Prospective cohort study of prone sleeping position and sudden infant death syndrome

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Studies of the link between prone sleeping position and sudden infant death syndrome have been criticised on grounds of recall bias and for not taking into account possible confounding effects. To avoid recall bias and to allow measurement of important biological factors a prospective cohort study of the cause of sudden infant death syndrome (SIDS) is being conducted. The infants included are those at high risk of the syndrome as assessed by a perinatal score. Of the 3110 members of the cohort born between January, 1988, and end of March, 1990, 23 infants later died of SIDS. Sleep position information was available for 15 of these. Matched analysis to control for the confounding effects of infant birthweight and maternal age indicated that prone sleeping position was associated with an increased risk of SIDS (OR 4·47 95% CI [1·30–15·43]). The findings are strengthened by the results of a concurrent retrospective case-control study of 42 SIDS cases in which the prone position was also associated with an increased risk of SIDS (unadjusted OR 3·45 [1·59–7·49]).

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Introduction

Despite extensive research, sudden infant death syndrome (SIDS) remains a major determinant of infant mortality in developed countries. The apparent lack of progress in this disorder is due to the failure to find, in human studies, consistent strong associations that might be putative risk factors and that might readily be altered by public health measures. However, there is increasing evidence that the prone sleeping position is related to the risk of sudden infant death syndrome. The prone sleeping position has been found to be commoner among cases than controls in retrospective work, although this relation has not always been statistically significant, with odds ratios for prone sleeping position and SIDS varying from 1·7 to 12·5.[1-11] In communities where infants rarely sleep prone, sudden infant death syndrome is uncommon.[2,12]

Clearly such findings have important implications for prevention of SIDS. Already, in some locations these findings have stimulated a change in the way babies are positioned, with—in South Australia and the Netherlands, for example—a concomitant decline in SIDS incidence.[13,14] Nevertheless, these observations and the inference that prone position might be an important causal factor in SIDS have not been received uncritically. Two important issues have been raised. The first issue is that of recall bias in the interview of bereaved parents;[15-17] prospectively collected information is required to establish the validity of the data on risk factors such as prone position in sudden infant death.[15] The second concern is that potentially important confounders, such as low birthweight and maternal education,[18] have not been taken into account in much of the previous work.

Here we present data from a prospective study on the relation between SIDS and prone sleeping position. Several likely confounders are controlled for. In addition, the strength of association between SIDS and prone or non-prone position on the basis of prospectively collected data was compared with that found by retrospective data collected on the same infants.

Methods

Tasmania, the island state of Australia, has approximately 7000 livebirths per annum, and its rate of SIDS—3·5 per 1000 livebirths—is considerably higher than that in other Australian states.[19] A prospective cohort study was started in January, 1988, to investigate the cause of SIDS in Tasmania. The six obstetric hospitals taking part cover approximately 93% of livebirths in the state. Infants born within these hospitals are assessed according to a local scoring system[20] to predict infants at high risk of SIDS. The composite score is based on maternal age, birthweight, season of birth, sex, duration of the second stage of labour, and infant feeding. Infants with a score over a cut-off point[20] are eligible for the study. The cut-off point identifies a group which represents approximately one fifth of livebirths in the state. Multiple births are also included in the study. Infants with severe neonatal disease or a major congenital anomaly and infants for adoption are excluded from the study.

Prospective cohort study

From January, 1988, until March, 1990, 3110 infants (20% of all livebirths) were eligible for the survey. 2977 (96%) of these eligible infants participated in the hospital interview and 2607 (84%) participated in both the hospital and home interviews.

