Original Research

Evaluation of a Diet Containing Probiotics and Zinc for the Treatment of Mild Diarrheal Illness in Children Younger Than One Year of Age

Raanan Shamir, MD, Imad R. Makhoul, MD, DSc, Amos Etzioni, MD, and Naim Shehadeh, MD

Division of Pediatric Gastroenterology and Nutrition (R.S.), Department of Neonatology (I.R.M.), Department of Pediatrics A (A.E., N.S.), Meyer Children's Hospital of Haifa, Primary Pediatric Clinic, Tamra, Western Galilee (I.R.M., N.S.), Bruce Rappaport School of Medicine, Technion-Institute of Technology, Haifa, ISRAEL

Key words: Acute gastroenteritis, probiotics, *Streptococcus thermophilus*, *Bifidobacterium lactis*, *Lactobacillus acidophilus*, zinc

Objectives: Supplementation of probiotics and supplementation of zinc during acute gastroenteritis in children have been shown to exert positive effects on diarrhea duration and severity. Our aim was to evaluate a new diet enriched with zinc and probiotic bacteria in the treatment of acute gastroenteritis in young children.

Methods: In a double blind prospective study, 65 children aged 6–12 months were randomized to receive 6×10^9 colony forming units of *Streptococcus thermophilus*, *Bifidobacterium lactis*, *Lactobacillus acidophilus* (2×10^9 of each strain), 10 mg of zinc/day, and 0.3 grams of fructo-oligosaccharides in the supplemented group ($n = 33$) or placebo ($n = 32$), given in a soy protein based rice cereal. For each child, age, sex, weight, degree of dehydration, the presence of fever or vomiting, stool frequency and consistency were recorded daily until diarrhea resolution.

Results: Diarrhea resolution occurred after 1.43 ± 0.71 days in the supplemented group vs. 1.96 ± 1.24 in the control group ($p = 0.017$). In the subset of children who presented with vomiting, time to vomiting resolution was 0.27 ± 0.59 vs. 0.81 ± 0.91 days in the supplemented and control groups, respectively ($p = 0.06$). On day 3, there was only 1 child with watery stools in the supplemented group versus 10 children in the control group ($p = 0.02$).

Conclusions: In our series, the feeding of a cereal containing *Streptococcus thermophilus*, *Bifidobacterium lactis*, *Lactobacillus acidophilus* and zinc, reduced the severity and duration of acute gastroenteritis in young children. However, whether this combination is better than either the addition of probiotics or zinc alone is yet to be determined.

INTRODUCTION

Diarrheal diseases are a leading cause of mortality in infants and children world wide, and continue to be a significant cause for morbidity in industrialized countries [1]. In recent years, the major advance in the treatment of acute gastroenteritis in children was the introduction of oral rehydration solution (ORS) in the early stages of illness [2,3]. In addition, rice water and rice based ORS are superior to ORS alone in reducing the frequency and stool volume in acute gastroenteritis [4,5]. However, nutritional interventions during the diarrheal illness are usually not helpful in reducing the duration of diarrhea, and current recommendations call for the continuation of age-appropriate diets during mild diarrhea [1–3].

Two meta-analyses have demonstrated a therapeutic effect of probiotics, mainly *Lactobacillus GG*, on acute diarrhea caused by rota virus [6,7]. This treatment usually reduces the duration of diarrhea by a few hours [6,7]. Possible explanations

Address reprint requests to: Raanan Shamir, MD, Division of Pediatric Gastroenterology and Nutrition, Meyer Children's Hospital of Haifa, Rambam Medical Center, POB 9602, Haifa 31096, ISRAEL. E-mail: shamirr@netvision.net.il

Financial interest: Dr. Shehadeh and Dr. Shamir served as consultants to Remedia, Israel, in the design of this product. Remedia, Israel, supplied the study cereals free of charge.

for the observed effects include inhibition of adhesion of pathogens, enhanced mucosal integrity, beneficial effects on the dysregulated immune response, production of antimicrobial substances, and intestinal receptor modification [6–10].

