Eat, Sleep, Console and Adjunctive Buprenorphine Improved Outcomes in Neonatal Opioid Withdrawal Syndrome

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ABSTRACT

Background: The worsening opioid crisis has increased the number of infants exposed to maternal opioids. Standard treatment of newborns exposed to opioids prenatally often requires prolonged hospitalization and separation of the mother–infant dyad. These practices can potentially increase severity of withdrawal symptoms, interrupt breastfeeding, and disturb mother–infant bonding. Use of the Eat, Sleep, Console (ESC) model may ameliorate symptoms, decrease mother–infant separation, and decrease hospital length of stay.

Purpose: To manage opioid exposed infants in a more holistic manner to decrease neonatal intensive care unit (NICU) admissions, reduce the need for pharmacotherapy, and evaluate response and total length of treatment after a unit protocol change from morphine to buprenorphine.

Methods: Implemented ESC model, optimized nonpharmacologic bundle, and prescribed buprenorphine therapy instead of morphine as needed for adjunctive therapy.

Results: Admissions of opioid-exposed infants from the Mother–Baby Unit (MBU) to the NICU decreased by 22%, and the number of infants who required pharmacotherapy was reduced by 50%. The average length of pharmacotherapy fell from 14 to 6.5 days.

Implications for Practice: The successful implementation of the ESC model helped keep the mother–infant dyad together, reduced admissions to the NICU, and lessened the need for pharmacotherapy. The change to buprenorphine further reduced our average length of treatment.

Implications for Research: Investigation of monotherapy with buprenorphine needs to be evaluated as a valid treatment option. The buprenorphine dosing and weaning chart will need to be revised and modified if indicated.

Key Words: buprenorphine, comfort assessment, multidisciplinary, neonatal abstinence syndrome, neonatal opioid withdrawal syndrome, quality improvement

The worsening national opioid crisis led to a 4-fold increase in infants with neonatal opioid withdrawal syndrome (NOWS) from 2008 to 2012.[1-3] Admissions to our neonatal intensive care unit (NICU) for NOWS increased from 18 opioid-exposed infants per year in 2008 to 51 infants in 2012. The number of admissions was consistent at 55 to 65 infants per year through 2017. Our multidisciplinary team addressed this public health concern through quality improvement (QI) methodology over the past decade. We continue to explore best practices for nonpharmacologic and pharmacologic management of infants with NOWS.

Conventional assessment and treatment approaches to the infant with signs of NOWS often result in separation of the infant from the mother.[4] The Finnegan Neonatal Abstinence Scoring System (FNASS), developed in 1975, is the most common tool used to evaluate infants with opioid exposure in the United States.[5] The tool assigns points from 1 to 3 for the 21 most common withdrawal symptoms seen in infants with NOWS. Generally, an infant with a score above 8 requires pharmacologic treatment. The FNASS requires initial and repetitive training for caregivers, may create subjectivity, and suffers from lack of interrater reliability. Despite its use for decades to assess need for NICU admission and medication, it may not be valid for infants with NOWS at present. Our previous practice included observation of these infants utilizing the FNASS for 5 days in the Mother–Baby Unit (MBU), resulting in separation of the mother and the infant at the time of maternal discharge. Infants were admitted to the NICU for 2 FNASS scores greater than 8 or one FNASS score greater than 12. Upon admission to the NICU and confirmation of the FNASS scores, the infants were treated with phenobarbital. Morphine was added for persistent elevation of FNASS scores.

Maintaining an intact maternal–infant dyad improves infant outcomes by decreasing admission to

