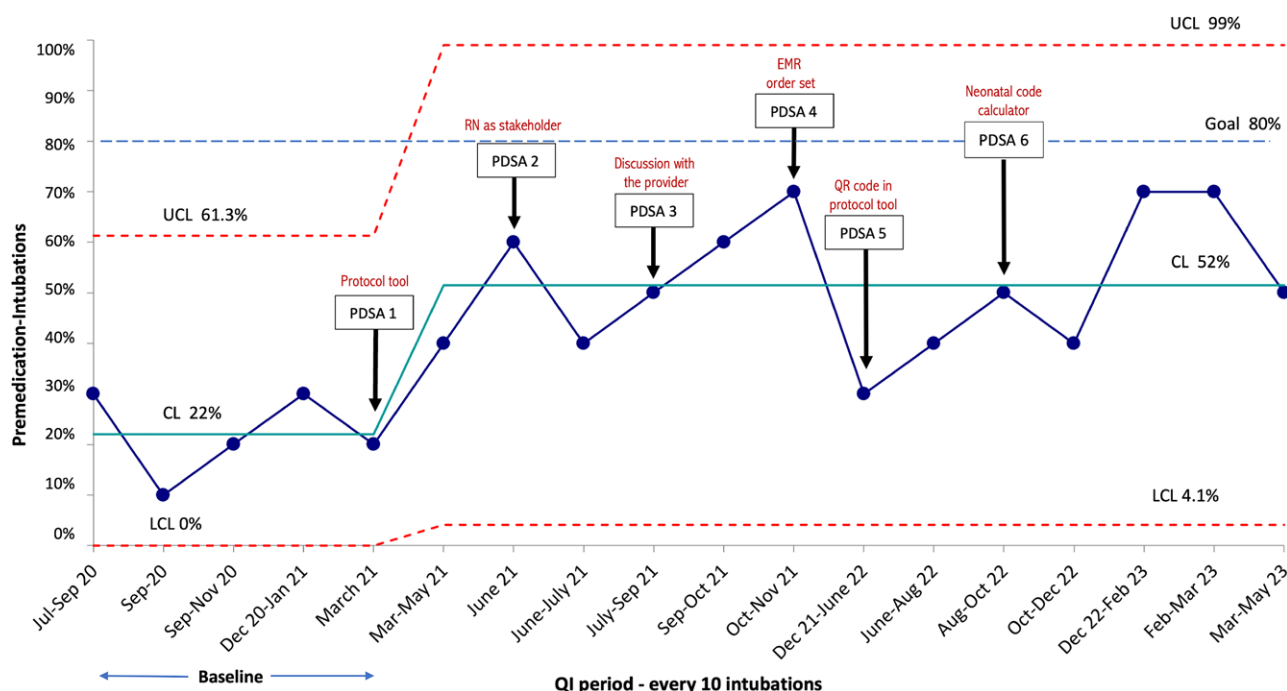


Fig. 4. Premedication-intubations NP chart. CL, center line; LCL, lower control limit; PDSA, plan-do-study-act; UCL, upper control limit.

as this NICU implemented two successful QI projects recently, increasing birth-dose hepatitis B vaccination²⁴ and skin-to-skin care duration in preterm infants.²⁵ We attribute not reaching our goal to the difficulty in mindset change; a 2-year window was not enough time for our protocol to become embedded as a unit practice. We also defined premedication as analgesics and muscle relaxants, unlike other studies that analyzed partial use of the medications in their guidelines.^{26,27} Some of our limitations were related to the lack of baseline data on the NP chart, restricting conclusions about the system's stability before the intervention. Another was associated with the short period of this QI initiative, with decreased data points on the statistical process control chart and the inability to detect another SCV during the protocol application.

Numerous pivotal factors contributed to the increase in premedication utilization. Implementing a customized bundle tailored to our NICU, combined with thorough team education and enthusiastic support from nursing staff during the first PDSA cycle, established a strong foundation for this upward trend. However, the effectiveness of subsequent PDSA cycles was absent. The involvement of an RN as a stakeholder during PDSA cycle 2 yielded suboptimal results compared with the engagement of the intubating provider in PDSA cycle 3, both without the expected success. Implementing an order set within the EMR system materialized in PDSA cycle 4, albeit with a slight delay in seamlessly integrating into NICU routines. During PDSA cycle 5, introducing a user-friendly protocol accessible via QR code, allowing team members to download the protocol tool easily, emerged as a well-accepted intervention, even though the documented

increase was not an SCV. Moreover, creating a comprehensive "code sheet" during PDSA cycle 6 empowered nurses to promptly update medication doses. However, it only reflected a common cause variation in the NP chart.

A 2015 survey of 693 neonatologists across all unit levels showed that the national average for using premedication for nonemergent intubations was close to 30%.¹² Neches et al²⁶ evaluated 352 encounters over more than 4 years, with the most frequent use of full premedication in infants ≥ 28 days before an elective procedure. Our hospital has many deliveries and few outside transfers. Therefore, there will be a significant number of intubations in the delivery room, lowering the use of premedication in general, as demonstrated in the exclusion criteria data, as 38.4% (78/203).

Despite the recommendations in the neonatal literature, there is an increased variability among guidelines and medications.^{8,9} This protocol included an opioid analgesic (fentanyl), a sedative (midazolam) if PMA is 37 weeks or more, and a muscle relaxant (rocuronium). We did not include atropine in our algorithm, as we did not encounter frequent bradycardia in the baseline data. However, this could change in a future updated protocol following other published intubation guidelines.^{26,28,29} We prioritized the use of analgesics to prevent procedural pain as we are mindful of the neurodevelopmental outcomes associated with repeated painful stimuli in premature infants.⁷ This guideline was the best for our unit to ensure safety, optimize the workflow, and improve compliance.^{2,9}

Diego et al³⁰ showed higher intubation rates in the first attempt among the premedication group; this QI initiative could not confirm these data as there was no

statistical difference compared with the nonpremedication group, similar to the Seattle group findings in 2023.²⁶ Desaturations were the most common complication. It is challenging to link desaturations to the procedure, administered medications, or the primary reason for intubation. We reported complications in fewer than 30% of cases; however, the flowsheet and procedure notes provided these data, increasing the underreporting risk. The small number of complications and the retrospective nature of these data led to limitations in our statistical analysis.

Our improvement rate, from the baseline to the PDSA cycle 1, was possible due to the collaborative work of professionals in the NICU and the involvement of the nurses. Our future directions include shortening the time to administer the medications³¹ and increasing buy-in from team members. We will also work on a culture change in the NICU, introducing this subject to the residents, fellows, and freshly hired nurses within their first months in the new environment. For the maintenance phase of this QI project, we plan to include a parent representative who will advocate for pain-free intubation and decreased number of attempts. Furthermore, a respiratory therapist who is actively involved in the intubation process should be one of the key stakeholders, and the flowsheet must include specific pain scores during the intubation, adding objective data to encourage more frequent premedication.

CONCLUSIONS

Intubation stands as a routine procedure within any NICU, demanding careful consideration of associated pain. Over 2 years, this cohort witnessed a 30% increase in premedication for nonemergent endotracheal intubations from its baseline. Despite this improvement, the desired target of 80% of intubations utilizing medications within the bundle remained unachieved. Establishing a unit-specific premedication bundle is an initial stride toward enhancing analgesia/sedation practices within the NICU. Effective teamwork and addressing common barriers to premedication are crucial for achieving the goals of implementing the premedication protocol.

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