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Intervention Bundle for Optimization of Procedural Sedation for Newborns Undergoing Magnetic Resonance Imaging: A Single-Center Quality Improvement Project in Qatar

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Magnetic resonance imaging · Procedural sedation · Neonatal care · Radiology

Abstract
Introduction: Magnetic resonance imaging (MRI) is a common procedure in tertiary care neonatal intensive care units (NICUs). MRIs aid in detailing structural anatomy and are increasingly utilized for prognostication. Keeping babies calm and motion-free in the MRI suite is challenging, and various approaches have been adopted to obtain the best image quality. We share our experience of intervention bundle for procedural sedation with the novel use of buccal midazolam in our NICU for babies undergoing MRI. ***Methods:*** This single-center quality improvement project comprised two epochs. Epoch 1 from April 2018 to December 2020 provided baseline data regarding sedation use and helped identify causes for suboptimal images and the adverse event rate. Following the implementation of an interventional bundle comprising specific midazolam dose recommendations tailored to background risk factors and streamlining the procedural sedation process, similar comparative data were collected in epoch 2 (May 2021 to December 2022) after a washout period. ***Results:*** Of 424 patients, 238 and 108 had MRI done under either procedural sedation protocol or feed and wrap technique in epoch 1 and 2, respectively. After excluding babies whose MRIs were performed under sedative infusions, 30 (13%) babies had adverse events in epoch 1, while only 8 (7%) events occurred in epoch 2. There was also a 37% improvement in the documentation of procedural sedation between the two epochs. ***Conclusion:*** Procedural sedation with buccal midazolam under neonatologist supervision is safe, efficient, and effective in babies undergoing MRI in this single-center study. More extensive studies may be warranted to assess the suitability of this sedation modality for broader use.

Introduction

Advances in neonatal care have improved survival in extremely preterm infants. Good antenatal care, use of antenatal steroids, noninvasive use of surfactant, standardized feeding protocol, use of exclusive breast milk and donor milk, family integrated care and skin-to-skin care, etc., have revolutionized the care of preterm and, as such, not only the survival is improved but also the rate

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and severity of brain injuries are reduced [1]. Cranial magnetic resonance imaging (cMRI) at term equivalent age (TEA) or before discharge from the neonatal intensive care unit (NICU) is increasingly becoming a part of standard practice [2]. Detailed cMRI, in conjunction with other clinical tools, helps in prognostication and guides early intervention therapy [3]. In addition, central nervous system (CNS) anomalies, pre-, and post-congenital heart disease surgery, hypoxic-ischemic encephalopathy, genetic abnormalities, seizure disorder, and post-major surgery in the neonatal period such as congenital diaphragmatic hernia repair are a few other indications/reasons for cMRI.

However, obtaining magnetic resonance imaging (MRI) for various diagnostic purposes warrants the patient to remain quiet and motion-free for the duration of the scan, which varies based on the anatomical area of interest and clinical indication for which the scan is recommended. Therefore, there is a potential need for safe and effective sedation to obtain high-quality images free from motion artifacts [4]. Procedural sedation for MRI is defined as moderate to deep sedation, putting the infant in a less responsive state with an ability to maintain an airway for spontaneous breathing and minimal requirement for resuscitative measures [5].

Many pharmacological and non-pharmacological strategies have been formulated to immobilize infants during MRI procedural sedation. Non-pharmacological methods, often grouped under umbrella terms such as "feed and wrap" [4], include swaddling, nonnutritive sucking, human or formula milk feeding, or providing skin-to-skin before the procedure [6, 7]. Ideally, these strategies should always be attempted. However, they may not always facilitate optimal images, and pharmacotherapy is warranted to sedate the infants. Moreover, the feed and wrap technique may sometimes not be feasible due to "nil by mouth" status. Hence, there is a need for medications to provide safe procedural sedation to avoid delays, exam cancellation, and frustration for both clinical teams and the patient's family.

Pharmacological strategies include using sedatives with appropriate doses to be used either during procedural sedation or during general anesthesia. Since general anesthesia is invasive, has significant associated risks [8], and may warrant the presence of an anesthesiologist, sedative medicines used for procedural sedation remain popular among neonatologists to facilitate the timely completion of MRI. Even though the concerns regarding the impact of sedation on long-term neurodevelopmental outcomes in both the term and preterm population are well studied, this does not entirely preclude the use of appropriate medications [9, 10]. Dexmedetomidine, an alpha-2 receptor agonist, is emerging as a suitable sedative for procedural sedation in term and preterm newborns undergoing MRI; however, large-scale prospective data are required before these are generalized for procedural sedative in neonates [11, 12].

