The Effect of Sleeping Environment on Sleep-Wake Organization in Preterm Infants

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BACKGROUND

Study Purpose and Rationale:

Technological advances in the treatment of preterm infants have dramatically improved survival in recent decades.[1] With increased survival, there has been a shift in emphasis from survival only to improved quality of life. Many factors in the intensive care units, both physical and social, influence development and behavior of these infants.[2-4] It is becoming clear that some of the long-term disabilities of high-risk infants are a result of the environment and care practices and are not attributable to the original disease or conditions that necessitated intensive care.[5-8]

Based on the hypothesis that the NICU environment is a source of sensory excess or deprivation for preterm infant, [9, 10] various types of stimulation such as auditory, kinesthetic, tactile, proprioceptive, olfactory, and visual have been offered.[11-14] Supplementary stimulation has shown some benefits ranging from weight gain, changes in activity level to better performance on developmental assessments. However, there continues to be lack of objective tools to objectively measure the immediate effects of these interventions.

Sleep-wake organization is a potential tool to assess the effects of altering neonates' environment. Neonatal sleep is comprised of four distinct stages: quiet sleep, active sleep, transitional sleep, and wakefulness.[15] Sleep is vital for the continuation of preterm infants' brain development, synaptic plasticity, and maturation, although preterm sleep demonstrates many altered patterns from that of term infants.[16] Preterm infants spend more time asleep, are more likely to initiate a sleep cycle in active sleep, have longer quiet sleep latency, and have decreased quiet sleep duration.[17] Furthermore, the environment of the neonatal intensive care unit predisposes to sleep disturbances given the necessity of frequent clinical handling and exposure to loud alarms.[18-20] Disordered sleep has adverse effects on neurocognitive development and may increase the frequency of cardiorespiratory events.[2]

Interventions that promote uninterrupted, restful sleep in preterm neonates in the NICU by simulating the intra-uterine environment are lacking. The SNOO Smart Sleeper (SNOO)— a responsive bassinet that mimics the sensory environment of the womb through swaddling, continuous rocking motion, and soft white noise—may mitigate the interruption of sleep in the NICU and promote maturation of the sleep-wake cycle in these fragile neonates.[21] These maturational changes in sleep-wake organization can potentially prevent long-term morbidity and improve neurodevelopmental outcomes.[16]

Study Design:

We propose an inpatient, prospective, non-blinded, randomized controlled trial comparing the effects of the SNOO to a traditional bassinet on sleep states and sleep-wake cycling of premature infants in the neonatal intensive care unit.

The SNOO is a commercially-available, responsive bassinet that simultaneously uses a secure swaddle, white noise, and continuous rocking movement to calm infants. The SNOO assists sleep by sensing when infants awaken with cries or fussiness and responding by increasing its delivered level of swaying (at its highest level, less than a quarter of an inch back and forth) and volume of white noise. Once infants are calmed and fall back asleep, the SNOO's degree of movement and volume return to baseline.

The SNOO is designed for infants from birth to six months of age weighing 4-25 pounds. Available in retail since 2016, it has been used by more than 200,000 babies for over 350 million cumulative hours. It has been certified by the Consumer Product Safety Commission, American Society for Testing Materials, and Juvenile Products Manufacturers Association. In 2021, the SNOO received the designation of “Breakthrough Device” by the FDA and is currently in review for approval as a SIDS/SUID prevention device. In addition, the SNOO prevents dangerous rolling by securely anchoring the baby in a flat, supine sleep position in accordance with safe sleep recommendations from the American Academy of Pediatrics.[22]

Statistical Procedures:

Sample Size:
- To control for any impact of baseline intrinsic sleep maturity on the effect of the intervention on sleep-wake cycle maturity, equal numbers of infants in each gestational age group (very preterm, 28w0d to 31w6d, or moderate-to-late preterm, 32w0d to 36w6d) in each intervention arm will be recruited.

- For 80% power, 20 infants will need to be included in the study.

- The Type I error probability associated with this test of our null hypothesis is 0.05.

- Our target enrollment is 50 infants to account for the possibility of study non-completion (participants discharged before their second sleep study is performed).

Data analysis:
- Behavioral sleep coding during the sleep assessments, EEG (Epilog) data during the sleep assessments, and vital sign data from both during the sleep assessments and throughout the participants’ hospital admission will be analyzed to calculate the percentage of time spent in each sleep stage (quiet, active, and indeterminate sleep).

- The EEG data will be analyzed to assess sleep-wake cycling.

- Heart rate variability will be determined from cardiorespiratory monitoring.

- Oxygen saturation profiles will be grouped as the percentage of time spent in 85-89% or 90-95% SpO2.

- Comparative statistical analyses will be performed to determine differences between the infants placed in the SNOO intervention arm and the traditional bassinet conditions.

