Auricular Acupressure as an Adjunct Treatment for Opioid Tapering in a Pediatric Cardiac Intensive Care Unit: A Pilot Feasibility Study

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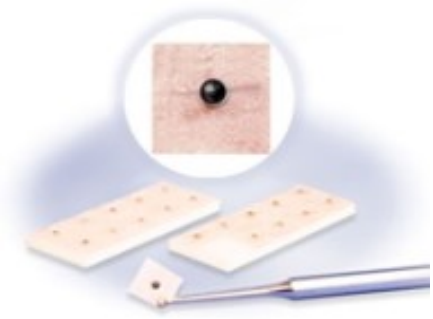
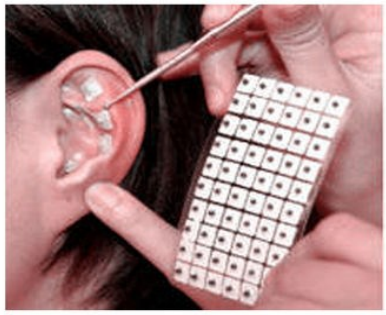
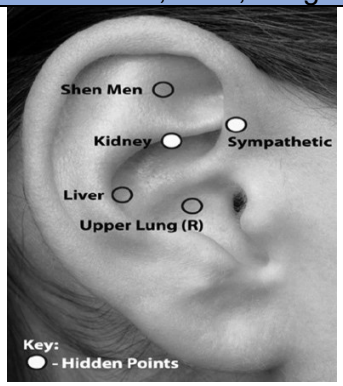
Study Overview

This **intervention pilot feasibility study** will assess the impact of auricular acupressure as an additional non-pharmacologic therapy for infants at risk for developing Iatrogenic Withdrawal Syndrome (IWS) in the Pediatric Cardiac Intensive Care Unit (PCICU) of Monroe Carrell Jr Children's Hospital at Vanderbilt (MCJCHV). We will recruit **40 healthy, 34 weeks gestational age or older infants** exposed to prolonged medications (greater than 5 days) for cardiac procedures that may cause withdrawal upon cessation such as opioids, benzodiazepines, or other sedative medications. Participants will receive the auricular acupressure in addition to the standard of care such as clustered nursing care, touch, position change, environmental controls, holding, and swaddling. Within 24 hours of implementing a weaning protocol, acupressure will be applied to three designated points of one ear following the NADA protocol acupuncture technique while also incorporating the Near-Term Infant (NTI) conceptual framework identified elements (see figure 3). Acupressure will be administered via stickers that are adhesive to the skin like a Band-Aid (see figure 1). These stickers include a vaccaria plant seed in the center that applies continuous light pressure on the designated points. This form of acupressure was selected as it is organic and does not contain metal which may interfere with emergency medical care such as imaging. After the initial 24 hours of application, stickers will be removed, the infant's skin will be assessed for any disruption such as bruising or discoloration, and the stickers will be rotated to the infant's other ear at the same NADA protocol auricular sites. Acupressure stickers will be removed and applied to the opposite ear every 48-72 hours until withdrawal symptoms improve (1). Withdrawal symptoms are measured every 6 hours with the enhanced Withdrawal Assessment tool (WAT) as part of the standard of care. Upon completion of the weaning regimen, infants with a score of less than or equal to 3 or less than 2 above baseline with no more than 2 rescue medication doses in 24 hours will have the acupressure removed.

Figure 1: Auricular Acupressure to NADA Protocol Sites

Acupressure Sticker	Auricular Application	NADA Protocol Points: Shen Men, Liver, Lung
		

1.0 Background

Opioid and benzodiazepine medications are necessitated in the treatment of critically ill infants in the cardiac intensive care unit to provide pain relief and anxiolysis. However, use of these modalities are associated with a multitude of uncomfortable symptoms surrounding physical dependence and may lead to withdrawal syndrome, bowel dysfunction, as well as exacerbation of delirium (2). Additionally, long term use of opioids and benzodiazepines in the infant population may impair neurodevelopment (3-5). This is especially concerning for infants undergoing cardiopulmonary bypass as this intervention further places this population at risk for impaired neurological development (6). These medications further contribute to prolonged hospital stays as they must be gradually weaned (7, 8).