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the NICU and reducing use of pharmacotherapy.[4,6,7] Recent evidence indicates that the Eat, Sleep, Console (ESC) model encourages a holistic approach to infants with NOWS.[8,9] The ESC approach to infants with opioid exposure in utero was published in 2017 by Grossman and colleagues.[10] This program is based on an infant's ability to perform activities of daily living. Three critical functions are assessed every 3 to 4 hours. (1) *Eat*: Can the infant take ½ to 1 oz or breastfeed effectively? (2) *Sleep*: Can the newborn sleep undisturbed for an hour? They may be held during this time to support sleep. (3) *Console*: Is the newborn consolable within 10 to 20 minutes? A second caregiver may attempt to console the newborn before a decision is made to use pharmacologic therapy. Grossman and colleagues[11] demonstrated a marked decrease in admissions to the NICU, a decrease in initiation of pharmacotherapy, and a decrease in length of treatment. In October 2017, our QI team incorporated this new care approach for the opioid-exposed infants in the MBU and the NICU. The Comfort Assessment Tool (CAT) was our interpretation of the ESC model of care, making it more descriptive. Providers and staff were encouraged to ask the aforementioned 3 questions. The bedside nurse documented either "Yes" or "No" in the flow sheet. We did not use a numerical score to evaluate the infant. Rather, if there were 2 consecutive "No's" or 3 "No's" at one time, the infant was evaluated by the physician for possible pharmacologic therapy.

Multiple medications have been utilized to treat NOWS with wide institutional variability.[12] Through QI initiatives using the Plan, Do, Study, Act (PDSA) method, our treatment plan evolved over time.[13] Medications changed from phenobarbital with methadone to phenobarbital with morphine to morphine alone, with the occasional use of adjunctive clonidine, and finally to phenobarbital with morphine if needed as second-line therapy.[14]

Sublingual buprenorphine treatment of NOWS decreases length of treatment and length of stay (LOS).[15] Buprenorphine is a partial opioid μ receptor agonist and a full opioid κ receptor agonist that has been used successfully to treat opioid withdrawal in adults.[16] Several buprenorphine trials in newborns with NOWS have shown comparable results when comparing morphine with methadone. The Blinded Buprenorphine or Neonatal Morphine Solution (BBORN) trial was a single-site, randomized, double-masked, double-dummy trial in which sublingual buprenorphine was compared with oral morphine in 63 infants with neonatal abstinence syndrome (NAS).[17] The median duration of treatment (15 days vs 28 days) and the median length of hospital stay (21 days vs 33 days) were shorter in the buprenorphine group versus the morphine group. On the basis of the initial and corroborated data, we adopted buprenorphine as our first-line opioid therapy in November 2018.[17-19]

The aims of this project were to decrease NICU admission rate of opioid-exposed infants from 50% to 30%, decrease the number of infants who require pharmacotherapy by 25%, and reduce average length of pharmacologic treatment from 14 to 10 days.

METHODS

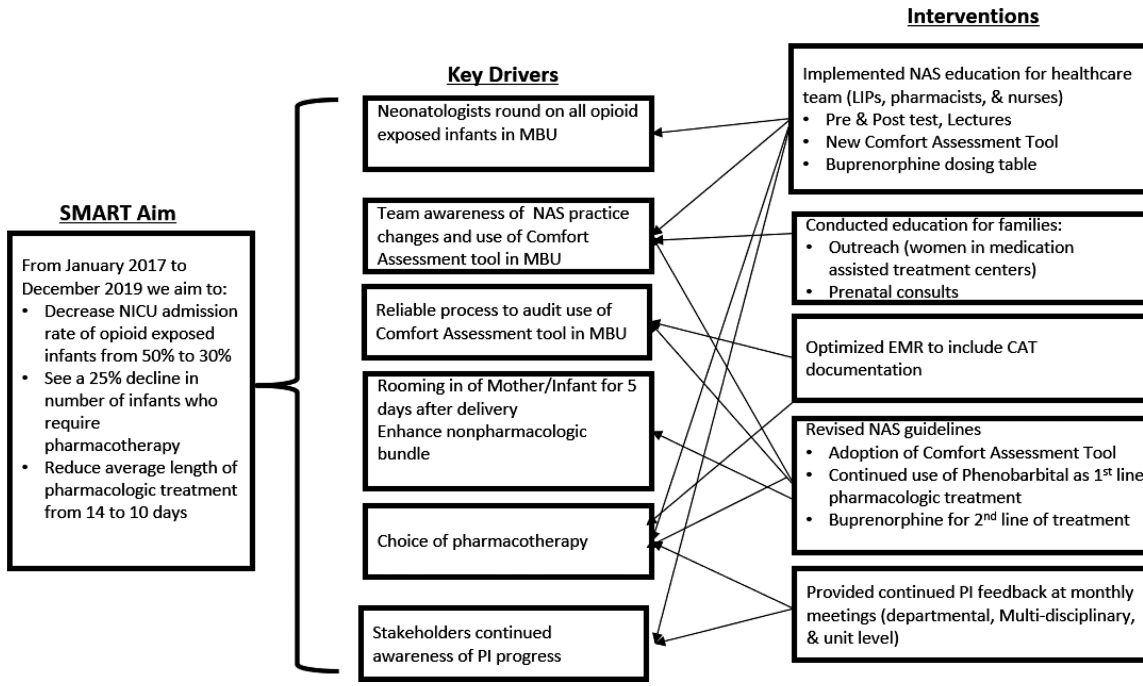
This project occurred in a children's hospital within an adult hospital where approximately 3500 live births occur annually. The level 3 NICU has 43 single patient rooms (25 NICU and 18 Special Care Nursery [SCN] beds) staffed by neonatologists and neonatal nurse practitioners 24 hours a day, with an average of 500 admissions per year. In February 2016, the mother–baby and neonatology teams collaborated on the care of opioid-exposed infants. In an effort to reduce clinical variation, the neonatologists assumed care of nearly all opioid-exposed infants in the MBU. Akron Children's Hospital Institutional Review Board approved this QI project.