Chloral hydrate has been extensively evaluated for pediatric MRI procedural sedation, with a success rate up to 95%. However, concerns have been raised about post-procedural oxygen desaturation and bradycardia in the term and preterm population [13, 14] and its impact on auditory perceptions even after a single dose in neonates, plus increased apoptosis in animal models [15]. Chloral hydrate was unavailable at our institutional pharmacy; hence, other options were considered, balancing the requirement of minimal adverse effects while providing adequate procedural sedation.

Midazolam, a short-acting sedative-hypnotic drug, works by slowing brain activity, allowing muscle relaxation and sleep, and can be administered via multiple invasive and noninvasive routes [16]. Evidence about the use of buccal midazolam suggests higher bioavailability, therapeutic efficacy, and tolerability [17]. Although the intranasal route for midazolam is well studied, a significant proportion of preterm babies at TEA require nasal cannula or CPAP. Utilizing the intranasal route might pose problems with instilling and briefly disconnecting the nasal interface and causing discomfort and burning sensation intranasally [18–20]. Hence, we proposed a novel approach of using buccal midazolam as the agent of choice for providing procedural sedation for MRI in patients who were not on mechanical ventilation. The buccal route was chosen as it is well tolerated with high bioavailability [17], quick onset of action, and ease of administration. However, to our knowledge, buccal midazolam has not been studied for procedural sedation in neonates. An initial audit showed about 17% of infants experience side effects related to buccal midazolam, including the escalation of respiratory support to invasive ventilation. A cause-effect diagram is shown below in Figure 1, outlining various reasons for the delay in acquiring MRIs and also in suboptimal images.

A consensus MRI procedural sedation intervention bundle was formalized, balancing the risk of adverse events and yet achieving optimal images by formulating recommendations for safe dosing for buccal midazolam, accounting for baseline risk characteristics. The bundle included standardized guidelines and algorithms (online suppl. material 1; for all online suppl. material, see https://doi.org/10.1159/000538762) buccal midazolam dose recommendations tailored to baseline clinical

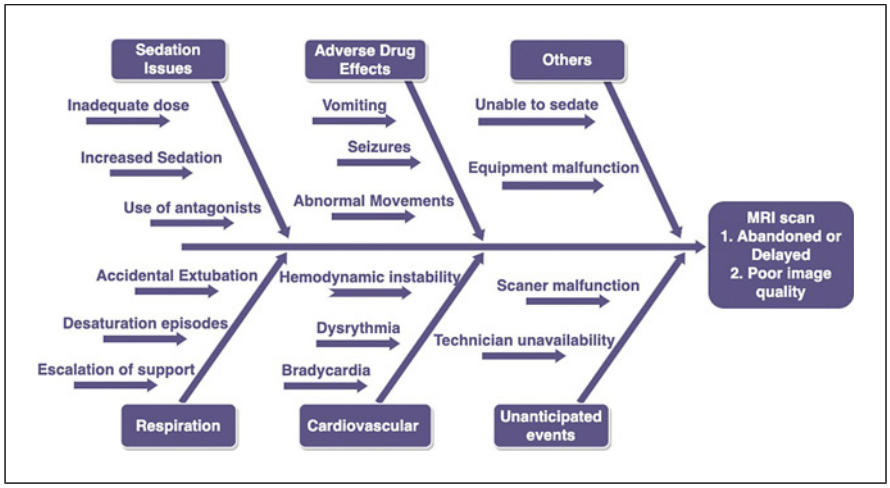

Fig. 1. Cause-effects diagram.

characteristics, a transportation checklist, establishing monitoring requirements in the MRI suite, and a standardized template to document events during the procedural sedation.

We studied the adverse event rate and image quality outcomes post-implementation of this bundle under this quality improvement project for all newborns undergoing MRI procedural sedation. This study aimed to assess if the safety and efficacy of buccal midazolam can be optimized for NICU in patients undergoing procedural sedation for MRI.