Given the sequelae of the prolonged opioid and benzodiazepine exposure in this vulnerable population, first line treatments involve the maximization of non-pharmacologic therapies. These treatments include swaddling, reduction in environmental stimulation, use of sound machines or music, vibration, and soothing touch (9, 10). Yet, these treatments are not always successful in significantly reducing symptoms of withdrawal (with significance referring to reductions that do not require additional medication administrations).

The NADA protocol uses an auricular acupuncture technique created by a physician for the treatment of addiction and has demonstrated efficacy in the adult population (11-13). Acupuncture and acupressure studies in pediatric populations have also demonstrated improvement in multiple symptoms commonly experienced by infants in withdrawal. These symptoms include pain, agitation, crying, feeding difficulties with subsequent growth impairment, and sleep disturbance (14-25). Current evidence suggests acupuncture and acupressure are safe on neonates, but high quality randomized controlled trials are needed to confirm efficacy for the treatment of withdrawal (1, 23-28). This study, with the use of the NTI, will establish efficacy and provide a framework to guide future acupuncture and acupressure studies.

2.0 Rationale and Specific Aims

Sedative medications such as opioids and benzodiazepines are commonly administered to improve comfort of infants undergoing cardiac surgical procedures. Unfortunately cessation of these medications are commonly associated with onset of uncomfortable withdrawal as infants become physically dependent on these medications (29, 30). This condition is known as Iatrogenic Withdrawal Syndrome (IWS) and is further associated with impaired neurological development as well as prolonged mechanical ventilation and hospital stays (3-5, 31-33).

Infants with IWS experience a multitude of symptoms shared by other infant conditions that have been improved with acupuncture including tremors, hypertonicity, agitation, disrupted sleep, feeding difficulty, vomiting, diarrhea, temperature instability, tachypnea, and impaired weight gain (34-37). Treatments focus on non-pharmacologic adjuncts that support physiologic stability and prevent further developmental difficulties, prolonged hospital stays, and interrupted maternal bonding (9, 38, 39). These therapies include swaddling, position change, soothing touch, and environmental controls; however, *they have not traditionally included acupressure as a non-pharmacologic adjunct*. Although standard interventions are helpful, there remains a need to optimize these interventions and further reduce or prevent the use of medication.

Current evidence suggests that acupuncture is safe and beneficial for multiple conditions that impact neonatal and pediatric populations including withdrawal, yet this therapy remains underutilized as there is a lack of high-quality studies evaluating feasibility and therapeutic efficacy in the treatment of dependence (1,10-24). A less invasive acupuncture therapy is acupressure, a technique that applies mild pressure via stickers, similar to Band-Aids, to designated body points rather than needle insertion to provide a therapeutic benefit. Acupressure may serve as an additional *non-pharmacological adjunct to ease the severe discomfort of withdrawal in infants physically dependent on medications.*

In addition to therapeutic utility of acupressure, it may be cost effective by decreasing hospital stays and the need for more expensive and invasive pharmacologic interventions (9). **In this pilot feasibility study, acupressure will be used as an additional intervention to current, standard therapies**. The Near-Term Infant conceptual framework (NTI) guided the creation of our acupressure protocol to ensure incorporation of standard of care as well as optimization of acupressure elements to produce healthy outcomes in infants at risk for developing iatrogenic withdrawal syndrome. This acupressure protocol has been implemented at MCJCHV in the neonatal abstinence syndrome (NAS) population and was deemed feasible, accepted by healthcare providers and mothers, as well as safe. If proven feasible and beneficial within a PCICU population, further studies may be conducted to evaluate the efficacy of acupressure in easing with withdrawal symptoms as measured by the enhanced withdrawal assessment tool (WAT-1), when applied in conjunction with standard treatments.

