Randomised trial of different rates of feeding in acute diarrhoea

Chaomin Wan, Michael R Phillips, Michael J Dibley, Zhengle Liu

Abstract

***Objective*—To compare the effect of different feeding frequencies on the speed of recovery from diarrhoea.**

***Methods*—A randomised, non-blinded trial provided 0.452 MJ/kg/day as either 6 or 12 feeds of cows' milk each day to 262 hospitalised male infants aged 3–12 months with acute diarrhoea. Stool frequency, stool weight, body weight, and diarrhoea complications were monitored until recovery or for 14 days.**

***Results*—A proportional hazards regression model controlling for age, diarrhoea aetiology, and severity of dehydration on admission revealed that the frequently fed group had a significantly shorter duration of diarrhoea (hazards ratio, 1.29; 95% confidence interval, 1.002 to 1.653). Frequently fed infants had a significantly greater weight gain and significantly lower faecal frequency and faecal weight.**

***Conclusions*—Breast feeding remains the preferred method of feeding infants with acute diarrhoea, but feeding cows' milk to adequately nourished infants with acute diarrhoea is safe and is more rapidly effective if provided in frequent feeds with low energy loads.**

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Keywords: acute diarrhoea; diet treatment; cows' milk; nutrition

Departments of Pediatrics and Clinical Epidemiology, West China University of Medical Sciences, Chengdu 610041, People's Republic of China
C Wan
Z Liu

Research Center of Clinical Epidemiology, Beijing Hui Long Guan Hospital, Beijing 100096, People's Republic of China
M R Phillips

Centre for Clinical Epidemiology and Biostatistics, University of Newcastle, Newcastle, NSW 2300, Australia
M J Dibley

Correspondence to:
Dr Wan
email: wangzy_76@hotmail.com

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Diarrhoea is a leading cause of morbidity and mortality in children from developing countries.[1 2] The World Health Organisation reports that children less than 5 years of age in developing countries experience from 1.6 to 2.3 episodes of diarrhoea each year.[3] The prevalence of diarrhoea peaks in children 6–11 months of age and then decreases with increasing age.[4 5] There is a strong relation between diarrhoeal disease and malnutrition,[6] so the identification of optimal feeding regimens might reduce the nutritional deficits commonly found in children with diarrhoeal diseases.

For infants who are breast fed exclusively, continued breast feeding during diarrhoea results in decreased stool output and is generally recommended.[7] Most infants who are bottle fed cows' milk can safely continue drinking milk during diarrhoea, but a sizeable subgroup experience a prolonged duration of diarrhoea, a greater number of treatment failures, and potentially life threatening complications, such as increased faecal frequency, vomiting, and recurrent dehydration; these complications are more likely to occur among young infants with relatively severe diarrhoea.[7] A commonly proposed reason for these adverse effects of feeding cows' milk during diarrhoea is lactose intolerance, but human milk has an even greater lactose content than cows' milk, so lactose intolerance is unlikely to be the only reason for the poor outcomes.[8] An alternative explanation is that human milk is usually provided more frequently and in smaller amounts than cows' milk, thus reducing the lactose load and promoting absorption.

Few studies have evaluated the effect of different feeding frequencies on recovery from acute infantile diarrhoea. A previous study demonstrated an advantage of continuous 24 hour intragastric feeding compared with intermittent four hourly bolus feeding in infants with bowel disease.[9] Our study compares the speed of recovery from diarrhoea in infants fed six high energy feeds of cows' milk each day to that of infants given the same total daily energy intake for each kilogram body mass in 12 low energy feeds each day.

Methods

SUBJECTS

Enrolled subjects comprised 282 boys, 3 to 12 months of age, admitted to four tertiary hospitals in Chengdu, China between November 1994 and February 1995 with acute diarrhoea and mild to severe dehydration. Acute diarrhoea was defined as liquid, mucous, or bloody stools passed at least two times more frequently than usual each day for a minimum of 24 hours before admission but not for longer than 72 hours. Infants were excluded if they had malnutrition (weight more than two standard deviations below the mean Chinese weight for length criteria), were exclusively breast fed, had systemic infections such as pneumonia or septicaemia, or had other diseases requiring additional treatments, such as surgery. Only male patients were enrolled because of the difficulty of separating urine and stool in female infants. Informed consent was obtained from the children's parents or guardians and the study was approved by the scientific and ethics committee of the West China University of Medical Sciences.

