JPPT | Single-System Multicenter Retrospective Study

Evaluating the Impact of Eat, Sleep, Console in Neonatal Abstinence Syndrome Treatment for Infants Exposed to Substance Use *In Utero*

Shannon V. McGrath, PharmD, MSPH; Allie Rivera, PharmD, MHSA; Christopher Kennie-Richardson, PharmD; David Ehrmann, MD; Julie Cline, PharmD; Kaye Gable, MD; and Victoria Forrest, PharmD

OBJECTIVE An increase in maternal use of licit or illicit substances, alcohol, and tobacco has resulted in an increased incidence of neonatal abstinence syndrome (NAS). In recent years, NAS management has shifted to initiating an Eat, Sleep, Console (ESC) approach prior to pharmacologic treatment. The objective of this study was to evaluate the impact of ESC in combination with pharmacologic treatment in the management of NAS for infants exposed to substance use *in utero*.

METHODS This single system, multisite, retrospective cohort study evaluated infants with known exposure to substance or polysubstance use *in utero* or those who had signs and symptoms of withdrawal with a positive toxicology screen. The primary outcome of rate of pharmacologic therapy initiated was evaluated pre and post implementation of ESC. Secondary outcomes included hospital length of stay, day of life that pharmacologic therapy was initiated, and an evaluation of the ESC guideline. A subgroup analysis with similar outcomes was also performed for patients with maternal polysubstance use.

RESULTS A total of 2843 patients were screened, and 50 patients were randomly selected for inclusion in both pre- and post-groups. The rate of pharmacologic therapy initiated post implementation of ESC decreased from 58% to 30% ($p < 0.01$). In the post-group, there was a decrease in the number of patients requiring scheduled morphine (33%, $p < 0.01$) and duration of pharmacologic therapy (14.6 days vs 6.47 days, $p < 0.01$).

CONCLUSIONS Implementing an ESC guideline decreased the length of stay and rate of pharmacologic intervention needed for infants with NAS at our institution.

ABBREVIATIONS CDS, cord drug screen; ESC, Eat, Sleep, Console; FNASS, Finnegan Neonatal Abstinence Scoring System; MDS, meconium drug screen; NAS, neonatal abstinence syndrome; NICU, neonatal intensive care unit; NOWS, neonatal opioid withdrawal syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; THC, cannabis; UDS, urine drug screen

KEYWORDS infant; neonatal abstinence syndrome; pregnancy

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Introduction

A recent increase in maternal use of licit or illicit substances, alcohol, and tobacco has resulted in an increased incidence of neonatal abstinence syndrome (NAS).[1] NAS occurs owing to the rapid discontinuation of substances the fetus was exposed to during pregnancy, which may cause disturbances in neurologic, autonomic, gastrointestinal, and musculoskeletal system function.[1,2] The term *neonatal abstinence syndrome* has often been used interchangeably with a more recent classification of withdrawal—neonatal opioid withdrawal syndrome (NOWS). A relevant distinction, however, is that NAS refers to neonatal polysubstance exposure, whereas NOWS is used when exposure is limited to opioids alone.[3] The onset, duration, and severity of NAS is affected by the substance type, duration of exposure, total accumulation during exposure, and the number of substances the neonate encountered during pregnancy.[1] Recent studies have also identified a relationship between non-opioid medication use, including psychotropic medications, and decreased head circumference and increased risk and severity of NAS symptoms when used in addition to opioids.[4,5] Infants who are born at term have delayed drug metabolism, which places those with polysubstance exposure at greater risk for severe and prolonged withdrawal.[1]

Management of NAS includes both pharmacologic and non-pharmacologic care. Historically, pharmacologic

intervention has been required for upwards of 90% of neonates presenting with NAS.[1] Recently, a shift in the management of NAS has occurred leading to a significant impact on the average length of stay, medication use, breastfeeding, and hospitalization costs.[6–12] The Eat, Sleep, Console (ESC) approach has been adopted as a substitute to the Finnegan Neonatal Abstinence Scoring System (FNASS)–driven management by several institutions and has resulted in significant improvements in the quality of care of infants with NAS.[6–12] ESC focuses on feeding, sleeping, and consoling along with prenatal counseling and parental support for a nonintrusive approach in assessing infants with NAS.[8] Patients are assessed every 2 to 6 hours and non-pharmacologic interventions are maximized prior to initiating pharmacologic treatment with as-needed or scheduled morphine.[8]