Aim 1: Assess feasibility of delivering an acupressure protocol for the treatment of withdrawal in a pediatric cardiac intensive care unit. Feasibility will be assessed with successful completion of the following objectives:

a. Achieve recruitment and consent of 4 parents per month whose infant has been exposed to opioids and/or benzodiazepines for greater than 5 days, with a retention of 80% or higher during a 24 month time period (n=40).
b. Deliver the acupressure protocol to 20 infants at risk for developing withdrawal within the standard of care as an additional non-pharmacologic intervention (20 infants will receive standard of care).

Aim 2: Assess impact of auricular acupressure on withdrawal symptoms for an infant physically dependent on opioid and/or benzodiazepine medications. Efficacy of auricular acupressure will be assessed, in line with the standard of care, with comparison of the following assessments among intervention and control groups:

a. Duration of opioid and/or benzodiazepine exposure
b. Duration of wean phase
c. Duration of mechanical ventilation
d. Total medication dosage as measured in morphine equivalents and benzodiazepine dosages (mg/kg/patient)
e. Hospital length of stay
f. Severity of withdrawal symptoms as measured by the Enhanced Withdrawal Assessment Tool (WAT-1)
g. Presence and/or severity of delirium as measured by the Pediatric Confusion Assessment Method for the Intensive Care Unit (psCAM-ICU)
h. Severity of agitation as measured by the Richmond Agitation Sedation Scale (RASS)
i. Infant Pain scores as measured by Faces, Leg, Activity, Cry, Consolability Scale (FLACC)

Aim 3: Assess acceptability and implementation of the acupressure protocol as an adjunct treatment for withdrawal syndrome within the standard of care.

a. Examine parental satisfaction of acupressure as an additional treatment as measured by the Client Satisfaction Questionnaire (CSQ8).
b. Assess provider and staff satisfaction of acupressure as an additional therapy as measured by Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM).
c. Assess qualitative feedback as reported by parents and healthcare providers.

Impact: Results from this proposed study may expand first line, non-pharmacological therapy for infants experiencing withdrawal symptoms. Offering enhanced care for IWS infants while reducing costs related to hospital treatments is a public health concern during an opioid epidemic. Acupressure is safe, noninvasive, inexpensive, and efficiently implemented for

disorders with similar conditions to withdrawal syndrome, thus warranting additional investigation for consideration as an included standard of practice for post procedural infants.

3.0 Animal Studies and Previous Human Studies

There is a multitude of research, which has demonstrated efficacy and safety of acupuncture and acupressure in the neonatal and pediatric population; including research within MCJCHV by the PI yielding no adverse outcomes (28). This treatment has also exhibited therapeutic results in veterinary medicine (40). In pediatrics, acupuncture has demonstrated improved myofascial pain and postoperative nausea/vomiting (41, 42). For infants, acupuncture and acupressure has reduced crying in infants with colic and reduced pain during procedures (14, 19, 22, 43). Incidentally, these positive effects can lead to better attachment with mothers. Several studies have outlined the presence of active ear points in the neonate which propose the use of auricular acupuncture or acupressure should be considered as an adjunct treatment (44-47). More specific research studies in NAS reveal acupuncture and acupressure are practical non-pharmacologic interventions (1, 9). Laser acupuncture has been performed on infants with NAS and resulted in reduction in morphine use, diarrhea, length of stay and improved feeding as well as sleep (23-25). Acupressure in combination with massage has also demonstrated efficacy in premature infants weight gain (21). Acupressure is the least invasive technique and very well tolerated (48). A similar study performed acupressure on NAS infants in 1992-1996 with several limitations but there were no adverse reactions or skin disruption noted (1). In this study, ear seeds were left in place for up to 72 hours, following the NADA protocol without any negative effects. Limitations included lack of control for additional acupressure applied by mothers, lack of blinding (sham), and timely application of the seeds (within 24 hours of birth).

