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Lactose vs. Lactose free regimen in children with acute diarrhoea: a randomized controlled trial

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SUMMARY. *Objective.* To determine whether the routine use of a lactose free formula (AL-110, Nestle Labs.) in hospitalized children aged one to 24 months reduces the duration of acute diarrhea (AD). *Methods.* After being stratified according to age and nutritional state, 28 and 24 patients were randomly allocated to receive AL-110 or lactose formula, respectively. The main outcome was the duration of diarrhoea after refeeding, both in hours and days. Secondary outcomes were evaluated by blind observers. Results were compared using t test, the Mann-Whitney test and Chi square.*Results.* No differences were found between the diets without and with lactose regarding duration of diarrhoea in hours (mean, 41,9 h vs 54.4 h; p=0.247) or days (median, 0 d vs 0 d; p=0.717), the percentage of failures (3.6% vs 8.3; p=0.2), and the mean weight increment (0.78 kg vs. 0.82 kg; p=0.788). The study power to find a 50% (27h) reduction of AD duration was 71%. *Conclusion.* Although the power of this trial was slightly below that previously fixed (80%), the results suggest that routine use of lactose free formula does not reduce the duration of AD in hospitalized children. Key Words: Acute diarrhoea, Lactose, Diet, Infant, Children, Randomized trial.

RESUMEN. Dieta con o sin lactosa en niños con diarrea aguda: un experimento clínico aleatorio.*Objetivo.* Determinar si el uso rutinari o de una fórmula láctea sin lactosa (AL-110, Lab. Nestlé) en niños entre uno y 24 meses de edad y hospitalizados reduce la duración de la diarrea aguda (DA). *Métodos.* Luego de ser estratificados por edad y estado nutriiconal, 28 y 24 pacientes fueron asignados al azar a recibir AL-110 o una fórmula con lactosa, respectivamente. La variable dependiente principal fue la duración de la diarrea luego de inciar la alimentación, medida en horas y en días. La proporción de fallas terapéuticas y el incremento del peso corporal fueron variables secundarias. Estas variables fueron evaluadas por observadores ciegos. Los resultados fueron analizados usando las pruebas t, de Mann-Whitney y de Chi cuadrado.*Resultados.* No se encontraron diferencias significativas entre las dietas sin y con lactosa en la duración de la DA medida en horas (media, 41.9 h vs. 54.5 h; p=0.247) o en días (mediana, 0 d vs. 0 d; p=0.717), la proporción de fallas terapéuticas (3.6% vs 8.3; p=0.2), o el incremento promedio del peso corporal (0.78 kg vs. 0.82 kg; p=0.788). El poder del estudio para encontrar una reducción del 50% (27h) en la duración de la DA fue 71%. *Conclusión.* Aunque el poder de este experimento fue ligeramente inferior al calculado previamente (80%), los resultados sugieren que el uso rutinario de esta dieta sin lactosa no reduce la duración de la DA en niños hospitalizados. Palabras clave: Diarrea Aguda, Lactosa, Dieta, Lactante, Niño, Experimento Clínico Aleatorio.

INTRODUCTION

Acute diarrhoea (AD) is one of the leading causes of disease and death among children in developing countries, producing 700-1000 million illness episodes and 4,6 million deaths every year (1). It is also well known that AD is a signficant contributor to malnutrition (2,3,4). Thus, rapid reintroduction of food during the disease after rehydration is now considered a priority (5,6,7). However, the damage caused to the intestinal mucosa by the illness can temporarily reduce the activity of lactase, the enzyme responsible for the hydrolysis of lactose. The non hydrolysed lactose produces movement of water from the instestinal wall into the lumen, thereby worsening the diarrhoea. This complication has been reported in 15% to 50% of children with AD (8,9,10,11,12), and is more common in cases of viral etiology or when malnutrition is already present.