INTERVENTION

Enrolled infants were classified into 12 strata by hospital and initial hydration status (mild, moderate, or severe); subjects in each stratum were randomly assigned to one of two treatment groups in blocks of four. All infants were given intravenous rehydration solutions (without energy) as needed, based on eight hourly assessments of hydration status, and infants with blood or mucus in their stools were treated with appropriate antimicrobial agents. Both groups of infants were exclusively fed cows' milk: subjects in the "high volume group" were fed 18 ml/kg body weight every three hours over 18 waking hours (six feeds; total of 0.452 MJ/kg/day); subjects in the "low volume group" were fed 9 ml/kg body weight every 1.5 hours over 18 waking hours (12 feeds; total of 0.452 MJ/kg/day). These feeding schedules continued until the infant recovered, until the appearance of complications that required withdrawal from the study, or for 14 days, whichever came sooner. If the infant consumed less milk than planned the nutrition nurse would increase the amount of milk at the next feed to compensate. Parents were instructed not to give their infant additional feeds of any kind; staff members observed their care of the infants to ensure that they abided by this request.

MEASUREMENTS

Body weight, length, head circumference, and abdominal skinfold thickness were measured on admission and 24 hours after admission. Leucocyte counts, serum electrolytes, and microscopic examination of the stool and urine (for white blood cells, red blood cells, and pus) were performed on admission and repeated daily if abnormal. Stool cultures were obtained on admission and on the second day after admission. These stool samples were tested using standard microbiological methods to identify shigella, salmonella, and pathogenic *Escherichia coli.*[10] Enzyme linked immunosorbent assays (ELISAs) were used to identify rotavirus.[11]

Infants' weights were measured each morning at 08:00 on a platform scale with 10 g accuracy. Infants were placed in a cot lined with standardised cotton batting to collect stools and vomitus. The separate collection of stools and urine was achieved by using urine collection bags; if the bag leaked the cotton batting was immediately replaced. Each time the infant had a bowel movement or vomited, the family members (who always accompany admitted infants in China) immediately notified the duty nurse; the cotton batting was weighed as soon as possible in a balance with a sensitivity of 1 g.

Recovery from diarrhoea was defined as two days of formed stools at the pre-diarrhoea frequency and a 24 hour stool weight of less than 30 g/kg body weight. Treatment failures were defined as follows: the recurrence or continuation of dehydration of more than 5% of body weight after the third day of admission; the occurrence of serious complications (such as severe vomiting); persistent electrolyte abnormalities (serum sodium concentration > 150 mmol/litre or < 125 mmol/litre; serum potassium concentrations > 6 mmol/litre or < 2.5 mmol/litre) after the second day of admission; prolonged severe diarrhoea (stool weight > 10% of body weight) on the seventh day of admission; and continuing diarrhoea after 14 days of treatment.

Table 1 Characteristics of patients who completed the trial

	High volume group (n = 128)	*Low volume group (n = 134)*	*p Value*
Age (months)	7.77 (2.35)	8.22 (2.42)	0.124*
Weight (kg)	8.25 (1.09)	8.48 (0.99)	0.065*
Length (cm)	69.15 (4.12)	69.67 (4.48)	0.337*
Head circumference (cm)	40.75 (2.59)	40.99 (2.64)	0.451*
Skinfold thickness of abdomen (cm)	1.10 (0.12)	1.10 (0.11)	0.942*
Duration of diarrhoea before admission (hours)	42.52 (15.10)	40.89 (14.43)	0.362*
Stool frequency before admission (times/day)	15.66 (10.56)	14.37 (8.13)	0.274*
Usual stool frequency (times/day)	1.49 (0.65)	1.44 (0.58)	0.504*
Vomiting before admission (n (%))	72 (56.3)	84 (62.7)	0.287†
Temperature >37.5°C on admission (n (%))	99 (77.3)	101 (75.4)	0.713†
Estimated degree of dehydration			
Mild (n (%))	64 (50.0)	70 (52.2)	
Moderate (n (%))	46 (35.9)	44 (32.9)	0.868†
Severe (n (%))	18 (14.1)	20 (14.9)	
Characteristic of stool			
Watery (n (%))	122 (95.3)	122 (91.0)	0.172†
Mucous or blood (n (%))	6 (4.7)	12 (9.0)	
Aetiology			
Rotavirus (n (%))	57 (44.5)	78 (58.2)	
‡Bacteria (n (%))	15 (12.7)	19 (14.2)	0.027†
No pathogen identified (n (%))	56 (43.8)	37 (27.6)	