Materials and Methods

Study Design

This quality improvement project was done at Sidra Medicine, NICU, a level IV center. We used retrospective and prospective data utilizing the "DMAIC" (Define, Measure, Analyze, Improve, Control) framework. Initially, data were collected for all infants who underwent MRI procedural sedation in our NICU from April 2018 to December 2020 and were defined as epoch 1. This retrospective baseline data analysis identified underlying risk factors associated with adverse events during the MRI procedure. It enabled the formulation of recommendations for an optimal buccal midazolam dosing regimen. After studying the baseline data in epoch 1, we proposed the ideal first dose of buccal midazolam for premature babies with chronic lung disease on baseline respiratory support (i.e., nasal cannula or noninvasive ventilation [NIV]) as 100 μg/kg/dose. The rationale behind such a dose was to avoid respiratory depression. On the other hand, the ideal first dose of buccal midazolam for full-term babies not on respiratory support was set at 200 μg/kg/dose to reduce the need for repeat dosing and decrease scanning time. The intervention bundle was implemented in March 2021, and prospective data collection similar to epoch 1 was conducted after a 2-month washout period from May 2021 to December 2022 to assess for improvement in obtaining optimal MRI images and rates of adverse events.

We included all newborns admitted to the NICU at Sidra Medicine who underwent MRI as inpatients. We excluded babies with MRIs performed at the pediatric or cardiac ICU who were subsequently readmitted to the NICU after cardiac surgery or extra corporeal membrane oxygenation.

Patient demographic data, such as gestational age (GA) at birth and at the time of MRI, birth weight, current weight at the time of MRI, indication for MRI, respiratory support before, during, and after MRI procedure, medications used along with their doses, the number of doses, and any adverse events either related to drugs or cardiorespiratory instability, were collected via electronic medical record.

Following informed written consent for MRI procedural sedation, the patients were fed formula or human milk via nasogastric tube or bottle (unless they were nil by mouth for other reasons) approximately 60 min before the procedure. If required, a pacifier was used to calm the infant. MRI-compatible chest electrodes and an oxygen saturation (SpO_2), monitoring device were attached to the baby's chest and right hand. After the application of noise-canceling earmuffs, the patient was swaddled in a blanket to minimize disturbance and placed in an MR-compatible incubator (Lammers Medical Technology, Lübeck, Germany) in a supine position with the head in the midline with all monitoring and sensor devices attached. Baseline vital signs were recorded, and SpO_2 and heart rate monitoring continued throughout the procedure. It was documented every 5 min in a standardized template, which included a tick box section listing potential adverse events. This document was subsequently uploaded to the electronic medical record (online suppl. material 2).

Imaging was performed using a 3T MRI scanner (Philips Achieva) in a Lammers incubator using an eight-channel coil. Routine imaging included sagittal T1 3D with multiplanar reformats (TE 4.6 ms, TR 1.7 ms, FOV 16.0 cm) and high-resolution T2-weighted sequences (TE 130 ms, TR 8,000 ms, FOV 140 cm).

The patient was accompanied by a physician, registered nurse in charge, and respiratory therapist (when on respiratory support, i.e., nasal continuous positive airway pressure or mechanical ventilation) to the MRI suite and were responsible for close monitoring of any respiratory compromise or any adverse events related to medication.

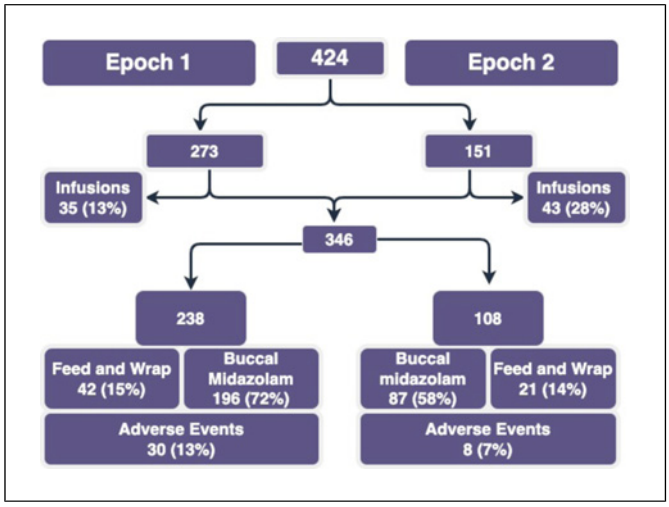

Fig. 2. Flowchart of study participants.