Beginning June 1, 2019, the NAS Committee at Cone Health Women's and Children's Center and Alamance Regional Medical Center implemented an update to the inpatient guidelines for patients with or being observed for NAS. This committee is composed of nurses, providers, pharmacists, and social workers who care for neonates at Cone Health. Owing to prolonged length of stays for patients managed with FNASS, family-centered care, and pharmacologic therapy, along with the improved outcomes found with the ESC approach, our practice was updated to adopt an ESC guideline to minimize drug therapy. Prior to the implementation of ESC, patients requiring pharmacologic treatment for NAS were transferred to the neonatal intensive care unit (NICU) for symptom management. This guideline implemented a standardized approach using the ESC methodology in all hospital units for the assessment of infants at risk owing to *in utero* exposure and those with withdrawal symptoms who may also require pharmacologic treatment. Infants can now receive care on mother-baby and pediatric units. Infants with known exposure to substance(s) *in utero* or those who have signs and symptoms of withdrawal with positive toxicology screens are observed on the mother-baby units for up to 5 days. During this time, mothers and caregivers are allowed to continue rooming-in, even after the mother is discharged, so they can actively participate in the infant's ongoing care and management, using the ESC approach. Infants with known or suspected substance use exposure may be admitted to an intensive care or pediatric unit if the infant has NAS symptoms requiring further intervention or has other acute medical needs. Further details regarding Cone Health's ESC approach are outlined in Supplemental Materials (Appendix A).

To further improve the care for infants with NAS at our institution, the aim of this study was to evaluate the rate of pharmacologic therapy initiated pre and post implementation of ESC. We also assessed hospital length of stay and the average day of life that pharmacologic therapy was initiated, and completed an evaluation of our ESC guideline and the management of polysubstance-exposed patients.

Materials and Methods

Study Design. This single system, multisite, retrospective cohort evaluation was conducted in neonatal patients treated for NAS during an admission at Cone Health Women's and Children's Center and Alamance Regional Medical Center. Moses H. Cone Hospital is a 628-bed, level II hospital that provides pediatric emergency department services and offers an 18-bed pediatric unit. Cone Health Women's and Children's Center was recently added to Moses Cone Hospital; averages greater than 6000 births a year; and offers a 45-bed, level III NICU and 50 mother-baby beds. Alamance Regional Medical Center is a 238-bed, level II hospital that offers 19 mother-baby beds and a 12-bed level II/III special care nursery. Infants were included if they had a known exposure to substance or polysubstance use *in utero* or had signs and symptoms of withdrawal and had a positive fetal or maternal urine drug screen (UDS), meconium drug screen (MDS), or cord drug screen (CDS) between January 1, 2018, and April 30, 2019 (pre-group) or July 1, 2019, and December 31, 2020 (post-group). Patients were considered substance exposed if they were exposed to opioids, benzodiazepines, amphetamines, cocaine, gabapentin, or barbiturates *in utero*. Polysubstance-exposed patients were infants exposed to more than 1 substance *in utero*. Cannabis (THC) was not included as a positive substance exposure because it is not known to result in withdrawal symptoms, be a contraindication to breastfeeding, or alter outcomes in the perinatal period. Infants received care in the NICU, pediatric unit, or mother-baby units depending on need for maintenance pharmacologic intervention, along with severity and timing of symptom onset. Infants were excluded if they had a gestational age <35 weeks, required surgery during their hospital stay, or had an acute exposure to opioids for an indication other than NAS during their hospital stay. Patients were also excluded if maternal care required an acute exposure to opioids prior to delivery (Table 1). Potential patients in both groups were identified retrospectively using a clinical surveillance tool that created a comprehensive list of those with an ICD-10 diagnosis for neonatal withdrawal symptoms from maternal use of drugs of addiction and newborns affected by maternal use of drugs of addiction, patients initiated on the institutional NAS order set, or patients with a positive UDS or CDS.[13] Urine or cord blood drug screening criteria included mothers who mentioned substance use during pregnancy; methadone, suboxone, or buprenorphine treatment during pregnancy; late prenatal care (during the third trimester); or mothers with fewer than 3 prenatal visits. Data collection was completed by one of the coinvestigators for continuity. All patients

