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(Accepted 17 June 1996)

Case-control study of risk of dehydrating diarrhoea in infants in vulnerable period after full weaning

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Abstract

***Objectives*—To investigate risk factors for dehydrating diarrhoea in infants, with special interest in the weaning period.**

***Design*—Case-control study.**

***Setting*—Metropolitan area of Porto Alegre, Brazil.**

***Subjects*—Cases were 192 children aged 0-23 months hospitalised with acute diarrhoea and moderate to severe dehydration. Controls were 192 children matched for age and neighbourhood who did not have diarrhoea in the previous week.**

***Main outcome measures*—Associations between dehydrating diarrhoea and child's age, type of milk consumed, time since breast feeding stopped, and breast feeding status.**

***Results*—In infants aged <12 months the risk of dehydrating diarrhoea was significantly higher in the first 9 months of life (P<0.001), and in those aged 12-23 months the risk was again greater in younger children (12-17 months) (P = 0.03). The type of milk consumed before start of diarrhoea episode was strongly associated with dehydration independent of socioeconomic, environmental, maternal reproductive, demographic, and health services factors. Compared with infants exclusively breast fed, bottle fed infants were at higher risk (odds ratio (95% confidence interval) for cow's milk 6.0 (1.8 to 19.8), for formula milk 6.9 (1.4 to 33.3)). Compared with those still breast feeding, children who stopped in the previous two months were more likely to develop dehydrating diarrhoea (odds ratio 8.4 (2.4 to 29.6)). This risk decreased with time since breast feeding stopped.**

***Conclusion*—These results confirm the protective effect of breast feeding and suggest there is a vulnerable period soon after breast feeding is stopped, which may be of relevance for developing preventive strategies.**

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BMJ 1996;313:391–4

Introduction

Diarrhoea is still an important cause of death among young children in developing countries. Combinations of exposure to environmental pathogens, inappropriate diet, and malnutrition contribute to morbidity and mortality from diarrhoea. There may be up to 1000 million episodes of diarrhoea each year, of which about 2-3% may lead to life threatening dehydration.[1]

Poverty, lack of safe water and sanitation, early motherhood, and inadequate health care have been associated with a poor prognosis for diarrhoea among young children.[2] Lack of breast feeding also increases the risk of diarrhoea mortality.[3 4] In an earlier Brazilian study completely weaned infants had 14.2 times the risk of death from diarrhoea compared with breast feeding infants.[3] This protection can be explained by the anti-infective properties of breast milk, lower exposure to contaminated food and water, and improved nutritional status.[5 6]

The advantages of breast feeding have been highlighted by the World Health Organisation, which recommends that infants be fed exclusively with breast milk for the first 4-6 months.[7] In many countries, however, breast feeding is seldom exclusive and is of short duration.[8] In Brazil, for example, the median duration was 90 days among mothers of low socioeconomic status.[9] The intrinsic properties of breast milk suggest that protection is directly related to its presence in the diet.[5 10] No study, however, has attempted to assess whether the protection afforded by breast feeding against dehydration ceases immediately after full weaning or whether there is a carry over effect.

In this report we describe the results of our case-control study of dehydrating diarrhoea, with special emphasis on risk factors related to the weaning period.

Subjects and methods

The study was carried out in the metropolitan area of Porto Alegre (about 2.5 million inhabitants), in southern Brazil. Cases were children hospitalised with dehydrating diarrhoea, aged 0-23 months. They were enrolled from the two largest paediatric hospitals during the summer diarrhoea season, from December 1987 to April 1988. The eligibility criteria included a diarrhoea episode lasting less than eight days and the presence of moderate or severe dehydration—identified by a persistent skin fold plus at least one of the following signs: sunken fontanelle, dry mouth and tongue, sunken eyes, reduced urinary output, weak pulse, and irritable or sleepy condition. Physical examination was carried out by a trained paediatrician using a standardised protocol.

