(9) mm Hg; blood flow 45 (28) v 49 (41) ml/min; diastolic diameter 4.82 (0.60) v 4.47 (1.05) mm; distensibility 4.8 (1.4) v 5.9 (1.6) per kPa. During reactive hyperaemia, heart rate, blood pressure, and the increase in brachial artery blood flow (554.8%

(99.5%) v 590% (106.6%)) were similar in diabetic and normal subjects (figure 1) but the increases in brachial artery diastolic diameter (1.2% (2.7%) v 9.1% (4.4%); difference 6.9% (95% confidence interval 4.9% to 11%)) and distensibility (-15.3% (10.4%) v 31% (31.7%); difference 46.3% (25.5% to 67.1%)) were significantly less in diabetic subjects (both $P < 0.001$). After 10 μ g glyceryl trinitrate or 400 μ g glyceryl trinitrate the increase in flow, diameter, and distensibility was similar in diabetic and normal subjects (figure 1).

Fig 1—Mean changes in blood flow, diastolic diameter, and distensibility of brachial artery in 12 diabetic subjects and 12 controls during reactive hyperaemia, 10 μ g glyceryl trinitrate, and 400 μ g glyceryl trinitrate. Bars show 95% confidence intervals

Comment

Endothelium dependent, flow related dilatation and increase in distensibility of the brachial artery are greatly impaired in patients with non-insulin dependent diabetes, but endothelium independent responses induced by glyceryl trinitrate are similar to those in normal subjects. Loss of flow related increase in arterial distensibility will augment systolic pressure, myocardial wall stress, and heart work relative to stroke output, potentially promoting left ventricular hypertrophy and lowering ischaemic threshold. Late systolic pressure will be further augmented by early wave reflection from the periphery³ because pulse wave velocity is increased when distensibility is reduced. Loss of flow mediated vasodilatation reflects endothelial dysfunction and may thus also provide a marker of atherogenic susceptibility. Our data provide evidence of vascular dysfunction in non-insulin dependent diabetes before the appearance of microalbuminuria, previously regarded as its earliest marker.⁴

We thank Dr J R Peters for allowing us to study patients under his care and Wendy Simons and Julie-Ann Davies for their secretarial assistance.

Funding: British Heart Foundation.

Conflict of interest: None.

- 1 Ramsey MW, Goodfellow J, Jones CJH, Luddington LA, Lewis MJ, Henderson AH. Endothelial maintenance of arterial distensibility is impaired in chronic heart failure. *Circulation* 1995;92:3212-9.
- 2 Coates PA, Ollerton RL, Luzio SD, Ismail IS, Owens DR. Reduced sampling protocols in estimation of insulin sensitivity and glucose effectiveness using the minimal model in NIDDM. *Diabetes* 1993;42:1635-41.
- 3 O'Rourke MF. Systolic blood pressure: arterial compliance and early wave reflection, and their modification by anti-hypertensive therapy. *J Hum Hypertens* 1989;10:47-52.
- 4 Stehouwer CD, Nauta JJ, Zeldenrust GC, Hackeng WH, Donker AJ, den Otterlander GJ. Urinary albumin excretion, cardiovascular disease, and endothelial dysfunction in non-insulin dependent diabetes. *Lancet* 1992;340:319-23.

(Accepted 9 January 1996)

Breast feeding and hypertrophic pyloric stenosis: population based case-control study

Alfredo Pisacane, Ugo de Luca, Luciano Criscuolo, Filomena Vaccaro, Adriana Valiante, Angelina Inglese, Giuseppe Caracciolo, Luciano Pinto

Hypertrophic pyloric stenosis is a common infantile disorder characterised by enlarged pyloric musculature and gastric outlet obstruction. Although there is a genetic component,¹ some evidence suggests that postnatal factors may also play an important part. Pyloric stenosis has been associated with birth rank, maternal anxiety and drug use, and feeding practices.² We investigated the association between pyloric

stenosis and infant feeding in a population based case-control study.

Patients, methods, and results

All 102 infants admitted to Santobono Paediatric Hospital, Naples between 1 July 1992 and 31 December 1993 with surgically confirmed pyloric stenosis were recruited for the study. All were born and lived in Campania province. Controls were 204 infants randomly selected from around 600 enrolled from a provincial birth list for a child health survey; all were born in 1993 and were matched to cases of the same sex. Two medical students, unaware of the objectives of the study, interviewed the mothers at around the first birthday of their infants. Sample size was based on the assumption that a 15% difference in the prevalence of breast feeding between the two groups would be clinically significant. Relative risk was estimated by the odds ratio; 95% confidence intervals were calculated by Cornfield's method. The potentially confounding

Department of Paediatrics,
University of Naples, 80131
Naples, Italy

Alfredo Pisacane, senior
lecturer

Luciano Criscuolo,
postgraduate trainee
Filomena Vaccaro,
postgraduate trainee
Adriana Valiante,
postgraduate trainee

Santobono Paediatric
Hospital, Naples

Ugo de Luca, senior surgical
registrar
Giuseppe Caracciolo,
consultant surgeon
Luciano Pinto, consultant
neonatologist

variables of sex; birth order; birth weight; maternal education, age, and smoking; and type of birth were studied by stratified analysis. The percentage population attributable risk was calculated on the assumption that the controls' feeding pattern was representative of that of the general infant population of our province.