In addition to probiotics, intervention trials have demonstrated that the addition of oral zinc can also reduce the duration and severity of acute diarrhea in children [7,11,12]. The rationale for the beneficial effect of zinc supplementation is based on the depletion of zinc due to diarrhea [11,13] and the deleterious effects of zinc deficiency on the immune system, leading to more severe enteric infections [14]. In support of zinc supplementation is that there is no evidence that zinc cause harm when given to non-septic immunocompetent children [15].

On the other hand, results of zinc supplementation studies were not consistent, with a very modest effect observed when zinc was added to an ORS solution [16].

Since zinc and probiotics work via different mechanisms it is possible that adding both would have a synergistic effect. One study, in rhesus monkeys, showed a prophylactic effect of the combination of probiotics and zinc [17]. However, the combination of probiotics and zinc in the treatment of acute diarrheal illness in children has not been tested.

Our study aim was to evaluate the effectiveness of a new diet enriched with zinc and probiotic bacteria in the treatment of acute diarrhea in young children.

PATIENTS AND METHODS

Patients

Sixty five consecutive children attending the Primary Pediatric Clinic, Tamra, Western Galilee, Israel, were prospectively enrolled to this double blind placebo controlled randomized study between April 2002 and April 2003. At enrollment children were randomized using sealed envelopes containing a note assigning the patient to one of the 2 study arms. There were 33 children (19 males) in the study group (supplemented), and 32 (14 males) in the control group. One child in the supplemented group (9 month old female) and 2 children in the control group (an 11 month old male and a 12 month old female) did not drink the formula in the amount specified by the protocol, but their data were collected when available (see footnotes for Table 2), and the analysis was based on intention to treat.

Inclusion criteria for the children were age between 6–12 months, the presence of acute diarrheal illness, and the presence of mild to moderate dehydration. Acute diarrheal illness was defined as passage of four or more watery stools in 24 hours for more than one day and less than 7 days [11]. The presence of mild to moderate dehydration was established as previously defined [18]. Exclusion criteria included severe dehydration, exclusively breast-feeding, clinical dysentery, toxic clinical appearance, and immuno-suppressed children.

For each child age, sex, weight, degree of dehydration, the presence of fever or vomiting, number of bowel movements and stool consistency (watery, loose or solid) were recorded. Children were seen every day, and weight, degree of dehydration, presence of fever or vomiting, number of bowel movements and stool consistency were recorded. Diarrhea resolution was established when stool consistency ceased to be watery, or when the number of bowel movements was lower than 3 in 24 hours. Due to the ambulatory setting of the study, after diarrhea resolution, parents were instructed to return to the clinic if diarrhea resumed, and daily telephone calls were made to ensure that there are no relapses.

The Institutional Ethics Committee approved the study. All parents gave informed consent for their child's participation in the study.

Methods

Children diagnosed with acute gastroenteritis were instructed to drink an ORS solution according to previously established guidelines [3,18]. In short, oral rehydration with ORS was calculated to replace the estimated fluid deficit, and given over 4 hours. After that, parents were instructed to continue ORS supplementation with 10 ml/kg of fluids for each watery stool or vomitus. In addition, rapid introduction of feedings were practiced (three hours after the beginning of ORS). After randomization (see patients section) patients were assigned to group 1 or 2 in a double blind manner (cereals were sealed as cereal 1 and 2 by the manufacturer). Both groups were instructed to consume 600 ml of cereals (Baby-Biocal, Remedia, Israel) with or without added probiotics and zinc, in a lactose free, soy protein-based formula (Remedia Tsimchit, Remedia, Israel). The instructions were to provide the rest of the infant's feeding regimen with the regular diet used before the episode of diarrhea. The composition of the soy based formula is shown in Table 1, as well as the nutrient composition of the study and control formula and the probiotic content of the study formula. The viability of the probiotic strains was examined after six months of storage and determined to be 7×10^9 colony forming units/100 g cereal. All cereals used in this study were consumed within 6 months of addition of the probiotics.

Statistical Analysis

Differences between groups were evaluated using two-tailed Student t-test. For single parameters, the Fisher Exact test was used. P values less or equal to 0.05 were considered statistically significant.

