Relationship between Sleep Position and Risk of Extreme Cardiorespiratory Events

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Objective To determine whether infants at sleep in the prone side positions are at higher risk for an extreme cardiorespiratory event compared with infants at sleep in the supine position.

Study design We used a case-control study to compare sleep position, determined with an accelerometer, in 116 infants during an extreme cardiorespiratory event with that in 231 matched control subjects (2 per case) who did not experience any extreme events during monitoring.

Results From calculation of adjusted ORs and 95% CIs, infants placed in the prone or side position were no more likely to experience an extreme cardiorespiratory event compared with infants at sleep in the supine position. We used conditional logistic regression to account for the matched design of the study and to adjust for potential confounders or effect-modifiers.

Conclusion These findings, coupled with our earlier observation that the peak incidence of severe cardiorespiratory events occurred before the peak incidence of sudden infant death syndrome, strongly suggest that the supine sleeping position decreases the risk of sudden infant death syndrome by mechanisms other than by decreasing extreme cardiorespiratory events detected by monitoring. *(J Pediatr 2012;161:22-5)*.

Since 1994, and on the basis of a recommendation of the American Academy of Pediatrics,[1] there has been a national public education campaign to reduce the risk of sudden infant death syndrome (SIDS). Coincident with the reported reduction in prone sleeping in this country, there has been a substantial decrease in SIDS to approximately 50% of the rate per 1000 live births that was reported before the recommendation.[2-4] Despite the success of this public health intervention, this observation immediately prompts the question of how prone sleep affects the risk of SIDS.

We previously conducted a National Institutes of Health-sponsored multicenter study of the usefulness of home monitoring in infants thought to be at increased risk for SIDS (the Collaborative Home Infant Monitoring Evaluation [CHIME]). Toward this end, we recorded cardiorespiratory data in 1070 infants for 700 000 hours to detect episodes of extremely prolonged apnea or bradycardia, because it had been presumed for many years that apnea or bradycardia was the prelude to sudden death.[5] The "at-risk" infant groups enrolled in the CHIME study included infants born prematurely (<1750 g and ≤34 weeks at birth), siblings of SIDS victims, and infants with a history of an apparent life-threatening event, in addition to a group of healthy term infants. We reported that, when compared with healthy term infants, extreme events (EEs) of apnea or bradycardia were more likely to occur only in premature infants and only before 43 weeks postmenstrual age (PMA), well before the peak incidence of SIDS, especially in infants born full term.[6]

Although our earlier findings suggested that extreme cardiorespiratory events were not immediate precursors of SIDS, it is important to test the validity of that inference. Thus, if there is no relationship between EEs and non-supine sleep position, it would strongly suggest that supine position decreases the risk of SIDS by means other than decreasing extreme apnea or bradycardia. In contrast, if there is a strong relationship, this should prompt additional study to understand this precise mechanism. The central question we addressed was whether infants in the prone position or infants in side position are at higher risk for an extreme cardiorespiratory event compared with infants in the supine position. We had a unique opportunity to answer this question because the monitors had been equipped with a sensor to track infant position, rather than relying on the report of an observer.

CHIME	Collaborative Home Infant Monitoring Evaluation
EE	Extreme event
PMA	Postmenstrual age
SIDS	Sudden infant death syndrome

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Methods

We designed a case-control study with infants previously enrolled in the CHIME study. We selected "cases" as infants who experienced at least one EE. For each case, we selected two control subjects from infants who did not experience any EE. For each of the cases, we assessed the infant's position at a period immediately before the first extreme cardiorespiratory event; for each of the two matched control subjects, we assessed the infant's position at a period comparable with the time of the case's first extreme cardiorespiratory event. As reported previously,[5] all home recordings were collected between May 1994 and February 1998, the institutional review board at each site approved the study (**Appendix**), and the parents of all subjects gave written informed consent.