PROCEDURES

Study Population:
- Participants will be 50 infants ranging from 28 to 36w6d weeks gestational age at birth. They will be randomized to either the traditional bassinet condition (n = 25) or the SNOO (n = 25).
- Participants will be further stratified into two groups based on their gestational age at birth: very preterm (28w0d to 31w6d) or moderate-to-late preterm (32w0d to 36w6d).
- Only viable neonates will be enrolled in the study. The Morgan Stanley Children's Hospital Neonatal Intensive Care Unit medical team is responsible for assessing the viability of the neonates. Members of the research team will not be involved in determining the viability of the neonates.

Inclusion Criteria:
(a) Inpatients at the Morgan Stanley Children's Hospital 7 Tower Neonatal Intensive Care Unit.
(b) Singleton gestation.
(c) Gestational age 28w0d to 36w6d at birth.
(d) Postmenstrual age 35w0d to 36w6d at the time of the first intervention.
(e) Weight greater than 1.8 kg and less than 11.3 kg.
(f) Stable thermoregulation in an open crib.
(g) Stable respiratory status on room air (no nasal cannula or CPAP).
(h) Normal head ultrasound (if obtained). (If the patient has not had a clinical head ultrasound obtained by their medical team, a research-driven head ultrasound will not be obtained.)

Exclusion Criteria:
(a) Congenital brain or spinal anomalies.
(b) Intracranial hemorrhage.
(c) Severe encephalopathy.
(d) Known or suspected genetic syndromes that could result in cerebral dysfunction.
(e) Airway anomalies that could result in sleep-disordered breathing.
(f) Bleeding diatheses.
(g) Status post surgery or minor surgical procedures (i.e. inguinal hernia repair, circumcision).
(h) Fetal opioid exposure.
(i) Administration of sedating agents over the past 24 hours.
(j) Ability to independently roll to hands and knees.

Materials:
- SNOO Smart Sleeper hospital bassinet
- SNOO mobility platform

- Disposable mesh cover
- SNOO hospital mattress
- Disposable mattress covers
- Disposable fitted cotton mattress sheets
- Disposable cotton SNOO sleep sacks
- Hospital blankets
- Pulse oximetry probes
- Heart rate leads
- Epilog single-lead EEG
- Cerebral NIRS lead
- Infant hats

Study Protocol:
Once enrolled infants are considered to be medically stable by the primary clinical team (no respiratory support) and have been maintained out of the isolette for at least 24 hours, their study participation will begin. Prior to and immediately following the study interventions, infants will receive routine nursing care per the MSCH NICU clinical standards of care.

Each enrolled infant will have sleep studies performed at two time points: within one week of weaning from the isolette to open crib (35w0d to 36w6d postmenstrual age, T1), and within one week of discharge from the NICU to home (at approximately term-equivalent age, 37w0d postmenstrual age or greater, T2). There will be at least one week between the two sleep studies. Each sleep study will take place between the infant's 14:00 and 17:00 feeds. The duration of each sleep study will be approximately 3 hours. Parents will not be present during either the feeding or the sleep study. Parents will be given at least one day's notice by the researcher that each of the sleep studies will be occurring the following afternoon. This will ensure that any planned parental visitation occurs outside the hours of the sleep study.

Before the 14:00 feed, the researcher will attach stick-on sensors to the infant for physiologic measurements (heart rate monitor, pulse oximetry, and cerebral NIRS) per unit standard of care. The Epilog single-lead scalp EEG will have been cleaned with an alcohol swab. A new pressure-activated sticker will be affixed to the underside of the Epilog. The sticker liner will be discarded and the Epilog adhesive side will be pressed on the infant's right forehead for 10 seconds.

All infants will receive their 14:00 feeds via mouth, feeding tube, or both, as directed by their primary medical team. Thirty minutes after initiation of the feed, the experimental period will begin. All infants will then be placed in the SNOO bassinet.

Traditional bassinet group (control arm):
The researcher will swaddle the infants using a standard hospital blanket and place the infant in the center of the SNOO. The SNOO will be left powered-off. Data collection will then begin.

SNOO group (intervention arm):

The researcher will unzip the SNOO Sleep Sack and spread open the inner bands. The infant will be laid down on top of the unzipped SNOO sack with the shoulders placed 2-3 inches higher than the top of the sack. The infant's arms will be straightened, the inner bands will be pulled around, and then the bands will be attached snugly. To ensure correct placement, the researcher will check that the bottom of the edge of the bands will cover most of the infant's hands. The diaper flap will be pulled up and secured over the band. Then the fabric at the top will be pulled up and over each shoulder. Lastly, the Sleep Sack will be completely zipped with the infant now fully swaddled.

If the infant is close to 1.8 kg and thus relatively small in relation to the SNOO Sleep Sack, per manufacturer instructions, they will first be swaddled in a standard hospital blanket before being placed in the SNOO sack. The positioning of the inner bands, diaper flag, securement, and zippering will then progress in the same order (as stated above). The SNOO Sleep Sacks have vented panels to avoid overheating, even in the event that an interior swaddle blanket is required.