Data are obtained by research assistants on three occasions. At the hospital interview conducted on day 4 of life, sociodemographic, obstetric, and perinatal data (including information on maternal nutrition and alcohol and smoking practice during pregnancy), birthweight, height, head circumference, and triceps and subscapular skinfold thicknesses are recorded. The second occasion is a home visit conducted during the fifth postnatal week, but for premature infants ($\leq$36 weeks' gestation) this visit is done at 40 weeks post conceptional age. For babies kept in hospital because of complications the home visit is delayed until the infant has been at home for at least 2 weeks. At the home visit a comprehensive questionnaire is used to elicit information on usual sleep position, usual sleep pattern, body movement during sleep, infant illness and health service attendance, pattern and type of infant feeding, parental smoking practice, child's overnight clothing and bedding, home heating and housing, and other characteristics of the infant and of parental care. Anthropometric and temperature measurements are made on the infant and a developmental assessment is conducted. The physical features of the house are noted and humidity and 24 hour max-min infant bedroom temperature on day of home visit is recorded. The third occasion is a phone interview conducted when the infant is 10 weeks old to review infant progress, illness history, feeding, and immunisation.

To collect information on sleeping position mothers are asked verbally "What position does your baby usually sleep in?". The prone position refers to the infant positions "on stomach, face to

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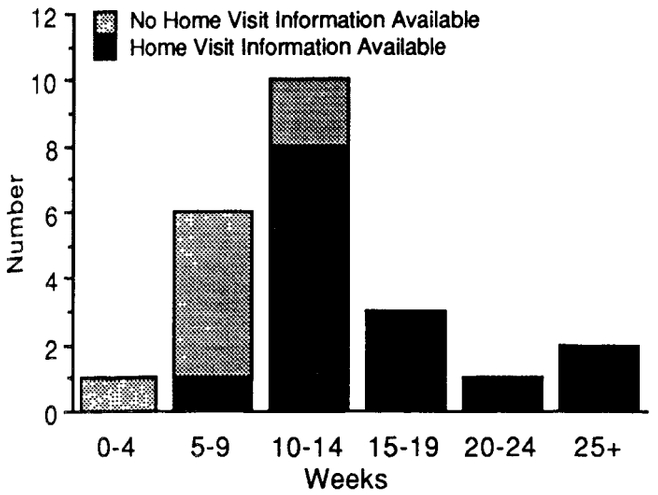

Age at death distribution of the cohort members who later died of SIDS.

side" and "on stomach, face down", whereas "on side", "on back, face to the side", "on back, face up", and "other" are classified as non-prone.

Retrospective case-control study

A retrospective case-control study has been conducted since October, 1988, with cases being all infants dying suddenly and unexpectedly in Tasmania. 2 matched controls are selected for each case, control A being matched for hospital of birth and postnatal age, and control B for hospital of birth, postnatal age, and birthweight (< 1500 g, 1500–2500 g, > 2500 g). Case information on usual sleeping position was collected by an interviewer, who administered a questionnaire to parents 5 weeks after the death of an infant. Control infants are interviewed within a month of the index case's death, and they are chosen to be the same postnatal age at interview as the SIDS infant was at death. Information on usual sleeping position is included in the data recorded.

From October, 1988, until the end of June, 1990, 42 of the 43 SIDS cases occurring during this interval were entered into the study. 83% of the controls initially chosen were interviewed. If a control infant was unable to be interviewed another appropriate infant was chosen.

All infants dying suddenly and unexpectedly in Tasmania during both study periods underwent a postmortem examination by a hospital pathologist. Toxicological and bacteriological studies were done routinely.

Statistical methods

Prospective data—The relative risk for prone sleeping position and SIDS was estimated for the entire birth cohort. To identify potential confounders data were subjected to univariate relative risk analysis.[21] The individual effect of the identified confounders was assessed by traditional stratified analysis.[22] In the third stage of the analysis a "nested" case-control analysis was done, with controls selected from the non-SIDS population of the cohort for each case. The controls were matched on birthweight, maternal age, and availability for interviews, and were born within 1 month of the case. 4–10 controls were selected for each case, depending on available matches. The matching of the cases and controls was preserved in the analysis. Multiple conditional logistic regression[22] was used on this prospectively collected case-control data to obtain an odds ratio for prone sleeping position and SIDS and to assess additional variables as potential confounders. The odds ratio and 95% confidence interval from the conditional logistic regression are logit-based.[22] All other odds ratios and relative risks use Mantel-Haenszel estimates with test-based 95% confidence intervals.[23]

Retrospective data.—Parents of 13 of the 15 SIDS cases on whom information on sleeping position was collected at 1 month of age in the cohort study answered the retrospective questionnaire section of the case-control study. Unadjusted odds ratios for usual sleeping position and SIDS outcome were calculated for these cases and controls. The same odds ratios were also calculated for the entire retrospective case-control study.