The occurrence of EEs and the methods used to identify these EEs in the CHIME study were reported previously[5] and were extensively validated to reduce the possibility of technical artifact.[7] An EE was defined[5] as: apnea ≥30 seconds or a heart rate <60 bpm for ≥10 seconds (when <44 weeks PMA) or <50 bpm for ≥10 seconds. (when ≥44 weeks PMA). On the basis of these selection criteria, the cases included all 116 infants in whom a total of 653 EEs occurred during the CHIME study. For this report, those infants who had an EE were selected and matched to the control infants as follows. An infant was selected on the basis of having the first EE within 180 days from the start of monitoring. This frame was used because it was the target duration of home monitoring in the CHIME study. When there was more than one EE, only the first event was used, because the first EE, when noticed by the caregiver, might have prompted a change in care of the infant and confounded assessment of the hypothesis. Furthermore, for a given infant, sleeping position rarely changed during a particular night or between nights. Thus, the position observed in subsequent events would not be independent of the position observed in the first event, so that inclusion of many events from the same infant would not substantially add to the power of our analyses.

For control infants, epochs were obtained from the 3-minute "non-event" recording that we obtained hourly in all infants as part of our study protocol.[8]

We matched control infants with case infants in these ways: (1) gestational age at birth (all control infants had a gestational age at birth that was within 1 week of their matched case infant); (2) PMA at event (all control infants had a 3-minute non-event epoch recorded at a PMA that was within 1 week of the PMA at which the event occurred in the matched case infant); (3) time of day of event (all control infants had a 3-minute non-event epoch recorded at a time of day that was within 1 hour of the time at which the event occurred in the matched case infant); and (4) date and site of enrollment (as the last criteria for matching, when multiple potential control infants met all the aforementioned criteria, then infants were selected with the study identification numbers that were closest in proximity). Because identification numbers were assigned sequentially, by site, this process served to match, to the extent possible, site and date of enrollment. There were two control epochs from two different control infants chosen to compare with each EE for the cases. Our rationale for not using an infant as its own control was that these young infants rarely changed position during the course of their sleep.

Infant position (supine, prone, side, or indeterminate) was determined by using an accelerometer as the sensor.[8] The prone and supine positions were measured directly, and the assignment of side position was inferred by comparison with when the infant was also observed sometime during the monitoring in either the supine or prone position. Specifically, an accelerometer placed on the infant's back showed a force of plus or minus 1 g (ie, the force of gravity on a 1 g mass) when the infant was in the prone or supine position, respectively, but it showed 0 g when the child was side (neutral position) or when the accelerometer was not connected (indeterminate). Thus, registration of a change in force was confirmation that the accelerometer was indeed attached to the infant's back. When we could not confirm attachment, 0 g was considered "indeterminate." The period during which the position was determined was either the 75 seconds preceding any event for the cases or during the "non-event" recordings of control subjects.

Statistical Analysis

We examined the association between infant sleep position (supine, prone, side, or indeterminate) and being an infant with at least one EE (ie, being a case) by calculating ORs and their 95% CIs. Side and indeterminate position were combined because it was not always possible to determine whether an infant was in the side position or the position was indeterminate. We used conditional logistic regression to account for the matched design of the study and to adjust for these potential confounders or effect-modifiers: sex, age, race, birth weight, PMA at birth, being sibling of SIDS victim, being born preterm, history of apparent life-threatening event, mother's age, and mother's education. The associations were expressed as adjusted ORs with corresponding 95% CIs. In addition, we ran a model that included all first-order interactions with the aforementioned variables to explore whether there was any effect-modification with these variables.

Maternal and infant characteristics of the cases and control subjects were compared through the independent samples t test for continuous measures and the χ^2 test for categorical measures. For all tests, the type I error level was set at 0.05. All analyses were performed with SAS software version 9.2 (SAS Institute, Cary, North Carolina).

