



Treatment for Neonatal Abstinence Syndrome using Nonpharmacological Interventions

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Abstract

Objective Management of neonatal abstinence syndrome includes nonpharmacological interventions, but their effectiveness may not be verified before implemented. The objective of this study is to evaluate the effectiveness of a type of bassinet in the treatment of infants with neonatal abstinence syndrome.

Study Design This is a retrospective observational cohort study. Study setting involved a 24-bed open-bay Level III neonatal intensive care unit located in a metropolitan academic trauma facility. Participant inclusion criteria involved prenatally opioid-exposed infants ≥ 35 weeks with confirmed maternal opioid urine toxicology, required pharmacological treatment for withdrawal symptoms, and were admitted to the neonatal intensive care unit. Three subsets of study participants were analyzed over three different time periods: Group 1 were infants admitted during 2019 without nonpharmacological intervention, Group 2 who were admitted from September 2021 to February 2022 and received nonpharmacological interventions, and Group 3 included those admitted from February 2022 to March 2023 who received the same interventions as Group 2 but were managed in bassinets being used in other local facilities for neonatal abstinence syndrome.

Results Group 3 had significant increases in length of stay compared with Group 1 ($p = 0.006$) and Group 2 ($p = 0.013$). Group 3 had a significantly greater length of treatment than Group 1 ($p = 0.041$) and a significantly higher total mg/kg morphine exposure than Group 1 ($p = 0.006$).

Conclusion Addition of the bassinet for nonpharmacological management of infants with neonatal abstinence syndrome appeared to prolong length of stay, length of treatment, and increase total mg/kg morphine exposure. As a retrospective nonrandomized study, weakness of low certainty of causality is of concern but findings strongly warrant further research before devices such as the bassinet used in this study are adopted for routine neonatal abstinence syndrome care.

Keywords

- ▶ withdrawal
- ▶ addiction
- ▶ opioids
- ▶ neonate
- ▶ bassinet

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Key Points

- Special bassinets are promoted to enhance sleep and decrease agitation.
- Such bassinets may assist infants undergoing drug withdrawal.
- Study of the bassinet failed to show benefit to this population.

Treatment for infants with neonatal abstinence syndrome (NAS) has historically involved medications such as morphine, clonidine, phenobarbital, and methadone.

These medications can have concerning side effects, interfere with the mother–infant dyad, extend hospitalization with prolonged drug tapering, and subsequently increase costs.^{1–7} To limit the need for these medications, a greater focus is now on nonpharmacological interventions (NPIs) to assist in the management of NAS.^{7–11} As an example of these interventions, Ryan et al¹² found breast feeding, swaddling, rooming in, environmental control, and skin-to-skin contact to be effective in the management of NAS including those infants that required pharmacological therapy.

In 2020, our academic, metropolitan medical center received a 2019 facility state registry summary for NAS. Length of stay (LOS) for infants treated for NAS was 47% (22.6 days) longer than statewide average (12 days) and 74% of the infants admitted for NAS received pharmacological therapy compared with 42% statewide. As a quality improvement (QI) initiative to lessen pharmacological treatment and reduce LOS, we implemented NPIs felt to be feasible for an open-bay neonatal intensive care unit (NICU) with a significant population of homeless mothers, no or limited prenatal care, polysubstance abuse, and noncompliance with substance abuse programs. Polysubstance abuse and noncompliance with substance abuse programs restricted breastfeeding while rooming in was not an option for an open-bay NICU. Thus, environmental control was selected as our focus for nonpharmacological management of NAS with the emphasis to provide quiet, dimly lit areas of care, minimal stimulation, and soothing techniques. During the QI initiative, access to novel bassinets became available and were included as part of our NPI bundle. Bassinets as a means to alter the proximal environment of infants with NAS is not well documented, but there are reports of using various modified bassinet mattresses. Oro and Dixon¹³ found infants with NAS placed on a commercially available nonoscillating waterbed required significantly less pharmacological treatment, had lower withdrawal scores, and earlier consistent weight gain compared with controls. The authors attributed the findings as a favorable behavioral response to proximal tactile and vestibular stimuli input provided by the nonoscillating waterbed upon movement by the infant. Bloch-Salisbury et al,¹⁴ in a randomized-controlled study compared a vibrating crib mattress of continuous 3-hour on–off cycled low stochastic vibrotactile stimulus (SVS) to a standard bassinet mattress for newborns prenatally exposed to opioids. Results indicated daily duration of SVS was associated with a 50% reduction in the need for morphine compared with controls. Subanalysis of caretaker bedside logs found caretaker holding time