If the baby was noted to be well settled after the initial feed and wrap technique, physician discretion allowed for the procedure to be completed without using medication for sedation. However, if the baby was awake or moved during the procedure while inside the MRI scanner, causing motion artifact in images, midazolam was given via a 1 mL needless sterilized syringe, and the solution was dripped evenly over the buccal mucosa followed by a pacifier. There was an option of a repeat dose if the patient was not sedated. Patients on mechanical ventilation and sedation medications via infusion pumps or intravenous intermittent boluses continued to receive them without the need for "feed and wrap" or buccal midazolam; however, other steps of preparing the patient for MRI procedural sedation remained the same.

Adverse events evaluated during and after the MRI procedure were based on either of the following events:

1. Assisted ventilation for periods of apnea (cessation of breathing >20 s) at any time during the procedure.
2. Oxygen desaturation episodes are defined as a decrease in SpO_2 of 10% from the pre-procedure baseline for 5 min or longer during the procedure.
3. Episodes of unplanned extubation
4. Heart rate changes are defined as tachycardia with a heart rate above 180 beats/min or bradycardia with a heart rate less than 70 beats/min and any hemodynamic instability at any time during the procedure.
5. The procedure is discontinued or interrupted due to adverse drug reactions, like new-onset seizures, abnormal movements, vomiting, etc.
6. The scan was abandoned because the baby remained awake despite sedation medications or contraindicated feed and wrapping, unable to make the baby sleep.

The above information collected from the standardized documentation template and information related to MRI images, including the duration of the scan time, the number of images taken, and the quality of images, were then entered into an Excel sheet designed for this purpose. MRI scan time duration was defined as the time in minutes between the first and last image acquisition. The quality of the images was assessed from the comments, if any, by the reporting neuroradiologist.

Results

Patient Characteristics

Four hundred twenty four patients underwent MRI using either procedural sedation protocol or feed and wrap technique, 273 during epoch 1 and 151 in epoch 2, respectively, as shown in Figure 2. Their baseline demographic data are shown in Table 1. In epoch 1, we had more mature babies, as demonstrated by their respective GA and birth weight compared to epoch 2; however, there was not much difference in gender distribution between the two epochs. Babies in epoch 2 were more appropriate for their GA, while only 6% of babies in epoch 2 were small for GA as compared to epoch 1.

Similarly, MRI-related information for babies in epoch 2 was slightly different for babies in epoch 1 regarding their corrected gestational age, day of life the MRI took place and, weight at that time, duration of the scan, and number of images taken, as shown in Table 1. There was no significant difference in the image quality between the two epochs. Interestingly, documentation was significantly improved in epoch 2. The scan was abandoned in 2% of babies in both epochs.

Most scans in both epochs were done at TEA due to prematurity-related CNS complications, like severe IVH or white matter injuries, to predict the neurodevelopmental outcome and screen underlying CNS anomalies. Other clinical indications/reasons for MRI are summarized in Table 1.

After excluding babies on sedatives and narcotics infusions, 72% of babies in epoch 1 and 58% in epoch 2 required buccal midazolam for procedural sedation, and interestingly, most babies in epoch 2 received less buccal midazolam as compared to epoch 1. MRI images were acquired using feed and wrap techniques equally in both epochs, as shown in Table 1.

Adverse Events

In epoch 1, about 13% of babies who underwent MRI procedures either as feed and wrap technique or with buccal midazolam experienced adverse events; however, in epoch 2, only 7% of babies had adverse events. Adverse events mainly related to a decrease in peripheral SpO_2 occurred in both epochs, although less frequent in epoch 2; however, other serious events, including unplanned extubation in the MRI suite, assisted ventilation requiring positive pressure ventilation, and other clinically significant changes occurred only in epoch 1 as shown in Figure 3 and summarized in Table 1. Subgroup analysis of babies with