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The enzymes responsible for the hydrolysis of other carbohydrates (sucrose, maltose) are not affected in the same proportion during AD. Thus, routine withdrawal of lactose from the diet during the disease, replacing cow's milk by a formula with a differente carbohydrate, would be a form of rapid refeeding avoiding lactose intolerance. However, this change in the formula may be both inconvenient and confusing, and for low-income families, it may be a significant financial burden as well. Several randomized trails comparing lactose and lactose free regimens during diarrhoea in children have produced contradictory results, and have used mainly soy based formulas in the lactose free group, changing simultaneously the carbohydrate and the protein, which makes difficult to isolate the effect of avoiding lactose (13,14,15,16,17,18,19,20,21,22,23,24,25,26). The goal of this randomized controlled trial was to determine whether the routine use of a lactose free formula containing cow's milk protein (AL-110, Nestle Labs.) in hospitalized children aged one to 24 mo reduces the duration of AD, when compared with a lactose formula.

METHODS

During the months of October of 1989 to July of 1990 we studied a group of children aged one to 24 mo inclusive, hospitalized in the Clinica Infantil Colsubsidio, a tertiary social security center located in Bogota, Colombia. All subjects were admitted due to dehydration secondary to AD (defined as four or more watery stools in a period of 24 h, with a total duration less than or equal to one week (7), that in most cases had not been corrected with oral rehydration therapy. Subjects were excluded if they were receiving more than 50% of their daily milk as breast milk or were not receiving lactose milk/formula prior to illness, if they had diarrhoea caused by *E. histolytica*, if they had received antibiotic therapy during a 48 h period prior to admission, if they had history of chronic malabsorption syndrome, or if their parents refused to take part in the trial. The study protocol was approved by the Research Committees of both the Javeriana University and the Colsubsio Children's Clinic. Written informed consent was obtained from all parents.

Eligible patients received the same rehydration therapy, first with parenteral fluids and later with oral electrolyte solution. Parenteral solutions included Ringer's lactate in case of shock (30 ml/kg in 30 min to 60 min followed by 70 ml/kg in five hours), and a solution of 5% dextrose with 50 mmol/L of sodium and 20 mmol/L of potassium for less severe cases or for maintenance. The oral solution used was that recommended by the WHO (7), usually started within four to six hours after admission. After rehydration subjects were stratified according to age (one to six months inclusive, and seven to 24 months) and to nutritonal state (normal and abnormal, where normal was a weight/height index >91%) (27) and then allocated to intervention or control group within their strata using block randomization.

Feeding was started within 12 hours after admission. The lactose free group received AL-110 (Nestle Lab.). The lactose formula for children under six months of age was NAN 1 (Nestle Lab.), which is similar to human milk and for older children it was NAN 2, that is similar to cow's milk (Table 1). All children received the day one prescribed formula in half strength concentration to provide at least 50% of the calculated fluid requirements for 24 h. The concentration was normal from day two on. Food different to milk, the same for both groups, was reintroduced after the first day. Therefore, children were receiving full feedings within 24 h to 26 h after admission. Since the appearance, odour and taste of the lactose free formula were very different from those of lactose formulas, the study did not have a blinded manoeuvre.

TABLE 1
COMPOSITION OF THE FORMULAS USED

	Without Lactose	With Lactose	
	AL-110	NAN1	NAN2
Protein source	Casein	Casein	Casein
Protein (gm/l)	19	16	33
Fat source	Corn	Cow's milk	Cow's milk
Fat (gm/l)	33	34	33
Carbohydrate	Glucose pols.	Lactose	Lactose
Lactose (gm/l)	0.00	74	71
Cal/ml	0.66	0.66	0.66