RESULTS

The characteristics of the study groups are presented in Table 2. There were 32 children with mild dehydration in the

Table 1. Composition of Study and Control Formulas

		Nutritional content per 100 g cereal*		Nutritional values per 100 ml of formula**	Nutrition content for daily consumption***	
		Study cereal	Control cereal	Study and control group	Study group	Control group
Energy	Kcal	366	366	68	517.8	517.8
Proteins	gr	5.7	5.7	1.8	12.51	12.51
Carbohydrate	gr	83.7	83.7	7.9	72.51	72.51
Fibers	gr	3.5	2.5		1.05	0.75
FOS (fructo-oligosaccharides) (as part of fibers)	gr	1.0	0		0.3	0
Fat	gr	0.9	0.9	3.3	20.07	20.07
Na	mg	15.7	15.7	27.6	170.31	170.31
Ca	mg	800.0	800.0	74.4	686.4	686.4
P	mg	540.0	540.0	41.4	410.4	410.4
K	mg			77.2	463.2	463.2
Cl	mg			51.0	306	306
Mg	mg	30.0	30.0	6.3	46.8	46.8
Fe	mg	40.0	40.0	1.2	19.2	19.2
Zn	mg	40.0	7.0	0.6	15.6	5.7
I	mcg	60.0	60.0	10.1	78.6	78.6
Se	mcg	25.0	25.0	2.1	20.1	20.1
Taurin	mg			7.6	45.6	45.6
Cu	mcg	700.0	700.0	54.4	536.4	536.4
Mn	mcg			37.9	227.4	227.4
Vit A	mcg	600.0	600.0	62.0	552	552
Vit D3	mcg	12.5	12.5	1.0	9.75	9.75
Vitamin K	mcg	14.0	14.0	10.3	66	66
Vit E	mg	7.0	7.0	1.5	11.1	11.1
Vit C	mg	80.0	80.0	10.6	87.6	87.6
Vit B1	mcg	1000.0	1000.0	53.1	618.6	618.6
Vit B2	mcg	1200.0	1200.0	68.2	769.2	769.2
Vit B6	mcg	600.0	600.0	49.6	477.6	477.6
Vitamin B12	mcg	1.2	1.2	0.2	1.74	1.74
Niacin	mg	10.0	10.0	1.1	9.6	9.6
Pant. Acid mg	mg	5.0	5.0	0.7	5.7	5.7
Folic Acid mcg	mcg	90.0	90.0	11.4	95.4	95.4
Biotin mcg	mcg	22.0	22.0	3.8	29.4	29.4
Choline mg	mg			8.3	49.8	49.8
Inositol mg	mg			3.4	20.4	20.4
Nucleotides	mg			3.4	20.4	20.4
Carnitine	mg			1.4	8.4	8.4
Bifidobacterium lactis	CFU	0.66×10^{10}			2×10^{9}	0
Streptococcus termophilus	CFU	0.66×10^{10}			2×10^{9}	0
Lactobacillus acidophilus	CFU	0.66×10^{10}			2×10^{9}	0

* Composition of the cereals provided to the study group and the control group (per 100 gr).

** Composition of the soy based formula (Remedia Tsimchit, Remedia, Israel) consumed by study and control groups (per 100 ml).

*** Composition of the daily amounts consumed by study and control groups, respectively, based on an intake of 600 ml of the soy protein based formula and 30 grams of cereals as directed.

CFU = Colony forming units.

supplemented group (plus one with moderate dehydration), and 32 children with mild dehydration in the control group.

Season of gastroenteritis occurrence was similar in both groups. Most of the cases occurred between May and July (12 in the supplemented group and 12 in controls) and between November and February (14 in the supplemented group and 12 in controls).

Clinical characteristics of the study groups are shown in Table 3. The mean duration of diarrhea was 0.62 days (14 hours and 53 minutes) shorter in the supplemented group compared to the control group ($p = 0.017$). On daily follow up for 7 days after diarrhea resolution, none of the children in both study arms had a repeated diarrheal episode.