TABLE I—USUAL INFANT SLEEPING POSITION AS RECORDED AT ONE-MONTH INTERVIEW

Sleeping position	Cases	Other infants	Total
Prone, face side	9 *(60%)*	821 *(32%)*	830
Prone, face down	0 *(0%)*	16 *(1%)*	16
On side	6 *(40%)*	1579 *(61%)*	1585
On back	0	118 *(5%)*	118
Other	0	58 *(2%)*	58
Total	15	2592	2607

Results

Prospective cohort study

Among the 3110 infants born between January, 1988, and March, 1990, and who met the inclusion criteria, 23 infants had later died suddenly and unexpectedly, with no cause being identified at necropsy, as of June, 1990. The rate of SIDS for infants in the cohort study was 7·4 per 1000 livebirths. The age-at-death distribution for SIDS cases is outlined in the figure. 3 SIDS infants died before home visit age. Home information was obtained prospectively for 15 of the 20 eligible SIDS infants, giving a response rate of 75%. The overall response rate for the entire cohort was 84%. The 23 SIDS deaths represent 46% of all infants dying from SIDS in Tasmania who were born between January, 1988, and March, 1990, and who died before the end of June, 1990.

The distribution of infant sleeping position is given in table I. The relative risk for usual prone sleeping position at 1 month of age and SIDS is 3·12 (95% CL 1·18, 8·29).

Of the variables examined, infant birthweight, maternal age, and maternal smoking habit were found to be likely confounders of the relation between prone sleeping position and SIDS (table II). The individual effect on each of these factors was then assessed by stratified analysis. In the study sample 45% of low birthweight (< 2500 g) infants and 29% of normal birthweight (≥ 2500 g) infants were sleeping in the prone sleeping position at 1 month of age. The adjusted relative risk for the prone sleeping position and SIDS was 2·69 (1·05, 6·94) after stratification by birthweight; 3·43 (1·29, 9·15) after stratification by maternal age (< 20 yr, ≥ 20 yr); and 3·58 (1·21, 10·64) after stratification by maternal postnatal smoking habit (non-smoker, smoker). Maternal age and smoking habit were found to be closely related and, unlike birthweight, maternal smoking habit became non significant after controlling for maternal age.

For the multiple regression procedure, controls were matched on maternal age and birthweight, as well as on

TABLE II—RELATIVE RISKS FOR SIDS AND PRONE SLEEPING POSITION FOR SELECTED STUDY VARIABLES AMONG ALL COHORT INFANTS

Risk factor	Relative risk (95% CL)	
	SIDS	Prone sleeping position
Birthweight < 2500 g	1·50 (0 62, 3·61)	1·55 (1·38, 1·75)
Gestation < 37 weeks	1·16 (0·43, 3·12)	1·72 (1·53, 1·94)
Maternal age < 25 yr	2·53 (0·97, 6·55)	0·70 (0·63, 0·78)
Mother smoking postnatally	3·13 (1·06, 9 26)	0·88 (0·84, 0·93)
Infant food: some or all formula milk	1·50 (0·48, 4·65)	0·77 (0·68, 0·86)
Male infant sex	1·26 (0·50, 3·17)	1·03 (0·92, 1·17)
Family income < $250 per week	1·34 (0·57, 3·18)	0·77 (0·68, 0·88)
Mother's education ≤ 10th grade	0·89 (0·37, 2·15)	0·75 (0·67, 0·84)
Father's education ≤ 10th grade	1·19 (0·47, 3·00)	0·73 (0·65, 0·82)

