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Patient Report

Reduced frequency of apnea and bradycardia episodes caused by exposure to biological maternal sounds

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Preterm infants tend to have irregular breathing patterns due to decreased autonomic and self-regulatory abilities. This is typically characterized by brief cessation of breathing (apnea), often followed by a sudden drop in heart rate (bradycardia). In preterm infants, apnea is known to be secondary to the physiologic immaturity of the central nervous system.[1] Although mild apnea is not thought to have long-term effects, the common medical impression is that preventing multiple or severe episodes of apnea, bradycardia and oxygen desaturation is better for the baby in the long term.[2]

Preventing apnea and bradycardia episodes (ABE) becomes a greater challenge when considering the loud environmental noise typically present in a multi-bed neonatal intensive care unit (NICU). Loud noise is highly noxious for the preterm infant and can result in detrimental health effects.[3] Preterm infants are especially vulnerable to unpredictable noise due to their inability to filter and process toxic auditory stimuli. Excessive exposure to a noisy environment has been shown to negatively affect the cardiovascular and respiratory systems,[4] and increase the risk for ABE.[5]

We present a case of an extremely preterm infant who showed significant improved respiratory and cardiovascular stability when exposed to sounds of her mother's voice and heartbeat. Low-frequency maternal sounds are audible *in utero* and are thus thought to be crucial for healthy growth and development.[6] Early auditory aptitude for maternal sounds is thought to subserve a variety of developmental functions such as mother – infant bonding and language acquisition.[7] The specific effects of maternal auditory stimulation on short-term physoiological stability, however, are still unclear. This case study was conducted as part of a larger study currently underway at Brigham and Women's Hospital. The infant's mother gave written, informed consent.

Case report

A female infant was born at 26 weeks 6 days gestational age (GA) by emergency cesarean section for abruption with vaginal bleeding of approximately 1 h duration and fetal bradycardia. Birthweight was 750 g, length was 31 cm and head circumference was 31 cm. Prenatal history was benign. Ultrasound at 12 weeks appeared normal. Pregnancy was complicated by abruption on day of delivery. The mother received general anesthesia for cesarean section. The infant was born limp, pale, with a heart rate (HR) <60 beats/min. The infant was warmed, dried, stimulated and positive pressure ventilation was given. Thirty seconds of chest compressions were given. At 1 min of life, HR had risen to >60 beats/min. The infant was intubated at 5 min of life. Apgar scores were 1, 2, and 8 at 1, 5, and 10 min, respectively. The infant was given surfactant and required synchronized intermittent mandatory ventilation for 2 days, followed by continuous positive airway pressure (CPAP). The infant returned to birthweight on day of life (DOL) 8, reaching full feeds on DOL 19. On DOL 48, the infant was transitioned from CPAP to room air. Cerebral ultrasonography was normal and there were no signs of bleeding. Patent ductus arteriosus closed on medical management. Apnea of prematurity was medically managed with caffeine, and the last dose was given on DOL 57. The last apneic episode was documented on DOL 77. The infant passed brainstem-evoked response audiometry testing on DOL 80 and was discharged from the NICU on DOL 83.

Data was collected from study documents, nursing flow sheets and electronic medical records. The exact time of ABE was recorded by the bedside nurse as part of routine documentation. Apnea was defined as a cessation of breathing lasting >20 s; bradycardia was defined as a single HR drop below 100 beats/min when the infant was <34 weeks GA, and 80 beats/min when the infant was >34 weeks GA. ABE documented as being associated with feeding or gastroesophageal reflux were excluded from analysis.

The maternal heartbeat and voice were recorded from the infant's mother by an expert audio technician on the study team. The biological maternal sounds (BMS) recording was loaded onto an MP3 player connected to a specialized micro-audio system that had been validated in a previous safety and feasibility study.[8] BMS were applied by the bedside nurse approximately four times per day, in intervals of 30 min, from DOL 7 until NICU discharge. We intentionally did not set specific times for

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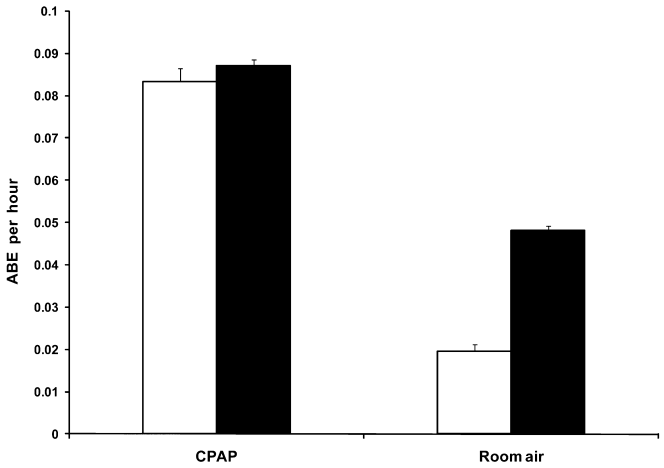