Table 1—*Odds ratios for dehydrating diarrhoea by age and sex of Brazilian infants*

	No (%) of cases (n = 192)	No (%) of controls (n = 192)	Odds ratio (95% confidence interval)
Younger infants (0-11 months old)			
Age (months):			
0-1	30 (16)	27 (14)	2.6 (1.3 to 5.5)
2-3	45 (23)	18 (9)	7.1 (3.0 to 16.5)
4-5	33 (17)	25 (13)	3.5 (1.6 to 7.5)
6-8	38 (20)	47 (24)	2.4 (1.2 to 4.8)
9-11	18 (9)	48 (25)	1.0
			P<0.001
Older infants (12-23 months old)			
Age (months):			
12-17	18 (9)	10 (5)	3.7 (1.0 to 13.1)
18-23	10 (5)	17 (9)	1.0
			P = 0.03
Sex of infants			
Male	101 (53)	97 (51)	1.0
Female	91 (47)	95 (49)	0.9 (0.6 to 1.4)

All 184 cases who fulfilled these criteria were included, as well as 16 children whose skin folds were not assessed but who showed a weight gain of 5% or more after rehydration.

We selected one control for each case, matched by age (0-11 months or 12-23 months) and neighbourhood, who had not presented with diarrhoea in the previous seven days. After finding the case's home, the field worker moved on in a systematic way in the neighbourhood, asking at every house about the presence of children of appropriate age. Mothers or child minders were interviewed about socioeconomic, maternal reproductive, demographic, nutritional, and health care characteristics. The mother's skin colour and some environmental characteristics were assessed by observation. The variables studied included age of the children (0-1, 2-3, 4-5, 6-8, 9-11, 12-17, or 18-23 months); type of milk consumed (breast only, breast and cow's, breast and formula, cow's only, formula only); breast feeding status (continuing, stopped, never breast fed); interval since breast feeding stopped (≤2 months, 3-5 months, >5 months, never breast fed). Breast feeding variables were adjusted for confounding factors such as family income (measured in minimum wages: ≤3.6 times or >3.6 times); father's presence and education (absent or illiterate, or one or more years of school attended); mother's education (expressed as years of school attended: ≤8 or >8); mother's skin colour (observed as white, black, or mixed); type of housing (observed as well built or shack); availability of water (piped in the house, piped in the plot, piped to a public source, well, or river); number of children aged under 5 living in the house (1-2 or 3-6); cleanliness of housing (index based on observation of availability of soap for handwashing and towel for drying, food scraps in uncovered pans, pans kept covered on the cooker, presence and number of flies in the kitchen or living room, faeces or still water in the yard, presence of pets); mother's age (≤20 years old or >20); presence of twins (yes or no); birth weight (informed by mother or recorded in birth card as <2500 g, 2500-2999 g, ≥3000 g); weight for age (calculated by z score and categorised as ≤−2, −1.9 to −1, >−1); previous hospitalisation for any reason (yes or no). The cut points for quantitative variables were those where the odds ratios for diarrhoea increased sharply.

This information was gathered by trained interviewers using a standardised precoded questionnaire. The feeding information for cases was related to the day before the start of symptoms. For controls, the feeding information was asked for the same date as recorded for their matched cases. Cases and controls were weighed naked with portable spring scales that were calibrated daily. Cases were weighed at admission and after signs of dehydration had disappeared. Their weight for age z score was calculated from their weight after rehydration.

STATISTICAL ANALYSIS

The results were analysed by conditional logistic regression using the EGRET statistical package.[11] Age adjusted odds ratios were obtained for the variables studied as they changed with age, and they were also adjusted for confounding factors. Statistical significance was assessed by the likelihood ratio test, in which the number of degrees of freedom was equal to the number of categories minus one. The study was designed to have a sample size that would be sufficient to detect an odds ratio of 1.5 with α 0.05 and 80% power, given a prevalence of exposure of 20% to 65%.