From January 2017 through December 2019, data were collected on all opioid-exposed infants 35 weeks' gestation or more. A key driver diagram was completed, baseline data were collected, and interventions were implemented (Figure 1). The CAT using the ESC model was introduced in the NICU in October 2017 and in the MBU in December 2017. These assessments were initially recorded on the paper chart, and after a 6-month trial period, the electronic medical record (EMR) was optimized to include the CAT. Documentation of the Finnegan score above the CAT in the EMR provided an opportunity to compare the 2 models.

Interventions

The multidisciplinary team included physicians, a pediatric pharmacist, a nurse educator, a clinical nurse practice coordinator, neonatal nurse practitioners, and parents. A number of mothers with opioid use disorder (OUD) were participants in the Maternal Opiate Medical Supports Plus (MOMS+) program, which is funded by the Ohio Mental Health and Addiction Services (OHMAS) and by the Substance Abuse and Mental Health Services Administration (SAMHSA). This program, introduced in January 2018, combines medication-assisted treatment (MAT) with counseling, community resources, housing, and transportation for expectant mothers. A member of our QI team makes monthly visits to the MOMS+ group meetings to discuss issues relating to pregnancy and birth of opioid-exposed infants. Discussions also include the new CAT model of care used in the MBU, the nonpharmacologic bundle, and the change from morphine to buprenorphine therapy when an opioid is required for the infant with NOWS.

FIGURE 1



Key driver diagram. NICU indicates neonatal intensive care unit; MBU, Mother–Baby Unit; PI, performance improvement; LIP, Licensed Independent Practitioner; EMR, electronic medical record; CAT, Comfort Assessment Tool; NAS, neonatal abstinence syndrome.

We utilized QI methodology for this project, which incorporated PDSA cycles. Support of the intact maternal–infant dyad was studied in PDSA cycle 1, by facilitating 5 days of rooming-in while infants were observed in the MBU. Mothers received a 2- to 3-day courtesy stay after discharge from the MBU. An enhanced nonpharmacologic bundle of care including kangaroo care, quiet environment, soothing techniques (rocking, white noise machine, music, cuddling, pacifier, swaddling) was developed. A greater emphasis on kangaroo care and breastfeeding was encouraged. The CAT was introduced during PDSA cycle 2. This new tool, based on the ESC model of care, was first introduced to the staff via a PowerPoint presentation and lectures by the neonatologists to the multidisciplinary team, nursing staff on the MBU and the NICU, ancillary staff, pediatric staff educators, and parents. Small group discussions and pre- and posttest surveys served to ensure understanding of the ESC process and correct use of the CAT. NOWS guidelines were revised to reflect the new approach to care and evaluation of the opioid-exposed infant. The CAT was utilized in conjunction with the FNASS in order to compare the results. Two consecutive "No" assessments on the CAT or one assessment of all "No" warranted NICU admission and possible need for pharmacotherapy. PDSA cycle 3 began in November 2018, with the change from morphine to buprenorphine in those infants who required opioid therapy in the NICU.