Table 1. Baseline Patient Characteristics

	Pre-Group (n = 50)	Post-Group (n = 50)	p value
Gestational age, mean ± SD, wk Unknown age, n (%)	38 wk 6 days ± 1wk 5 days 1 (2)	38 wk 6 days ± 1 wk 2 days 1 (2)	0.62
Sex, Female, n (%)	19 (38)	23 (46)	0.66
Birth weight, mean ± SD, kg	3.04 ± 0.41	3.02 ± 0.47	0.82
Apgar score, mean ± SD, n	8.2 ± 1	7.94 ± 1.11	0.22
Maximum percent weight loss, mean ± SD, %	6.9 ± 3	7.96 ± 3.85	0.14
Head circumference, mean ± SD, cm	33 ±1.5	33 ± 1.3	1.00
No documented parent contact, n (%)	4 (8)	9 (18)	0.137
Hospital unit, n (%) Women's and Children's Center NICU Mother-baby unit Pediatrics unit Alamance Regional Medical Center Special care nursery Mother-baby unit	 24 (48) 13 (26) 4 (8) 4 (8) 5 (10)	 8 (16) 23 (46) 8 (26) 5 (10) 6 (12)	 <0.01 0.04 0.21 0.73 0.75
Infant urine drug screen obtained, n (%) Positive UDS Polysubstance found on UDS	43 (86) 24 (59) 7 (16)	41 (82) 18 (44) 1 (2)	
Cord drug screen obtained, n (%) Positive CDS Polysubstance found on CDS	49 (98) 49 (100) 16 (33)	49 (98) 49 (100) 21 (43)	
Meconium drug screen obtained, n (%) Positive MDS Polysubstance found on MDS	1 (2) 1 (100) 0 (0)	1 (2) 1 (100) 1 (100)	

CDS, cord drug screen; MDS, meconium drug screen; NICU, neonatal intensive care unit; UDS, urine drug screen

identified for the study underwent electronic medical record review to ensure they met inclusion criteria. Of the patients who met inclusion criteria, 100 patients (50 in each arm) were randomly selected using the online research randomizer by Geoffrey C. Urbaniak and Scott Plous for inclusion and analysis.[14]

Per the guideline, infants are assessed and managed with the ESC approach beginning at 24 hours of age. Every 3 to 5 hours, the following parameters are assessed: the infant is able to eat at least 1 ounce per feed or breastfeeds well; sleeps at least 1 hour between feedings; and consoles within 10 minutes with comfort measures. If 1 or more of these parameters are not met, the pediatrician or neonatologist will be contacted for an assessment to determine if any further action is needed. If non-pharmacologic interventions have already been maximized, an as-needed dose of morphine will be considered and the infant will be reassessed in 4 hours. For infants who are unable to meet ESC criteria after 2 as-needed doses of morphine, a scheduled morphine dose will be ordered and the escalation or weaning of doses will be determined by the interdisciplinary team. Morphine doses are increased by 10% to 20% and weaned by 10% of the maximum dose once the patient is meeting ESC criteria for 12 to 24 hours. Patients unable to meet ESC criteria while receiving morphine may require adjunctive therapy with oral clonidine and phenobarbital. Further details regarding Cone Health's ESC approach are outlined in Supplemental Materials (Appendix A).

The primary endpoint was the rate of pharmacologic therapy initiated post implementation of the ESC guideline. Secondary endpoints included hospital length of stay; the average day of life that pharmacologic therapy was initiated; and an evaluation of the ESC guideline and management of polysubstance-exposed patients. This was assessed by an evaluation of the average number of as-needed morphine doses administered prior to initiating maintenance medication, the average initial starting dose for pharmacologic therapy, the average maximum dose for pharmacologic therapy, the average total doses of pharmacologic therapy, the average dose at which pharmacologic therapy was discontinued, the rate of pharmacologic doses

weaned outside of goal, the rate of neonates requiring adjunct therapy, and the rate of treatment failures after de-escalation of therapy that required re-escalation of therapy.

