Study Protocol approved by the UPMC Hamot IRB on 10/14/2015 and by the University of Pittsburgh IRB on 4/28/2016

Brief Title: A Pilot Study to Evaluate Patient Tolerance and Nursing Ease-of-use of a Novel Hearing Protection Device (NEATCAP)

Identifiers: NCT02744066

Unique Protocol ID: PR016010220

Research Proposal

A Pilot Study to Evaluate Patient Tolerance and Nursing Ease-of Use of a Novel Hearing Protection Device to Reduce Exposure to Excessive Noise among Patients Undergoing Neonatal Intensive Care

Michael J. Balsan, MD[1]; Emily Hirsch, MSN, MHA, RNC-NIC[1]; Jeanne Burns, RN[1]; Fred Kimock, PhD [2]; Andrew Unger, MD[2,3]; Timothy Cooney, MS[4]

[1]UPMC Hamot Women's Hospital, Erie, PA

[2]Neatcap, LLC, Bethlehem, PA

[3]Sacred Heart Hospital, Allentown, PA

[4]UPMC Hamot Medical Center, Erie, PA

Background

There were 3,932,181 births in the United States in 2013 and 11.39% of these infants were born prematurely, delivered before the 37th week of gestation.[1] Many of these infants presented with respiratory distress requiring neonatal intensive care. An additional 25-30,000 infant were born to substance abusing mothers, requiring prolonged neonatal intensive care unit (NICU) admissions for the management of Neonatal Abstinence Syndrome, related to substance withdrawal.[2]

These populations of vulnerable neonates are at significantly higher risks of sensory and neurodevelopmental delays when compared to normal full term infants.[3] Although the genesis of these delays are clearly multifactorial, a growing body of evidence supports the theory that post-natal exposure to noise, particularly high frequency sounds, may play a significant role in these problems.[4]

The acoustic environment of the developing human fetus in utero is difficult to evaluate directly for obvious ethical reasons, but animal models afford an opportunity to examine this environment closely.[5] The developing fetus within the womb is exposed to low frequency sounds produced by the mother's body (including maternal speech), presumably important for the optimal neurosensory development.[6] However, high frequency sounds are diminished by the mother's body, effectively protecting the growing fetus from potentially adverse sound exposures.[FIG 1]

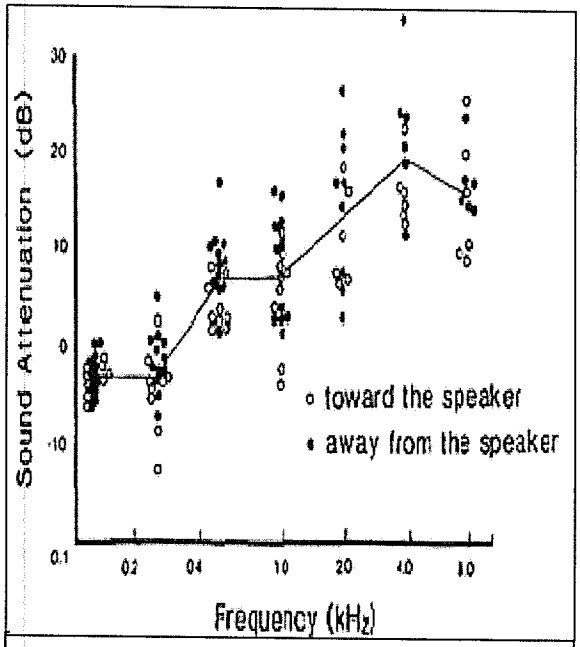

FIG 1. Sound attenuation of the pregnant sheep uterus. From Ref [5].