reduced the need for morphine administration equivalent to SVS. Authors concluded the greater exposure to tactile stimulation, whether mechanosensory SVS vibration or direct human contact provided by caretakers, resulted in less need for pharmacological treatment of infants with NAS withdrawal symptoms.

In this study commercially available bassinets marketed toward healthy infants in the first 6 months of life to enhance sleep and decrease agitation are reviewed. Their inclusion as an NPI was anticipated to favorably alter the proximal environment of infants with NAS as it was similarly implied by Gellasch et al¹⁵ who reported these bassinets improved quality of patient care, including infants undergoing drug withdrawal. It was hypothesized the bassinet would lessen pharmacological treatment, reduce LOS, and enhance nonpharmacological management of NAS. Concerns, however, after implementing the new bassinets prompted a retrospective review of short-term outcomes compared with other time periods that did not involve use of the bassinet. This study summarizes the data and results of that review.

Materials and Methods

Study Design

A retrospective observational cohort study was performed involving infants ≥ 35 -week gestation admitted to our NICU for pharmacological treatment of NAS. Approval from the institutional review board (IRB) was obtained (IRB # 21.0555) and the medical center's research office. All aspects of the research were performed in accordance with the Declaration of Helsinki. Total number of study participants were determined by the total number of qualifying NAS infants pharmacologically treated within each period and not by determination of power/effect size. Per definition as a retrospective observational study, the research was not registered as a clinical trial.

Three patient subsets were analyzed. Group 1 ($n = 39$) included prenatally opioid-exposed infants admitted to the NICU in 2019 for pharmacological treatment of NAS. This group represents the cohort of patients included in our 2019 facility state registry summary for NAS and prior to our QI initiative for NPI management of NAS. Group 2 ($n = 21$) included prenatally opioid-exposed infants admitted after September 2021 to the NICU for pharmacological treatment of NAS. As part of our original QI efforts, all infants in Group 2 received NPIs for the management of NAS. Group 3 ($n = 20$) included those admitted to the NICU for pharmacological treatment of NAS from February 2022 to the end of using the bassinet in March 2023. Infants in Group 3 not only received the same specific NPIs as Group 2 but also received care in

newly obtained bassinets (SNOO Smart Sleeper, Happiest Baby, Los Angeles, California). Use of the bassinet was discontinued March 2023 after conducting an interim review of length of treatment (LOT) and LOS data for infants using the bassinet.

Homogeneity of the three groups were ensured regarding predetermined metrics (e.g., Finnegan scores and initiation of morphine to treat withdrawal symptoms) prior to assessing outcomes due to small sample size limitations of each group, the strict inclusion criteria regarding participant enrollment in a population affected by polysubstance use, and lack of randomization to these groups. Four separate dependent variables of NAS severity were calculated: average Finnegan crying score, average Finnegan sleeping score, average Finnegan total score (i.e., prior to treatment), and day of life that treatment was initiated for NAS. The Finnegan sleep and crying scores were selected from the total Finnegan score, since they reflected bassinet characteristics to enhance sleep and decrease agitation (crying). A one-way analysis of variance (ANOVA) was conducted for each of these dependent variables compared across the three patient groups and no statistically significant differences were found (–Table 1) suggesting the three patient subset groups over three different time periods were homogeneous as they related to NAS severity.