Table 1. Baseline demographics

Variables	Epoch 1 (*n* = 238)	Epoch 2 (*n* = 108)
GA at birth, weeks, mean±SD	34.42±5.33	32.46±5.79
Birth weight, g, median (IQR)	2,500 (500–4,200)	1,845 (540–4,590)
Male, *n* (%)	142 (60)	62 (57)
Growth, *n* (%)		
Appropriate for gestational age (AGA)	204 (86)	102 (94)
Small for gestational age (SGA)	33 (14)	6 (6)
MRI clinical indications/reasons, *n* (%)		
Suspected seizures	2 (0.8)	0
Seizures	12 (5)	9 (8)
Prematurity	50 (21)	36 (33)
CNS anomalies	73 (31)	26 (24)
Post-hypoxic-ischemic encephalopathy	13 (5.5)	2 (2)
Pre-cardiac surgery	22 (9)	3 (3)
Post-cardiac surgery	5 (2)	1 (1)
Genetic anomaly	12 (5)	5 (5)
Post-congenital diaphragmatic hernia	6 (2.5)	3 (3)
Others (more than 1 indication/reason)	43 (18)	23 (21)
MRI-related information		
Corrected gestational age (CGA) at scan, weeks, mean±SD	41.31±4.95	42.59±6.23
Chronological age at MRI scan, days, median (IQR)	30 (1–301)	61 (1–261)
Weight at the time of scan, g, mean±SD	3,146±860	3,276±923
Duration of scan, min, median (IQR)	46 (7–180)	35 (11–105)
Quality of images (optimal), %	92	87
Number of images, median (IQR)	24 (2–84)	20 (5–39)
Additional scan (MRA/MRV/MRS), *n* (%)	120 (50)	10 (9)
Documentation (optimal), *n* (%)	59 (25)	67 (62)
Scan abandoned, *n* (%)	5 (2)	2 (2)
Sedation, *n* (%)		
No (feed and wrap only)	42 (18)	21 (19)
Midazolam 100 μg/kg	69 (29)	77 (72)
Midazolam >100 μg/kg	127 (53)	10 (9)
Adverse events, *n* (%)		
None	203 (85)	98 (91)
Assisted ventilation required	4 (2)	0
Oxygen desaturation during the procedure	23 (10)	8 (7)
Unplanned extubation	1 (0.4)	
Other clinically significant changes (vomiting, seizures, etc.)	2 (0.8)	0

IQR, interquartile range; MRA, magnetic resonance angiography; MRV, magnetic resonance venography; MRS, magnetic resonance spectroscopy; SD, standard deviation.

adverse events revealed that about 24 babies in epoch 1 versus 6 in epoch 2 received buccal midazolam of >100 μg/kg, as shown in Table 2.

Respiratory Outcomes

Epoch 1

171 (72%) patients were spontaneously breathing in room air pre-procedure, and 45 (19%) were on noninvasive respiratory support, which, together with 19 babies who required noninvasive ventilation (NIV) from the spontaneously breathing group, constituted 64 patients (27%). This NIV included oxygen delivered via nasal cannula, face mask, or high-flow nasal cannula to maintain normal SpO_2 between 91 and 95%. After the procedure, 15 patients were successfully weaned off from NIV and joined the group of babies who were initially self-ventilating in room air and comprised 167 (70%). On the other hand, 49 (21%) patients continued to be on noninvasive respiratory support at the end of MRI imaging.