The primary outcome measure was the total duration of diarrhoea fron the moment of reintroduction of formula. One day of diarrhoea was defined as the presence of four or more watery stools during a 24 h period. The duration was also measured as the total number of hours up to the last liquid evacuation. The reappearance of watery stools after a period of normal evacuations of seven days or less was considered part of the same episode; otherwise it was considered as a second episode. Both the proportion of failures during the reintroduction of food and the change of corporal weight during the first six weeks were secondary outcomes. Failure was defined as the persistence of diarrhoea for more than seven days after the reintroduction of food, an increment of more than 50% in the number of stools/24 h following refeeding, when compared with the number during the previous 24 h, and/or the persistence of vomiting/refusal with the adminstration of milk/formula in two consecutive opportunities after a second six hours period of fasting. Failures were not excluded for measuring the total duration of the disease. The corporal weight gain was the difference between the body weight obtained after six weeks and the observed after the period of rehydration, measured with the same instrument. The outcomes were evaluated by nursing personnel who did

not have knowledge about the treatment received by each subject.

Patients were discharged from hospital when they were receiving the formula in normal concentration and after at least one day without diarrhoea. Follow-up visits were scheduled at one, three and six weeks, when data about food tolerance, number and consistency of evacuations, problems with the administration of milk/formula and corporal weight were collected. Parents were instructed to bring the empty cans of milk to these visits to evaluate compliance with the formulas used. A consumption equal to or higher than 80% of the formula was considered as good compliance. After three weeks patients allocated to lactose free formula returned to the lactose regimen they were using prior to illness. In case of recurrence of diarrhoea during this change, the patient was maintained with lactose free regimen for one more week, when the change was tried again.

During August/89 17 eligible patients participated in a pilot study that showed that the mean duration of diarrhoea after admission was 2.0 d (SD=1.1 d). A difference equal to or larger than one day between the two treatment groups was considered clinically important. Assuming 10% of drop-outs, a sample size of 21 subjects/group was needed (alpha=0.05, two tailed test; power=80%). The baseline comparability of the treatment groups was assessed according to the demographic and medical data collected at admission. Discrete variables were compared using X2 or Fisher exact test, and continuous variables with Student t test. Since the duration of AD measured in days was not normally distributed, the Mann-Whitney test was used.

RESULTS

During the study period 59 eligible children were admitted to hospital. Two of these subjects were not included due to parental refusal to participate. Fifty seven patients were randomized, 29 and 28 to the lactose free and the lactose groups, respectively. Two children allocated to lactose formula were later excluded because their disease was secondary to *E. histolytica*, found in their faeces after randomization but before starting the study diets. One patient on the lactose group was excluded due to referral to another hospital due to economical reasons, and two additional patients, one from each group, dropped out after leaving the clinic. Since complete information regarding the duration of diarrhoea and body weight could not be obtained from the two children that dropped out, they were excluded for the analysis of these variables, but they were included in the failures count. The baseline characteristics of children excluded were not different to those found in the 52 subjects finally included. The baseline characteristics of the groups are summarized on Table 2. No differences were found between the group except for the mean duration of diarrhoea before admission (3.5 d and 2.3 d for lactose free and lactose groups, respectively; p=0.01).

TABLE 2
FEATURES OF THE TREATMENT GROUPS ON ADMISSION[a]

Feature	Lactose free	Lactose
Total in group	28	24
Age (mo)	13.1(5.8)	11.6(4.6)
Male	18(64)	13(54)
Body weight after rehydration (kg)	8.8(2.4)	8.5(1.8)
ORT during current illness	24(86)	19(79)
History of breast feeding	26(93)	20(83)
Duration of breast feeding (mo)	5.1(3.8)	5.0(5.6)
Days of diarrhoea before admission	3.5(2.0)	2.3(1.0)b
Number of stools last 24 h	7.2(3.8)	7.1(3.4)
Heart rate on admission	125(12.2)	122(8.8)
Serum sodium (mmol/1)	139(7.4)	140(6.2)
Serum creatinine (μmol/1)	62(27)	62(27)
Estimated degree of dehydration		
Mild (4-5%)	13(46)	16(67)
Moderate (6-9%)	15(54)	7(30)
Severe(>9%)	—	1(3)
Estimated nutritional status		
Normal	16(57)	18(75)
Mild malnutrition	10(36)	4(17)
Moderate malnutrition	2(7)	2(8)
Highest maternal education		
Elementary	9(32)	6(25)
High school	14(50)	10(42)
University	5(18)	8(33)
Number of house bedrooms		
One	4(15)	2(8)
Two	14(52)	13(54)
Three or more	9(33)	9(38)
Pathogens identified in stools		
Proteus sp.	11	13
C. freundii	9	7
Klebsiella sp.	3	3
Y. enterocolytica	1	-
Enterobacter sp.	1	-
Rotavirus	11/20	14/20