Inclusion and Exclusion Criteria

Inclusion criteria was based on confirmed opioid maternal urine toxicology of any prenatally opioid-exposed infant \geq 35-week gestation admitted to the NICU in 2019, and from September 2021 to March 2023, for pharmacological treatment of opioid withdrawal symptoms. NAS patients admitted in 2020 were excluded based on extensive coronavirus disease 2019 restrictions during that year. Other exclusions included infants $<$ 35-week gestation, those with neurologic impairment not consistent with NAS withdrawal, evidence of significant congenital malformations, and infants receiving pharmacological treatment for pain or sedation.

Neonatal Abstinence Scoring

Standardized Finnegan-based scoring for monitoring withdrawal symptoms and initiating, escalating, and weaning pharmacological therapy was utilized for all NAS study participants.¹⁶ Patients with three consecutive scores \geq 8 or 2 consecutive scores \geq 12 were initiated on pharmacological therapy and admitted to the NICU, if not already in the NICU for observation. Morphine was the primary agent used for pharmacological treatment with clonidine used as adjunctive therapy. Weaning began when scores remained $<$ 8 within a 24-hour time frame. Infants were not discharged on medication. Standard hospital guideline was followed to monitor all perinatally substance exposed infants for a minimum of 5 days in the mother/baby unit or NICU prior to discharge.

To ensure consistent scoring by nursing, periodic competencies are required, and new hires are required to be trained on the Finnegan scoring system. Scores obtained by a nurse are to be verified by another NICU nurse before recorded in the infant's electronic medical record.

Nonpharmacological Interventions

Reviewing the literature, we identified and implemented reported common NPIs^{7–11} as a QI initiative represented by Group 2 and continued the NPIs for infants in study Group 3. NPIs included the 5S's method for infant soothing,¹⁷ identification of specific NICU bed locations for NAS patients to minimize noise and light intensity, incorporation of white noise (White Noise Sound Machine, Anescra, Fujian, China) for infant agitation, and increased volunteer availability to hold infants in need of calming. In February 2022, we received four courtesy novel bassinets to complement our NPI bundle for NAS management. The same management practices of Group 2 were maintained for Group 3 with the exception infants in Group 3 were secured in the newly available horizontal rocking bassinet. The bassinet was equipped with a speaker that provided white noise and a sound sensor that detected noise made by the infant. Based on noise and activity of the infant, the bassinet responded by adjusting the side-to-side motion and the volume of the white noise. The settings utilized were based on manufacturer setting recommendations for healthy infants. The motion level was maintained at baseline, the white noise volume was set at normal (\sim 70 dB), the responsive selection was set at normal, and the level lock was selected to limit motion between baseline to level 2. Settings were maintained for all Group 3 participants until they were able to wean from the bassinet.

Infants in Group 3 were weaned from the novel bassinet 48 hours before pharmacological treatment was discontinued using the following protocol:

- Morphine dose 0.04 mg.
- Select weaning mode (no motion but white noise). Continue swaddling using sleep sack per the manufacturer's recommendations.
- Once weaning mode tolerated (withdrawal scores return to baseline), move to standard open crib.
- Once in standard open crib wrap with waffle weave blanket (facility's standard of care)
- Place separate white noise machine at the bedside.
- NAS scoring continues during weaning process.
- Educate parents/guardian on use of appropriate white noise in preparation for discharge.

Data Analysis

Descriptive analysis of infant demographic data was analyzed, and categorical data were reported as frequencies and percentages. Continuous data were reported as means and standard deviations (–Tables 2 and 3). Shapiro–Wilk tests indicated the assumption of normality was violated for LOS, LOT, morphine, clonidine, crying, and sleeping. Levene's statistic demonstrated homogeneity of variances; thus, one-way ANOVA was conducted for LOS, LOT, clonidine, crying, and sleeping. Post hoc comparisons with one-way ANOVA used Scheffe's test. Levene's statistic demonstrated homogeneity of variances assumption was violated for morphine and nonparametric testing was used. Inferential analyses using one-way ANOVA determined differences between groups with follow-up post hoc tests as applicable to LOS, LOT, morphine, and clonidine exposure,