All the NICU and SCN beds are private rooms with beds for the mother. The nonpharmacologic bundle was therefore easily continued upon admission to the NICU or SCN. In some cases, the infants did better than on the MBU because they did not experience the noise and bright lights of the Newborn Nursery. Mother and any family members who stayed with the infant were encouraged to continue the soothing techniques, kangaroo care, and consoling methods they were taught on the MBU. The nursing staff in the NICU were trained in these nonpharmacologic methods of calming a newborn with opioid exposure. Specially trained volunteers, known as cuddlers, were utilized when mother or her identified caregivers were not available.

The CAT was the primary means of evaluation of the opioid-exposed infant in the NICU. If indicated, phenobarbital was started per protocol. To avoid the high percentage of alcohol contained in the phenobarbital suspension, a loading dose of 15 mg/kg was administered via a tablet crushed in a small amount of water or formula. The infant received twice-daily maintenance oral phenobarbital at 4 mg/kg/d. If symptoms were not effectively controlled in 24 to 48 hours, oral morphine was added at a dose of 0.05 mg/kg/dose every 3 hours.

Sublingual buprenorphine replaced morphine in November 2018 as the first-line opioid treatment. The dose was approximately 5.3 μg/kg/dose given

TABLE 1. Buprenorphine (0.075 mg/mL) Dosing Table

Weight, kg	Starting Dose	Dose Increase 25%
1.5-1.99	9.3 μg (0.12 mL) q8h	12 μg q8h
2-2.49	12 μg (0.16 mL) q8h	15 μg q8h
2.5-2.99	15 μg (0.2 mL) q8h	19 μg q8h
3-3.49	18 μg (0.24 mL) q8h	22 μg q8h
3.5-3.99	20 μg (0.27 mL) q8h	25 μg q8h
4-4.99	23 μg (0.3 mL) q8h	29 μg q8h

Abbreviation: q8h, every 8 hours.

every 8 hours. The sublingual buprenorphine was compounded into a 0.075 mg/mL solution using the buprenorphine injectable, 95% ethanol alcohol, and simple syrup.[20,21] A detailed dosing and weaning chart was developed and implemented to decrease variability and provide standard dose volumes (Tables 1 and 2). Weaning began after 48 hours of consistent "NO's" on the CAT and continued daily. Need for increased dosing was evaluated daily on interdisciplinary rounds. Criteria included 2 or 3 consecutive "No's" on the CAT or 3 "No's" at one assessment. The physician evaluated the infant and determined whether a dose increase was warranted. The nursing and medical staff received education on buprenorphine administration, and the unit policy was revised to include the transition from morphine to buprenorphine therapy.

Measures

Data were collected monthly from January 2017 through December 2019 on all opioid-exposed infants 35 weeks' gestation or more through manual chart audits and validated through EMR coding searches. The diagnosis codes included P04.49, P96.1, and P04.89. Opioid exposure was confirmed through maternal history, maternal and infant urine toxicology, and umbilical cord toxicology sampling. We excluded one infant who was transferred from an outside hospital at 2 weeks of age.

Annotated process run charts were utilized to analyze improvement over time (Figures 2-4).[22] Outcome measures included percentage of opioid-exposed infants transferred to the NICU from the MBU, number of infants requiring pharmacotherapy, length of opioid treatment, and length of phenobarbital treatment. Length of pharmacotherapy was calculated from the day treatment began until the last day of treatment. Balancing measures included need for increased doses, reinstitution of treatment, and readmission for NOWS symptoms.

RESULTS

A total of 191 opioid-exposed infants from the MBU were included in this project. The neonatology team rounded on 54 infants during the baseline period from January through November 2017. Demographic characteristics are listed (Table 3). Of those 54 infants, 27 (50%) were admitted from the MBU to the NICU for NOWS and 17 (31%) required pharmacotherapy. During the post-CAT implementation period, December 2017 through December 2019, 44 of 137 (31%) infants were admitted to the NICU, with 32 (24%) requiring pharmacotherapy (Figure 2). No infants were admitted in December 2019.