4.0 Inclusion/Exclusion Criteria

This prospective pilot study will be conducted over a 24-month period and will enroll a total of 40 infants. Infants will be randomized in a 1:1 ratio to the two groups; randomization will occur within REDCap. Inclusion criteria are as follows: infants, 34 weeks or greater gestation, exposure to opioids and/or benzodiazepine medications for 5 days or more, beginning a stable wean, and maternal age of 18 or older as these individuals are able to consent for themselves (see Table 2). Exclusion criteria will be captured in the medical record as follows: hemodynamic instability, transfer to another facility prior to completion of the weaning regimen or death. Parents identified by health care providers in the PCICU will be approached by study providers (Jackson, Terrell, Sweeney, Weber, or Williams) in the PCICU. Project procedures will be described and if participants would like to enroll in the study, the consent process will be completed by study providers. Following informed consent, acupressure will be administered within 24 hours MCJCHV. Healthcare providers caring for these infants will be identified through the medical record and subsequent surveys sent through their VUMC email. No ethnic group will be targeted or excluded from this study.

Table 2: Inclusion and Exclusion Criteria

Inclusion	Exclusion
34 weeks gestational age to 1 year of age	Transfer to another facility prior to wean completion
Maternal age 18 or older	Re-escalation of care/Worsening Illness
English speaking	Death
Hemodynamically stable	

Exposure to opioid and/or benzodiazepine for 5 days or more	

5.0 Enrollment

A purposeful sampling technique will be utilized to recruit participants from MCJCHV as referred by healthcare providers caring for infants exposed to opioids and/or benzodiazepines for surgical procedures. Informational flyers (Appendix A) will be produced and provided by healthcare providers to parents interested in participating in the study and asked if they would like to be contacted by the PI or research team. At that time, parents may contact the PI, ask the PI to call them, or the PI will be available during the week (Monday-Friday) to discuss the study immediately following their discussion with their healthcare provider. Additionally, infants at risk for developing withdrawal may be identified by following the census in the PCICU. Daily monitoring of the PCICU census via the electronic medical record will be performed by the PI.

Previous infant studies, including a pilot feasibility study conducted by the PI at MCJCHV, have reported high retention rates of mother's that consent to acupuncture for the treatment of withdrawal but we are mindful of challenges in enrollment and retention (1, 23, 24, 28). Enrolled participants will remain in the study until cessation of opioid and/or benzodiazepine unless they are transferred to another facility (see Table 2 Exclusion Criteria) or parents voluntarily withdrawal. If an infant is transferred, acupressure will not be continued but surveys will be provided to assess satisfaction and acceptability (Aim 3). Healthcare providers will be identified through the medical record and surveys sent through their VUMC email.

6.0 Study Procedures (Design)

6.1. Interventions.

Acupressure Administration (Aim1). All participants will receive the standard non-pharmacological treatment, which may include any variety of the following treatments: rooming in, soothing tough, swaddling, skin to skin, positioning, reduced stimulation, and sound machines, as needed and tolerated. These treatments are documented by nurses in the medical record. The essential characteristics for neonatal acupuncture (Figure 3) as guided by the Near-Term Infant conceptual framework (Figure 2) are included in the delivery of this acupressure protocol.

Within 24 hours of weaning medications, one of five specialty trained advanced practice providers will apply acupressure stickers to one ear (left or right depending on access to site) in accordance with the NADA protocol acupuncture technique. Application will occur at designated points including Shen Men, Liver, and Lung: in the room with the mother; and potentially during breast feeding, holding, skin to skin contact or bottle feeds. Administrators and nurses will document the activities of the infant during acupressure placement in the medical record. Stickers will remain in place for 24 hours.