Results

Of the 200 cases identified, 192 were studied, as were their 192 controls. The addresses of six cases could not be located and the mothers of two cases refused to be interviewed, but there were no losses or refusals among controls. Most of the cases (76%) and controls (83%) were cared for and fed by their own mothers.

AGE

Table 1 shows the age distributions of cases and controls with their corresponding odds ratios. Although the study was matched by age group (0-11 and 12-23 months), a substantial age effect was still observed within each group. The risk of developing dehydrating diarrhoea was greater in the first 9 months of life, and especially for infants aged 2-3 months. These children were about seven times more likely to develop dehydrating diarrhoea than those aged 9-11 months. In the second year of life a greater risk was detected for the younger group (aged 12-17 months). Sex was not associated with the risk of dehydrating diarrhoea.

MILK FEEDING

The type of milk consumed before the start of the diarrhoea episode was strongly associated with dehydration (table 2). Only 8% of cases and 23% of controls received breast milk alone without any other milk or food. Virtually all of these children received water or herbal teas in addition to breast milk. Children who were not breast fed had greater risks of dehydration when they were fed with artificial milk. The type of milk was associated with dehydration independently of age, nutritional status, birth weight, and other confounding variables. Children who were never breast fed were at low risk of suffering from dehydrating diarrhoea, contrasting with the odds ratio of 6.4 for children who had been breast fed but who had stopped. The risk was greatest just after stopping breast milk and decreased thereafter. However, it was still high and significant after six months of full weaning (table 2).

In the crude analysis, confidence intervals for all categories of weaned children excluded unity. For most categories, the odds ratios were even higher after adjustment for confounders, showing the presence of negative confounding. Among the variables included in the model, those responsible for such negative confounding were weight for age, father's presence and schooling, mother's skin colour, and family income.

Discussion

These results suggest that breast feeding offered strong protection against dehydrating diarrhoea, particularly when compared with feeding with formula milk. This protection persisted after extensive adjustment for confounding variables. The effect of breast milk was in accordance with previous studies of mortality from diarrhoea[3, 12] and other infectious diseases such as pneumonia.[13]

Although most studies on the overall incidence of diarrhoea suggest that protection vanishes after stopping breast feeding,[14-16] one study detected the persistence of protection after its cessation.[4] Our results contrast with the latter observation, showing that recent interruption of breast feeding was a strong risk factor for dehydrating diarrhoea. Insufficient adjustment for confounding by Howie *et al*[4] can explain the difference in the results. The reliability of our finding is strengthened by the presence of a time-response curve—the risk was greater immediately after breast feeding was stopped and decreased thereafter.

PROTECTIVE EFFECT OF BREAST FEEDING

Whether the protection afforded by breast feeding persists after its interruption will depend on several factors, including the target organ of the infection. For example, breast feeding has a long term effect against otitis media.[17-19] Although the mechanisms are not clear,[18] anatomical development of the eustachian tubes may play a role.

Breast milk has various properties that may be responsible for its protective effect against diarrhoea. Breast fed children have enterobacterial flora rich in *Escherichia coli* that have the adhesin type 1 fimbriae, which promotes phagocytosis, and are less virulent than other forms of *E coli*.[20 21] Other adhesins linked with virulence factors seem to be suppressed by breast milk (L Hanson, personal communication). When breast feeding is stopped these properties are no longer present and children are exposed to contaminated food, kitchen utensils, and bottles.[6] The time-response curve indicating a vulnerable period after full weaning could reflect a lack of or retarded immunological response to this higher infectious load.

Another possible explanation is that breast milk has both local (gastrointestinal) as well as systemic protective factors. Local factors such as IgA would be stopped soon after interruption and lead to a vulnerable period for gastrointestinal tract infections. Systemic factors would continue to act for several months after breast feeding is stopped. Factors that stimulate the development of the child's own immune system (such as thymic stimulant factors) might even lead to protection for several years.

