Effect of breast feeding in infancy on blood pressure in later life: systematic review and meta-analysis

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Abstract

Objective To determine whether breast feeding in infancy compared with bottle feeding formula milk is associated with lower mean blood pressure at different ages.
Design Systematic review.
Data sources Embase, Medline, and Web of Science databases.
Study selection Studies showing the effects of feeding in infancy on blood pressure at different ages.
Data extraction Pooled mean differences in blood pressure between breast fed infants and those bottle fed formula milk, based on random effects models.
Data synthesis The pooled mean difference in systolic blood pressure was −1.10 mm Hg (95% confidence interval −1.79 to −0.42 mm Hg) but with significant heterogeneity between estimates ($P<0.001$). The difference was largest in studies of <300 participants (−2.05 mm Hg, −3.30 to −0.80 mm Hg), intermediate in studies of 300-1000 participants (1.13 mm Hg, −2.53 to 0.27 mm Hg), and smallest in studies of >1000 participants (−0.16 mm Hg, −0.60 to 0.28 mm Hg). An Egger test but not Begg test was statistically significant for publication bias. The difference was unaltered by adjustment for current size and was independent of age at measurement of blood pressure and year of birth. Diastolic blood pressure was not significantly related to type of feeding in infancy.
Conclusions Selective publication of small studies with positive findings may have exaggerated claims that breast feeding in infancy reduces systolic blood pressure in later life. The results of larger studies suggest that feeding in infancy has at most a modest effect on blood pressure, which is of limited clinical or public health importance.

Introduction

It has been postulated that nutrition early in life may programme subsequent blood pressure. The influence of breast feeding is of interest because of the differing composition of breast milk and formula milk, particularly the sodium and fatty acid content. Until the 1980s the sodium content of breast milk in Western countries was much lower than that of formula milk.[1 2] Low sodium intake in infancy has been related to lower levels of blood pressure both in the short term and in the long term.[3 4] Long chain polyunsaturated fatty acids are present in breast milk but not in formula milk. These play an important part in the vascular endothelium and, when given as nutritional supplements, seem to reduce blood pressure in adults and children.[5–8]

Small observational studies suggest that breast feeding may be related to noticeably lower blood pressure in childhood.[9–11] Similar conclusions were reached by a follow up study of participants in a randomised controlled trial of feeding in preterm infants.[12] Not all published studies have reported an association.[13] We performed a systematic review to examine whether there are consistent mean differences in blood pressure between adults who were initially breast fed or bottle fed with formula milk.

Methods

We searched Embase, Medline, and Web of Science databases for publications on the effects of feeding in infancy on blood pressure. The electronic search (completed March 2003) identified 339 references. Of these, 29 papers were considered relevant because either the abstract indicated that blood pressure had been measured in different infant feeding groups or because the data were provided. For all studies we sought the difference in systolic and diastolic blood pressure between those exclusively breast fed and those exclusively bottle fed, adjusted for current age and sex (if appropriate) and for height and body mass index. In studies including different ethnic groups, we sought additional adjustment for ethnicity. After obtaining data from the studies and further review there were, overall, 26 estimates of systolic blood pressure and 23 estimates of diastolic blood pressure (see bmj.com for details).

Statistical analysis and study quality

In the meta-analysis we used the mean difference in systolic blood pressure between infant feeding groups (breast fed and bottle fed)and the standard error of the difference from individual studies. Because heterogeneity was noticeable, we produced pooled estimates of the difference in systolic blood pressure using random effects models. Publication bias was assessed with funnel plots.[14] Begg and Egger tests were also performed.[15 16] Analyses were carried out after stratifying by study size in three groups chosen a priori: less than 300 participants; 300 to 1000 participants; and more