Values are mean (SD) unless otherwise stated.
**t* test; †χ^2 test.
‡In the high volume group nine patients were infected with shigellae and six with *Escherichia coli*; in the low volume group 13 were infected with shigellae and six with *E coli*.

STATISTICAL ANALYSIS

The characteristics of infants in the two groups at the time of enrolment were compared using *t* tests for normally distributed continuous variables and χ^2 tests for categorical variables. The rates of recovery from acute diarrhoea between treatment groups were compared using survival analysis; Cox's proportional hazard regression analysis was used to compare the rates of recovery after adjusting for age, dehydration status on admission, and aetiology of the diarrhoea (rotavirus versus other).

Most of the infants recovered and were discharged before the end of the 14 day study period, so the analyses of the change in body weight, stool frequency, faecal weight, and volume of cows' milk consumed were limited to the first five days of our study when all patients were still in hospital. The rate of increase in body weight for each patient was estimated by fitting a regression line to the patient's weights on days 1–5; the two interventions were then compared by comparing the median of the slopes of the regression lines of patients in each group. The post-treatment summary measurements for each patient included average body weight, stool frequency, and faecal weight on days 2–5; these measurements were compared across treatment groups by comparing the median values in the two groups. The changes in body weights for the two groups were assessed by comparing the median of the difference between the pretreatment and post-treatment weights (that is, average weight on days 2–5 minus weight on day 1).

Results

Twenty of the 282 enrolled patients were withdrawn during the course of the study: eight were withdrawn from the low volume group because of premature discharge by the parents (n = 4), unscheduled feeding of rice water by the parents (a commonly used folk treatment

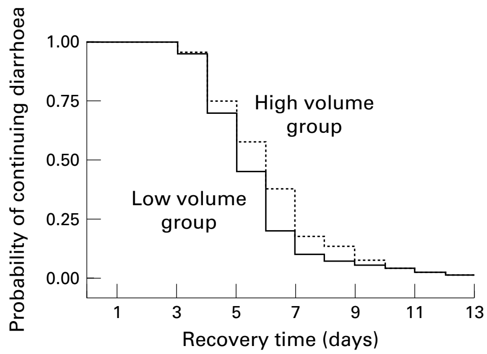

Figure 1 Kaplan–Meier plots for recovery from diarrhoea in 128 infants given six feeds of cows' milk a day (high volume group) and 134 infants given the same energy load/kg body weight in 12 feeds of cows' milk each day (low volume group).

for diarrhoea in China) (n = 2), pneumonia (n = 1), and surgery (n = 1); 12 were withdrawn from the high volume group because of premature discharge (n = 5), septicaemia (n = 3), unscheduled feeding of rice water (n = 2), pneumonia (n = 1), and surgery (n = 1). There were no significant differences in the admission characteristics of the infants who did and did not complete our study. Table 1 gives the admission characteristics of the 134 patients enrolled in the low volume group and the 128 patients enrolled in the high volume group who completed our study. The clinical and demographic characteristics were similar between the groups but more of the infants in the low volume group were infected with rotavirus.

Only one of the 262 infants (a patient in the low volume group) did not meet the criteria for recovery at the end of the 14 day trial, and none of the infants met the other criteria for treatment failure (see above). All patients in both treatment groups consumed from 75% to 125% of the targeted milk consumption level of 0.452 MJ/kg/day. The median (interquartile range) amount of milk consumed on the first five days of treatment was 0.430 (0.376–0.467) MJ/kg/day in the low volume group and 0.431 (0.369–0.474) MJ/kg/day in the high volume group (Wilcoxon rank sum test, Z = 1.27; p = 0.204).