At 24 hours, skin will be assessed, and stickers will then be rotated to the opposite ear every 48-72 hours if there are no adverse effects such as skin irritation. Should skin irritation be present after the 24-hour period, the sticker applied to the opposing ear will be removed in 12 hours and skin assessed. If skin irritation continues, acupressure will be discontinued, and the participant will be withdrawn from the intervention portion of the study. Parents and health care providers of the infant will still be provided surveys to assess satisfaction and acceptability of acupressure. If no skin irritation occurs, stickers may be rotated for these participants every 12 hours. Assessment of the ear skin will be documented at the time of acupressure removal in the medical record. In accordance with previous neonatal studies that applied auricular acupressure under these guidelines (48-72 hour acupressure placement), we do not anticipate skin irritation but will continue to monitor throughout hospitalization (1, 20, 28). Acupressure will be discontinued when withdrawal symptoms measure less than or equal to 3 or less than 2 above baseline with no more than 2 rescue medication doses in 24 hours. Study participants will

receive the same assessments as non-participants and must meet the same weaning qualifications in line with the standard of care.

Acupressure Efficacy (Aim 2). As part of the standard of care, multiple metrics will be captured and compared among the intervention and control group. These include duration of opioid and/or benzodiazepine medications, duration of weaning phase, duration of mechanical ventilation, and hospital length of stay. To ensure appropriate opioid dosage comparisons, all opioid medications will be converted to morphine equivalents (mg/kg/patient); benzodiazepine medications and dosages will also be captured. Consistent with the current standard of care for infants treated in the PCICU the following assessments will be conducted: Withdrawal Assessment Tool (WAT-1) for Pediatric Withdrawal every 6 hours, Preschool Confusion Assessment Method for the ICU (psCAM-ICU) every 12 hours, Richmond Agitation-Sedation Scale (RASS) every 2-4 hours and Faces Legs Activity Cry Consolability Scale (FLACC) every 4 hours.

Acupressure Acceptability (Aim 3). Prior to discharge and after completion of the weaning protocol, parent(s) will receive the Client Satisfaction Questionnaire (CSQ8) to assess parental satisfaction of acupressure as an additional therapy. Staff and providers who cared for participants will also receive three brief electronic surveys via REDCap directly to their email prior to discharge. This survey will include 12 questions: Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM) to evaluate acceptability of acupressure as a complementary therapy. Qualitative feedback back from healthcare providers and parents will be documented by administrators at time of acupressure application and skin assessment. Such feedback would include observations reported to the research team by healthcare providers or parents.

6.2. Conceptual Framework & Innovation. An important innovation of this study is the development of a standardized protocol specific for infants that is guided by the Near-Term Infant (NTI) conceptual framework to ensure that essential components of infant care are incorporated in this adjunctive treatment within the standard of care (49). To our knowledge, the use of a conceptual framework has only been implemented in one neonatal acupressure study (performed by the PI) and no consistent framework has been outlined for future studies. Use of the NTI guided the development of our acupressure protocol to ensure optimal delivery of this therapy as a complementary treatment for IWS. Based on previous evidence related to acceptability of acupressure with neonates, we will eliminate a treatment room during application, allowing the infant to be with his/her parents. An auricular technique is supported by the NTI to improve physiologic symptoms within the standard of care by reducing stimulation to the infant, as full body administration would require unwrapping, exposing body points, and laying the infant down. All of the elements defined by the NTI ensure maternal-infant bonding, as well as incorporation of family and other human interactions. These are novel elements the NADA protocol did not consider as it was developed for the adult population. Use of the NTI is innovative and significant in our study as it ensures adaptations to the NADA protocol including evidence-based strategies of acupressure that are imperative for the IWS population. Cumulatively, these considerations allow for the inclusion of acupressure within the standard of care for infants thereby promoting future feasibility and acceptance of this novel treatment by parents, health care providers, and institutions.