TABLE III—CHARACTERISTICS OF CASES AND MATCHED CONTROLS, CHOSEN FROM THE STUDY COHORT

Variable	SIDS cases (n=15)	Controls* (n=116)
Mean (SD) birthweight	2643 g (778)	2866 g (745)
Mean (SD) gestation	38·0 wk (2·8)	38·1 wk (3 1)
Mean (SD) maternal age	21·7 yr (5·1)	21 6 yr (3·7)
Mothers smoking postnatally	73%	63%
Infant food: some or all formula milk	73%	73%
Male sex	67%	64%
Family income under $250 per week	60%	63%
Mother's education 10th grade or less	73%	81%
Father's education 10th grade or less	73%	80%
Sleeping position†		
Prone	9 *(60%)*	33 *(28%)*
Not prone	6 *(40%)*	83 *(72%)*

*Control infants matched on birthweight, maternal age, availability for interviews and born within one month of case.
†As recorded at the 1-month interview

availability for interviews and date of birth. Three of the variables used in selecting the cohort—infant sex, infant feeding practice, and duration of second stage labour—were not used as matching variables in selecting cases for this analysis. However, these three variables were found not to affect the relation between prone sleeping position and SIDS. A total of 116 controls were chosen for the 15 cases (table III). A comparison of the distribution of selected variables between cases and controls chosen from the cohort study is shown in table III.

Multivariate analysis was used to test the effects of the following possible confounders: infant post-conceptional or postnatal age at interview, maternal age, maternal cigarette smoking, infant sex, length of gestation, birthweight, cot type, mattress lining and type, pillow type, heater use in infant's room, breast feeding, breathing and feeding problems, history of an upper respiratory tract infection, perspiring when not febrile, visiting a doctor, developmental prone posture, sleep movement, birth as a public hospital patient, region of Tasmania, family income, and parents' education. None of these factors was a confounder of the relation between prone position and SIDS. In addition, the association between prone sleeping position and SIDS did not vary by season. Therefore, in the matched analysis on the "nested" case-control data only birthweight, maternal age, availability for interview, and month of birth were held constant. In this multivariate analysis the odds ratio for prone sleeping position at 1 month of age and SIDS is 4·47 (1·30, 15·43).

Comparison of prospective and retrospective data on sleeping position

For infants for whom both prospectively and retrospectively collected data on usual sleeping position were available, there was close agreement between both sets of data (table IV). Prone position was significantly associated with an increased risk of SIDS in both the cohort and case-control study ($p < 0.05$) (table V). The odds ratio for prone position and SIDS based on the prospectively collected data (n = 15) was similar to the odds ratio obtained from analysis of the retrospective data on the subset of SIDS cases (n = 13) on whom both prospective and retrospective data were available.

TABLE IV—PROSPECTIVE VS RETROSPECTIVE INFORMATION ON SLEEPING POSITION

Prospective study	Retrospective study		Total
	Prone	Not prone	
Prone	8	1	9
Not prone	3	1	4
Total	11	2	13

TABLE V—COMPARISON OF THE RISK OF SIDS IN RELATION TO USUAL SLEEPING POSITION IN COHORT AND CASE-CONTROL STUDIES

Sample	Percentage of infants in prone sleeping position		Unadjusted OR (95% CL)
	% cases*	% controls†	
Prospective cohort study	60 *(15)*	32	3 14 (1 18, 8·40)
Retrospective data from case-control study on cohort SIDS cases only	69 *(13)*	46	2 66 (0·64, 11 06)
Retrospective case control study	67 *(42)*	37	3·45 (1·59, 7·49)

*Numbers in parentheses refer to number of cases
†Controls from the prospective study and retrospective study as described in the text

Retrospective information on sleeping position for cohort infants on whom prospective data were not available

All the 8 cases in the cohort study without prospective information on sleeping position were in the retrospective study. 6 of these 8 infants were classified as prone by retrospective questionnaire and were also reported to have died in the prone position.

