Protocol

Time to accurate Heart Rate on Neonatal Outcomes

Sponsor:

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Purpose and Background

The goal of this trial is to compare the time to first heart rate displayed for iRes Warmer with ResusView and using iRes Warmer without ResusView when used in the resuscitation (e.g. CPR or breathing assistance) of premature newborns (23 to 32+6 weeks gestation).

Our primary hypothesis is that the use of electrocardiogram (ECG) leads during resuscitation of premature infants born at 23+0 to 32+6 weeks gestational age using iRes Warmer with ResusView will display a heart rate within 30 sec of lead placement and allow for earlier response to low heart rate by clinical team during transition following delivery. We hypothesize that the use of ECG leads during resuscitation of premature infants born at 23+0 to 32+6 weeks gestational age using iRes Warmer without ResusView will display a heart rate on a standalone ECG monitor at or after 30 seconds of placement of leads leading to delayed intervention to low heart rate.

Our experience with the current GE ECG standalone monitor has shown the time to pick up a heart rate is delayed 30-60 seconds from time of lead placement. It has not been established whether a faster ECG algorithm would have an impact on neonatal resuscitation outcomes. Therefore, we will conduct a randomized trial to determine whether the new algorithm would provide a heart rate sooner and have an impact on neonatal resuscitation of infants born at 23 to 32+6 weeks gestational age.

The American Academy of Pediatrics Neonatal Resuscitation Program recommends the use of a cardiac monitor in infants that need resuscitation [1]. Previous trials have looked at how the availability of electrocardiogram (ECG) affects clinical interventions in the delivery room [2] and point toward the need for further evaluation of ECG use in preterm infants. Accurate, reliable, and fast heart rate (HR) display ensures interventions are delivered immediately. Ineffective HR assessment can increases the risk of hypoxic injury and infant mortality. [3] Standalone ECG monitors currently in use with the iRes Warmer without ResusView has a delay in displaying heat rate from the time of lead placement greater than 30 seconds from time of lead placement. [2]

Subjects

40 infants delivered at 23+0 to 32+6 weeks EGA will be enrolled from Sharp Mary Birch Hospital for Women & Newborns. Premature newborn from 23+0 to 32+6 weeks gestation meeting inclusion criteria and consented prior to delivery at Sharp Mary Birch will be considered for enrollment until we reach our target of 40 newborns over the one-year period. This study will include subjects from a vulnerable population and will safeguard subjects through implementation of an augmented consent process with added time and simplification of consent language.

Inclusion Criteria

- Infants who are delivered to mothers 16 years of age or older
- Infants delivered at 23+0 to 32+6 weeks EGA (estimated gestational age) based on the best obstetric estimate at the time of delivery.
- Infants without known congenital malformations prior to delivery
- Antenatal consent

Exclusion Criteria

- Infants who are delivered to mothers under the age of 16 years of age
- Known congenital anomalies of newborn prior to delivery
- Cardiac defects other than small VSD and PDA
- Declined consent
- iRes Warmer with ResusView not available at time of delivery
- Multiples of more than two

Methods and Procedures

This is a prospective interventional randomized control trial. Infants born between 23 weeks and 32+6 gestational age will be randomized using a computer generate allocation sequence stratified by gestational age. Randomization cards will be placed in opaque envelopes. For the intervention group, the care team will use the Panda iRes Warmer with ResusView Bed during resuscitation interventions in the first 10 minutes of life. During use of the iRes warmer, standard nursing care of an infant on a radiant warmer will be followed. Participants assigned to the control group will receive interventions using the same model Panda bed without ResusView and a standalone cardiac monitor. There is no minimum time for monitoring, and the maximum time depends on clinical determination for use of HR feature for each resuscitation event. Data including the infant's gestational age, ECG monitor type and activities that occurred during resuscitation will be recorded for the first 10 minutes of life.