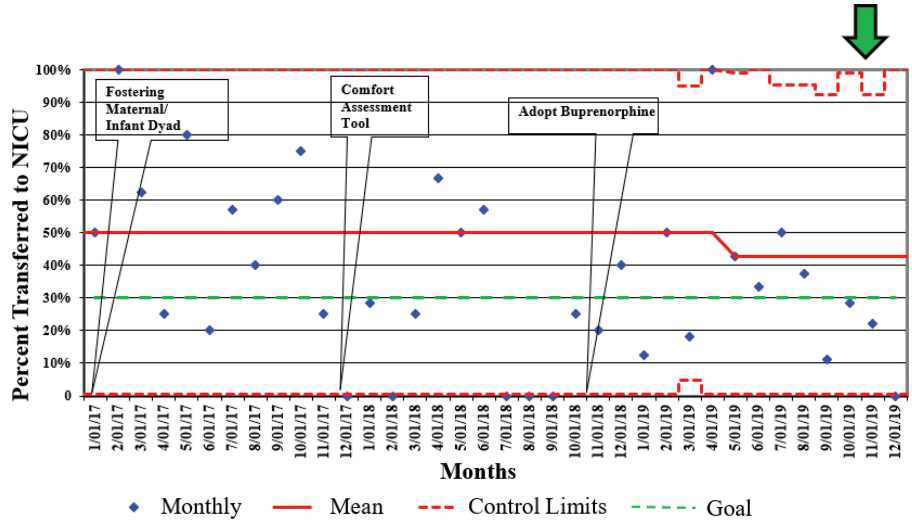
Confirmed opioid-exposed infants who required pharmacologic treatment in the NICU were given phenobarbital first and received only an opioid as

TABLE 2. Buprenorphine Weaning[a]

Weight, kg	Starting Dose q8h	First Wean From Starting Dose	Next Wean	Next Wean	Next Wean	Next Wean	Next Wean	Next Wean	Next Wean	Next Wean
1.5-1.99	9.3 μg	8 μg q8h	7 μg q8h	6 μg q8h	6 μg q12h or off					
2-2.49	12 μg	10 μg q8h	8 μg q8h	7 μg q8h	6 μg q8h	6 μg q12h or off				
2.5-2.99	15 μg	13 μg q8h	12 μg q8h	10 μg q8h	8 μg q8h	6 μg q8h	6 μg q12h or off			
3-3.49	18 μg	16 μg q8h	14 μg q8h	12 μg q8h	10 μg q8h	8 μg q8h	6 μg q8h	6 μg q12h or off		
3.5-3.99	20 μg	18 μg q8h	16 μg q8h	14 μg q8h	12 μg q8h	10 μg q8h	8 μg q8h	6 μg q8h	6 μg q12h or off	
4-4.49	23 μg	20 μg q8h	18 μg q8h	16 μg q8h	14 μg q8h	12 μg q8h	10 μg q8h	8 μg q8h	6 μg q8h	6 μg q12h or off

Abbreviations: q8h, every 8 hours; q12h, every 12 hours.
[a]*All doses are shown in total dose.*