a Values in parentheses are SD or percentages in each group
b p=0.01

TABLE 3
FINAL OUTCOME MEASURES ON THE TREATMENT GROUPS[a]

Outcome measure	Lactose free	Lactose	P
Median duration of diarrhoea (d)	0(0-3)	0(0-5)	.717
Mean duration of diarrhoea (h)	41.9(32)	54.5(40)	.247
Body weight increment (kg)			
All third visit attendants	.80(.5)	.82(.5)	.918
Mean time follow up (d)	43.1(3.5)	43.2(3.6)	.945
Therapeutic failures	1/29(3.4)	2/25(8.0)	.584

a Values in parentheses are SD or percentages, except for the median duration of diarrhoea in days, were they are range.

Table 3 summarizes the results on the dependent variables. The median number of days of diarrhoea after the reintroduction of food was zero for both groups, with a range of zero to three on the lactose free group, and of zero to five on the lactose group (p=.717, Mann-Whitney test). Although there was a tendency to a reduction in the mean duration of the disease in hours in the lactose free group, this difference was not statistically signficant (p=.247, t test). Twenty six (93%) patients from the lactose free group and 22 (92%) from the lactose group attended the third follow up appointment. No differences were found on the body weight increment up to this visit (p=.918, t test). The mean time between the onset of the study regimen and this follow up visit was almost the same for both groups. There was one treatment failure in the lactose free group, due to persistent refusal of the patient to the formula, and two in the lactose group, due to increment in the number of stools of more than 50% after the reintroduction of milk. This difference was not statistically signficant (p=.584, Fisher exact test).

In order to determine whether the difference in the duration of the disease before admission between the treatment groups could have modified the results, the relationship of this variable with the outcome measures was explored. The correlation coefficients with the duration of diarrhoea after food reintroduction (both in days and hours), and the body weight increment were -.06, -.14 and -.13, respectively (p>0.05). Thus, the baseline difference between the groups seems to have had no relation with the final results.

No complications or complaints were found during the administration of the study formulas. Parents' compliance with the treatments was considered adequate in all subjects that completed the follow up. All children allocated to the lactose free formula were given lactose formula after three weeks without recurrence of the illness.

DISCUSSION

At least 14 randomized trials comparing lactose and lactose free regimens during diarrhoea in children have been published since 1968 (13-26). As expected, there is great variability in the characteristics of these studies. Although 10 studies (15,20,21,25) included only inpatients, the severity of the disease seems to differ signficantly among them. Most trials evaluated only one diet in the lactose free group; however, three studies (18,23,26) used two formulas without lactose and two more (20,22) three lactose free regimens. Ten studies assessed soy based formulas in the lactose free groups (13-18,20,23-25), two used food mixtures free of milk (19,21), and one cow's milk treated with lactase (26). Five studies measured the mean number of days with diarrhoea as an outcome (15,16,18,19,21), while three more measured this length in hours (13,24,26); only one of these trials found statistically significant differences in the duration of the disease between the treatments (13). Significant differences in the proportion of failures during refeeding were found in three out of nine studies that measured this outcome (13,14,17).