The swaddled infant will then be laid inside the SNOO on her back. The loop on the end of each swaddle wing will be slid over the safety clips that are attached to either side of the platform. The SNOO will not operate unless the elastic wing loops are fully slid onto both safety clips. The smart bassinet will then be powered on by pressing the activity button on the front of the SNOO. The front light will blink a white, but will then turn blue when the SNOO is ready to function. The SNOO's movement will be set to a maximum level of 3 out of 5, and its volume set to a maximum of 2 out of 4. The SNOO's movement and sound settings will automatically ramp up and down as needed in response to the infant's sensed level of fussiness or crying per the manufacturer's programming. Data collection will then begin.

Data collected will include EEG (during the sleep assessments), vital sign (during the participant's hospitalization), cerebral oxygenation (during the sleep assessments), and behavioral state data (during the sleep assessments) (see "Measurement Details," below). We will also place sensors beside each SNOO bassinet to measure environmental light and sound levels for the entire duration of the sleep studies. Data collection will continue for 3 consecutive hours or until the 17:00 feed is due, whichever comes first.

If the SNOO senses that an infant is crying or fussing for more than three minutes, the SNOO will automatically shut off. This feature is meant to alert the caregiver that the infant needs further attention such a diaper change. In the SNOO intervention arm, in the case of the SNOO shutting off, the researcher will pause the sleep study and manually calm the infant using a pacifier until their fussing ceases. The sleep study will then resume.

Upon completion of the sleep study, the SNOOs in the intervention arm will be powered off. Infants who had been in SNOO sleep sacks will be unswaddled. Epilog and cerebral NIRS probes will be removed, and all infants will be placed back in their standard bassinet or crib. Sound and light recorders will be shut off.

Cleaning Protocols:
Prior to use:

- The blue disposable mesh cover will be placed in the bassinet to completely cover the bassinet walls.
- The sealed mattress will be placed inside the disposable blue waterproof cover.
- A clean mattress sheet will be placed over the covered mattress.

After use:

- A hydrogen peroxide-based disinfectant or wipes will be used to wet all exposed surfaces of the bassinet. The surfaces will be wiped so that they remain visibly wet for at least 1 minute at room temperature.
- The cleaned SNOO will be covered with a clean plastic bag so that it remains ready for the next experimental use.

Measurement Details:
Variables to be collected at the time of the sleep studies and from vital sign sensors throughout the participant's hospital admission:
(a) Behavioral sleep states: Behavioral state will be assessed by a member of the study team as described by Sahni et al. (1995). In brief, the researcher will continuously code the infant's behavioral sleep states at bedside for the duration of the roughly 3 hour sleep study. Code 1 will be designated as quiet sleep, and Codes 2 and 3 will be grouped as active sleep. Behavioral state codes will include:
i. Code 1: Eyes are closed with predominantly flaccid "rag doll" appearance. Body movements are limited to startles. Rhythmic jaw jerks lasting 1 to 2 seconds are also seen.
ii. Code 2: Small body movements are seen. Motor activity includes low intermittent writhing movements, jerky startles, small movements of an extremity or its parts, frowns, smiles, chewing and sucking movements, grimaces, grunts and occasional whimpers.
iii. Code 3: Rapid eye movements observed. Eyes may occasionally open or close or remain briefly half open.
iv. Code 4: Wakeful behavior.
v. Code 5: Crying.
vi. Code 6: Feeding.

(b) EEG activity (Epilog): The study investigator analyzing the EEG data for sleep state identification will be blinded to the infants' assigned study groups.
(c) Cardiorespiratory measurement
(d) Oxygen saturation measurement
(e) Cerebral oxygenation
(f) Cardiorespiratory events monitoring: Heart rate, respiratory rate, oxygen saturation, and cerebral oxygenation (NIRS) will be collected using Phillips and bedside monitors, which is the standard practice in the NICU.
(g) Environmental sound levels
(h) Environmental light levels

Variables to be collected from retrospective chart review:

(a) Date and time of birth
(b) Sex
(c) Race
(d) Ethnicity
(e) Gestational age at birth
(f) Birth weight
(g) APGAR scores
(h) Intrauterine growth restriction diagnosis in pregnancy
(i) Symmetric, appropriate, or large for gestational age diagnosis
(j) Maternal betamethasone administration
(k) Early-onset sepsis evaluation
(l) Late-onset sepsis evaluation
(m) Positive blood culture
(n) Pneumothorax
(o) Respiratory support at birth
(p) Necrotizing enterocolitis diagnosis
(q) Head ultrasound findings
(r) Current medications
(s) Previous medications
(t) Caffeine use
(u) Day of life at study
(v) Postmenstrual age at study
(w) Weight at study
(x) Days since last lab draw
(y) Date of last painful procedure
(z) Feed prior to study
(aa) Date and time of discharge

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