The acoustic environment in the NICU is radically different from that experienced in the womb. Incubators, ventilators and cardiorespiratory monitors all contain high frequency auditory alarms specifically designed to optimally alert NICU caregivers to critical changes in infant conditions, and they do so with astounding frequency. In fact, the concept of caregiver "monitor fatigue" has entered the NICU lexicon and is the subject of current quality assurance efforts by the Vermont-Oxford Neonatal Network and others.[7] These adverse stimuli have been shown to increase markers of neonatal stress, interfere with evolving normal sleep patterns and potentially contribute to auditory and neurodevelopmental deficits.[4]

As neonatal clinicians have become aware of the potential adverse effects of noise in the NICU, multiple interventions have been proposed in the past to deal with this issue. Acoustic monitors, visually alerting staff to high levels of noise in the NICU, have been trialed with limited success.[8] Ear plugs have been proposed and abandoned as ineffective and problematic, given the anatomy of the neonatal auditory canal and the non-frequency selective nature of their noise

diminution.[9] A commercially available ear muff, the "MiniMuff" has been utilized on a short term basis, but the adhesive used to fix the appliance to the skin can rapidly lead to skin irritation, prompting the manufacture's recommendation to limit the use of the device to a maximum period of 24 hours.[10] Another approach to this problem has been the multi-million dollar redesign of NICU's throughout the country, in order to provide single patient rooms. There is controversial evidence that such an approach leads to an increase, rather than a decrease in neurodevelopmental delays, potentially related to relative "sensory deprivation".[11] None of the previous proposed solutions to this issue have been shown to be practical and/or effective.

Methods

Our proposed study is a phased pilot study to evaluate patient tolerance and nursing ease-of-use of a novel hearing protection device to reduce exposure to excessive noise among patients undergoing neonatal intensive care. The study device has been engineered by NEATCAP, LLC, to provide a circumaural hearing protector ("ear muff") with a "low pass" filtering of sound, preferentially blocking high frequency sounds while transmitting low frequency sounds such as a mother's voice.[FIG 2]

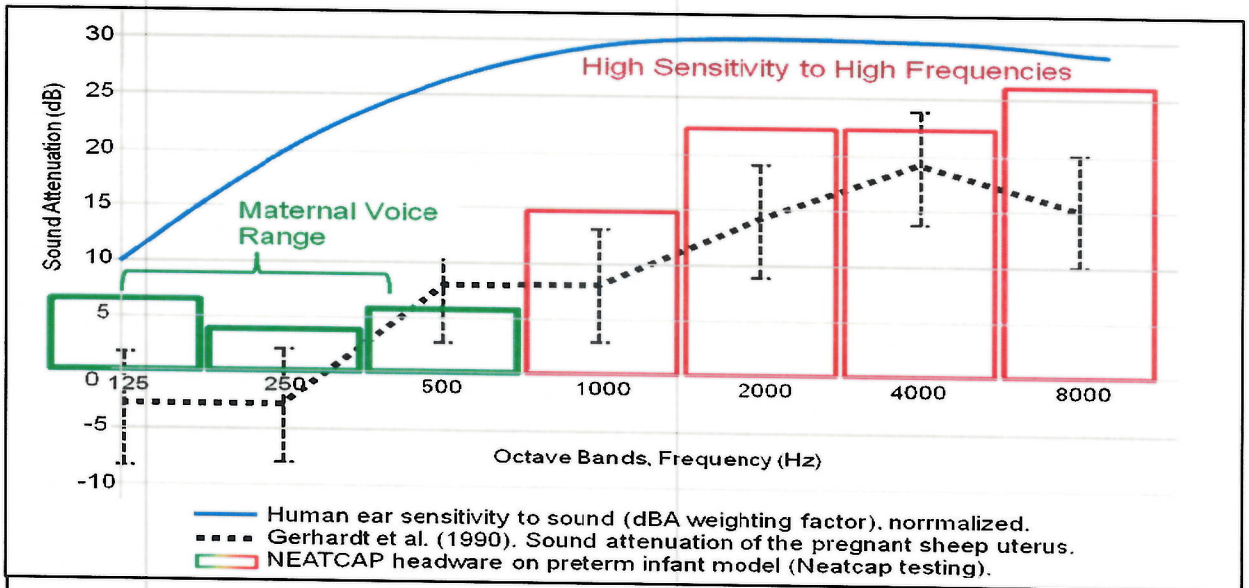

FIG 2. Human ear sensitivity to sound as a function of frequency, representative sound attenuation of pregnant sheep uterus (see also FIG 1), and bench testing results of headware device on preterm infant model.