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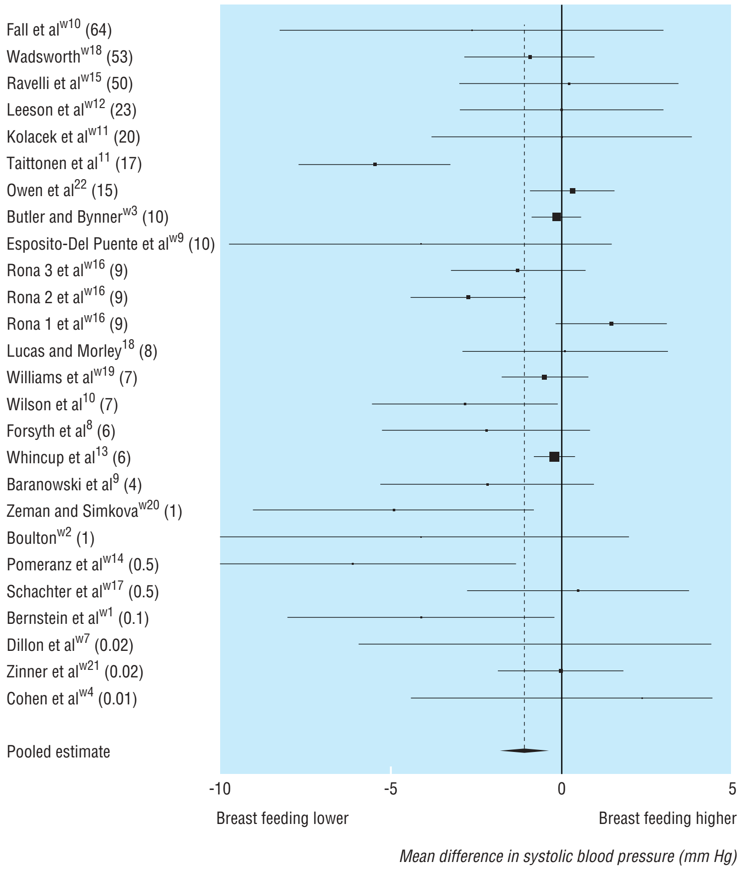

Mean differences in systolic blood pressure (95% confidence intervals) between breastfed and bottle fed participants. Box area proportional to inverse of variance, with horizontal lines showing 95% confidence intervals. y axis in ascending order of mean age (years) at which blood pressure was measured. Dashed vertical line and diamond (95% confidence interval) is pooled estimate based on a random effects model

than 1000 participants. We explored whether there were differences between age groups based on the mean age of the sample (infants ≤ 1 year, children > 1 to 16 years, adolescents and adults > 16 years), dates of birth (including whether born before or after 1980), the impact of ascertaining infant feeding status in infancy or by parental questionnaire at least three years after birth, and the difference in effect size between studies that reported on the association between infant feeding and blood pressure and those that did not. The effect of adjustment for current body size (height and body mass index) was also examined in 10 studies (12 observations), with data before and after adjustment.

We used sensitivity analyses to examine the effects of different methods of ascertaining exposure and to examine the effects of excluding groups that used mixed feeding methods. It was not possible to distinguish formally on quality of blood pressure measurement (nearly all studies used automated machines) or on response rates, which were not provided for many studies.

Results

From 24 studies we obtained 26 mean differences in systolic blood pressure and 23 in diastolic blood pressure (see bmj.com). All were observational studies, except for one randomised controlled trial in preterm infants. Eight observations on systolic blood pressure were in infants, 12 were in children, and six were in adults (figure). In a random effects model including all studies, mean systolic blood pressure was lower in breastfed participants than in bottle fed participants (−1.10 mm Hg, 95% confidence interval −1.78 to −0.42 mm Hg). We found noticeable heterogeneity between studies ($\chi^2 = 59.4$, df = 25, $P < 0.001$). No consistent difference was, however, found either between the three age groups (P = 0.601) or between studies in participants born before and after 1980 (P = 0.832, table).