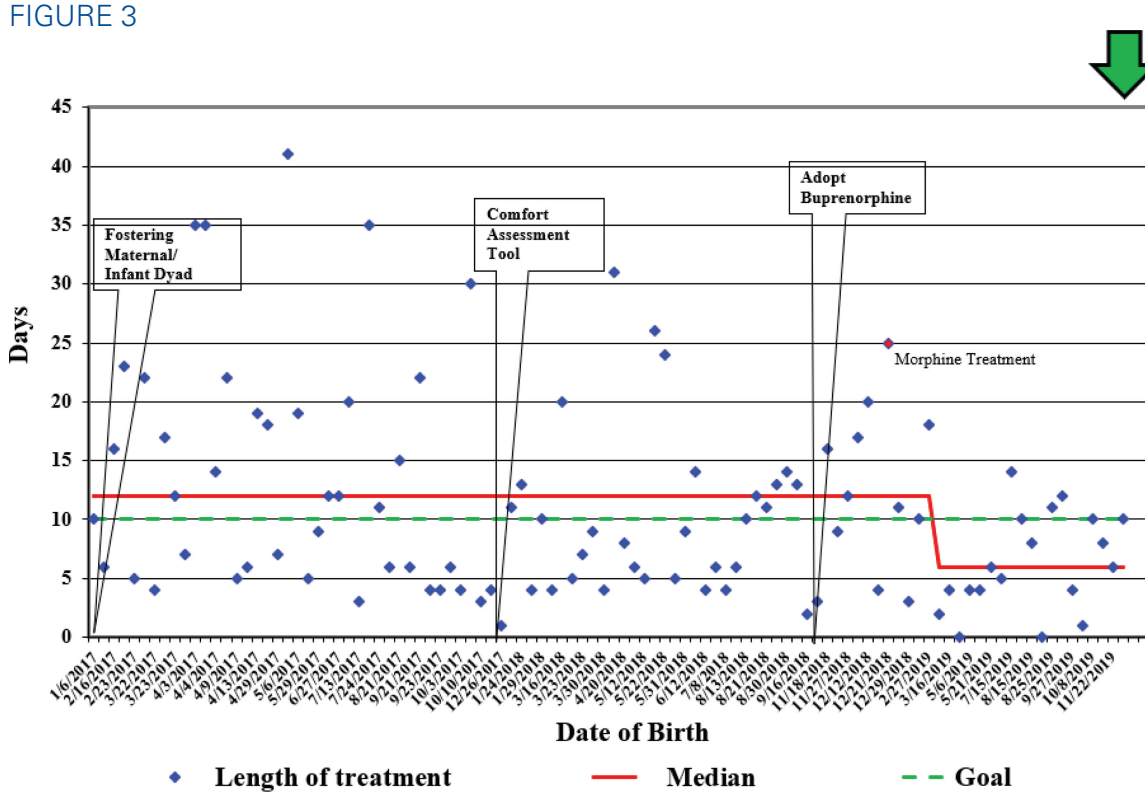
FIGURE 2



Percentage of opioid-exposed infants transferred to the NICU. NICU indicates neonatal intensive care unit.

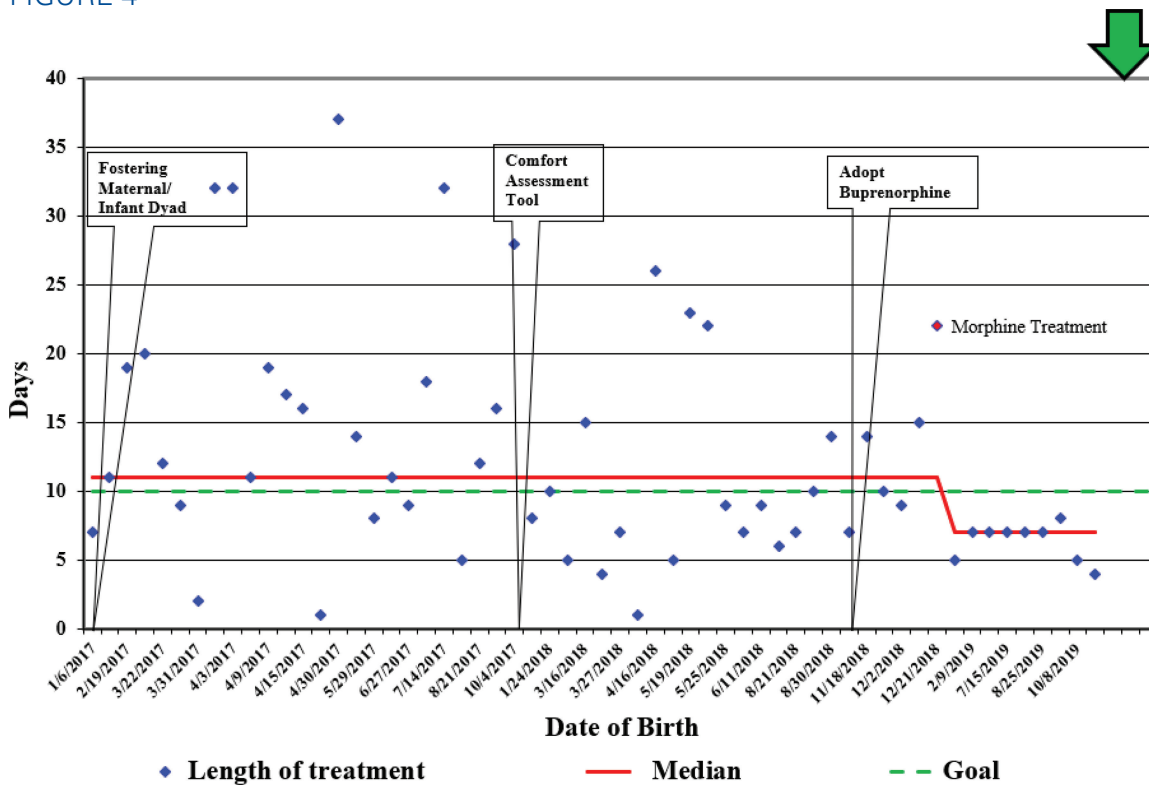
adjunct therapy. During the 11-month baseline period, there were 27 infants admitted to the NICU for evaluation and possible pharmacologic treatment. Seventeen of the 27 infants received medication. Five of the 27 required only phenobarbital (18%). During the 2-year post-CAT implementation period, there were 44 infants admitted for NOWS. Thirty-two infants required medication and 19 (59%) of those infants received only phenobarbital (Figure 3). The last infant to receive adjunctive opioid therapy was admitted in October 2019. The remaining infants admitted for NOWS received only phenobarbital or did not require medication.