There were no differences in weight change from base line (weight on study entry) between the supplemented group and the control group (Fig. 1). Although these numbers are too small for statistical comparison, after 3 days, the supplemented group as regained their mean base line weight while the mean

Table 2. Characteristics of Participants at Study Entry

	Supplemented group n = 33	Control group n = 32	p value
Age (months)	9.42 ± 1.98	9.13 ± 2.07	0.55
Weight (grams)	9470 ± 1153	9020 ± 1300	0.14
Fever > 38.0 C°	16 children	12 children	0.45
Vomiting	16 children	16 children	1
Diarrhea prior to enrollment (days)	2.15 ± 0.75	2.59 ± 1.31	0.1

Data also include children who did not complete the study (one child in the supplemented group and 2 children in the control group). Data are expressed as Mean ± Standard Deviation.

weight of the control group remained below their base line weight.

There were no differences between the groups in the number of bowel movements per day (Fig. 2). Regarding stool consistency, there was no difference between the groups on day 1 and day 2. However, on day 3, there was only 1 child with watery stools in the supplemented group compared with 10 children in the control group (p = 0.02).

DISCUSSION

Supplementation of *Lactobacillus* during acute gastroenteritis in children has been consistently demonstrated to have a beneficial effect on both diarrhea duration and severity [6,7]. Since the effect of *Lactobacillus* is not limited to rota virus infection, this treatment may be useful not only in the hospital setting but also in the ambulatory setting, where a variety of pathogens are most likely to be at play [6]. In the present study of children in the community, we were able to demonstrate similar beneficial effects of a combination of probiotic bacteria.

Administration of several probiotics species, namely VSL#3, that contains three species of *Bifidobacteriae*, four

Table 3. Clinical Characteristics of Study Groups

	Supplemented group n = 33	Control group n = 32	p value
Time to resolution of fever (days)*	0.44 ± 0.63	0.75 ± 0.87	0.45
Time to resolution of vomiting (days)*	0.27 ± 0.59	0.81 ± 0.91	0.059
Time to resolution of diarrhea (days)	1.34 ± 0.71	1.97 ± 1.24	0.017

Data includes children who did not complete the study (one child in the supplemented group and 2 children in the control group). Data are available for all study participants until day 2. From day 2, data is missing for one child in the supplemented group (9-month old male) and one child from the control group (11-month old male) who were lost to follow up.

* Data provided for the children who presented with fever in the supplemented (n = 16) and control (n = 12) groups and the 16 children who presented with vomiting in each group.

Data are expressed as Mean ± Standard Deviation.

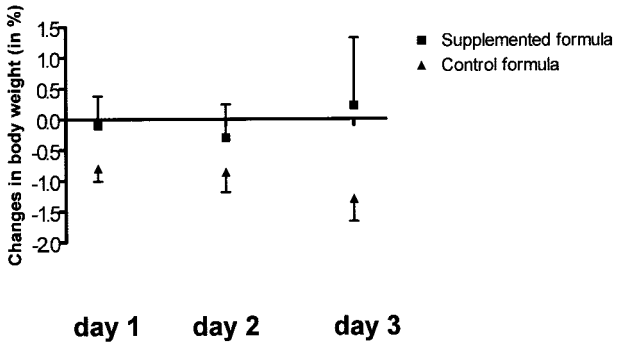

Fig. 1. Changes in % body weight in study groups. Changes in % body weight (base line referred to as zero for both groups) are presented for both groups as mean ± standard deviation. Children who recovered ceased to attend the Pediatric Clinic; therefore, of the supplemented group, there were 33 children on day 1, 27 on day 2, and 12 on day 3, and of the control group, there were 32 children on day 1, 30 on day 2, and 17 on day 3.

strains of lactic acid bacteria and one strain of *Streptococcus*, has been demonstrated to be useful in the treatment of adults with various gastrointestinal disorders including prevention of acute pouchitis [19], prevention of flare-ups in chronic pouchitis [20], irritable bowel syndrome [21], and radiotherapy induced diarrhea [22]. Although the concept of using a mixture of probiotic bacteria was successful in gastrointestinal inflammation, this combination has not been studied in acute gastroenteritis, and it is unknown whether specific bacteria contained in the VSL#3 combination are responsible for the observed effect. Since we did not compare the effect of adding one probiotic bacteria to that of a combination of probiotic species, the rationale for a combination of species for the treatment of acute gastroenteritis is yet to be evaluated.

