Key messages

- The most appropriate treatment for patients with non-insulin dependent diabetes is not known
- In this study after three years chlorpropamide, glibenclamide, insulin, and metformin were all more effective than diet alone with no differences in efficacy in reducing glycaemia
- Sulphonylureas and insulin tended to increase body weight, plasma insulin, and the risk of hypoglycaemia, whereas metformin did not affect weight, reduced insulin, and was associated with less frequent hypoglycaemia
- Long term follow up is required to determine the risk benefit ratio for each of these treatments

It is not possible to assess from the present data which treatment will be the most effective in the long term. While chlorpropamide and metformin seem to be the most effective in reducing hyperglycaemia with the least incidence of hypoglycaemic reactions, it is important to remember that in the only other large scale intervention study of diabetes, the University Group Diabetes Programme, the therapeutic allocations to a similar first generation sulphonylurea (tolbutamide) and a similar biguanide (phenformin) were ended because of a tendency to increase rather than decrease the incidence of major cardiovascular events.[17]

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Bottle feeding and the sudden infant death syndrome

R E Gilbert, R E Wigfield, P J Fleming, P J Berry, P T Rudd

Department of Epidemiology and Biostatistics, Institute of Child Health, London, WC1N 1EH
R E Gilbert, *lecturer in epidemiology*

Department of Child Health, St Michael's Hospital, Bristol BS2 8EG
R E Wigfield, *research fellow*
P J Fleming, *consultant paediatrician*

Bath Unit for Research into Paediatrics, Royal United Hospital, Bath BA1 3NG
P T Rudd, *consultant paediatrician*

Department of Paediatric Pathology, St Michael's Hospital, Bristol BS2 8EG
P J Berry, *professor of perinatal pathology*

Correspondence to:
Dr Gilbert.

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Abstract

***Objective*—To determine whether the risk of the sudden infant death syndrome is increased in bottle fed babies.**

***Design*—Population based case-control study matching for age and time.**

***Subjects*—All babies aged 1 week to 1 year dying of sudden infant death syndrome during November 1987 to April 1989 or February 1990 to June 1991 and two live controls.**

***Setting*—Avon and north Somerset.**

***Main outcome measures*—Breast or bottle feeding, sleeping position, maternal smoking, parental employment, and length of gestation.**

***Results*—Compared with being fully breast fed, the crude odds ratio for sudden infant death in fully bottle fed babies was 3·1 and for mixed breast and bottle fed babies 1·5. These odds ratios fell to 1·8 (95% confidence interval 0·7 to 4·8) and 1·2 (0·5 to 2·7) respectively after maternal smoking, parental employment, preterm gestation, and sleeping position had been adjusted for. Sleeping position partly masked the effect of being bottle fed on sudden infant death as breast fed babies were more likely to have slept prone than bottle fed babies.**

***Conclusions*—Bottle feeding is not a significant independent risk factor for the sudden infant death syndrome. Patterns of maternal smoking, preterm gestation, and parental employment status account for most of the apparent association with bottle feeding.**

Introduction

Over the past 25 years the effect of method of feeding on the risk of the sudden infant death syndrome has been analysed in 17 case-control studies[1-17] and one cohort study.[18] These studies were designed to investigate a variety of risk factors for the sudden infant death syndrome, including bottle feeding. Eleven studies[7-17] found an increased risk of sudden death in bottle fed babies and seven found no effect.[1-6 18] Reasons for such inconsistent results include different ways of measuring type of feeding and variations in the degree to which confounding factors were taken into account.

Bottle feeding is largely determined by social and cultural factors and is strongly associated with maternal smoking.[19 20] Of the 11 studies which found a positive association between being bottle fed and the sudden infant death syndrome, only two accounted for con-

founding due to social factors and preterm gestation or low birth weight,[15 17] and only one study in New Zealand[17] included maternal smoking and sleeping position as potential confounders in the analysis. In the New Zealand study the adjusted odds ratio for the sudden infant death syndrome associated with being fully bottle fed at postnatal discharge from hospital was 2·45 (95% confidence interval 1·32 to 4·55). This result led to the promotion of breast feeding as part of a national cot death prevention programme launched in 1991.[21] In Britain calls for the promotion of breast feeding in order to protect against the sudden infant death syndrome[22] have met with concern that the New Zealand findings should be supported by other studies.[23] The aim of this study was to determine whether being bottle fed has an independent effect on the sudden infant death syndrome.