Table 1 Inferential analyses					
Variable	M	SD	<i>n</i>	<i>F</i>	<i>p</i>
Length of stay (d)					
Treatment 1	32.26	15.98	39	6.398	0.003 ^a
Treatment 2	31.76	11.94	21	–	–
Treatment 3	46.29	17.28	20	–	–
Length of treatment (d)					
Treatment 1	28.18	16.48	39	3.993	0.022 ^a
Treatment 2	27.38	10.98	21	–	–
Treatment 3	39.70	18.84	20	–	–
Clonidine (mg/kg)					
Treatment 1	248.61	353.01	39	2.177	0.120
Treatment 2	174.39	203.66	21	–	–
Treatment 3	376.60	328.73	20	–	–
Crying (in Finnegan Scoring)					
Treatment 1	1.92	0.453	39	0.582	0.561
Treatment 2	1.95	0.454	21	–	–
Treatment 3	2.03	0.054	20	–	–
Sleeping (in Finnegan Scoring)					
Treatment 1	1.55	0.179	39	4.412	0.015 ^a
Treatment 2	1.42	0.155	21	–	–
Treatment 3	1.48	1.141	20	–	–
Day of life receiving treatment					
Treatment 1	2.15	1.46	39	0.183	0.833
Treatment 2	1.95	0.86	21	–	–
Treatment 3	2.15	1.35	20	–	–
Average crying prior to morphine					
Treatment 1	1.22	1.04	39	0.097	0.907
Treatment 2	1.17	1.04	21	–	–
Treatment 3	1.31	0.98	20	–	–
Average sleeping prior to morphine					
Treatment 1	1.38	0.848	39	0.357	0.701
Treatment 2	1.26	0.815	21	–	–
Treatment 3	1.19	0.853	20	–	–
Average Finnegan prior to morphine					
Treatment 1	7.35	1.36	39	0.333	0.718
Treatment 2	7.72	2.15	21	–	–
Treatment 3	7.45	1.70	20	–	–
	Median ^b	–	<i>n</i>	<i>H</i>	<i>p</i>
Morphine (mg/kg)					
Treatment 1	5.22	–	39	7.485	0.024 ^a
Treatment 2	7.24	–	21	–	–
Treatment 3	10.98	–	20	–	–

Abbreviations: ANOVA, analysis of variance; LOS, length of stay; LOT, length of treatment; M, mean; SD, standard deviation.

Note: One-way ANOVA used for LOS, LOT, Clonidine, Crying, and Sleeping.

^a $p < 0.05$, statistically significant result. Kruskal–Wallis test used for morphine.

^bMedian, nonparametric testing.

Table 2 Demographic data			
Infant characteristics	Group 1 N = 39	Group 2 N = 21	Group 3 N = 20
Gestational age (wk)	38	38	39
	M (SD)	M (SD)	M (SD)
Maternal age (y)	29 (4.39)	30.05 (4.63)	31.25 (4.80)
Birth weight (g)	2,913 (514.89)	2,793 (505.10)	3,057 (532.65)
Birth head circumference (cm)	32.5 (1.5)	32.7 (1.5)	33.4 (2.2)
	Median	Median	Median
Apgar Score			
1 min	8	8	8
5 min	9	9	9
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)
Race			
White	32 (82)	15 (71)	16 (80)
Black	7 (18)	6 (29)	4 (20)
Ethnicity			
Non-Hispanic	39 (100)	21 (100)	20(100)
Gender			
Male	23 (59)	9 (43)	12 (60)
Female	16 (41)	12 (57)	8 (40)
C-section	13 (33)	12 (57)	6 (30)
Scheduled	0 (0)	4 (19)	1 (5)
Routine	2 (5)	5 (24)	1 (5)
Emergent	11 (28)	7 (33)	4 (20)
Vaginal delivery	26 (67)	9 (43)	14 (70)
Spontaneous	23 (59)	8 (38)	12 (60)
Operative/vacuum	3 (8)	1 (5)	1 (5)
Exposed to maternal polysubstance use	38 (97)	19 (90)	20 (100)

Abbreviations: C-section, cesarean section; M, mean; SD, standard deviation.

crying, and sleeping using Finnegan scoring (→Table 1). Finnegan scores specific for crying and sleeping were analyzed for each infant group to reflect reported bassinet characteristics to enhance sleep and decrease agitation (crying).