Statistical Analysis. Standard descriptive statistics were used to evaluate baseline characteristics in both groups. Chi-square tests were used to compare nonparametric, categorical variables including the primary endpoint, the rate of pharmacologic therapy initiated post implementation of the ESC guideline, and several secondary endpoints. Student *t* tests were used to compare parametric continuous variables. Multiple logistic regression models were conducted to evaluate the differences between age groups, polysubstance use, and patients receiving care at Alamance Regional Medical Center. For all calculations, statistical significance was defined as a p value of <0.05. Statistical analysis was completed in Microsoft Excel 2008.

Based on previous literature available and the current patient population at Cone Health, it was anticipated that a total of 70 patients (35 in the pre-group and 35 in the post-group) were needed to see a 66% reduction in the need for pharmacologic treatment outside of ESC to reach 80% power with an alpha of 0.05.

Results

A total of 2843 patients (1352 pre-group, 1491 post-group) were screened (see Supplemental Figure). Of these patients, 379 (162 pre-group, 217 post-group) met inclusion criteria and 100 patients (50 in each arm) were randomly selected for inclusion and analysis. Infant and maternal baseline characteristics are reported in Tables 1 and 2. Baseline characteristics were similar in both groups. The infants' growth and maturity characteristics are described in Table 1. No statistically significant differences were noted between the amount of documented parent contact time and care times between groups; however, fewer patients in the pre-group had limited or no documented parent contact time (Table 1). Mothers receiving good, late, or no prenatal care were dispersed evenly between both groups; however, a correlation in the number of patients receiving late or no prenatal care can be seen in the polysubstance-exposed infant group (Table 2). Most mothers (~80%) in both groups had documented tobacco use during pregnancy (Table 2). More mothers were prescribed antipsychotic medications in the post-group (Table 2). The only significant difference between infant groups was the decreased number of NICU admissions and the increased number of patients able to be managed in the mother-baby unit in the post-group after the implementation of ESC (p < 0.01). Most infants included had a cord blood drug screen positive for buprenorphine, methadone, methamphetamine, or cocaine. In the pre-group, methadone and cocaine were most commonly observed in comparison to buprenorphine and cocaine in the post-group. In the post-group, a rise in the number of patients with a positive screen for amphetamines and methamphetamines was also observed. Seventeen infants in the pre-group (34%) and 22 patients in the post-group (44%) had polysubstance exposure identified on their UDS, MDS, or CDS (Table 1).

Table 2. Baseline Maternal Characteristics

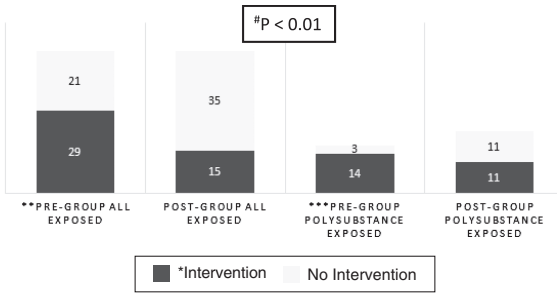
	Pre-Group (n = 50)	Post-Group (n = 50)
Age, mean ± SD, yr	28 ± 4.7	30 ± 5
Delivery, n (%)		
Vaginal	38 (76)	35 (70)
Cesarean	12 (24)	15 (30)
Prenatal care, n (%)		
Good (throughout pregnancy)	24 (48)	22 (44)
Late (care after the third trimester)	17 (34)	20 (40)
None	9 (18)	8 (16)
Cigarette smoker, n (%)	39 (78)	43 (86)
Alcohol, any time during pregnancy, n (%)	11 (22)	12 (24)
Tetrahydrocannabinol, n (%)	20 (40)	23 (46)
Psychiatric medication prescription, n (%)	1 (2)	4 (8)
Opiate prescription, n (%)	38 (76)	34 (68)
Maternal urine drug screen obtained, n (%)	37 (74)	33 (66)
Positive UDS	27 (73)	19 (58)
Polysubstance found on UDS	8 (22)	5 (15)