FIGURE 3



Length of phenobarbital pharmacotherapy.

FIGURE 4



Length of opioid treatment.

At the start of this project, the average length of pharmacotherapy was 14 days. After implementation of the CAT, the average length of treatment fell to 10 days. The change from morphine to buprenorphine further reduced length of treatment to 6.5 days (Figure 4).

DISCUSSION

Implementation of a modified nonpharmacologic bundle, which included the ESC model, successfully reduced admission to the NICU for NOWS. This change in evaluation of the opioid-exposed infant also reduced the percentage of infants who required pharmacologic treatment. An increased number of infants with NOWS were only treated with phenobarbital and subsequently had an average LOS of 5 days. The transition to buprenorphine from morphine for those infants who required an opioid further reduced our length of treatment and LOS.

Several interventions were important to our success and indicate the major strength of this QI initiative. The focus on keeping the mother–infant dyad

TABLE 3. Demographics of Opioid-Exposed Infants Admitted From the Mother–Baby Unit for Neonatal Opioid Withdrawal Syndrome

	Baseline Jan-Nov 2017	Post-CAT Implementation Dec 2017-Dec 2019	*P*
Total N	27	44	
Race, n (%)			<.1
White	25 (93)	35 (81)	
African American	2 (7)	8 (19)	
Males, n (%)	12 (44)	22 (53)	<.3
Birth weight, mean ± SD, kg	2.92 ± 0.4	2.96 ± 0.4	<.1
Maternal polypharmacy, n (%)	16 (59)	22 (51)	<.5

Abbreviation: CAT, Comfort Assessment Tool.

together during the postpartum stay was crucial for provision of a calm, soothing environment and facilitation of breastfeeding. Use of the CAT emphasized the most clinically significant symptoms, notably the ability to eat, sleep for an hour, and be consoled within 10 minutes. After extensive education and discussion, this tool is now readily accepted by the MBU and NICU staff.

Participation in the MOMS+ program increased steadily and contributed to the successful implementation of the nonpharmacologic bundle in the MBU. Mothers enrolled in the MOMS+ group were more knowledgeable about NOWS and the various soothing methods available to them. They were aware of the new model of assessment (CAT) and expressed more comfort with the care of their infants while observing for signs of NOWS. In our observation, mothers have expressed dissatisfaction with the Finnegan scoring system. Emphasis on the CAT model of care increased mothers' sense of control and feelings of empowerment during their stay in the MBU.