Results

Three subsets of patients were retrospectively analyzed with respect to NPI for the treatment of NAS. Overall, there was a

Table 3 Infant outcome data for each group			
Infant outcomes	Group 1 N = 39	Group 2 N = 21	Group 3 N = 20
	M (SD)	M (SD)	M (SD)
Therapeutic morphine total dose exposure, mg/kg ^a	9.86 (9.94)	9.52 (7.79)	19.71 (21.72)
Therapeutic clonidine total dose exposure, µg/kg	248.61 (353.01)	174.39 (203.66)	376.6 (328.73)
Discharge weight (g)	3,611 (743)	3,403 (611)	4,030 (841)
Discharge head circumference (cm)	35.6 (2.0)	35.3 (1.8)	36.9 (2.1)
Length of hospitalization, days ^a	32 (16)	32 (12)	46 (17)
Length of time in SNOO, days	N/A	N/A	34 (19)
Length of treatment, days ^a	28 (16)	27 (11)	40 (20)

Abbreviations: M, mean; N/A, not applicable; SD, standard deviation.

^a*p* < 0.05, statistically significant result.

significant difference in LOS ($p = 0.003$) and LOT ($p = 0.022$) in days, morphine exposure ($p = 0.024$) in mg/kg, and Finnegan sleep scores ($p = 0.015$). There were no significant differences in clonidine exposure ($p = 0.120$) in mg/kg and Finnegan crying scores ($p = 0.561$).

Length of Stay

One-way ANOVA revealed a significant difference in mean LOS in days, $F(2, 77) = [6.398]$, ($p = 0.003$). Post hoc comparisons indicated the mean difference between LOS for Group 1 ($p = 0.006$, 95% confidence interval [CI] = [3.47, 24.59]) and Group 2 ($p = 0.013$, 95% CI = [2.52, 26.52]) were significantly decreased from Group 3.

Length of Treatment

One-way ANOVA revealed a significant difference in LOT in days, $F(2, 79) = [3.993]$, ($p = 0.022$). Post hoc comparisons indicated that the mean difference between LOT for Group 1 was significantly decreased from Group 3 ($p = 0.041$, 95% CI = [0.40, 22.64]).

Morphine

The Kruskal–Wallis test revealed a significant difference in morphine exposure in mg/kg across the three groups, $H(2, n = 80) = [7.485]$, ($p = 0.024$). Group 3 recorded a significantly higher median morphine exposure in mg/kg (median [Md] = 10.98) than Group 1 (Md = 5.22) and Group 2 (Md = 7.24). Post hoc comparisons using a Bonferroni-adjusted α level revealed a significant difference and higher mg/kg morphine exposure of Group 3 compared with Group 1 ($p = 0.006$).

Sleeping

One-way ANOVA revealed a significant difference in mean sleeping in Finnegan scores, $F(2, 77) = [4.412]$, ($p = 0.015$). Post hoc comparisons indicated a mean difference between sleeping for Group 1 was significantly higher than Group 2 ($p = 0.018$, 95% CI = [0.0181, 0.2401]).

Clonidine/Crying

One-way ANOVA revealed a nonsignificant difference in clonidine exposure in mg/kg, $F(2, 77) = [2.177]$, ($p = 0.120$) and mean Finnegan crying scores and Groups, $F(2, 77) = [0.582]$. Post hoc comparisons also indicated no significant differences.

Discussion

Our study suggests the bassinet used in this study failed to enhance nonpharmacological management of infants with NAS admitted to an open-bay NICU. Findings were contrary to our original hypothesis that the novel bassinet would decrease LOS and pharmacological exposure. It was presumed the novel bassinet's unique features would collectively act as an effective calming NPI for NAS, especially in an open-bay NICU. Its ability to adjust the intensity of rocking to the infant's intensity of agitation was assumed would have a beneficial effect on sensory stimulation and

behavioral responses analogous to other studies involving reactions to sensory input by infants with intrauterine drug exposure.^{17–22} Instead, the bassinet was found to be associated with an increased length of hospitalization and exposure to pharmacological treatment of NAS.