The device employs a soft neoprene/nylon headband to fix the ear covers in place, with multiple sizes of both the ear covers and headbands to accommodate multiple sizes of infants. [FIG 3] A patent for the device is pending. Recent Food and Drug Administration rulings have waived a requirement for an Investigational Device Exemption ("IDE") for this type of device (see attached letter).

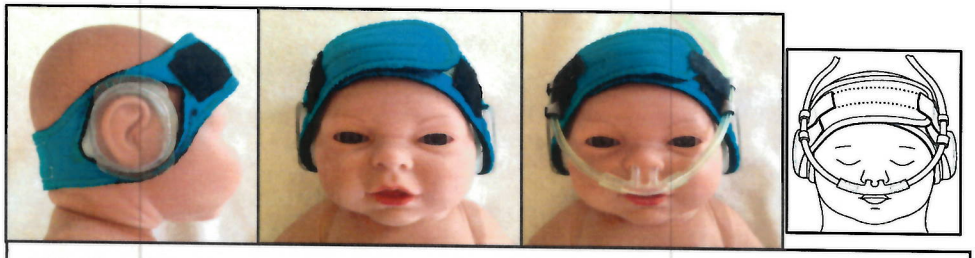

FIG 3. NEATCAP prototype noise protection device on premature infant model, illustrating circumaural ear covers, fabric band and

Phase 1 of the study will entail a 60-minute initial size and fit evaluation of the device on a convenience sample of 25 infants admitted to the NICU. The inclusion criteria for the study include study initiation during the first two (2) weeks of NICU hospitalization and written signed informed consent from the parents of the study subjects. Exclusion criteria will include: age less than 12 hours, significant cranial trauma noted on admission, congenital anomalies of the head and/or neck, hemodynamic instability requiring pharmacologic intervention and a recommendation by the attending neonatologist not to enroll the patient for any reason.

In Phase 1, the device will be applied by a single trained senior neonatal intensive care nurse with experience in recognizing distress in NICU patients. Once proper fit of the device has been assured, it will be removed and a 30 minute "time out" interval will be employed. Baseline vital signs will then be obtained (see attached data collection sheet), the device will be re-applied and repeat vital signs will be obtained at 30- and 60-minute time periods. The device will be removed after 60 minutes and a fourth set of vital signs will be obtained 30 minutes after device removal. The primary endpoint of the study will be the absence of any device-related adverse events, including evidence of skin discomfort or irritation at the site of device application, or significant sustained changes in vital signs consistent with a stress response, as outlined in Table #1.

Table #1.

Significant elevated stress is defined as persistence of any of the following in the absence of intrusive manipulations of the patient (e.g.: IV insertions, nursing care procedures, etc.) based on the Cries Score for Pain Assessment:[12]
• Temperature: >0.6°F increase in temperature above baseline.
• Respiration: > 20% increase in respirations per minute above baseline
• Pulse: >20% increase in beats per minute above baseline
• Blood pressure: >20 mm Hg increase in systolic blood pressure above baseline
• Oximetry level: >5% pulse oximeter decrease below baseline

Secondary endpoints will include NEATCAP sizing options able to fit >90% of the target population and a >80% positive response to a multi-question ease-of-use questionnaire completed by the participating NICU staff (see the attached questionnaire). The data will be stored by the Study Coordinator and will undergo statistical analysis for repeated measures by T. Cooney, MS, with subsequent review by the primary investigator and the device consultants. If no specific negative findings are identified, Phase 2 will begin.