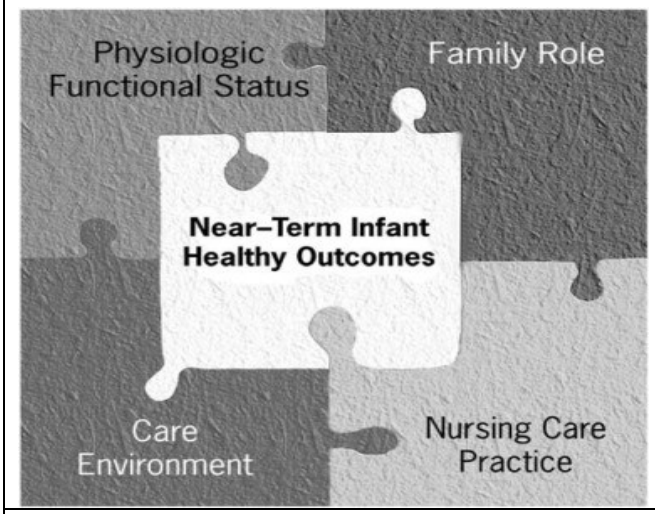


FIGURE 2: Near-Term Infant Conceptual Framework

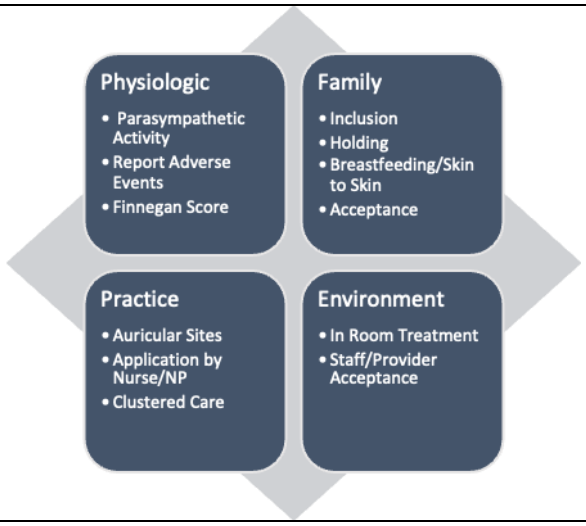


FIGURE 3: Essential Characteristics for Neonatal Acupuncture as Informed by the Near-Term Infant Conceptual Framework

7.0 Risks to Participants

This study includes an intervention trial that requires registry in ClinicalTrials.gov. There is minimal risk to human participants in the proposed study; nonetheless, rigorous efforts will be made to protect them. We will recruit a total of 40 infants at risk for experiencing withdrawal at Monroe Carrell Jr. Children's Hospital at Vanderbilt in Nashville, TN. Recruitment and consent will be conducted by the PI and research team. Written, electronic, or telephone informed consent will be obtained prior to initiating any study activities. All key personnel and study team members are licensed healthcare professionals with extensive substance dependence and neonatal experience that have been specially trained and credentialed to apply auricular acupressure.

The only known physical risk associated with auricular acupressure is the possibility of irritation to the infant's skin such as bruising or discoloration. Skin irritation will be defined as bruising, and severe redness as documented by the acupressure provider. Should skin irritation be present after the 24-hour period of acupressure application, the sticker applied to the opposing ear will be removed in 12 hours (as this is half the initial evaluation period designated in the protocol) and skin assessed. If skin irritation occurs in the opposing ear, acupressure will be discontinued, and the participant will be withdrawn from the study. If no skin irritation occurs, stickers will be rotated for these participants every 12 hours. In accordance with previous neonatal studies, including one performed by the PI at MCJCHV, we do not anticipate skin irritation when applying auricular acupressure under these guidelines (48-72 hour acupressure placement) (1, 20, 28).

Protections for Infants. Infants in this study will be viable near term gestational age; individuals engaged in this research will have no part in determining viability of the neonate. Clinical studies have been conducted on the use of acupressure and (more invasive) acupuncture and provide data for assessing potential risks to infants. Every parent providing consent in this study will be fully informed regarding the reasonably foreseeable impact of acupressure in infants experiencing withdrawal from substances.