Fig. 1 Average apnea and bradycardia episodes (ABE) per hour during exposure to (□) biological maternal sounds (BMS) and (■) routine hospital sounds. A significant reduction of 59.3% in the frequency of ABE was observed during exposure to BMS when the infant was breathing room air ($P = 0.003$). A slight (4.2%) although statistically insignificant ($P = 0.14$) reduction in the frequency of ABE was observed when the infant was on continuous positive airway pressure (CPAP). Error bars, SEM.

when BMS should be applied. Instead, we instructed nurses to apply BMS four times per 24 h, when the infant was "tucked in" and ready to sleep. This included both daytime and night-time. This approach allowed us to ensure that the observed effect of BMS on ABE was representative of the entire 24 h period (rather than only certain times of the day). Three days in which BMS were not applied at all were excluded. The total hours of daily exposure to BMS were therefore much lower than the total hours of daily exposure to routine hospital sounds (RHS). To account for this difference, the frequency of ABE per hour during BMS was calculated for each day by dividing the total number of ABE during BMS by the total daily hours of BMS exposure. Similarly, the frequency of ABE per hour during RHS was calculated for every day of intervention by dividing the total number of ABE occurring during RHS by the total hours of RHS exposure. These calculations were necessary to normalize the frequency of ABE during each type of exposure while accounting for the much longer exposure time to RHS (mean, 22.77 ± 0.06 h/day) in comparison to BMS (mean, 1.23 ± 0.06 h/day).

The frequencies of ABE per hour were compared within each condition (BMS vs RHS) using a Wilcoxon signed rank test. An interesting trend was found when considering the type of ventilation support the infant received (Fig. 1). During the 40 days the infant was on CPAP, there was a slight decrease in the frequency of ABE per hour during exposure to BMS compared to RHS, although this effect was not significant ($P = 0.14$). During the 34 days the infant was breathing room air, however, ABE were reduced by 60% during exposure to BMS as compared to RHS ($P = 0.003$).

Other interesting findings were noted when looking specifically at severe ABE requiring vigorous stimulation (as per subjective nursing reports), regardless of whether the infant was on CPAP or breathing room air. None of the 39 episodes of severe ABE occurred while the infant was hearing her mother's voice and heartbeat.

Discussion

Here we report a case of a preterm infant who showed improved physiological stability when exposed to an audio recording of her mother's voice and heartbeat. This case demonstrates a significant reduction in the frequency of ABE during exposure to BMS but not to RHS. These findings suggest that the presence of maternal sounds increases the infants' physiological capacity to self-regulate, consistent with the view that external stimulation plays a role in promoting regular breathing in neonates.[9] We hypothesize that the soothing, rhythmic aspects of the maternal heartbeat,[10] along with the familiar, stimulating characteristics of the mother's voice,[11] enhanced the physiological alertness of the infant. Further studies are needed to confirm this hypothesis.

It is particularly interesting that the positive effects of BMS were observed when the infant was on room air but not when the infant was on CPAP. One possible explanation is that the BMS were partially (or perhaps entirely) masked by the loud noise generated by the CPAP device inside the incubator. It has been shown that CPAP devices in general, can generate a significant amount of noise, often exceeding 90 dBA.[12] These high levels of noise are possibly attributable to air turbulence in the upper airway. Assuming this high level of noise inside the incubator, it is very unlikely that the infant was able to clearly hear the maternal voice and heartbeat sounds, which were kept at a constant safe level of 60 dBA (equivalent to the level of normal conversation).

The absence of significant exposure effects while the infant was on CPAP could also be explained by mechanisms of natural maturation. The infant was transitioned off of CPAP at 33 weeks 5 days post-conceptual age, when her apnea of prematurity was presumably more manageable. It is therefore possible that the effective therapeutic window for BMS opens only later in gestation (at approximately 33 weeks GA) and that maternal auditory stimulation prior to that, at least in terms of reducing frequency of ABE, is ineffective due to the extreme physiologic immaturity of the central nervous system. Future investigations are needed to clarify this hypothesis.

A possible limitation of this report is that the method of data collection may not have captured the full scope of the observed cardiorespiratory events. Nurses objectively documented events based on the infant's bedside monitor, which was set to alarm whenever ABE occurred. In addition, we collected real-time data directly from the infant's cardiac monitor (Dash 3000; GE Healthcare, Waukesha, WI, USA), but these data did not have sufficient time resolution to back up the nursing documentation of ABE in the most reliable fashion. Thus, conclusions as to whether the observed decrease in ABE can be translated into clinically relevant outcomes should be made with caution.

Conclusion

There is much to learn about the effects of BMS and the development of the autonomic nervous system in the preterm infant. Because these results are based on a single patient, the capacity to

make a generalized conclusion is limited. The present case study, however, provides a glimpse of the potential benefits of using a non-invasive strategy to better envelop the infant in a more womb-like environment by compensating for the loss of exposure to the maternal voice and heartbeat while in the incubator. The present findings suggest that the implementation of recorded maternal sounds in routine NICU care should be further considered and rigorously studied.

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