UDS, urine drug screen

The rate of pharmacologic therapy initiated post implementation of the ESC guideline decreased from 58% to 30% (p < 0.01) (Figure 1). Similar trends were noted when evaluating infants who were polysubstance exposed, with a decrease in drug therapy from 82% to 50% (Figure 1). In the post-group, a significant decrease was noted in the amount of scheduled morphine doses (33%) compared with management with as-needed morphine doses alone (67%, p < 0.01) (Figure 2). The duration of pharmacologic therapy decreased from 14.6 days to 6.47 days (p < 0.01) (Table 3). Polysubstance-exposed infants had similar outcomes; however, patients in pre- and post-groups had longer durations of morphine therapy (17.5 vs 6.82 days) in comparison to patients exposed to only 1 substance (14.6 to 6.47 days) (Table 3). Along with the decrease in pharmacologic treatment and durations

of management, the starting and maximum doses of morphine were decreased after the implementation of ESC. No patients required the addition of an adjunct pharmacologic agent for the management of NAS, regardless of substance exposure.

Figure 1. Required pharmacologic intervention.

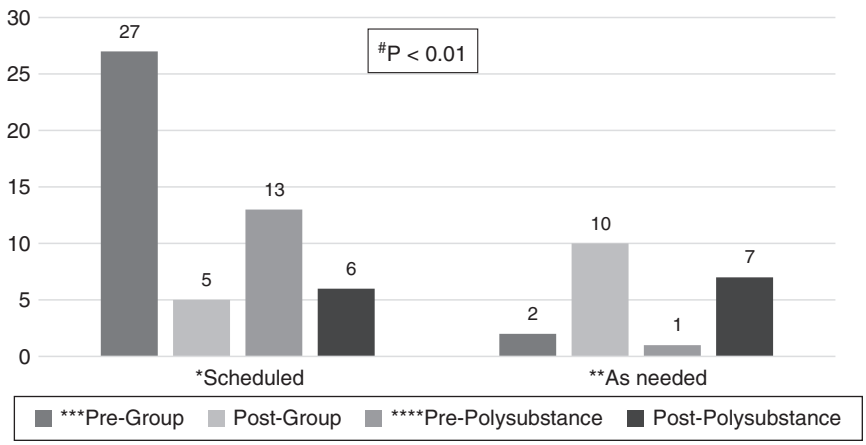


A p value of less than 0.05 was considered to be statistically significant.
* Patients in the intervention group who received pharmacologic treatment.
** "All exposed" included patients with substance and polysubstance exposure to the following medications: opioids including heroin, methadone, buprenorphine, oxycodone, hydrocodone, oxymorphone, tramadol, codeine, and fentanyl; benzodiazepines including midazolam, lorazepam, diazepam, temazepam, clonazepam, oxazepam, and zolpidem; amphetamines; cocaine; gabapentin; and barbiturates including butalbital and phenobarbital.
*** Polysubstance-exposed patients included infants with exposure to 2 or more of the medications listed above.

The day of life that pharmacologic therapy was initiated shifted from 2.3 to 3.5 days between pre- and post-groups. Similar trends were also captured in the polysubstance group (Table 3). The average length of stay for infants with NAS decreased from a baseline of 8 days to 5.5 days in the ESC group (Table 3). Polysubstance-exposed patients had longer durations of hospital stay at baseline (12 days), which also decreased after the implementation of ESC (7.5 days) (Table 3).

Eat, Sleep, Console was initiated within the first 24 hours of life in 90% of patients in the post-group. Most patients who did not receive ESC monitoring were those who had toxicology screening owing to late or limited prenatal care and were incidentally found to have a positive screen. Most patients who required escalation in their NAS management were inconsolable and had poor feeding by mouth, requiring the need for nasogastric feeds. When evaluating guideline adherence, deviations in weaning medications within the appropriate recommended dose and frequency goal range were identified; however, only 1 patient experienced a treatment failure that required the re-escalation of medication therapy after the guideline was implemented. Of note, infants in the post-group received an average of 3 doses of as-needed morphine. Although this exceeded our guideline recommendation of 2 doses before scheduling morphine, many of these doses were separated by several days rather than by 1 to 2 care times. There were no differences in pharmacologic intervention when comparing ESC

Figure 2. Pharmacologic interventions.