Adequacy of Protection Against Risks. All members of the team will have the required human participants research (CITI research ethics and compliance) and HIPPA training. All paper copies of data will be kept in a locked file cabinet in the PI's office at VUMC. Electronic

information will remain in the password protected, project number identification, REDCap database. The PI and research team will always be available to the healthcare providers and staff via cell phone. Participants' parents will be given a telephone number, pager number, and email address which will allow them to contact the PI at any time. Should there be any adverse events, PCICU providers are available to provide care for the infants.

Potential Benefits of the Proposed Research to Participants. Acupressure may serve as an additional non-pharmacologic intervention that improves symptoms of withdrawal in infants at risk of developing withdrawal syndrome. In addition to therapeutic utility of acupressure, it may be cost effective by decreasing hospital stays as well as the need for more expensive and invasive pharmacologic interventions.

Importance of the Knowledge to be Gained. Acupressure may augment current first line therapies assisting in the avoidance of medications, promoting maternal bonding, and reducing hospital length of stay. If proven feasible within a pediatric cardiac intensive care population, further studies may be conducted to evaluate the efficacy of acupressure in easing withdrawal symptoms as measured by the enhanced Withdrawal Assessment Tool (WAT), when applied in conjunction with standard treatments.

Data and Safety Monitoring Plan. The PI is responsible for the monitoring of the progress of the study and safety of all participants. Participants must meet all inclusion criteria and none of the exclusion criteria. All discussions with participants' parents will take place in confidential areas (private room or hospital room inpatient).

8.0 Reporting of Adverse Events or Unanticipated Problems involving Risk to Participants or Others

The study team is comprised of seven specialty trained and credentialed providers that will communicate any issues such as skin irritation to the PI immediately. Adverse events (AE) in this study will be minimal as there are no invasive procedures and the intervention may be administered within the standard of care as the PI has done previously at MCJCHV; with no reported AE (28). However, AE will be monitored throughout the study and any event will be followed to resolution or stabilization. An AE is defined as any unfavorable medical occurrence in a human study participant, whether or not it is considered to be related to participation in the research. Any AE will be reported to the VUMC IRB immediately. An unanticipated problem (UP) is any incident, experience, or outcome that meets all of the following criteria: a) unexpected given the research procedures and characteristics of the study population, b) related or possibly related to participation in the research and c) suggests that the research places participants or others at a greater risk of harm than was previously known or recognized. We will report any such events to the IRB. The PI will provide continuous, close monitoring of participants at VUMC with prompt reporting of AEs to the IRB and will follow VUMC reporting guidelines.

9.0 Study Withdrawal/Discontinuation

Participants may withdraw from the study at any time and continue standard care. Participants may be withdrawn if deemed medically necessary by an attending physician or study staff or if exclusion criteria are met. Participants may be withdrawn from the study by the principal investigator for repeated non-compliance. This would entail altering the seed placement for example. Participants will be reminded that participation will not affect their clinical services and the CSQ8 parental satisfaction survey will be provided to parents of participants.

10.0 Statistical Considerations: Analysis Plan

The study sample will be characterized using descriptive statistics including mean/median, standard deviations/interquartile range, proportions and percentages as outlined below. Benchmarks for success are summarized in Table 2.

Data Analysis Aim 1. The primary goal of this aim is to assess feasibility and implementation of this study including recruitment, retention, and execution of and adherence to the acupressure protocol. Feasibility measures will be reported as frequencies and proportions (% of eligible patients enrolled, % of patients prematurely terminating treatment, % of patients completing all study assessments, % of data collection procedures completed, % of missing medical record data). Feasibility will be determined through the following benchmarks: a) recruitment success: recruitment rate of 2 infants per month over the proposed 24-month time frame (80% of 40 (ex 32) enrolled); b) study retention: retention of >80% of participants through all assessment periods, c) adherence to the acupressure administration protocol: advanced practice providers will record at least 90% of all acupressure sessions in the REDCap database and medical record.