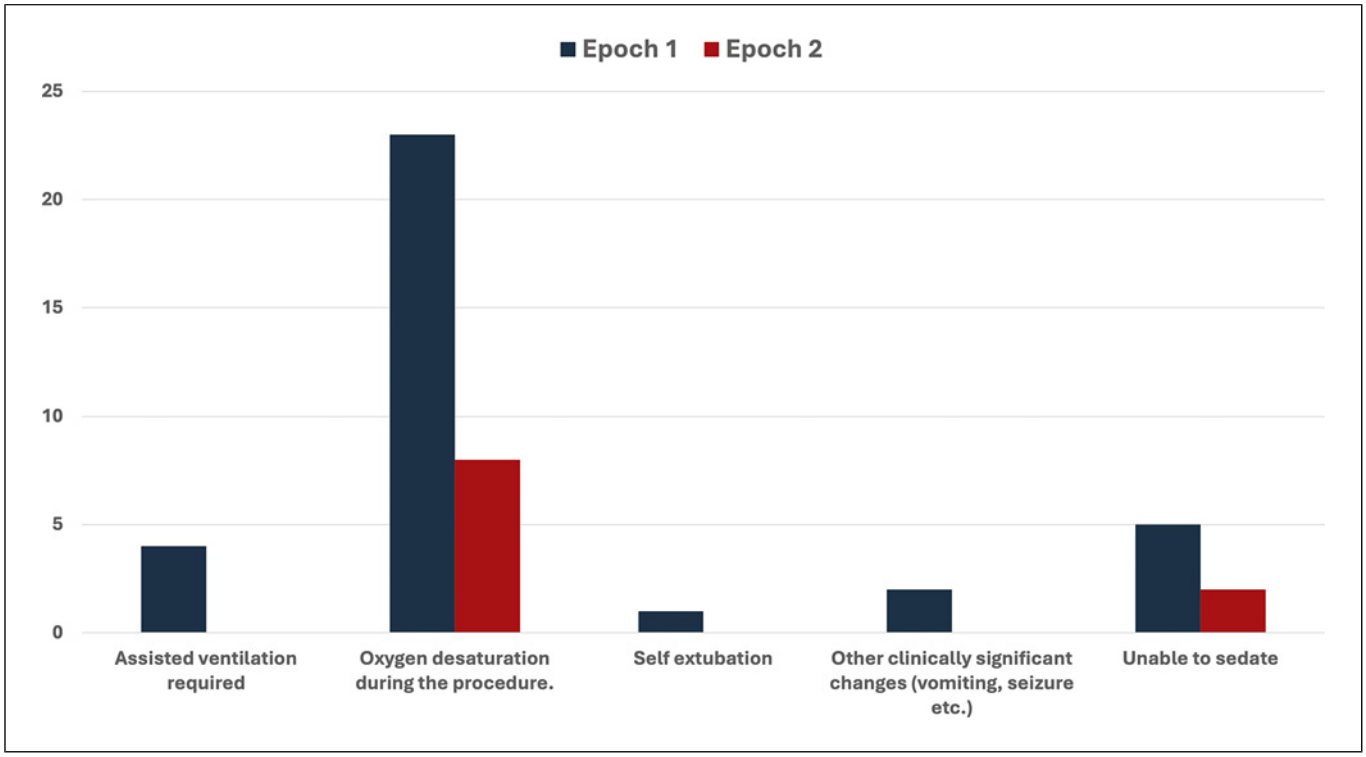

Fig. 3. Bar graph to show adverse events during epochs 1 and 2.

Table 2. Comparison of adverse events between single and multiple sedation doses

Variables	Epoch 1			Epoch 2		
	no dose	single dose (100 µg/kg)	multiple dose (>100 µg/kg)	no dose	single dose (100 µg/kg)	multiple dose (>100 µg/kg)
None	42	69	127	21	77	10
Assisted ventilation required	0	0	4	0	0	0
Oxygen desaturation during the procedure	1	4	18	0	2	6
Self-extubation	0	1	0			
Other clinically significant changes (vomiting, seizures, etc.)	0	0	2	0	0	0

2 (1%) infants received respiratory support via tracheostomy during pre- and post-procedural sedation. 20 (8%) babies on invasive ventilation remain on this support at the end of the MRI.

Epoch 2

Among 84 (78%) babies spontaneously breathing in room air before the MRI procedure, eight required NIV, and together with 13 (12%) babies already on noninvasive respiratory support constituted 21 (19%) during the procedure. However, five babies were successfully weaned off from NIV at the end of the MRI procedure, and together with other babies who remained spontaneously breathing in room air constituted 81 (75%). In contrast, the remaining 16 (15%) babies continued to be on NIV after the MRI procedure.

3 (3%) babies were breathing via tracheostomy tube during pre- and post-procedural sedation. 8 (7%) babies on invasive ventilation remain on this support at the end of the MRI. All changes in respiratory outcome during and after the MRI procedure are shown graphically in the flowchart in Figure 4a, b.