A p value of less than 0.05 was considered to be statistically significant.
* Patients in the intervention group who received scheduled pharmacologic treatment.
** Patients in the intervention group who received as-needed pharmacologic treatment.
*** Pre- and post-group patients including those with substance and polysubstance exposure to the following medications: opioids including heroin, methadone, buprenorphine, oxycodone, hydrocodone, oxymorphone, tramadol, codeine, and fentanyl; benzodiazepines including midazolam, lorazepam, diazepam, temazepam, clonazepam, oxazepam, and zolpidem; amphetamines; cocaine; gabapentin; and barbiturates including butalbital and phenobarbital.
**** Pre- and post-group patients with polysubstance exposure (infants with exposure to 2 or more of the medications listed above).

Table 3. Secondary Outcomes

	Pre-Group	Post-Group
Average duration of pharmacologic therapy, days		
All exposed patients	14.6	6.47
Polysubstance-exposed patients	17.5	6.82
Day of life pharmacologic therapy was initiated		
All exposed patients	2.3	3.5
Polysubstance-exposed patients	2.2	3.2
LOS assessment, days		
All exposed patients	8	5.5
Polysubstance-exposed patients	12	7.5

LOS,length of stay

management at Cone Health Women's and Children's Center with that at Alamance Region Medical Center.

Discussion

At our institution, implementation of the ESC approach has dramatically improved our ability to manage most infants with NOWS and NAS without pharmacologic therapy. Rates of NAS have drastically increased from 1.5 to 8.0 per 1000 hospital births in the United States from 2004 to 2014, contributing to a mean length of stay of 15.9 days and a total overall hospitalization cost of $572.7 million nationwide in 2016 alone.[15,16] In 2018, every 1-day increase in length of stay for patients with NAS increased the hospital cost by $1685 and was often compounded by other comorbidities.[17] Previous studies indicate a reduction in scheduled medication use, hospital length of stay, and relevant cost savings with implementation of ESC for patients exposed to 1 or more substances *in utero*.[2,5,7] Along with reductions in mean length of hospital stay and the proportion of infants who received opioid treatment, Young and colleagues[18] reported no differences in safety outcomes for patients following the ESC approach compared with the standard of care. Results of this study confirm there is a significant decrease in the hospital length of stay, duration of treatment, and the number of patients requiring pharmacologic intervention or adjunct therapy after implementing the ESC approach. Similar differences in treatment outcomes were noted between patients with a single substance and polysubstance exposure, indicating that as-needed doses of morphine should remain the standard treatment for management of polysubstance-exposed patients. Trends were also identified in the increased number of mothers who received late or no prenatal care in the post-group, in comparison to more patients having good or late care in the pre-group. In recent years, a standardized verbal screening tool and maternal urine drug screenings have been added into routine prenatal care in the outpatient setting to identify substance use disorders. With increased screening, our team hopes to capture substance exposure earlier in pregnancy to make earlier interventions and decrease the severity of NAS.

The FNASS has been used in the United States to evaluate the signs of neonatal withdrawal and determine future adjustments in treatment.[19] This comprehensive scoring tool assesses 21 items relating to signs of withdrawal to determine if escalation or de-escalation in treatment is required.[19] Non-pharmacologic care remains the mainstay for the initial management of NAS and focuses on minimizing environmental stimuli, avoiding auto-stimulation by careful swaddling, responding early to an infant's signals, adapting infant positioning and comforting techniques, and providing frequent, small volumes of hypercaloric formula or human milk to ensure proper growth.[1,19] Infants with moderate to severe signs of NAS who are unable to be managed with non-pharmacologic interventions alone have been treated with a variety of medications including opioids, phenobarbital, and clonidine.