In hospitalized children, the combination of *Bifidobacterium lactis* and *Streptococcus thermophilus* was proved useful in the prevention of acute gastroenteritis [23]. In another study

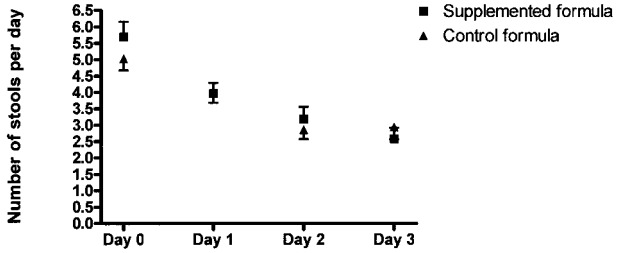

Fig. 2. Number of stools per day in study groups. At base line, the number of stools per day was higher in the supplemented group (5.7 ± 2.6) than in the control group (5.0 ± 2.1, p = 0.14), and was similar on day 3 (2.6 ± 1.2 in the supplemented group, 2.9 ± 1.6 in the control group). Since children who recovered ceased to attend the Pediatric Clinic, in the supplemented group, there were 33 children on day 1, 27 on day 2, and 12 on day 3. In the control group there were 32 children on day 1, 30 on day 2, and 17 on day 3. Data are presented for both groups as Mean ± Standard Deviation.

in hospitalized children with a wide age range (6 to 60 months), supplementation of the formula with *Bifidobacterium infantis* and *Lactobacillus acidophilus* reduced the duration of diarrhea by 0.5 days [24].

In the present study we were able to demonstrate, in a primary care setting, that the addition of 6×10^9 colony forming units of *Streptococcus thermophilus*, *Bifidobacterium lactis*, *Lactobacillus acidophilus* (2×10^9 of each strain) and 10 mg/day of zinc significantly reduced the duration of acute gastroenteritis in children aged 6–12 months (by close to 15 hours) and induced quicker resumption of normal stool consistency. At this stage, it is impossible to ascertain whether the observed effects were induced by the combination of probiotics or by any one of the strains in the mixture that was added to the formula. Furthermore, the presence of minimal amounts of oligosaccharides in the study formula may have contributed to the beneficial effects, since the addition of oligosaccharides to infant formula has a dose-dependent stimulating effect on *Bifidobacteria* and *Lactobacilli* [25].

Oligosaccharides have been shown to increase stool frequency and decrease stool consistency [26], but such effect was not demonstrated at a dosage as employed in our study [25]. Furthermore, since stools became harder in the supplemented group without a significant effect on the number of stools, it is unlikely that the observed effects on stool frequency and consistency were related to the oligosaccharides. One explanation for harder stools without a change in the number of stools could be that the treatment influenced electrolytes and fluids absorption and excretion rather than intestinal motility or immune responses.

In acute gastroenteritis, zinc supplementation reduces the duration and severity of the disease [11,12]. Furthermore, zinc supplementation for 4 months reduces the incidence of severe and prolonged diarrhea in children [27]. On the other hand, the addition of probiotics to infant formula in rhesus monkeys decreased the severity of experimentally induced diarrhea, but no additional benefit was obtained adding zinc to the probiotics [17]. Moreover, a study in young children in Peru reported that morbidity was greater following supplementation with zinc *plus* multivitamins and minerals than with supplementation with zinc alone [28]. Since a cereal containing only zinc was not included in our study, the potential specific (beneficial or detrimental) contribution of zinc to our results remains uncertain.

There are several limitations to our study. The sample size was small, due to the primary care setting, there was no isolation of pathogens, and all participants consumed a soy protein based formula and rice. Although stools were not examined for pathogens, the study and the control groups were recruited from the same villages with presented at the same season, suggesting a similar distribution of causative agents. Thus, our results demonstrate the efficiency of the investigated preparation in an ambulatory setting, but the efficiency related to specific pathogens can not be established. Soy protein and rice had probably no effect on the outcome since they were equally consumed by both groups. Despite the small sample size, we were able to demonstrate a significant effect of feeding a formula supplemented with a mixture of probiotics and zinc, although our study design precludes the possibility to determine whether one ingredient or a combination of ingredients was responsible for earlier resolution of diarrhea and improvement in stool consistency.