The Kaplan–Meier survival curves (fig 1) show a more rapid recovery in the low volume group than in the high volume group; the difference in the proportion of recovered patients between the two groups increases in a stepwise manner from the third to seventh day of treatment and then decreases in a stepwise manner as the high volume group subjects "catch up". Univariate analysis indicated that this decrease in the recovery time for the low volume group was not significant (log rank test, $\chi^2 = 3.65$; p = 0.056), but the difference became significant after controlling for age, dehydration status on admission, and aetiology of diarrhoea (table 2). The hazard ratio for the feeding method (1.29) indicated that after adjustment the probability ("hazard") of recovery from diarrhoea over the 14 day trial was 29% higher in the low volume group than in the high volume group. Cox's proportional hazards regression analysis (table 2) also revealed that the probability of recovery from diarrhoea decreases 19% (hazard ratio, 0.81) for each stepwise increase in the level of dehydration on admission (that is, from mild to moderate dehydration and from moderate to severe dehydration). However, the age of the infant and the aetiology of the diarrhoea were not significantly related to recovery time.

The median slope of the regression lines for body weight during the first five days of admission was significantly higher in the low volume group (median, 0.030; interquartile range, 0.010–0.050) than in the high volume group (median, 0.020; interquartile range, 0.002–0.030; Wilcoxon rank sum test, Z = −4.63, p < 0.001). This shows that the rate of increase in body weight was faster in patients fed 12 times each day than in patients fed six times each day. Table 3 shows that both the median of the average body weight over the second to fifth day of treatment and the increase in this post-treatment median weight from the median weight at admission were significantly greater in the more frequently fed group than in the less frequently fed group. Moreover, the medians of the average stool frequency and average stool weight over the second to fifth day of treatment were significantly lower in the low volume group than in the high volume group.

Table 2 The hazards ratios for recovery from acute diarrhoea by feeding method, hydration status, age, and aetiology of diarrhoea in 262 children admitted to four hospitals in Chengdu, China

	HR (SE)*	*Z Value†*	*p Value*	*95% CI*
Treatment regimen	1.29 (0.16)	−1.98	0.048	1.002 to 1.653
0 = high volume group				
1 = low volume group				
Degree of dehydration on admission	0.81 (0.07)	2.36	0.018	0.679 to 0.943
0 = mild				
1 = moderate				
2 = severe				
Aetiology (uses two variables)				
Rotavirus: R = 1, B = 0				
Bacteria: R = 0, B = 1				
No pathogen: R = 0, B = 0				
Rotavirus	0.97 (0.13)	−0.26	0.797	0.736 to 1.265
Bacteria	1.03 (0.21)	0.14	0.890	0.692 to 1.528
Age (in months, 3–12)	1.01 (0.03)	0.26	0.793	0.955 to 1.062

*From Cox's proportional hazards regression model.
†Wilcoxon rank sum test.
CI, confidence interval; HR, hazard ratio.

Table 3 Changes in body weight and stool characteristics over the first five days of treatment for acute diarrhoea

	High volume group (n = 128)	*Low volume group (n = 134)*	*Z Value**	*p Value*
Change in body weight with treatment†	0.05 (0.01–0.10)	0.10 (0.03–0.15)	−3.13	0.012
Post-treatment measurements‡				
Faecal frequency (stools/day)	5.5 (3.8–7.2)	4.6 (3.5–6.5)	2.21	0.027
Faecal weight (g/kg/day)	36.5 (22.7–45.0)	28.7 (21.9–40.0)	2.27	0.023
Body weight (kg)	8.49 (7.87–8.92)	8.71 (7.88–9.28)	−3.15	0.032

Values are medians (interquartile range).
Infants in the high volume group were given six feeds of cows' milk a day and infants in the low volume group were given the same energy load/kg body weight in 12 feeds of cows' milk a day.
*Wilcoxon rank sum test.
†Median of the average body weight from day 2 to 5 minus the median value for body weight on day 1.
‡Post-treatment median body weight, median faecal frequency, and median faecal weight were the median values of the average of the four serial measurements taken on days 2–5.