Subjects and methods

We carried out two case-control studies, each lasting 18 months, in a geographically defined population in Avon and north Somerset. The study periods were from November 1987 to April 1989 and from February 1990 to June 1991. The study design was similar for both study periods and has been described.[24 25] For each baby who died of the sudden infant death syndrome we selected two babies matched for age and time from the health visitor list for the index case.

Questions about feeding practice related to how the baby was fed after birth and whether there had been any subsequent change up until death or interview. The analysis was principally based on babies categorised as fully breast fed, mixed breast and bottle fed (representing either a mix of breast and bottle feeding or a change from breast to bottle feeding), and fully bottle fed (never breast fed). Solid feeds were excluded from this classification. Potential confounding variables were recorded at parental interview. These comprised employment status (registrar general's classification I-V compared with unemployed father or unsupported mother); maternal smoking (mother smoked or did not smoke during pregnancy); sleeping position on the night before death or interview (prone, compared with side, or back); gestation ($\geq$37 completed weeks of pregnancy compared with $<$37 weeks).

We combined data for the two study periods because the adjusted odds ratios for being bottle fed were similar in both study periods. Crude and adjusted odds ratios for the sudden infant death syndrome were derived by conditional logistic regression analysis. The confounding variable which most improved the fit of the logistic regression model was chosen first and additional variables were added in a stepwise multivariate analysis. Variables which did not significantly improve the fit of the model or significantly alter the odds ratio were discarded from the analysis. The study was designed to have 80% power at a 5% level of significance to detect an unadjusted twofold increased risk of sudden infant death in fully bottle fed compared with ever breast fed babies, assuming an unmatched design and given a prevalence of bottle feeding from birth of 25%. The EGRET statistical package was used to carry out the conditional logistic regression analysis. Confidence intervals were derived from standard errors of maximum likelihood estimates.

Results

A total of 107 sudden infant deaths occurred in the study area during the two study periods. Nine babies who died of the sudden infant death syndrome were excluded from the analysis because of insufficient data, but they did not differ from the group studied.[25 26] The mean age of the 98 babies dying of the sudden infant death syndrome who were included in the analysis was 103 days (5th to 95th centiles: 27-218 days). Sixty seven of the babies died during November 1987-April 1989 and 31 died during February 1990-June 1991. The large fall in the incidence of the sudden infant death syndrome in the second period seemed to be associated with local and national publicity about the increased risk of the sudden infant death syndrome in babies who sleep prone.[25]

The table gives the number of babies in each feed group and the crude and adjusted odds ratios. Analysis of the control group showed that fully breast fed babies were more likely to have non-smoking mothers (35% (46/131) *v* 19% (12/62) smoking mothers, P=0·002); to have fathers in employment (32% (56/176) *v* 15% (3/20) unemployed fathers or unsupported mothers, P=0·2); to be term babies (31% (59/192) *v* 0% (0/4) preterm P=0·3); and to have slept prone (34% (32/93) *v* 25% (25/100) slept on side or back, P=0·3).

We tested for an interaction between the adjusted odds ratio for the sudden infant death syndrome (any breast feeding compared with fully bottle fed) and the following variables using a multiplicative model: first and second study period (P=0·3; χ^2=2·4 df=2); maternal smoking (P=0·8; χ^2=0·53 df=2); and prone sleeping position (P=0·4, χ^2=0·80 df=1). The proportion of fully breast fed control babies who slept prone fell from 68% (26/38) to 32% (6/19) between the two study periods and the proportion who were mixed or fully bottle fed fell from 54% (50/93) to 26% (11/43).

We repeated the analysis using alternative categorisations for the type of feed. The odds ratios for the sudden infant death syndrome for bottle fed babies compared with babies who were ever breast fed was 2·3 (95% confidence interval 1·3 to 4·0), falling to 1·7 (0·7 to 3·7) after the confounders listed in the table were adjusted for. The mixed breast and bottle fed category was further subdivided into babies who were given both breast and bottle feeds beyond 28 days of age and babies who had been switched from breast to bottle before 28 days of age. The adjusted odds ratios for these categories were 1·0 (0·4 to 2·6; 20 cases, 46 controls) and 1·5 (0·5 to 4·5; 19 cases, 39 controls) respectively (χ^2 test for trend for four level categorisation, P=0·17).