Table 2—*Odds ratios for dehydrating diarrhoea in Brazilian infants by their milk feeding*

	No (%) of cases (n = 192)	No (%) of controls (n = 192)	Odds ratio (95% confidence interval): Adjusted for age	Odds ratio (95% confidence interval): Adjusted for age and other factors*
Type of milk fed to infants				
Breast only	15 (8)	44 (23)	1.0	1.0
Breast and cow's	27 (14)	40 (21)	1.7 (0.7 to 4.4)	1.3 (0.3 to 4.9)
Breast and formula	6 (3)	4 (2)	4.2 (0.9 to 20.2)	2.2 (0.3 to 17.2)
Cow's only	115 (60)	92 (48)	5.8 (2.5 to 13.5)	6.0 (1.8 to 19.8)
Formula only	29 (15)	12 (6)	10.1 (3.3 to 31.2)	6.9 (1.4 to 33.3)
			P<0.001	P = 0.006
Breast feeding status				
Continuing	46 (24)	88 (46)	1.0	1.0
Stopped	134 (70)	95 (49)	4.3 (2.3 to 8.2)	6.4 (2.3 to 17.3)
Never breast fed	12 (6)	9 (5)	3.7 (1.2 to 11.1)	0.7 (0.1 to 3.7)
			P<0.001	P<0.001
Interval since breast feeding stopped (months)				
Still breast feeding	47 (24)	88 (46)	1.0	1.0
≤2	60 (31)	22 (11)	4.9 (2.2 to 10.9)	8.4 (2.4 to 29.6)
3-5	37 (19)	31 (16)	4.4 (2.0 to 10.0)	7.3 (2.0 to 26.2)
≥6	37 (19)	42 (22)	3.5 (1.5 to 8.2)	3.9 (1.1 to 14.4)
Never breast fed	11 (6)	9 (5)	3.5 (1.2 to 10.8)	0.7 (0.1 to 3.6)
			P<0.001	P<0.001

*Family income, father's presence or education, mother's education, mother's skin colour, type of housing, availability of water, number of children aged <5 living in house, cleanliness of house, mother's age, presence of twins, birth weight, weight for age, and previous hospitalisation.

Key messages

- Diarrhoea is still a major cause of death among young children in developing countries, and breast feeding protects against diarrhoea
- In this study infants who were exclusively breast fed were six times less likely to have dehydrating diarrhoea than bottle fed infants
- Partially breast fed infants were at intermediate levels of risk
- Children who were recently weaned showed a higher risk of dehydrating diarrhoea than those who had been weaned for six months or more
- Recently weaned children presenting with diarrhoea should receive closer attention from health workers

POSSIBLE SHORTCOMINGS OF STUDY

Case-control studies have drawbacks which should be taken into account when interpreting results.[22] Reverse causality could lead to a biased estimate of odds ratio, since breast feeding may have stopped as a result of the diarrhoea episode. We tried to avoid this problem by collecting a detailed history of feeding and reasons for stopping. Children weaned during the diarrhoea episode were considered to be still receiving breast milk.

Recall bias might also distort the associations, since disease could stimulate a better recollection by the mothers of cases. Although our interviewers could not be blinded to case or control status, they were carefully trained not to induce answers and were unaware of the objectives of the study.

Overmatching could be a potential problem, since cases and neighbourhood controls were exposed to quite similar socioeconomic conditions. However, overmatching for these factors may be desirable since we wished to have groups that were similar in everything but breast feeding.

CONCLUSION

Our results show that breast feeding provided protection against dehydrating diarrhoea while the period soon after stopping breast feeding was a particularly vulnerable one. This finding may be relevant for further promotion of breast feeding as well as for directing the attention of health workers to children in this high risk period.

We thank Dr Flávio Fuchs (Universidade Federal do Rio Grande do Sul) and Dr L A Hanson (University of Gothenburg, Sweden) for their comments on an earlier manuscript.

Funding: World Health Organisation.

Conflict of interest: None.