Discussion

Our study has shown that more frequent feeds of cows' milk with low energy loads each feed have a beneficial effect on infants recovering from acute diarrhoea when compared with similar infants receiving the same total amount of energy each day but with less frequent, high energy feeds. Over the first five days of treatment (during which time all enrolled patients were hospitalised), the gain in body weight and the reduction in the frequency and weight of stools were significantly greater in the frequently fed group. Considering the entire 14 day trial, univariate assessment of the Kaplan–Meier survival curves show a non-significant decrease in the duration of diarrhoea for the frequently fed group; this difference becomes significant after controlling for the effects of age, aetiology of diarrhoea, and degree of dehydration on admission. The more rapid rate of recovery in the low volume group suggests that a relatively simple clinical manoeuvre—the adoption of treatment regimens that use frequent low energy feeds—will decrease the clinical, social, and economic burden of children hospitalised with acute infantile diarrhoea.

Our trial had a lower rate of treatment failure (0.4%; one of 262) than that usually reported for hospitalised infants with acute diarrhoea (5–10%).[12–14] There are several possible explanations. (1) The infants in our trial were older than in most previous studies (77% of infants were more than 6 months old at enrolment); most diarrhoea treatment failures occur in younger infants because of age related factors, such as IgA deficiency and a relative pancreatic insufficiency.[15] (2) None of our patients was malnourished; treatment failures are more common in malnourished infants,[16] probably because of the destruction of intestinal villi and diminished lactase activity.[17] (3) In comparison with other studies the infants in this trial had a shorter duration of diarrhoea before admission.[18] (4) Only 15% of the patients had severe dehydration, and individuals with systemic infections or other diseases were excluded, so the prevalence of these prognosticators of poor outcomes was lower than other studies.[19] (5) The volume of the milk feeds used during the trial (108 ml/kg/day) was deliberately smaller than in other studies because previous studies have reported a trend towards increasing failure rates with higher levels of dietary intake in diarrhoea.[20 21] (6) There was a rapid initiation of treatment on admission that included correction of dehydration and immediate introduction of feeds. (7) It is possible that the definition of treatment failure used in our trial was not as sensitive as that used in other studies.[22]

The low rate of treatment failure in our trial implies that infants fed with cows' milk who have acute diarrhoea probably do not need a lactose free formula. Allowing infants to continue to receive cows' milk would significantly reduce the cost and inconvenience of treatment for diarrhoea. Other investigators examining the role of diet in the treatment of diarrhoea have reached similar conclusions.[23 24]

Key messages

- In adequately nourished infants 3 to 12 months of age with acute diarrhoea, it is safe to feed cows' milk at either the standard frequency (six feeds each day) or at a higher frequency
- For adequately nourished infants with acute diarrhoea who are bottle fed cows' milk, the simple clinical manoeuvre of decreasing the volume of each feed and increasing the frequency of feeding (while maintaining the same total daily energy intake) speeds recovery, reduces faecal frequency and faecal weight, and increases weight gain during the recovery period

Over the first five days of treatment, the group given frequent low energy feeds had a significantly greater weight gain than the group given less frequent high energy feeds (mean, 100 g/day *v* 50 g/day, respectively). This greater weight gain was achieved despite a similar average milk consumption (energy intake) in both treatment groups and is not explained by differences in initial hydration status and subsequent fluid retention. These findings are similar to a previous study that compared continuous intragastric feeding with intermittent bolus feeding.[9] The explanation for the observed differences are not entirely clear, because absorption of the nutrients in the cows' milk by infants in the two groups was not measured. Increasing the frequency of feeding probably results in a lowering of the amount of lactose introduced into the intestine at any time.[25] The completeness of digestion depends on the molar relation between the amount of intraluminal lactose present for each unit of time, so the higher frequency of feeding might optimise the amount of lactose presented to the gut for absorption.