Studies that reported noticeable and statistically significant differences in blood pressure between feeding groups were mostly small, raising the possibility of publication bias (see figure). This was shown by a funnel plot. The Egger test was significant (P = 0.033) for publication bias but not the Begg test (P = 0.186). The estimate of effect size decreased with increasing study size; test for trend between groups P = 0.046 (table). However, a test for trend with study size treated as a continuous variable, was not significant (P = 0.209). In 10 studies (12 observations) in which we were able to examine the effect of adjustment for current body size, the difference was similar both before and after adjustment.

Mean diastolic blood pressure showed no noticeable difference between breastfed and bottle fed groups (table). In a random effects model, breastfed participants had similar mean diastolic blood pressure

Random effects meta-analyses by subgroup (study size, age group, and of those born before and after 1980)

Subgroup analysis	No of estimates of blood pressure: Systolic blood pressure	No of estimates of blood pressure: Diastolic blood pressure	No breast fed, No bottle fed	Mean (95% CI) difference in blood pressure, P value: Systolic blood pressure	P value	Diastolic blood pressure	P value
By study size							
<300 participants	13	11	681, 798	−2.05 (−3.30 to −0.80)	0.001	−0.53 (−1.52 to 0.46)	0.295
300-1000 participants	9	8	3131, 1995	−1.13 (−2.53 to 0.27)	0.112	−0.40 (−1.52 to 0.72)	0.485
>1000 participants	4	4	4659, 8499	−0.16 (−0.60 to 0.28)	0.480	−0.24 (−0.55 to 0.08)	0.142
By age group							
Infants (≤1 years)	7	5	269, 539	−1.43 (−3.69 to 0.84)	0.217	−0.83 (−2.88 to 1.22)	0.427
Children (>1 to 16 years)	13	13	4205, 9542	−0.78 (−1.48 to −0.07)	0.031	−0.37 (−0.93 to 0.18)	0.188
Adults (≥17 years)	7	6	4194, 1530	−1.75 (−3.51 to 0.02)	0.052	−0.45 (−1.27 to 0.37)	0.284
By year of birth							
Born before 1980	13	11	5394, 7142	−1.07 (−2.12 to −0.02)	0.045	−0.25 (−0.68 to 0.18)	0.256
Born after 1980	13	12	3077, 4150	−1.20 (−2.20 to −0.20)	0.018	−0.61 (−1.42 to 0.20)	0.138

to bottle fed participants (−0.36 mm Hg, −0.79 to 0.08 mm Hg). Significant heterogeneity was found between studies ($\chi^2 = 38.9$, df = 22, P = 0.014), although there was no consistent difference between age groups (P = 0.96) and no difference between participants born before and after 1980 (P = 0.80). This difference was unaltered when the analysis was restricted to studies that adjusted for current body size. We found no evidence of publication or inclusion bias, and the results were similar for studies of different sizes. The difference in blood pressure between feeding groups was unaltered by infant feeding status being recorded in infancy (n = 15) or by parent administered questionnaire (n = 11) at least three years after birth (P = 0.593).

Discussion

Our systematic review found that publication bias may partly explain the lower mean systolic blood pressure observed in participants that had been breast fed in infancy, with large studies showing little difference. Studies with more than 1000 participants, which are less subject to publication bias, reliably excluded a mean difference greater than 0.6 mm Hg, suggesting an effect of little clinical or public health importance. Feeding in infancy was not significantly associated with diastolic blood pressure.

Even if publication bias is discounted, the overall difference in systolic blood pressure of 1.1 mm Hg is modest. The relatively weak association between infant feeding and systolic blood pressure is not likely to reflect imprecise ascertainment of early feeding practices, as most were documented either during infancy from health records or from questionnaires administered to parents, the accuracy of which has shown to be valid up to 20 years after birth.[17] In addition, the difference in blood pressure between feeding groups was similar in studies that recorded infant feeding status in infancy to those based on a parental questionnaire later in life.