In summary, the supplementation of a *Streptococcus thermophilus*, *Bifidobacterium lactis*, *Lactobacillus acidophilus* and zinc combination to a soy-protein based rice cereal, can shorten the severity and duration of mild acute gastroenteritis in children six to twelve months of age. However, whether this combination is better than adding only probiotics or only zinc is yet to be determined.

ACKNOWLEDGMENT

This work was supported in part by Remedia, Israel.

REFERENCES

1. Shamir R, Zahavi I, Abramowich T, Poraz I, Tal D, Pollak S, Dinari G: Management of acute gastroenteritis in children in Israel. Pediatrics 101:892–894, 1998.
2. American Academy of Pediatrics. Provisional Committee on Quality Improvement, Subcommittee on Acute Gastroenteritis: Practice parameters: the management of acute gastroenteritis in young children. Pediatrics 97:424–433, 1996.
3. Walker-Smith JA, Sandhu BK, Isolauri E, Banchini G, van Caillie-Bertrand M, Dias JA, Fasano A, Guandalini S, Hoekstra JH, Juntunen M, Kolacek S, Marx D, Micetic-Turk D, Razenberg MC, Szajewska H, Taminiau J, Weizman Z, Zanacca C, Zetterstrom R: Guidelines prepared by the ESPGAN Working Group on Acute Diarrhoea. Recommendations for feeding in childhood gastroenteritis. European Society of Pediatric Gastroenterology and Nutrition J Pediatr Gastroenterol Nutr 24:619–620, 1997.
4. Wall CR, Swanson CE, Cleghorn GJ: A controlled trial comparing the efficacy of rice-based and hypotonic glucose oral rehydration solutions in infants and young children with gastroenteritis. J Gastroenterol Hepatol 12:24–28, 1997.
5. Mehta MN, Subramaniam S: Comparison of rice water, rice electrolyte solution, and glucose electrolyte solution in the management of infantile diarrhoea. Lancet 1:843–845, 1986.
6. Van Niel C, Feudtner C, Garrison MM, Christakis DA: Lactobacillus therapy for acute infectious diarrhea in children: A meta-analysis. Pediatrics 109:678–684, 2002.
7. Szajewska H, Mrukowicz J: Probiotics in the treatment and prevention of acute infectious diarrhea in infants and children: a systematic review of published randomized, double-blind, placebo controlled trials. J Pediatr Gastroenterol Nutr 33:S17–S25, 2001.
8. Isolauri E, Kirjavainen PV, Salminen S: Probiotics: a role in the treatment of intestinal infection and inflammation? Gut 50(Suppl III):iii54–iii59, 2002.