Data Analysis Aim 2. Descriptive data will be generated for the outcomes detailed in Table 2: Aim 2 by treatment group. Given the feasibility goal of this study, we will not conduct formal statistical tests of association between the two treatment groups, but we will provide descriptives by groups and measures of variability. These statistics will inform us of data trends. Descriptives will be generated based on the intent to treat principle.

Data Analysis Aim 3. Parental satisfaction with acupressure as an additional non-pharmacologic intervention will be reported as means with standard deviations and percentiles of the CSQ8 scores within each category of the following: excellent, good, fair and poor. Provider and staff acceptability of acupressure as an additional non-pharmacologic treatment will be measured with the Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM). These measures will be reported as frequency distributions and proportions (% of AIM scores, % of IAM scores, and % of FIM scores).

Table 2: Assessment Measures

Outcomes	Measures	Time Point
Aim 1 Feasibility of Acupressure Protocol	Demographics: age median & interquartile range, weight median & interquartile range, % male/female, % race (black, white, Hispanic)	Duration of study
	Recruitment Metrics: % of eligible patients enrolled, % of patients prematurely terminating treatment, % of patients completing all study assessments, % of data collection procedures completed, % of missing medical record data	Duration of study
	Enrollment Metrics: % of eligible patients enrolled, % of patients prematurely terminating treatment, % of patients completing all study assessments, % of data collection procedures completed, % of missing medical record data	Duration of study

	Acupressure Administration: % sticker displacement & reapplication, adverse events Infant Activity, Non-Pharmacologic Treatments	Every 24-72 hours Every 6 hours
Aim 2 Acupressure Efficacy	Duration of Medication Exposure (days): median, interquartile range Duration of Wean Phase (days): median, interquartile range Duration of Mechanical Ventilation (days): median, interquartile range Total Medication Equivalents (mg/kg/pt): median, interquartile range Hospital Length of Stay (days): median, interquartile range Exposure to adjunct medications: median, interquartile range WAT-1 Scores: median, interquartile range psCAM-ICU Scores: median, interquartile range RASS Scores: median, interquartile range FLACC Scores: median, interquartile range	Duration of study Duration of study Duration of study Every 24 hours Duration of study Every 24 hours Every 6 hours Every 12 hours Every 2-4 hours Every 4 hours
Aim 3 Acceptability	Parental Satisfaction: CSQ8 means, SD, % scores Staff/Provider Acceptability: % AIM scores, % IAM scores, % FIM scores Qualitative Feedback	Duration of study Completion of Study Every 24-72 hours

11.0 Privacy/Confidentiality Issues

There is a risk of breach in confidentially; however, steps will be taken to decrease this risk as all data will be collected by the PI from the medical record then input into REDCap. Databases will only be accessible by members of the study team, password protected, and a confidential project identification number will be assigned. This information will include recruitment metrics (Aim 1), and parental satisfaction and acceptability data (Aim 3) including the following surveys: CSQ8, AIM, IAM, FIM and qualitative.

Recruitment of parents will take place during routine care. Confidentially and privacy will be ensured by the PI and healthcare providers when discussing the study and potential participation.

12.0 Follow-up and Record Retention

All data will be stored in the Vanderbilt University Medical Center REDCap. Only authorized study personnel will have access to the password protected data tracking system and the project will have an identification number assigned. Paper copies of research records such as completed paper consent forms and surveys will be kept in a designated binder and locked cabinet in a restricted access office at Vanderbilt University Medical Center or uploaded into REDCap. The PI will manage data including quality assessment (completeness and accuracy) to ensure all variables are captured and entered into REDCap appropriately. At completion of the study, the PI will archive paper copies of research records in accordance with Vanderbilt University Medical Center's policy and as recommended by the institutional review board (IRB).

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