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(Accepted 11 June 1996)

Drinking, smoking, and illicit drug use among 15 and 16 year olds in the United Kingdom

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Abstract

***Objective*—To examine patterns of self reported drinking, smoking, and illicit drug use among a representative United Kingdom sample of people born in 1979.**

***Design*—Cross sectional, single phase survey based on a stratified cluster sample of 70 United Kingdom secondary schools during March and April 1995. Pupils completed a 406 item standardised questionnaire under examination conditions.**

***Setting*—United Kingdom state and private secondary schools.**

***Subjects*—7722 pupils aged 15 and 16.**

***Main outcome measures*—Reported use of alcohol, tobacco, and illicit drugs.**

***Results*—Almost all the pupils had drunk alcohol, 36% (2772/7689) had smoked cigarettes in the past 30 days, and 42.3% (3264/7722) had at some time used illicit drugs, mainly cannabis. 43% (1546/3546) of boys and 38% (1529/4009) of girls had tried cannabis. Higher levels of smoking were associated with poorer school performance (20.4% (783/3840) with average performance *v* 44.1% (214/486) with below average performance, $F = 79.06$, $P<0.01$). Levels of drug use in 15 and 16 year olds in 1995 were higher in Scotland than in England, Wales, or Northern Ireland.**

***Conclusions*—Drug experimentation was high among 15 and 16 year olds, and use of cannabis was particularly high among smokers. Cigarette smoking was more common among girls than boys.**

Introduction

The use of licit and illicit psychoactive drugs by young people has long been of scientific, political, and public concern. Recent evidence suggests that illicit drug use has been increasing steadily in the United Kingdom and many other countries and that a substantial minority of adolescents drink heavily and smoke tobacco.[1 2] National surveys of drinking and smoking have rarely been conducted simultaneously, and no United Kingdom wide survey of young people's drinking, smoking, and drug use has been carried out. An international study has been initiated by the Pompidou Group to examine and compare these behaviours in 15 and 16 year olds in 26 European countries. This paper reports the initial results of the United Kingdom part of that study.

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BMJ 1996;313:394–7

Subjects and methods

We studied individuals born in 1979 from 70 schools. The sample was chosen to be representative of Great Britain and Northern Ireland as a whole, to reflect different geographical regions within Great Britain and Northern Ireland, to represent both state and independent schools, and to allow analysis of urban and rural areas.

We divided the country into 13 regions based on local authority divisions: one each for Northern Ireland and Wales, two for Scotland, and nine for England. The regions chosen were comparable both in population size and in numbers of schools, except that London and the home counties was roughly three times larger than average and northern Scotland was about one quarter the size. We then selected 60 state schools, with a random sample being separately chosen from each region. London and the home counties was deliberately undersampled and northern Scotland oversampled. The sampling ratios varied from nine schools out of 952 for London and the home counties to four schools out of 90 for northern Scotland. In Northern Ireland we selected one Roman Catholic intermediate, one Roman Catholic grammar, one Protestant intermediate, and one Protestant grammar school. All 13 regions contained urban and rural areas and random sampling ensured that schools from both were chosen in each region.

Finally, we selected a sample of 10 independent schools. This gave nearly the correct proportion of state to independent schools (4088 to 758 in Britain). Six independent schools were randomly selected from the nine English regions and one each from Wales, northern Scotland, southern Scotland, and Northern Ireland. All eligible students in each school were approached, yielding a stratified, single stage cluster sample. For this report the nine English regions and the two in Scotland were combined and the results from independent schools were not analysed separately. The data were weighted according to the formula, weight = constant/probability of school selection. Two sets of weights were used with differing constants. The first set was applied to the United Kingdom as a whole and the second was used in the comparisons of the four areas within the United Kingdom. This ensured that the numbers added to the totals in the samples being analysed. Thirty seven of the schools originally chosen refused to participate, mainly on the ground that they had been over-researched. Each of these was replaced by the next school on the list. A large city school in Wales dropped out (because the local organiser was ill) too late for replacement.