All children studied by us had AD lasting up to seven days, and were receiving lactose formula until the illness onset. This feature differs from that in several previous papers, that do not give information about the duration of illness in their patients (13,14,19,21,22). As mentioned in the methods, we excluded children that had received antibiotics during a 48 hour period prior to admission because the long use of these drugs can produce diarrhoea, and those receiving more than 50% of their daily milk as breast milk (containing lactose) because the interruption of breast feeding during the study period in the subjects allocated to the lactose free group was considered inconvenient, both for ethical and practical reasons (28).

In general, previous trials that have reported differences seem to have included sicker patients. For this reason we decided to study only inpatients, who are expected to be sicker than those treated as outpatients. All subjects included in this trail were dehydrated on admissión, despite that most of them had received ambulatory care with oral rehydration therapy before admission. However, most cases had mild or moderate dehydration, with only one patient considered severely dehydrated. Although there were no cases with severe malnutrition, more than a third of the studied children were undernourished. It is necessary to point out that the study population included a reduced proportion of infants under six months of age, who may have more severe diarrhoea. This is due to the organization of the social security system in Bogota, that offers hospital care for children under one year at lower cost in other health facilities. All this means that our study population did not have enough number of children of the highest risk groups for lactose intolerance (i.e those under six mo of age, with severe dehydration and with severe malnutrition), which can limit the generalizability of the results in some extent. However, our findings will be applicable

to children at social security institutions whose general conditions are similar to those described in our population.

Table 2 shows that the study groups had similar baseline characteristics of all variables but for the duration of illness before admission. As it was shown, this difference did not have statistical association with the variables used as outcome measures. Several of the pathogens identified in stools are not generally considered enteric pathogens capable of causing diarrhoea; these data are provided to allow a better description of our subjects, and to compare the baseline characteristics of the study groups. Unfortunately, more precise typification of *E. coli* and cultures for Campylobacter could not be carried out.

As previously mentioned, most studies conducted up to date have used soy formulas in the lactose free group, which means that experimental intervention was different to the control both in the carbohydrate and in the protein source. This makes difficult to interpret the results of such studies. One reason we had to use AL-110 was that the protein content in this formula is similar to that in whole milk, which allows to rule out cointervention due to the simultaneous change in two ingredients of the formula. We believe that this constitutes a strength of our trial. Only the study conducted by Rajah (22) has evaluated this same formula as alternative for the routine withdrawal of lactose in children with AD. However, the lactose free treatment in Rajah's study included two more formulas, one of them soy-based, which makes difficult to isolate the effect of AL-110 and to compare our results with those reported in such study. On the other hand, it is necessary to emphasize that the milk formulas were offered at half strength during the first day, and that they were only one component of a mixed diet. These two facts may have diluted the effects of the lactose load in the evaluation, therefore reducing the possibility of finding differences between the study interventions. However, the intervention used may replicate closer the usual clinical practice, in which formula is not the only food provided to children with diarrhoea.

All subjets allocated to the control group in our study received formulas whose lactose concentration are similar to those found in human and cow's milk. It was necessary to use two formulas in this group in order to follow the usual clinical practices, according to which infants under six mo of age receive a product similar to breast milk while older children are given whole milk. This feature is different to the procedures followed in most previous studies, that have used the same lactose formula despite the age of the subjects included. In addition, it is necessary to mention that the study conducted by Leake et al (14) used a formula with a lactose content 50% higher than that of cow's milk in the control group during the first 48 h of refeeding, and as result it is impossible to say if the statistically signficant increase in the proportion of failures over the lactose free group could be explained by this non conventional procedure, or whether it would have been the same using regular formula.

No secondary reactions were reported in the study subjects, although some children allocated to the lactose free regimen seemed to perceive the different milk taste, secondary to the carbohydrate change. The formula was well tolerated for all patients. The study patient's compliance with the treatments was adquate, which rules out that the lack of differences on the results was due to no use of the experimental therapy in the group of patients allocated to this regimen. The very good compliance with the treatments observed in the study may be explained, at least partially, because the tolerance to the formula was known before discharging the patient, and because both lactose and lactose free formulas were provided to patients without cost during the study.