Currently, all infants taken to the resuscitation suite have recordings of heart rate, oxygenation, and airway pressure, along with simultaneous video recording. These recordings are reviewed monthly as part of our quality improvement process. Routine use of ECG monitoring may be used per physician preference. Therefore, the placement of electrodes (ECG) at the time of birth will not be an additional component of clinical care. Infants born between 23+0 – 32+6 weeks EGA are representative of the population that is expected to use the device in clinical practice.

Primary outcome:

1. Time to heart rate display [Time frame: 1 minute]
    a. Time to heart rate displayed on monitor following lead placement

Secondary outcome:

1. Time to first change in FiO2
    a. Time to first increase or decrease in FiO2 from first heart rate display
2. Time to first change in airway pressure
    a. Time to first increase or decrease in airway pressure from first heart rate display
3. Time to initiation of Positive Pressure Ventilation (PPV)
    a. Time to start PPV following first heart rate display

Exploratory Outcomes

4. Time of electrode placement [Time frame: 0- 10minutes]
    a. Time to application of ECG electrodes from time of birth
5. Is the rhythm recognized? [Time frame: 0- 10minutes]
    a. Is the rhythm recognized Y/N
6. Time to rhythm recognition [Time frame: 0- 10minutes]
    a. Measure at what time the Warmer displays the baby's cardiac rhythm

Subject Identification, Recruitment and Informed Consent

Pregnant women who are dated by their earliest ultrasound or last menstrual period at 23+0 – 32+6 weeks gestation will be identified, recruited and consented from the labor and delivery floor or perinatal special care unit. Parents will be approached for consent prior to delivery. Recruitment of prospective subjects will occur through pre-screening electronic medical records from pool of inpatient mothers admitted at 23+0 to 32+6 EGA to Sharp Mary Birch Hospital for Women & Newborns.

The primary investigator, a delegated sub-investigator or research associate will obtain consent prior to any research procedure. The mother, or legally authorized representative must sign the informed consent document. Mother, will sign a HIPAA authorization providing access to the child's medical records for data collection purposes. The subject's legally authorized representatives will be given ample time to read the informed consent, ask questions of the research team, and discuss the study with their family and/or the subject's physician. The informed consent process will be documented in the electronic medical record and copies of the signed and dated consent will be given to the subject's representatives, placed in the subject's physical chart, and stored in a locked cabinet in the offices of the Neonatal Research Institute.

Waiver of Informed Consent and Waiver of HIPAA Authorization for Pre-Screening

Waivers of informed consent and of HIPAA Authorization are requested for pre-screening medical records. The use or disclosure will not adversely affect the rights and welfare of the subjects. This research protocol cannot be conducted without partial waiver because investigators would be unable to identify eligible subjects. This will involve no more than minimal risk to the privacy of subjects. Only research investigators/assistants will access PHI for eligibility and screening purposes.

PHI that will be accessed for screening will be identifiable on research-related forms by a study number. We will take the following precautions to maintain the confidentiality of identifiable subject information. We will also keep subject's identity separate from their data on a Master log and coded. PHI will not be used or disclosed to any other person or entity, except as required by law.

1. Paper-based records will be kept in a secure location and accessible only to persons involved in the study
2. Computer-based files will be available only to persons involved in the study through the use of access privileges and passwords.
3. Prior to accessing any PHI, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable health information
4. Whenever feasible, identifiers will be removed from study-related information
5. PHI will not be disclosed or re-used for other purposes
6. Collect only the minimum necessary subject identifiers.
7. Limit physical access to any area or computer that contains subject identifiers.
8. Limit electronic access to any computer that contains subject identifiers.
9. Avoid storing subject identifiable data on portable devices (such as laptop computers, digital cameras, portable hard drives including flash drives, USB memory sticks, iPods or similar storage devices) as these devices are particularly susceptible to loss or theft. If there is a necessity to use portable devices for initial collection of subject identifiers, the data files must be encrypted, and subject identifiers transferred to a secure system as soon as possible.
10. Remove necessary subject identifiers from data files, and encrypt data files if stored electronically. Identifiers will be stored in a physically separate and secure location from the data files, and associated with the data files through a key code that is also stored in a separate and secure location.
11. Use only secure modes of transmission of data; subject identifiers submitted over a public network will be encrypted.
12. Review the Information Security & Privacy website for additional recommendations on how to best secure confidential data.
13. If there is an inadvertent breach of confidentiality of the research data which causes harm or places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm), the Lead Researcher will report this to the IRB through the electronic Unanticipated Problems reporting process within 5 working days of the researcher becoming aware of the event.
14. Assurance that the privacy of the subject will be maintained by avoiding discussions about the patient within earshot of other patients or non-participants.