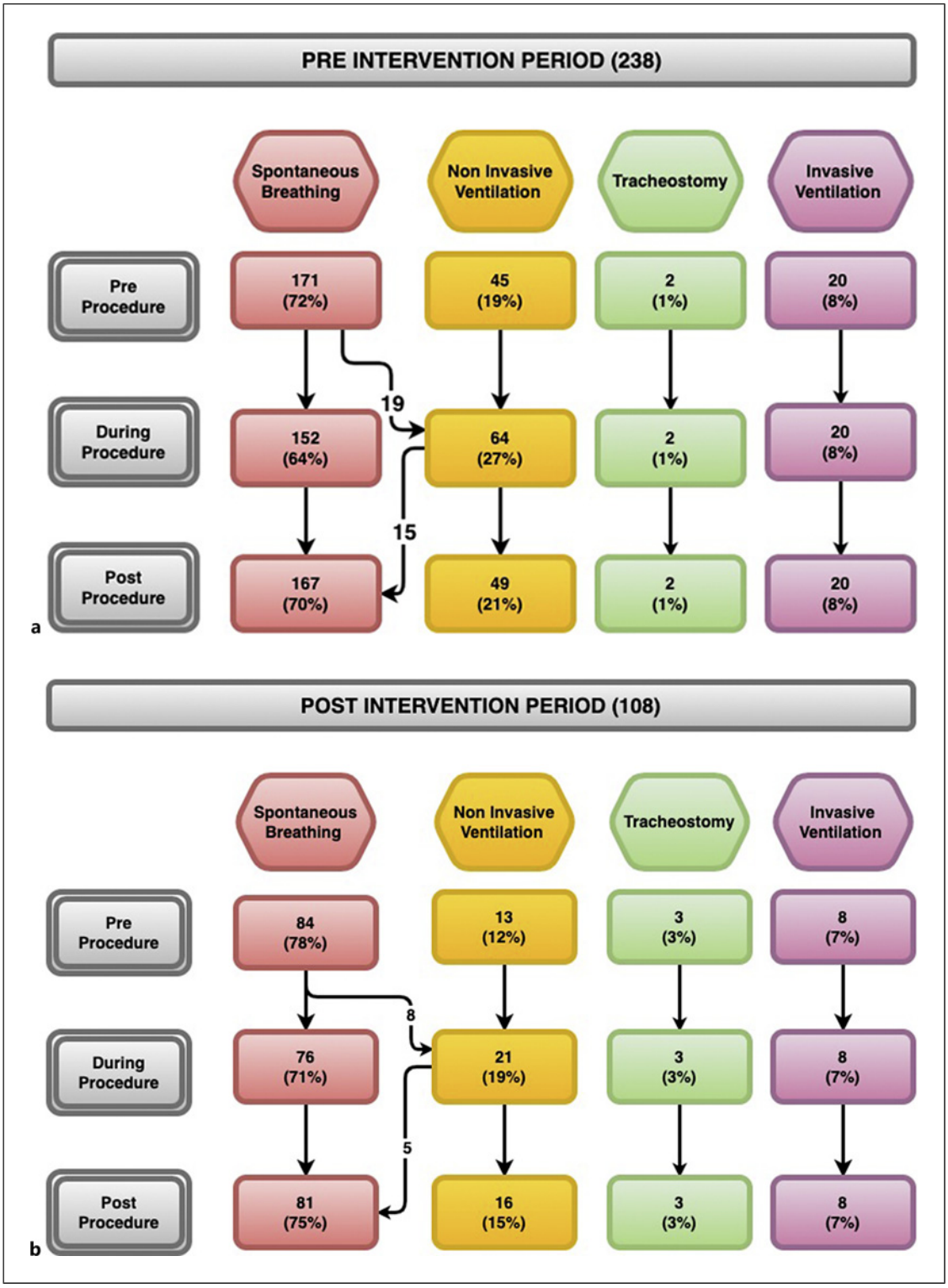

Fig. 4. a, **b** Respiratory outcomes of babies before, during, and after MRI procedure during epochs 1 and 2.

Discussion

Apart from routine diagnostic scans, MRIs are increasingly used for prognostication in the NICU. This applies especially to extremely preterm infants, where imaging is performed at TEA before discharge, and infants with complex underlying disease processes and who had a prolonged inpatient stay associated with major surgery. Hence, there is a need to develop a sedation regimen that can be administered to these relatively stable patient populations noninvasively, balancing both safety and efficacy. To accomplish this, we integrated the MRI procedural sedation care bundle with the novel use of buccal midazolam as our primary sedating medication, aiming to get an MRI done in the shortest possible time without compromising the image quality and with minimum adverse events. In this QI project, we have achieved a high success rate of >90% in completing MRI scans without any adverse events.

Due to the heterogeneous population in our quaternary surgical NICU, ranging from extreme preterm to infants close to 6 months of age at discharge, selecting a "one size fits all" dose for MRI procedural sedation was challenging. This, along with a series of adverse respiratory events associated with procedural sedation before the project was launched, was the primary driver for undertaking this QI project.