Although the main dependent variable in our study was the duration of diarrhoea after the reintroduction of food, we used the proportion of therapeutic failures as secondary outcome. Additonally, we decided to assess the change in the body weight during the period of use of the study intervention. These outcomes were evaluated by blind raters, which reduces the possbility of bias during the measurement. Although there was a tendency to a shorter duration of diarrhoea in the group receiving the lactose free formula when compared with the lactose group, this difference did not reach statistical signficance at the 0.05 level. No differences were found on the secondary outcomes either. It might be argued that the use of clinical variables to compare two diets could have contributed to the negative findings of our trial, and that it would have been of greater interest to monitor more «sensitive» variables, such as stool outputs during selected intervals of therapy. However, our study has demonstrated that there are no differences regarding clinical important outcomes. Should differences in stool output exist, their clinical meaning would be at most marginal.

Any trial that compares two treatments and that finds no differences must evaluate the probability of a Type II error, according to which the study can not demonstrate a true and signficative difference between the therapies due to a reduced sample size (29). The results of a pilot study conducted before starting the trial were used to estimate the number of subjects required to find a difference in the duration of the disease of at least one day, with a power of 80%. In accordance with the final results, the study power to find a 50% reduction (27 h) in the duration of diarrhoea after the reintroduction of food was 71%, slightly below the originally fixed. Using the data obtained in the control group, 35 subjects/group and 149 subjects/group would be required to demostrate a 50% and a 25% reduction in the duration of the disease, respectively (alpha 0.05, power 80%). Similary, the sample size required to show a reduction of 50% in the proportion of therapeutic failures found in accordance to the rate observed in the control group of this study would be much greater (519 subjects/group).

In conclusion, we think our study population was representative of the children under two years of age hospitalized due to AD in social security centres of Bogota,

and probably from other cities. However, the study sample included few infants under the age of six mo, and did not have severe malnourished subjects. Although the group of children receiving the lactose free regimen had a small reduction in the mean duration of the disease measured in hours after the reintroduction of food, this difference was not statistically significant. We could not find significant differences between the study groups regarding the median duration of the disease in days, the mean corporal weight increment, or the proportion of therapeutic failures either. Although the study power was slightly below the desired level, our findings suggest that the routine use a lactose free formula in hospitalized children has little effect, if any, over the course of this illness.