Although some women still receive methadone maintenance, most mothers in our demographic area are now prescribed buprenorphine for their MAT. From 2012 to 2019, methadone treatment of pregnant women with OUD in our population decreased from 40% to 26% and buprenorphine therapy rose from 27% to 58%. Infants exposed in utero to buprenorphine have shorter treatment times than those exposed to methadone.[21] This change in maternal medication likely has a positive effect on the maternal–infant dyad by decreasing need for pharmacologic treatment in their infants.

Discussion about the adoption of buprenorphine treatment in the NICU was met with enthusiasm among the mothers in the MOMS+ group due to their own experience with the medication. We have noted maternal comfort with either phenobarbital or buprenorphine treatment compared with morphine. Feedback from postpartum mothers on the MBU and in the MOMS+ group has indicated a preference for phenobarbital therapy alone when possible. From 2008 to the present, more than a third of the infants in our patient population with confirmed NOWS/NAS have required only a 3- to 5-day course of phenobarbital after admission to the NICU. This has resulted in an average LOS of 6.5 days. Because of sustained success with this approach, our team elected to continue phenobarbital as the first-line medication when indicated for NOWS.

One challenge was obtaining birth hospital administration buy-in for mothers to stay 5 days in a very busy postpartum unit. The administration was supportive of a "courtesy stay" for mothers as long as the census allowed. Additional challenges included need for extensive multidepartment education, development of the CAT in the EMR, and the requirement to continue documentation of FNASS scores for insurance billing. Following some initial resistance, nurses in the MBU and the NICU reported ease of use of the CAT versus the FNASS.

Sublingual buprenorphine was a new medication for the nursing staff. Therefore, a poster presentation was developed to review indications and dosing for infants. During this QI process, the ENFit oral syringe system was adopted, which required additional education to ensure correct administration of buprenorphine. Once education was complete, the ease of dispensing and administering buprenorphine 3 times a day versus every 3 hours of oral morphine was celebrated by the pharmacy as well as the nursing staff.

This QI project had some limitations. The ESC tool (CAT model of care in our unit) is not yet validated. We chose to implement this tool as a QI trial of care. This project did not control for exposure to substances other than opioids (eg, marijuana, amphetamine, cocaine, selective serotonin receptor inhibitor). More than half of the mothers in our patient population have a history of polypharmacy. We did not want to limit our interventions to those who used only opioids, thereby greatly diminishing the number of women who might benefit from the changes in approach.

Next steps for our QI project include at least 3 possibilities. First, examine the use of buprenorphine alone. A revised dosing and weaning schedule for buprenorphine will be developed and evaluated. Second, expand community resources for the MOMS+ program to enroll more women with OUD. This outreach would expose more women who may benefit from the extra support and education provided by the program. Unfortunately, the COVID-19 pandemic has necessitated a temporary halt to the monthly group meetings with the MOMS+ group. Alternative arrangements for virtual meetings are being explored. Third, increase breastfeeding emphasis and support for mothers with OUD on the MBU. This effort requires extra support from the providers as well as nursing management. It is imperative that all members of the healthcare team appreciate the immense benefits breastfeeding affords to infants who were exposed to opioids in utero.

The successful implementation of the ESC model helped maintain an intact mother–infant dyad, reduced admissions to the NICU, and lessened the need for pharmacotherapy. Phenobarbital monotherapy has been successful in treating infants who need minimal support. The change to buprenorphine further reduced average length of treatment of those who required an opioid.

Summary of Recommendations	
What we know:	• The incidence of NOWS has increased over the last decade. • The ESC method has improved the treatment of NOWS. • The CAT model of care has shown to be a promising tool to guide NOWS treatment. • Buprenorphine has decreased opioid length of treatment in our population.
What needs to be studied:	• The ESC model is effective in decreasing LOS and need for medication treatment. • Adjunctive use of buprenorphine may further decrease LOS.
What can we do today that would guide caregivers in the practice setting considering use of this evidence for guiding practices	• The ESC approach is an effective treatment of NOWS that limits pharmacologic treatment and may reduce LOS.

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