Results

The **Table** shows demographic and clinical data comparing cases and the control subjects and demonstrates no substantial differences in the groups. There were no differences in the cases and control subjects used in this

Table. Characteristics of cases and control subjects at enrollment

Characteristic	Cases (n = 116)	Controls (n = 231)
Male, n (%)	51 (44)	119 (51.5)
Race, n (%)		
Black/African American	15 (12.9)	33 (14.3)
Hispanic/Latino	27 (23.3)	53 (22.9)
White	49 (42.2)	109 (47.2)
Other	25 (21.6)	36 (15.6)
Birth weight, g (mean ± SD)	1749.1 ± 951	1752.3 ± 950.5
PMA at birth, weeks (mean ± SD)	31.8 ± 4.4	31.9 ± 4.4
PMA at recording, weeks (mean ± SD)	40.3 ± 5.0	40.5 ± 4.9
Sibling of SIDS victim, n (%)	16 (13.8)	33 (14.3)
Pre-term, n (%)	98 (84.5)	190 (82.3)
History of ALTE, n (%)	12 (10.3)	17 (7.4)
Mother's age, n (%)		
<20 years	19 (16.4)	22 (9.5)
20-30 years	49 (42.2)	112 (48.5)
30-40 years	43 (37.1)	88 (38.1)
>40 years	5 (4.3)	9 (3.9)
Mother's education, n (%)		
Less than high school	35 (30.2)	50 (21.6)
High school and higher	81 (69.8)	181 (78.4)

ALTE, apparent life-threatening event.

study compared with the original "risk" groups from which the infants were selected for the CHIME study.[5]

The **Figure** shows the percentage of cases and control subjects that were in each sleep position. When compared with the supine position, infants in the prone position were no more likely to have an EE than infants in the supine position (unadjusted OR, 1.08; 95% CI, 0.58-2.04); similarly, when compared with infants in the supine position, infants in the side or indeterminate position were also no more likely to have an EE (unadjusted OR, 1.49; 95% CI, 0.87-2.54). On the basis of multivariate analyses that accounted for all the variables aforementioned (see Methods), the odds of being a case still did not differ by position: compared with being in the supine position, infants in the prone position were no more likely to have an EE (adjusted OR, 0.91; 95% CI, 0.46-1.80); compared with being in the supine position, infants in the side or indeterminate position were no more likely to have an EE (OR, 1.3; 95% CI, 0.77-2.40).

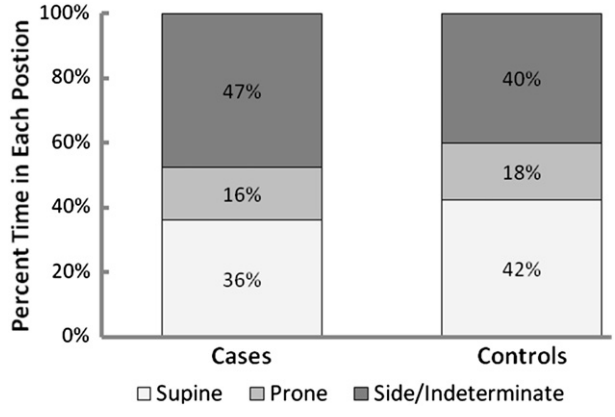

Figure. Percent of infants in each sleep position for 116 cases and 321 control subjects.

The multivariate analysis of the model with first-order interactions revealed no indication of effect modification for any of the variables considered.

Discussion

Our data show that infants placed in the prone position or in the side position are no more likely to experience an extreme cardiorespiratory event compared with infants placed in the supine position. This might have been surprising in light of: (1) the clear association between a reduction in prone sleeping position and a reduction in SIDS on the basis of autopsy and death scene investigation[4]; and (2) the common perception that the potential for having a life-threatening cardiorespiratory event is reduced when infants are sleeping in a supine position. Although the increased risk for SIDS when sleeping in a prone position seems incontrovertible, the second issue is unproven and remains a speculative mechanism for the reduction in SIDS. These findings, with our earlier observation that the peak incidence of severe cardiorespiratory events occurred before the peak incidence of SIDS,[5,6] strongly suggest that the supine sleeping position decreases the risk of SIDS by mechanisms other than decreasing the apnea or bradycardia commonly detected with monitoring. It is essential to emphasize, however, that our data do not disprove the possibility that EEs are "markers" of an infant at risk for SIDS.