Matched, crude and adjusted odds ratios for the sudden infant death syndrome associated with being bottle fed

Type of milk feed	No (%) dying of sudden infant death syndrome (n=98)	No (%) of controls (n=196)	Odds ratio (95% confidence interval)			
			Crude	Adjusted for sleeping position	Adjusted for sleeping position and maternal smoking	Adjusted for sleeping position, maternal smoking, gestation, and employment status*
Fully breast fed	17 (17)	59 (30)	1·0	1·0	1·0	1·0
Mixed breast/bottle	39 (40)	85 (43)	1·5 (0·8 to 3·0)	1·7 (0·8 to 3·5)	1·4 (0·7 to 3·0)	1·2 (0·5 to 2·7)
Fully bottle fed	42 (43)	52 (26)	3·1 (1·5 to 6·3)	3·3 (1·4 to 7·4)	2·4 (1·0 to 5·9)	1·8 (0·7 to 4·8)
P value†			0·005	0·012	0·12	0·44‡

*Analysis based on 98 sudden infant death syndrome victims and 190 control babies because of missing data.
†Based on likelihood ratio statistic for the addition of type of feed to the logistic regression model, two degrees of freedom.
‡χ^2 for trend=0·23.

Discussion

Babies who had been fully bottle fed from birth seemed to be at greater risk of the sudden infant death syndrome than babies who had been fully breast fed. However, this effect was not significant once confounding due to the prone sleeping position, maternal smoking, parental unemployment, and preterm gestation had been taken into account. Sleeping prone was an important negative confounder, being weakly associated with breast feeding in the control group (P=0·3) and strongly associated with the sudden infant death syndrome.[24 25] More breast fed babies may have slept prone because their mothers were more likely to adhere to previous advice to put babies to sleep prone. However, mothers who breast fed and those who bottle fed responded similarly to the publicity about the risks associated with prone sleeping. Alternatively, babies who are breast fed may be more likely to fall asleep prone on or at the side of the mother after feeding.

The crude association between being bottle fed and the sudden infant death syndrome was greatly reduced after maternal smoking, employment status, and preterm gestation were adjusted for. There was a trend for the risk of the sudden infant death syndrome to increase with the amount of bottle feeding, but this was not significant. Inclusion of more precise measurements of social and cultural determinants of bottle feeding would probably have further reduced the effect of being bottle fed on the sudden infant death syndrome. The importance of residual confounding due to social and cultural factors is likely to be greater if one type of feeding is particularly uncommon. For example, in the New Zealand study only 15% of control babies were fully bottle fed. In this relatively unusual group, bottle feeding may have been associated with specific social or cultural characteristics that may not have been included in the analysis of confounding factors.[17]

Although we did not find that bottle feeding was significantly associated with an increase risk of the sudden infant death syndrome, our results are consistent with an adjusted odds ratio for sudden infant death (fully bottle fed compared with ever breast fed) of up to 3.7. Larger studies may be able to distinguish a small independent effect of being bottle fed. However, the interpretation of the relation between bottle feeding and the sudden infant death syndrome should take account of two theoretical considerations which work in different directions. Firstly, the apparent effect of being bottle fed on sudden infant death may be the result of residual confounding due to social and cultural factors even after controlling for measures of these factors in the analysis. Secondly, being bottle fed may lie on a causal pathway between social and cultural factors and the sudden infant death syndrome; adjustment for these factors may therefore mask a real effect of being bottle fed on sudden infant death.

From a public health perspective promotion of breast feeding to protect against the sudden infant death syndrome cannot be justified without clear evidence of an independent effect from a range of studies. Nevertheless, there is sufficient evidence of the nutritional and immunological advantages of breast milk to justify the promotion of breast feeding as the optimal method of early infant feeding in both preterm[27-29] and term[30 31] babies in industrialised countries.

Key messages

- There is no clear evidence that breast feeding protects against the sudden infant death syndrome
- Bottle fed babies are more likely to have mothers who smoke, to be born preterm, and to come from poorer families, factors which are in themselves linked with the sudden infant death syndrome
- Inclusion of maternal smoking, preterm gestation, and parental unemployment in the analysis substantially reduced the association between risk of sudden death and being bottle fed
- Being fully bottle fed is not a significant independent risk factor for the sudden infant death syndrome

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