The additional weight gain of 50 g/day seen in the frequently fed infants might appear trivial in clinical practice, but it has considerable public health relevance in settings where diarrhoeal incidence is high, as is frequently reported in less privileged populations of children under 5 years of age.[1 3] Children living under these conditions might have insufficient time between episodes to permit full recovery from nutritional deficits imposed by inadequate dietary intake during illness.[20]

The more rapid reduction of faecal frequency and faecal weight in the low volume group might be related to the gastrocolic reflex and to an osmotic effect of unabsorbed sugar. The smaller amount of cows' milk in each feed given to the infants in the low volume group should have caused less distension of their stomach and small intestine and less mass propulsion of enteric contents.[26] Larger feeds might have resulted in lactose loads that could not be absorbed and a subsequent osmotic effect that increased stool frequency and weight.

STUDY LIMITATIONS

The difficulty of separating urine from faeces in female infants resulted in a restriction of the study to male patients so, strictly speaking, the results might not be applicable to female infants. There is, however, no biological reason to expect different results in female infants who have the same characteristics as the male infants studied here: adequately nourished infants 3 to 12 months of age with uncomplicated acute diarrhoea.

The randomisation was not entirely successful. The demographic and clinical characteristics of the patients in the two groups were similar at baseline, but the aetiology of the diarrhoea was significantly different. However, multivariate analysis found no relation between aetiology and duration of diarrhoea—a finding similar to several previous studies[27–29]—so it is unlikely that the higher prevalence of rotavirus infection in the low volume group had a major effect on the outcome.

One of the important limitations of the trial was the limited masking of the interventions. Feeding interventions cannot be completely blinded because differences in type of feeds or feeding frequency are apparent to both the care providers and the parents of infants with diarrhoea. To reduce potential information bias, the study hypotheses and the specific outcome measures used in the analysis were not revealed to the nursing and medical staff involved in the trial.

Another limitation of our study was the failure to assess the nutrient content of the cows' milk fed to the infants and the faecal loss of nutrients. Net absorption of macronutrients is not only related to the amount of food consumed but also to the rate of absorption of the component nutrients in the food. In previous studies, the change in the balance of nutrients was compared between groups by assessing the difference between dietary intake and faecal losses in the groups.[18] Practical considerations prevented us from making these measurements in our study, so we can only speculate about the reasons for the improved weight gain and reduced stool frequency and stool weight in children given frequent low energy feeds.

Infants with diarrhoea are usually allowed to feed ad libitum so the restriction of milk feeds to a volume of 108 ml/kg/day in our study might not be representative of typical feeding practices during recovery from diarrhoea. The low rate of treatment failure and improved outcomes when providing frequent low energy feeds might not generalise to treatment regimens that use higher total daily milk intakes or ad libitum feeds.