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REFERENCES

1. Snyder JD, Merson MH. The magnitude of the global problem of acute diarrheal disease; a review of active surveillance data. Bull WHO 60:605-613, 1982.
2. Black RE, Brown KH, Becker S, et al. Longitudinal studies of infectious diseases and physical growth of children in rural Bangladesh: I. Paterns of morbidity. Am J. Epidemiol, 115:305-314, 1982.
3. Black RE, Brown KH, Becker S, et al. *Londitudinal studies of* infectious diseases and physical growth of children in rural Bangladesh: II. Incidence of diarrhea and association with known pathogens. Am J Epidemiol, 115:315-324, 1982.
4. Black RE, Brown KH, Becker S. Effects of diarrhea associated with specific enterpathogens on the growth of children in rural Bangladesh. Pediatrics, 73: 799-805, 1984.
5. Wharton a, Pugh RE, Taitz LS, Walker-Smith JA, Booth IW. Dietary management of gastroenteritis in Britain. BR Med J, 296:450-452, 1988.
6. Madkour AA. Feeding during and after diarrhea. In: Maternal and child care in developing countries. Kessel E, Awan AK, eds. Switzerland: Ott Publishers, 1989, p.221-233.
7. Anonymous. A manual for the treatment of diarrhoea. For use by physicians and other senior health workers, WHO/CDD/SER80. 2 Rev 2, 1990.
8. Brown KH, Black RE, Parry L. The effects of diarrhea on incidence of lactose malabsorption among Bangladeshi children. Am J Clin Nutr, 33:2226-2227, 1980.
9. Hyams JS, Krause PJ, Geason PA. Lactose malbsorption following rotavirus infection in young children. J Pediatr, 99:916-918, 1981.
10. Davidson GP, Goodwing D, Robb TA. Incidence and duration of lactose malabsorption in children hospitalized with acute enteritis; study in a well nourished urban population. J Pediatr, 105:587-590, 1984.
11. Davidson GP, Goodwing D, Robb TA. Incidence and duration of lactose malabsorption in children hospitalized with acute enteritis; study in a well nourished urban population. J Pediatr, 105:587-590, 1984.
12. Trounce JQ, Wlaker-Smith JA. Sugar intolerance complicating acute gastroenteritis. Arch Dis Child, 60:986-990, 1985.
13. Sutton RE, Hamilton JR. Tolerance of young children with severe gastroenteritis to dietary lactose: a controlled study. Can Med Assoc J, 99:980-982, 1968.
14. Leake RD, Schroeder KC, BEnton DA, Oh W. Soy based formula in the treatment of infantile diarrhea. Am J Dis Child, 127:374-376, 1974.
15. Gabr M, Maraghi S, Morsi S. Management of lactose intolerance secondary to acute diarrhea with a soy based lactose free formula. Clin Therap. 2:271-276, 1979.
16. Noah MA. Soy based formula for infantile diarrhea: a controlled trial. Nig Med J, 9:243-245, 1979.
17. Naidoo BT, Chunterpurshad I, Mahyoodeen ABG, Pather G. The use of a soy Isolate based formula in the treatment of infantile diarrhoea. J Int Med Res, 9:232-235, 1981.
18. Bard-el-Din A, Kassem AS, Hussein ZM. Feeding during acute diarrhea. Gazz Egyp Paediatr Assoc, 31:89-93, 1983.
19. Isoulari E, Vesikari T, Saha P, Viander M. Milk versus no milk in rapid refeeding after acute gastroenteritis. J Ped Gastroen Nutr, 5:254-261.
20. Groothuis JR, Berman S, Chapman J. Effect of carbohydrate ingested on outcome in infants with mild gastroenteritis. J Pediatr, 108:903-906., 1986.
21. Bhan MK, Arora NK, Kloshoo B, Raj P, Sazawal S, Sharma K. Comparison of a lactose-free cereal based formula and cow's milk in infants and children with acute gastroenteritis. J Pediatr Gastroenterol Nutr, 7:208-213, 1988.
22. Rajah R. The effect of feeding four different formulas on stool weights in prolonged dehydrating infantile gastroenteritis. J Pediatr Gastroenterl Nutr, 7:203-207, 1988.
23. Conway SP, Ireson A. Acute gastroenteritis in well nourished infants: comparison of four feeding regimenes. Arch Dis Child, 64:87-91, 1989.
24. Haffejee IE. Cow's milk/based formula, human milk and soya feeds in acute infantile diarrhea: a therapeutic trial. J Pediatr Gastroenterl Nutr, 10:193-198, 1990.
25. Margolis PA, Litteer T, et al. Effects of unrestricted diet on mild infantile diarrhea. A practice based study. Am J Dis Child, 144:162-164, 1990.
26. Brown KH, Pérez F, Gastañaduy AS. Clinical trial of modified whole milk, lactose hydrolyzed whole milk, or cereal-milk mixtures for the dietary management of acute childhood diarrhea. J Pediatr Gastroenterol Nutr, 12:340-350, 1991.
27. Waterlow JC. Classification and definition of protein calorie malnutrition. Br Med J, 3:566-569, 1972.
28. Khin-Maung-U, Nyunt-Nyunt-W, Myo-Khin, Mu-Mu-Khin, Tin-U, Thane-Toe. Effect of clinical outcome of breast feeding during acute diarrhoea. Br Med J, 290:587-9, 1985.
29. Sackett DL, Haynes RB, Tugwell P. Clinical Epidemiology. A basic science for clinical medicine. Boston: Little, Brown and Company, 1985.

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