It is important to comment on both limitations and strengths of the data. Our findings about supine versus prone sleeping position are consistent with the null hypothesis of no effect. However, because of statistical power considerations, we cannot eliminate the possibility of a real effect that was less than two-fold, as shown by the upper confidence limit on the adjusted OR. We also recognize that many infants were in the side or indeterminate position rather than just prone or supine; this reflects some of the ambiguity in recommendations for sleep position at the time our data were collected. However, this study represents the sole opportunity to analyze data about cardiorespiratory events in a large cohort of infants in relation to an unbiased assessment of sleep position. Furthermore, this study obviates two major problems inherent in parental reporting: (1) we are able to detect position when the infant is not being witnessed; and (2) reporting is not subject to the influence of knowing what position is recommended. Finally, because of the marked decrease in the incidence of SIDS with the simultaneously reported change in sleep position in the past 15 years, it is highly unlikely that anyone can ever conduct a study in which sleep position is deliberately altered to test the effect on a potentially lethal outcome.

To the extent that sleep position influences the risk of SIDS, our data do not support the proposition that altering the frequency of an extreme cardiorespiratory event is the mechanism by which this occurs. Regrettably, our conclusions do not readily suggest alternative mechanisms by which sleep position might reduce the incidence of SIDS. However,

our data are entirely compatible with the notion that extreme cardiorespiratory events captured by contemporary home physiologic monitoring are not linked temporally with SIDS, and this is important both for clinical decisionmaking and for future research related to SIDS. ■

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50 Years Ago in *The Journal of Pediatrics*

Some Aspects of Respiratory Problems in the Newborn

Cook CD. J Pediatric 1962;61:105-10

Fifty years ago, mortality from respiratory failure was not an unexpected outcome for a prematurely born baby. Clinicians knew all too well that shortly after birth respiratory distress would develop and worsen over the next 2 to 3 days. At this point the condition would either spontaneously resolve, or the infant would succumb to unremitting hypoxemia, hypercarbia, and acidosis.

In this review article, Cook eloquently describes the clinician's dilemma in the early 1960s. The clinical course had been described, as well as the associated physiologic and biochemical aberrations; however, "the mystery of the pathogenesis" remained unsolved. Seminal work by Avery, Mead, Finley, and Gardner had demonstrated that a deficiency of a surface active material (which Cook called AAF, or antiatelectasis factor) increased the surface tension in diseased lungs. Cook noted that the absence of animal models, as well as the assumption that the disease started before birth, stymied the study of hyaline membrane disease. Despite these limitations, he concluded that active research would lead to interventions to both prevent and treat hyaline membrane disease.

Two of the most effective therapies for preterm neonates used today—antenatal steroids to prevent respiratory distress syndrome and surfactant replacement to treat it—grew out of the investigations that Cook wrote about. Importantly, these investigations were inspired by events Cook could not have predicted when he was writing his review in 1962. Nearly a year after this review was published, Jackie Kennedy went into preterm labor at 34 weeks, and Patrick B. Kennedy was delivered via cesarean section. The baby was rushed to Children's Hospital of Boston, where undoubtedly Cook's expertise and teachings helped shape the infant's care. Unfortunately, Patrick's clinical condition gradually worsened, and, despite being placed in a hyperbaric chamber, he died after struggling to breathe for 40 hours. This tragedy gripped the nation, with reports of President Kennedy sitting at the bedside of his infant son watching as doctors employed state-of-the art treatments in the futile effort to save his son. It was exactly this drama that brought neonatal respiratory disease into the public eye, stimulated increased study of neonatal conditions, and led to the advances that Cook predicted.

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