Explaining why the bassinet used in our study failed to enhance nonpharmacological management of prenatally opioid-exposed infants is a challenge. Different motion effects are employed by the study bassinet compared with the waterbed and vibrating mattress that could result in different tactile, proprioceptive, and vestibular inputs. Subjecting NAS infants to a specific type, duration, and intensity of motion may result in different tactile and vestibular sensory input and limit the management of these patients.

In 1999 D'Apolito²³ compared the use of a mechanical rocking bed with a standard bassinet for drug-affected infants. Infants randomized to the rocking bassinet had increased withdrawal symptoms, sleep deprivation, and suboptimal neurobehavioral function on day of life seven as defined by lower cluster scores on the Brazelton Neonatal Behavioral Assessment Scale. The author suggested the ineffectiveness of the rocking bed possibly was related to excessive stimulation during the acute phase of infants experiencing withdrawal from prenatal opioid exposure. Bassinet settings in our study were based on manufacturer recommendations for healthy infants in the first 6 months of life and may have been similarly excessive and a potential explanation for the ineffectiveness of the bassinet.

The bassinet has not been specifically studied or marketed as a device to assist in nonpharmacological management of infants exposed to opioids but nonetheless utilized in NICUs for this purpose. How nonopioid-exposed infants versus those with NAS process and respond to various tactile and vestibular stimuli is beyond the scope of this study, but our results suggest infants with NAS may respond differently to position and specific type, duration, and intensity of motion.

Limitations

We acknowledge several limitations in our study. The patient sample size was small, especially Group 3, which included infants after the initiation of NPIs and the bassinet for management of NAS. This was in part due to terminating use of the bassinet after preliminary review revealed an increase in LOS, LOT, and morphine exposure after implementation of the bassinet. With a small sample size and a retrospective design, we understand the accuracy of our interpretation may have been jeopardized by coincidental associations.

We acknowledge Group 3 participants were not randomized and limit the generalizability of the findings and control of confounding variables. The study, however, was conducted at a single facility, which enhances consistent care and providers; demographic data of subjects were comparable between Groups (→Table 2) and NAS symptoms were similar

between groups before treatment was initiated. Between the groups there was no significant difference between the day of life pharmacological treatment was initiated, averaged total Finnegan scores prior to pharmacological treatment or the average scores for sleeping and crying before initiation of morphine (→ [Table 1](#)).

As a retrospective study, we recognize the data gathered depended on the accuracy and completeness of the medical records, which did not document potential confounding factors including details regarding overall maternal health and socioeconomic status, the level of maternal care in the antenatal period, and the severity of maternal medication or substance use. Although all study infants had documented prenatal exposure to opioids based on maternal urine toxicology, over 90% of our study participants were subject prenatally to variable polysubstance use. What role other substances played in our data are unattainable and a limitation of the study, but polysubstance use was equally evident between the groups. Our State Public Health NAS Registry reported no major changes in the ranking of substances over the study period with opioids (~90%) followed by (meth) amphetamines as consistently the most frequent prenatal exposures for NAS in the state. There was also no significant change in opioid classification exposures during the study with buprenorphine, heroin, and methadone, respectively, as the most frequent opioids reported to the state based on maternal and/or infant positive toxicology.

We acknowledge other confounding variables such as degree of parental involvement, extent of skin-to-skin care, time spent being held were not documented or controlled for, and may have changed outcomes between groups. Lacking also is long-term follow-up of our study population, which would greatly validate our short-term outcomes and concerns regarding the novel bassinet as an NPI for the management of NAS.

Conclusion

The horizontal rocking bassinet used in this study was not effective as an NPI for infants pharmacologically treated for NAS in an open-bay NICU. Modifications may be indicated, and specific guidelines established if this device is to be implemented in the management of infants experiencing NAS. Further research that incorporates multidisciplinary perspectives is needed to assess responses to the bassinet and its impact on long-term outcome for NAS patients.

Ethical Approval

Institutional review board (IRB) and organizational approval were obtained for this study, IRB # 21.0555.

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None.

Conflict of Interest

None declared.

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