Random allocation of infants to breast feeding or bottle feeding has been regarded as inappropriate, except in the special circumstances of preterm birth, in which one randomised trial has been carried out.[18] That trial showed no marked difference in blood pressure between 8 year old children who were breast fed or bottle fed as infants. A follow up examination showing noticeably higher mean blood pressures among bottle fed infants was based on only a quarter of the study population; at such low follow up rates the validity of the comparisons cannot be assumed, and the degree of control for the original study centre has been questioned.[19] The other studies in this review were observational, so that there is a possibility of confounding, particularly by social factors, current body size, and diet in later life. However, since bottle feeding tends to be related to lower social class, a greater tendency to obesity, and a less healthy diet in later life, all of which are likely to be related to higher mean blood pressure, any confounding effects are likely to have exaggerated, rather than reduced, the extent to which mean blood pressure levels are higher among participants that were bottle fed.[20 21]

The results do not suggest that naturally occurring long chain polyunsaturated fatty acids in breast milk have an appreciable effect on blood pressure. The results from large studies effectively exclude the effect size observed in the recently reported small trial of supplementation with long chain polyunsaturated fatty acids, although the confidence intervals around that estimate were wide.[8] The absence of marked differences in blood pressure between infant feeding groups (either before or after 1980) are also of interest because of the higher sodium content of formula milk up to 1980.[1 2]

What is already known on this topic

Early studies suggested that breast feeding in infancy may protect against high blood pressure in later life

Many studies examining this effect have been small, raising the possibility of publication bias

What this study adds

Selective publication of small studies shows that breast feeding reduces blood pressure in later life

The effect in larger studies seems to be small and of limited clinical or public health importance

Conclusions

Our analysis suggests that any effect of breast feeding on blood pressure is modest and of limited clinical or public health importance. However, blood pressure is not the only relevant outcome; the case for breast feeding rests on a combination of short and long term benefits, including improved neural and psychosocial development, potential protection against obesity and allergic disease, and lower blood cholesterol levels in later life.[20 22–26]

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ELPS

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Mortality and morbidity in gastro-oesophageal cancer surgery: initial results of ASCOT multicentre prospective cohort study

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Abstract

Objective To evaluate the effect of comorbidity and other risk factors on postoperative mortality and morbidity in patients undergoing major oesophageal and gastric surgery.
Design Multicentre cohort study with data on postoperative mortality and morbidity in hospital.
Data source and methods The ASCOT prospective database, comprising 2087 patients with newly diagnosed oesophageal and gastric cancer in 24 hospitals in England and Wales between 1 January 1999 and 31 December 2002. Multivariate logistic regression analysis was used to model the risk of death and postoperative complications.
Results 955 patients underwent oesophagectomy or gastrectomy. Of these, 253 (27%) were graded ASA III or IV, and 187 (20%) had a high physiological POSSUM score (≥ 20). Operative mortality was 12% (111/955). Physiological POSSUM score, surgeon's assessment, type of operation, hospital case volume, and tumour stage independently predicted operative mortality. Medical complications were associated with higher physiological POSSUM scores and ASA grade, oesophagectomy or total gastrectomy, thoracotomy, and radical nodal dissection. Stage and additional organ resection predicted surgical (technical) complications.
Conclusions Many patients undergoing surgery for gastro-oesophageal cancer have major comorbid disease, which strongly influences their risk of postoperative death. Technical complications do not seem to be influenced by preoperative factors but reflect the extent of surgery and perhaps surgical judgment. Detailed prospective multicentre cooperative audit, with appropriate risk adjustment, is fundamental in the evaluation of cancer care and must be properly resourced.

Introduction

Oesophageal and gastric cancer are common diseases that pose considerable challenges to surgeons. Most patients present with advanced disease, and curative surgery requires considerable resources in the operating theatre and in critical care. Published data show large variations in practice and outcome from surgical treatment.[1–3] Both the optimal surgical techniques and the role of adjuvant therapy remain controversial because randomised trials have failed to resolve important questions or have not yet been performed. The applicability of data from trials to routine practice in gastro-oesophageal cancer surgery is difficult to determine because of the lack of reliable information about patients and outcomes in routine practice. This information gap obstructs the formulation of hypotheses for randomised trials and frustrates efforts to improve standards of treatment.