Eighty three cases were boys, giving a male:female ratio of 4.4:1. Two thirds of the infants started vomiting during the first four weeks of life but only seven (6.8%) during the first week. Several characteristics (birth weight; birth order; type of birth; maternal age, education, and smoking during pregnancy; family history of allergic disorders; and infant allergic disease until the first birthday) were similar in cases and controls. Table 1 shows the relative risk of pyloric stenosis analysed by the type of milk consumed. The association between breast feeding and disease was neither confounded nor modified by the factors we analysed. The proportions of controls who were bottle fed (12.2%; 25/204) or partially breast fed (20.6%; 42/204) at 1 week of age gave a percentage population attributable risk of 35% (95% confidence interval 6% to 72%).

Comment

This study indicates that infants with pyloric stenosis were less likely to have been exclusively breast fed during the first week of life. Our data are not consistent with those of Dodge³ and Webb,⁴ who reported that breast feeding was more common among such infants. The design of our study probably avoided selection bias as well as recall bias. Moreover, because in most patients the symptoms were not yet present at the age of 1 week, reverse causality bias was also unlikely.

Explanations for a protective effect of breast feeding in pyloric stenosis can only be speculative but include the presence in human milk of high levels of hormones like vasoactive intestinal peptide that can favour

Table 1—Relative risk for pyloric stenosis analysed by type of milk consumed during the first week of life

Type of milk	Cases	Controls	Odds ratio (95% confidence interval)
Breast only	48	137	1
Breast and formula	30	42	2.04 (1.1 to 3.76)
Formula only	24	25	2.74 (1.36 to 5.52)*

* χ^2 for trend=11.8, $P<0.001$.

pyloric relaxation; the increased plasma gastrin concentrations in infants fed by bottle, wholly or partially,⁵ which might be associated with pylorospasm, pyloric hypertrophy, and consequent damage of peptide containing nerve fibres; and, finally, the presence of unknown confounders. If this association is causal up to 35% of cases of pyloric stenosis in our population might be attributed to the lack of exclusive breast feeding during the early neonatal period. In view of conflicting results from other studies, however, and in the absence of biological supporting data, a causal interpretation for this association is not yet warranted.

Funding: Department of Paediatrics, University of Naples.
Conflict of interest: None.

- 1 Spence MA, Gladstien K. Pyloric stenosis and the simulation of Mendelism. In: Morton NE, Chung CS, eds. *Genetic epidemiology*. New York: Academic Press, 1978:331-51.
- 2 Jedd MB, Melton LJ, Griffin MR, Kaufman B, Hoffman AD, Broughton D, et al. Factors associated with infantile hypertrophic pyloric stenosis. *Am J Dis Child* 1986;142:334-7.
- 3 Dodge JA. Infantile hypertrophic pyloric stenosis in Belfast, 1957-1964. *Arch Dis Child* 1975;50:171-8.
- 4 Webb AR, Lari J, Dodge JA. Infantile hypertrophic pyloric stenosis in South Glamorgan 1970-9. *Arch Dis Child* 1983;58:586-90.
- 5 Marchini G, Simoni MR, Bartolini F, Uvnas-Moberg K. Plasma gastrin and somatostatin levels in newborn infants receiving supplementary formula feeding. *Acta Paediatr* 1994;83:374-7.

(Accepted 23 November 1995)

Breast feeding and tonsillectomy

Alfredo Pisacane, Nicola Impagliazzo,
Carmela De Caprio, Luciano Criscuolo,
Angelina Inglese,
Maria Claudia Mendes Pereira da Silva

Tonsillectomy is one of the commonest operations in children,¹ performed mainly for recurrent tonsillar and ear infections and severe nasal airway obstruction. The pathogenesis of tonsillar disease is probably multifactorial, and interactions among the anatomy, microbiology, and immunology of these structures may be important.² Infant feeding is one factor that may programme the immune response, and bottle feeding has been associated with diseases such as acute appendicitis.³ We performed a case-control study designed to investigate the relation between tonsillectomy and infant feeding.

Patients, methods, and results

The study was carried out in seven primary schools in Naples. The parents of all children were sent questionnaires asking whether the children had had their tonsils and adenoids removed, about maternal education and smoking, and the children's feeding habits. Cases were all children whose tonsils and

adenoids had been removed before 31 December 1994. For each case three controls were randomly selected from the same class. The parents of cases received a second questionnaire about the operation. All data were collected between February and April 1995. Sample size was determined after a pilot survey to assess the prevalence of the operation and based on the assumption that a 10% difference in frequency of breast feeding between study groups would be clinically important. Relative risks were estimated by odds ratios with 95% confidence intervals. Stratified analysis and unconditional multiple logistic regression were used to investigate the role of confounding and interaction.

Of the 2999 questionnaires sent 2458 (82%) were completed. Overall 238 children (9.6%) had had their tonsils removed, the main reasons being recurrent throat and ear infection (95%) and airway obstruction (91%). The relation between breast feeding and tonsillectomy was stratified by each of the other risk factors without evidence of confounding. Logistic regression analysis showed that factors independently associated with tonsillectomy were: breast feeding, maternal smoking, higher maternal education, and female sex (see table 1). A dose response relation was observed between tonsillectomy and breast feeding.

Comment

Our data show that, after adjustment for several potential confounders, children whose tonsils had been

Department of Paediatrics,
University of Naples,
80131 Naples, Italy

Alfredo Pisacane, senior
lecturer

Nicola Impagliazzo,
postgraduate trainee
Carmela De Caprio,
postgraduate trainee
Luciano Criscuolo,
postgraduate trainee
Angelina Inglese,
postgraduate trainee
Maria Claudia Mendes
Pereira da Silva, postgraduate
trainee

Correspondence to:
Dr Pisacane.

BMJ 1996;312:746-7