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1 World Health Report 1995. *World Health Forum* 1995;**6**:379–80.
2 *Programme for control of diarrhoeal disease. Eighth programme report 1990–1991.* Geneva: World Health Organisation, 1992:1–2 (WHO/CDD/92.38).
3 *Programme for control of diarrhoeal diseases. Interim programme report 1992.* Geneva: World Health Organisation, 1993: 57–59 (WHO/CDD/93.40).
4 Chen KC, Lin CS, Qiao QX, *et al.* The epidemiology of diarrhoeal diseases in Southeastern China. *J Diarrhoeal Dis Res* 1991;**9**:94–9.
5 Ise T, Tanabe Y, Sakuma F, Jordan O, Serrate E, Pena H. Clinical evaluation and bacterial survey in infants and young children with diarrhoea in the Santa Cruz district, Bolivia. *J Trop Pediatr* 1994;**40**:369–74.
6 Vella V, Tomkins A, Nviku J, Marshall T. Determinants of nutritional status in south-west Uganda. *J Trop Pediatr* 1995;**41**:89–98.
7 Brown KH, Lake A. Appropriate use of human and non-human milk for the dietary management of children with diarrhoea. *J Diarrhoeal Dis Res* 1991;**9**:168–85.
8 Brown KH. Dietary management of acute childhood diarrhoea: optimal timing of feeding and appropriate use of milks and mixed diets. *J Pediatr* 1991;**118**:S92–8.
9 Parker P, Stroop S, Greene H. A controlled comparison of continuous versus intermittent feeding in the treatment of infants with intestinal disease. *J Pediatr* 1981;**99**:360–4.
10 Edwards PR, Ewing WH. *Identification of entero-bacteriaceae.* 3rd ed. Minneapolis: Burgess, 1972:10–31.
11 Yolken RH, Kim HW, Clem T. Enzyme-linked immunoabsorbent assay (ELISA) for detection of human rotavirus-like agents of infantile gastroenteritis. *Lancet* 1977;ii:236–67.
12 Pizarro D. Oral rehydration therapy: its use in neonates and young infants. *J Pediatr Gastroenterol Nutr* 1986;**5**:6–8.
13 Brown KH, Perez F, Gastanaduy AS. Clinical trial of modified whole milk, lactose-hydrolysed whole milk, or cereal-milk mixtures for the dietary management of acute childhood diarrhoea. *J Pediatr Gastroenterol Nutr* 1991;**12**: 340–50.
14 Alarcon P, Montoya R, Perez F, *et al.* Clinical trial of home available, mixed diets versus a lactose-free, soy-protein formula for the dietary management of acute childhood diarrhoea. *J Pediatr Gastroenterol Nutr* 1991;**12**:224–32.
15 Penny EM, Brown KH. Lactose feeding during persistent diarrhoea. *Acta Paediatr Suppl* 1992;**381**:133–8.
16 Chew F, Penna FJ, Peret-Filho LA, *et al.* Is dilution of cows' milk formula necessary for dietary management of acute diarrhoea in infants aged less than 6 months? *Lancet* 1993; **341**:194–7.
17 Greene HL, McCabe DR, Menenstein GB. Protracted diarrhoea and malnutrition in infancy: changes in intestinal morphology and disaccharidase during treatment with total intravenous nutrition and elemental diets. *J Pediatr* 1975;**87**:695.
18 Brown KH, Gastanaduy AS, Saavedra JM, *et al.* Effect of continued oral feeding on clinical and nutritional outcomes of acute diarrhoea in children. *J Pediatr* 1988;**112**:191–200.
19 World Health Organisation. *Persistent diarrhoea in children in developing countries.* World Health Organisation, Diarrhoeal Diseases Control Programme, WHO/CDD/88.27, 1988: 1–12.
20 Alarcon P, Montoya R, Rivera J, Perez F, Peerson JM, Brown KH. Effect of inclusion of beans in a mixed diet for the treatment of Peruvian children with acute watery diarrhoea. *Pediatrics* 1992;**90**:58–65.
21 Sullivan PB, Mascie-Taylor CGN, Lunn PG, Northrop-Clewes CA, Neale G. The treatment of persistent diarrhea and malnutrition: long-term effects of in-patient rehabilitation. *Acta Paediatr Scand* 1991;**80**:1025–30.
22 Fox R, Leen CL, Dunbar EM, Ellis ME, Mandal BK. Acute gastroenteritis in infants under 6 months old. *Arch Dis Child* 1990;**65**:936–8.
23 Groothuis JR, Berman S, Chapman J. Effect of carbohydrate ingested on outcome in infants with mild gastroenteritis. *J Pediatr* 1986;**108**:903–6.
24 Lozano JM, Cespedes JA. Lactose vs. lactose free regimen in children with acute diarrhoea: a randomized controlled trial. *Arch Latinoam Nutr* 1994;**44**:6–11.
25 Ferry GD, Selby M, Pietro T. Clinical response to short-term nasogastric feeding in infants with gastro esophageal reflux and growth failure. *J Pediatr Gastroenter Nutr* 1983;**2**:57.
26 Barclay DV, Gil-Ramos J, Mora JO, Dirren H. A packaged rice-based oral rehydration solution for acute diarrhoea. *J Pediatr Gastroenter Nutr* 1995;**20**:408–16.
27 Lifshitz F, Olivo CAG, Friedman S. Refeeding of infants with acute diarrhoea disease. *J Pediatr* 1991;**4**:S99–108.
28 Hyams JS, Kranse PJ, Gleason PA. Lactose malabsorption following rotavirus infection in young children. *J Pediatr* 1981;**99**:916–18.
29 Mahalanabis D, Alam AN, Rahman N, Hasnat A. Prognostic indicators and risk factors for increased duration of acute diarrhoea and for persistent diarrhoea in children. *Int J Epidemiol* 1991;**20**:1064–72.