Since this project was novel in that, to our knowledge, the isolated use of buccal midazolam for MRI procedural sedation in neonates had never been studied before. Therefore, selecting the most appropriate dose for ex-preterm and full-term neonates was a challenge.

In their study, Li et al. [21] showed buccal midazolam in combination with intranasal dexmedetomidine was associated with a higher success rate and with a good safety profile for short-duration MRI in children between 1 month and 10 years. 93% success rate in our study using buccal midazolam as a sedation agent is comparable to studies using other sedatives, either a combination of intranasal midazolam and dexmedetomidine [22, 23] or chloral hydrate [4].

The most significant complication of MRI procedural sedation is respiratory depression manifested by decreased peripheral SpO_2 and apnea [24]. Most adverse events in our study were related to lower SpO_2 during procedures below 10% of the pre-procedure level. Most of these occurred in babies with underlying congenital anomalies, as shown in Table 1, for which MRI was done; however, there was a trend toward decreased adverse events in epoch 2, owing to strict adherence to dosage regimes separate for preterm and term newborns, following a consensus recommendation amongst the NICU multidisciplinary team. The extended scanning time in epoch 1 might suggest more interruptions during the scan to manage suboptimal sedation or to assess the higher frequency of respiratory instability. Patient movements or wide-awake states often alter the oxygenation saturation and heart rate on the monitor. In and out movement of team members within the MRI suite to adjust oxygenation and heart rate on the monitor may also cause a delay in scan time.

Our results related to adverse events of buccal midazolam are consistent with results reported by Sammons et al. [25]. Their systematic review assessed 27 studies evaluating the safety and effectiveness of various routes of midazolam in children undergoing imaging procedures. They reported that hypoxia was the most common adverse event and was completely reversible after using simple maneuvers like supplemental oxygen, while vomiting was the second most frequently reported adverse event.

Our study focuses on data obtained from a level IV NICU facility, which cares for a wide spectrum of inpatients ranging from extremely low GA newborns to older complex surgical infants with prolonged hospitalization. We have included both retrospective and prospective data to show improved scan time and less occurrence of adverse events by using a novel buccal route for midazolam.

Limitations include a lack of data about when the baby experienced a desaturation episode, and we relied mainly on documentation by physicians present during the procedural sedation. Though monitoring devices for measuring heart rate and SpO_2 were wireless, these episodes were not automatically transferred to electronic patient charts as captured in the NICU. Since patient safety is the priority during MRI procedural sedation, healthcare providers must attend to the patient's needs during the procedure to ensure whether the drop in SpO_2 is genuine or due to motion artifacts. Hence, the time duration for desaturation episodes was not captured.

Second, we relied on reports dictated by experienced radiologists for the quality of images, and if they commented on the poor-quality image, we included that as suboptimal images. Ideally, all MRI images included in our cohort should have been independently assessed and scored by radiologists other than those who reported the initial image to remove bias or were blinded to clinical data. However, we believe the study should have been canceled or reflected in the report if there were noticeable motion artifacts. We are confident that our study findings reporting suboptimal images are meaningful and reflect real-world imaging data.

Third, we have not included the acuity of the baby's condition or significant comorbidities present before MRI procedural sedation, which might have resulted in adverse events. However, we think they might not have caused a considerable impact on adverse events as MRI scans were done in hemodynamically stable babies.

Conclusion

Ideally, non-pharmacological strategies like feed and wrap should always be attempted first for MR imaging studies. If sedation is required, buccal midazolam under neonatologist supervision provides safe, efficient, and effective sedation. More extensive comparative studies and randomized trials will be essential to assess the long-term suitability and safety for the broader use of this sedation modality.

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Statement of Ethics

The Institutional Research Board (IRB) Committee at Sidra Medicine approved the project (1748578-5). All methods were carried out in accordance with relevant guidelines and regulations. Since data were collected retrospectively, hence, no patient consent was required as a waiver was obtained from the IRB at Sidra Medicine.

Conflict of Interest Statement

The authors declare no conflicts of interest.

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Author Contributions

Conceptualization and supervision: N.U.R.D.; methodology: S.A., G.D., and A.A.C.; data collection: G.D. and N.U.R.D.; writing – review, discussion, and editing: N.U.R.D., S.A., G.D., and A.A.C. All the authors have read, approved, and agreed to the published version of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its supplementary material files. Further inquiries can be directed to the corresponding author.

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