9. Markowitz JE, Bengmark S: Probiotics in health and disease in the pediatric patient. Pediatr Clin North Am 49:127–141, 2002.
10. Reid G, Jass J, Sebulsky MT, McCormick JK: Potential uses of probiotics in clinical practice. Clin Microbiol Rev 16:658–672, 2003.
11. Sazawal S, Black RE, Bhan MK, Bhandari N, Sinha A, Jalla S: Zinc supplementation in young children with acute diarrhea in India. N Engl J Med 333:839–844, 1995.
12. Strand TA, Chandyo RK, Bahl R, Sharma PR, Adhikari RK, Bhandari N, Ulvik RJ, Molbak K, Bhan NK, Sommerfelt H: Effectiveness and efficacy of zinc for the treatment of acute diarrhea in young children. Pediatrics 109:898–903, 2002.
13. Castillo-Duran C, Vial P, Uauy R: Trace mineral balance during acute diarrhea in infants. J Pediatr 113:452–457, 1988.
14. Bhandari N, Bahl R, Taneja S, Strand T, Molbak K, Ulvik RJ, Sommerfelt H, Bhan MK: Substantial reduction in severe diarrheal morbidity by daily zinc supplementation in young North Indian children. Pediatrics 109:e86, 2002.
15. Doherty CP, Weaver LT, Prentice AM: Micronutrient supplementation and infection: a double-edged sword?. J Pediatr Gastroenterol Nutr 34:346–552, 2002.
16. Bahl R, Bhandari N, Saksena M, Strand T, Kumar GT, Bhan MK, Sommerfelt H: Efficacy of zinc-fortified oral rehydration solution in 6- to 35-month-old children with acute diarrhea. J Pediatr 141:677–682, 2002.
17. Kelleher SL, Casas I, Carbajal N, Lonnerdal B: Supplementation of infant formula with the probiotic lactobacillus reuteri and zinc: impact on enteric infection and nutrition in infant rhesus monkeys. J Pediatr Gastroenterol Nutr 35:162–168, 2002.
18. Sandhu BK; European Society of Pediatric Gastroenterology, Hepatology and Nutrition Working Group on Acute Diarrhoea: Practical guidelines for the management of gastroenteritis in children. J Pediatr Gastroenterol Nutr 33(Suppl 2):S36–S39, 2001.
19. Gionchetti P, Rizzello F, Helwig U, Venturi A, Lammers KM, Brigidi P, Vitali B, Poggioli G, Miglioli M, Campieri M: Prophylaxis of pouchitis onset with probiotic therapy: a double-blind, placebo-controlled trial. Gastroenterology 124:1202–1209, 2003.
20. Gionchetti P, Gionchetti P, Rizzello F, Venturi A, Brigidi P, Matteuzzi D, Bazzocchi G, Poggioli G, Miglioli M, Campieri M: Oral bacteriotherapy as maintenance treatment in patients with chronic pouchitis: a double-blind, placebo-controlled trial. Gastroenterology 119:305–309, 2000.
21. Kim HJ, Camilleri M, McKinzie S, Lempke MB, Burton DD, Thomforde GM, Zinsmeister AR: A randomized controlled trial of a probiotic, VSL#3, on gut transit and symptoms in diarrhoea-predominant irritable bowel syndrome. Aliment Pharmacol Ther 17:895–904, 2003.
22. Delia P, Sansotta G, Donato V, Messina G, Frosina P, Pergolizzi S, De Renzis C: Prophylaxis of diarrhoea in patients submitted to radiotherapeutic treatment on pelvic district: personal experience. Dig Liver Dis 34(Suppl 2):S84–S86, 2002.
23. Saavedra JM, Bauman NA, Oung I, Perman JA, Yolken RH: Feeding of Bifidobacterium bifidum and Streptococcus thermophilus to infants in hospital for prevention of diarrhoea and shedding of rotavirus. Lancet 344:1046–1049, 1994.
24. Lee MC, Lin LH, Hung KL, Wu HY: Oral bacterial therapy promotes recovery from acute diarrhea in children. Acta Pediatrica Taiwanica 42:301–305, 2001.
25. Moro G, Minoli I, Mosca M, Fanaro S, Jelinek J, Stahl B, Boehm G: Dosage-related bifidogenic effects of galacto- and fructooligosaccharides in formula-fed term infants. J Pediatr Gastroenterol Nutr 34:291–295, 2002.
26. European Commission. Health and Consumer Protection Directorate-General. Scientific Committee on Food Statement on the Use of Resistant Short Chain Carbohydrates (Oligofructose and Oligogalactose) in Infant Formula and in Follow-on Formulae. http://europa.eu.int/comm/food/fs/sc/scf/index_en.html September 26, 2001.
27. Bhandari N, Bahl R, Taneja S, Strand T, Molbak K, Ulvik RJ, Sommerfelt H, Bhan MK: Substantial reduction in severe diarrheal morbidity by daily zinc supplementation in young north Indian children. Pediatrics 109:e86, 2002.
28. Penny ME, Marin RM, Duran A, Peerson JM, Lanata CF, Lonnerdal B, Black RE, Brown KH: Randomized controlled trial of the effect of daily supplementation with zinc or multiple micronutrients on the morbidity, growth, and micronutrient status of young Peruvian children. Am J Clin Nutr 79:457–465, 2004.

Received March 24, 2004; revision accepted March 20, 2005.