Discussion

These results support the hypothesis that prone sleeping position increases the risk of SIDS. The specific contribution of our finding is that it is based on prospective data collection and therefore is not subject to recall bias, a matter that had been of major concern in past reports. The additional finding that the association between prone sleeping position and SIDS was similar, whether prospective or retrospective information on sleeping position was used, adds weight to observations from other retrospective work on this topic. When confounding was controlled for, the estimate of association increased, the final adjusted odds ratio being 4·5. This point estimate is within the range reported in previous retrospective studies. This finding, taken in the context of the previous work, would, if a causal inference were accepted, have considerable public health implications. It is therefore important to make a judgment on the validity of these data, and to carefully assess whether the accumulated evidence establishes that there is a causal association.

The strength of these data, as stated above, is their relative freedom from measurement bias. In addition, any measurement bias that might occur is likely to bias results towards the null hypothesis. Their weaknesses are the small number of cases on which they are based and the response rate of 75% for information obtained at home visits among case families in the cohort study. The first problem will be addressed as more cases accumulate in our study. The second will be difficult to avoid in any study of this type. The overall study response rate of 84% is very high for a community-based study requiring measurements in the home, and it seems probable that families in whom a SIDS death is likely to occur will be particularly poor respondents. Nonetheless we were able to examine the retrospective data for the 5 non-respondents from the prospective study; all of them were reported to have been found prone at death and all 5 were classified as being placed usually prone by

retrospective questionnaire. The comparison of retrospective findings on respondent and non-respondent cases therefore suggests that inferences drawn from the infants on whom all data are available would not be altered if the missing data from non-respondents were available and included.

Another question that might be raised is whether the findings on a cohort consisting of infants at a slightly higher risk of SIDS than average for Tasmania can be extrapolated to the entire population. It is reassuring that the odds ratios for usual prone sleeping position and SIDS from all the subjects from the case-control study were similar to those for the cases in the cohort.

Is it reasonable to presume, then, on the basis of these findings and the previous work, that prone sleeping position is a factor in the causation of SIDS? There certainly are several plausible mechanisms that have been postulated to explain the association. These include oropharyngeal obstruction, obstructive apnoea secondary to partial nasal obstruction, and interactions between prone sleeping position and the thermal balance or arousal state of the infant[24-28] as well as others.[29-30] The benefits and disadvantages of various sleeping positions have been well discussed in a recent clinical review.[31] Our findings support the authors' view that the prone position should not be advocated for infants unless there are specific clinical indications.[32]

Hill has suggested a set of criteria for assessing causal associations.[33] Many of these criteria have been met for the association between prone position and sudden infant death syndrome. There is consistency between the findings from different studies. Furthermore, as indicated above, the association is biologically plausible. The association is strong, although a dose-response relation cannot be tested here. In addition, the analytical epidemiological studies are supported by the ecological observations, and there is evidence from our study that the putative cause precedes the effect. Nonetheless, it is possible that prone position is not a cause of SIDS but the factors that determine whether a parent places the baby prone are themselves causes of SIDS. Only a prospective randomised trial can remove this concern. Without such a trial the evidence for a causal association between prone position and the sudden infant death syndrome is compelling but not conclusive.

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From The Lancet

Quacks and quackery

Of the patronage of quacks and quackery, we shall say but little; but we would warn our lay readers, if they value their health and lives, to hesitate ere they entrust either to the hands of men whose names figure in the paragraphs and advertisements of the public papers. Nothing can be more disgusting to the educated and sensible man, than to see the editors of those journals prostituting their columns to the diffusion of ignorant and mendacious impositions; and we trust and feel convinced that before long no greater condemnation can attach itself to the reputation of a medical man, than to have his name vaunted and his deeds praised in the ignorant effusions of the political journals.

(April 24, 1841)