Compensation of Subjects and Costs

The study sponsor will provide the iRes Warmer with ResusView to Sharp Mary Birch Hospital for Women & Newborns at no cost for a 6 month period. There are no additional costs to study participants. Study Participants and health plan/insurance Company are responsible for the cost of participants' hospitalization and standard clinical care provided. Participants will be responsible for co-pays and deductibles in the same way as outside of a clinical trial.

Data Collection and Analysis

Study data will be maintained using REDCap data management system and managed by Sharp's Neonatal Research Institute. All collected variables are listed in the CRF forms (see attached). We will

describe / compare baseline demographics, clinical outcome variables between the two groups using univariate and appropriate bivariate analysis. A future detailed statistical analysis plan will be made available prior to completion of the trial.

Privacy, Confidentiality and Data Monitoring

All SAEs will be reported within 72 hours of discovery of event, to the PI and the IRB (if applicable) at the Sharp Data center.

Any Unexpected AE or Serious Deviation will be reported within 7 days of discovery of event to the Sharp Data Center.

Unexpected events that are Not Serious are reported not more than 14 days after the PI first learns of the event. All other expected outcomes of prematurity, i.e. BPD, IVH grades 1-4, ROP, NEC will be collected in the electronic database and reviewed in interim reports.

The study will meet FDA monitoring requirements by: Monitor data quality through routine review of submitted data to identify and follow-up on missing data, inconsistent data, data outliers, and potential protocol deviations that may be indicative of systemic or significant errors in data collection, study conduct.

FDA Requirements for investigational devices:

(1) The investigator will label the device in accordance with FDA regulations for investigational devices. (2) The investigator will comply with FDA requirements for records and reports. (3) The investigator will not market or promote the device.

Potential Benefits

There may or may not be direct benefits to participants in this study. We hope the information we learn will help babies born prematurely in the future.

Potential Risks

Loss of confidentiality: All data will be safeguarded in accordance with the Health Insurance Portability and Accountability Act (HIPAA) and the principles and practices of strict confidentiality. Data will be maintained by numerical code without personal identifiers. Computer-based files will be available only to persons involved in the study with access privileges and password protection. However, there is still a potential risk of loss of data and privacy. As with any study, there may be risks that currently are unforeseeable.

Only research team members (with appropriate research training relevant to protection of human subjects) shall have access to the study's databases.

All risks with conducting this study are associated with prematurity including severe IVH, death, retinopathy of prematurity, chronic lung disease and other lung problems. There should be no more risks for babies in this study than are possible for any Extreme Low Birth Weight (ELBW) baby needing resuscitation. However, as with all research, there may be risks that are unknown at this time.

References

1. *Neonatal Resuscitation*. Vol. 7th edition. 2016, Elk Grove Village, IL: American Academy of Pediatrics.
2. Katheria, A., et al., *A pilot randomized controlled trial of EKG for neonatal resuscitation.* PLoS One, 2017. **12**(11): p. e0187730.
3. Johnson, P.A. and G.M. Schmölzer, *Heart Rate Assessment during Neonatal Resuscitation.* Healthcare (Basel), 2020. **8**(1).