Phase 2 will entail a 3-day evaluation of tolerance of the device, entailing a total of three (3) eight-hour-long sessions of device use on three (3) consecutive days. The study population will consist of a convenience sample of 25 neonates with identical inclusion and exclusion criteria as outlined for Phase 1. After obtaining baseline vital signs prior to each session, the bedside NICU nurse assigned to the patient will apply the device under the supervision of the data collection RN. Temperature and blood pressure data will be obtained at 3 and 6 hours of device use and heart rate, respiratory rate and oxygen saturation levels will be recorded every hour. The device will be removed after eight hours, with continued monitoring of vital signs for another eight hours after device removal. The primary endpoint of the study will be the absence of device-related adverse events, including evidence of skin discomfort or irritation at the site of device application, or sustained changes in vital signs consistent with a stress response, as outlined in Table #1. Secondary endpoints will include a >80% positive

response to a multi-question ease-of-use questionnaire by the bedside nurse assigned to the patient and acceptance of the device by the patient's parents, by direct questioning by the principal investigator. Data for Phase 2 will be stored by the Study Coordinator with statistical analysis for repeated measures by T. Cooney, MS. All data will be de-identified by the Study Coordinator prior to analysis.

Risks/Benefits

The potential study risks to subjects include skin discomfort, irritation or pain at the site of device application and/or adverse changes in vital signs associated with device usage. The potential study benefits are to provide critical data for the product development of an optimally-designed circumaural hearing protection device for patients receiving neonatal intensive care. This pilot study will potentially lead to a trial of sustained use of this device in the NICU.

References

1. Osterman, M., Kochanek, K., MacDorman, M., Strobino, D. Guyer, B. (2015). Annual Summary of Vital Statistics: 2012-2013. Pediatrics, 135, 1115-1125.

2. Patrick, SW., Davis MM., Lehmann, CU., Cooper, WO. (2015). Increasing incidence and geographic distribution of neonatal abstinence syndrome: United States 2009 to 2012. J Perinatol. 2015 Aug; 35(8):650-5.

3. NICHD Neonatal Research Network (NRN): Extremely Preterm Birth Outcome Data. http://www.nichd.nih.gov/about/org/der/banches/ppd /programs /epbo/pages/epbo_case.aspx?start=17;31;31.

4. Graven, SN., Browne, JV. (2008). Sensory development in the fetus, neonate, and infant: Introduction and overview. Newborn & Infant Nursing Reviews, 8,169-172.

5. Gerhardt, KJ., Abrams, RM. (1990). Sound Environment of the Fetal Sheep. American Journal of Obstetrics and Gynecology, 162, 282-287.

6. Gerhardt, KJ., Abrams, RM. (2000). Fetal Exposures to Sound and Vibroacoustic Stimulation. Journal of Perinatology, 20, S20-S29.

7. Ketko, AK., Martin, CM., Nemshak, MA., Niedner, M., Vartanian, RJ. (2015). Balancing the Tension Between Hyperoxia Prevention and Alarm Fatigue in the NICU. Pediatrics 2015, 136, e496-e504.

8. Liu, W. (2012). The impact of a noise reduction quality improvement project upon sound levels in the open-unit-design neonatal intensive care unit. Journal of Perinatology, 30, 489-496.

9. Turk, CA., Williams, AL., Lasky, RE. (2009). A randomized clinical trial evaluating silicone earplugs for very low birth weight newborns in intensive care. Journal of Perinatology, 29, 358-363.

10. Abujarir, R., Salama, H., Greer, W., Al Thani, M., Vlisda, F. (2012). The Impact of Earmuffs on Vital Signs in a Neonatal Intensive Care Unit. Neonatology Today, 7, 1-8.

11. Pineda, RG., Neil, J., Dierker, D., Smyser, CD., Wallendorf, M., Kidokoro, H., Reynolds, L., Walker, S., Rogers, C., Mathur, AM., Van Essen, DC., Inder, T. (2014). Alterations in Brain Structure and Neurodevelopmental Outcome in Preterm Infants Hospitalized in Different Neonatal Intensive Care Unit Environments. Journal of Pediatrics, 2014 Jan; 164(1): 52-60.

12. Krechel, SW., Bildner, J. (1995). CRIES: a new neonatal postoperative pain measurement score. Initial testing of validity and reliability. Paediatric Anesthesia, 1995; 5(1):53.