We initially anticipated a 66% reduction in the rate of pharmacologic treatment needed for the management of infants after the implementation of ESC, based on previously published data. Although we did not find this large of a decrease, we saw a significant reduction in the number of scheduled, starting, and maximum morphine doses used for ESC patients. THC was not included in the definition of substance use exposure; however, no differences in outcomes or need for pharmacologic management was noted in either group for patients who had additional exposures to THC. Owing to the limited number of patients in the pre-group who were exposed to antipsychotics, we could not evaluate the outcomes of these medications on patient outcomes. Recent findings by Morris et al[20] reveal no difference in NOWS outcomes for concurrent exposure of antipsychotics with opioids; however, co-exposure of opioids with stimulants showed a reduction in length of treatment and need for adjunct therapy, which correlate with the findings of our study. Lastly, CDS results revealed that an increased number of patients in the pre-group were exposed to methadone, whereas in the post-group an increased number of patients were exposed to buprenorphine. This was due to the addition of prescribing authority of buprenorphine to obstetric providers in our health care system in the post-group and recent data suggesting decreased severity of neonatal withdrawal with buprenorphine use in pregnancy.[21] Further opportunities to evaluate other medications that may contribute to polysubstance and increased NAS severity are being prospectively evaluated by the NICU team as well as other treatment and management modalities.

Our analysis revealed deviations from the recommended morphine-tapering regimen found in our institution's

ESC guideline in all 4 patients in the post-group who required scheduled morphine. To improve adherence with guideline recommendations, we plan to review our findings with the NICU team and provide updated education to pharmacists, nursing staff, and providers to promote the use of guideline-directed dose tapering. A reassessment of guideline adherence after education will be conducted to evaluate future outcomes.

There are several limitations to our study. The retrospective study design and patient identification may have limited the number of patients included in the study. Limited virtual education and training were provided to nursing, pharmacists, or other health care staff regarding the implementation and use of the guideline. The guideline was also updated several times throughout the study period. At this time, we are unable to confirm whether all staff who have onboarded since the implementation of ESC have received formal training. Both of these limitations could have contributed to variances in guideline-directed therapy and medication management in the post-group.

At this time, we could not evaluate the impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on pregnancy outcomes; however, it did limit the number of volunteers who were available on site for contact time for patients between March 2020 and April 2021. Currently, we have "Rock and Hold" volunteers on-site during weekdays to provide routine non-pharmacologic care and support for patients with NAS. Unfortunately, owing to SARS-CoV-2 these services were not available in our NICU for 1 year, including the post-group in the study period. SARS-CoV-2 may have also affected the number of patients who received late prenatal care in the post-group.

Several mothers received opioids for the acute management of pain prior to delivery. Although these patients were evaluated and excluded on the basis of timing of their medications and the results of drug screening, there is a possibility that a mother may have taken a medication that causes false-positive results on a drug screen that was not accurately captured on the admission medication reconciliation.

Donor milk products and availability varied depending on patient weight and location during the transition between the Women's Hospital and the Women's and Children's Center at Moses Cone Hospital in February 2020. This variability may have positively affected the outcomes of patients in the post-group. Though we were unable to collect information on breastfeeding for all patients owing to inconsistent documentation in the electronic medical record, most patients in both pre- and post-groups received breast or donor milk with supplementation during their hospital stay. Along with breastfeeding limitations, we did not document whether patients had intrauterine growth restriction and we did not individually assess patients for all underlying comorbid conditions outside of our exclusion criteria. At this time, we could not rule out the impact of genetic abnormalities on NAS symptoms and management. Lastly, we did not review patient outcomes post discharge.

Conclusion

Our study showed a 28% reduction in the number of patients requiring pharmacologic management for NAS while using the ESC approach. The implementation of ESC can effectively decrease the hospital length of stay, duration of pharmacologic treatment, and the type of pharmacologic intervention needed for patients exposed to 1 or more substances *in utero*. Infants exposed to polysubstance use *in utero* and whose mothers had late or no prenatal care have an increased hospital length of stay and duration of pharmacologic treatment. Future studies should evaluate the use of maternal assessments during pregnancy on NAS outcomes and further assess the impact of combined opiate and non-opiate polysubstance exposure on the severity of NAS symptoms.

Article Information

Affiliations. Department of Pharmacy (SVM, JC, CK-R, AR, VF), Cone Health Women's and Children's Center, Neonatology (DE, KG), Cone Health Women's and Children's Center, Greensboro, NC; Neonatology (DE), Cone Health Alamance Regional Medical Center, Burlington, NC.

Correspondence. Shannon McGrath, PharmD, MSPH; svbrown0629@email.campbell.edu

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Ethical Approval and Informed Consent. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and have been approved by the appropriate committees at our institution.

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