Management of Lithuanian children's acute diarrhoea with Gastrolit solution and dioctahedral smectite

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Objective **Acute gastroenteritis represents a major cause of morbidity and mortality worldwide among children, and rehydration treatment has been one of the cornerstones in the management strategy. The natural clay dioctahedral smectite (Smecta) increases intestinal barrier function and is effective against infectious diarrhoea in children. The purpose of this work was to compare the efficacy and tolerance of Lithuanian children's diarrhoea treatment with dioctahedral smectite combined with hypotonic oral rehydration solution (ORS) – Gastrolit – versus Gastrolit alone to establish the influence of Smecta on serum electrolyte balance in young children with diarrhoea and mild or moderate dehydration.**

Methods **Smecta combined with ORS (study group) and ORS alone (control group) were evaluated in a multicentre, open, randomized trial in 54 children aged 6–48 months hospitalized for acute diarrhoea (mostly rotavirus aetiology) and signs of mild and moderate dehydration. The main outcomes examined were duration of diarrhoea, fever, number of vomiting episodes, and serum electrolyte balance before and after treatment.**

Results **The mean duration of diarrhoea was significantly shorter in the study group (42.3 ± 24.7 h) than in the control group (61.8 ± 33.9 h). No side effects of Smecta were observed. The changes of sodium, potassium, chloride and calcium concentrations after treatment were minimal and in the normal range.**

Conclusions **Smecta significantly reduced the duration of diarrhoea, was safe and well tolerated, and had no impact on the adsorption of electrolytes. Smecta could be used together with ORS in children suffering from acute gastroenteritis (without uncontrollable vomiting) with mild and moderate dehydration.** ***Eur J Gastroenterol Hepatol*** **14:419–424 © 2002 Lippincott Williams & Wilkins**

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Introduction

Acute diarrhoea is still an important cause of morbidity worldwide. The Lithuanian Centre for Communicable Diseases Prevention and Control reported 12 580 cases of infectious gastroenteritis in 1998, 14 147 in 1999, and 11 855 in 2000.

Management of acute diarrhoea in children consists of oral rehydration, appropriate nutritional treatment, and various auxiliary treatments aimed at shortening the diarrhoeal episode [1,2]. In 1992, the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) published guidelines recommending the use of hypo-osmolar oral rehydration solution (ORS) with a sodium content of 60 mmol/l and optimal osmolarity of 200–250 mosmol/l for European children [3]. Rehydration should normally be completed over a 3–4-h period. In Lithuania in 2000, we began to use a new ORS, Gastrolit, which corresponds to ESPGHAN recommendations.

Dioctahedral smectite (Smecta), an aluminosilicate of phyllitic structure, has been shown during in-vitro studies to protect the intestinal mucosal barrier. (Other names for this drug are also found in the literature, including Smectite® and Diosmectite®.) The drug adsorbs agents aggressing the intestinal mucosa, including rotavirus, *Escherichia coli*, *Campylobacter*, bile salts and non-digested sugars [4,5]. Double-blind or controlled clinical trials have shown that Smecta significantly reduces the duration of symptoms compared with oral rehydration alone [6–8].

The influence of Smecta on the serum electrolyte balance has not been studied in children with diarrhoea, but it has been demonstrated in experimental animals [9,10].

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The aim of this study was to compare the efficacy and tolerance of Lithuanian children's diarrhoea treatment with Smecta combined with Gastrolit solution and with Gastrolit alone to establish the influence of Smecta on the serum electrolyte balance in children with diarrhoea and mild or moderate dehydration.

Patients and methods

This was a multicentre, open, randomized clinical study conducted on 56 children from 4 February to 15 May 2000 in the Centre of Paediatrics, Vilnius University Children's Hospital and the Paediatric Clinic of Kaunas Hospital of Infectious Diseases, Lithuania.

To be enrolled in the study, children had to meet the following criteria: age 6–48 months; presenting with acute diarrhoea (excretion of three or more stools during 24 h but no more than 72 h before admission); and mild or moderate dehydration (classified according to the American Academy of Pediatrics guidelines [11]: mild, 3–5% weight loss; moderate, 6–9% weight loss).

Exclusion criteria were age < 6 months or > 48 months; duration of diarrhoea > 72 h; severe dehydration; concomitant illness (e.g. pneumonia, urinary tract infection, meningitis, malnutrition, shock); and acute infectious or other diseases requiring specific additional treatment.

Patients who developed a condition requiring intravenous fluid therapy were excluded from the analysis of the study.

Immediately after admission, a thorough clinical history of the patient was obtained, and a complete physical examination was performed. History and physical findings were recorded in a uniform clinical data sheet for each child. Patients who met the inclusion criteria were divided randomly into two treatment groups. Children born on odd-numbered days were treated with ORS only (control group), and those born on even-numbered days received ORS and Smecta (study group).

Weight was measured on admission, after initial rehydration, and daily thereafter during the hospital stay. The ward nurses recorded the number and quality of the stools passed (characterized as watery, loose, semisolid or solid), vomiting episodes, and temperature. Normal feeding (milk formula and supplement food as usual) for age was resumed immediately after the initial rehydration (3–6 h) period.

ORS (Gastrolit) consisted of 60 mmol/l sodium, 20 mmol/l potassium, 50 mmol/l chloride, 30 mmol/l bicarbonate, and 80 mmol/l of glucose (total osmolarity 240 mosmol/l). During the rehydration phase in the first 3–6 h, each child was given Gastrolit at a rate of 40–100 ml/kg to correct dehydration; no foods or other fluids were given during this phase. ORS was given 15–30 ml every 5–10 min. Children with vomiting received 5 ml every 2–3 min. Thereafter, the children were put on maintenance hydration therapy at approximately 100–150 ml/kg/day (including usual food and other fluids, e.g. tea, water, etc.). In both phases, losses due to vomit and stool were replaced with Gastrolit: 10 ml/kg for each diarrhoeal stool and 2 ml/kg for each emesis.

Smecta was available in sachets containing a powder composed of 3.0 g dioctahedral smectite, glucose monohydrate and vanilla to be dissolved in 30–50 ml boiled water or mixed with watery food. Children in the study group received 3 g at the beginning of rehydration and then 1.5 g every 8 h for children up to 10 kg body weight, and 1.5 g every 6 h for children with body weight of 10–20 kg. Treatment with Smecta was not continued for more than 24 h after normalization of the stools. Side effects (constipation, vomiting and others) of Smecta were evaluated. The evaluation criteria for both treatment groups were duration of diarrhoea, fever, number of vomiting episodes from initial therapy, and serum electrolyte balance at admission (before treatment) and at the time of discharge from hospital (after treatment). Clinical symptoms were evaluated during the follow-up after 4, 12, 24, 36, 48, 60, 72, 84, 96, 108 and 120 h. Diarrhoea was considered to have resolved at the time one of the following criteria was met: (i) passage of the first formed stool; (ii) passage of the second semisolid stool; (iii) passage of the last unformed (semisolid) stool if no stools were passed for 24 h. Duration of diarrhoea was therefore the period from the initiation of the treatment to the time of the last watery or semiliquid stool.

Venous blood was obtained at admission (first blood) and at the time of discharge from the hospital no more then 48 h after diarrhoea has stopped (second blood) for blood analysis and concentration of serum electrolytes (sodium, potassium, chloride, calcium). Serum electrolytes were determined with an Electrolyte Analyzer (Radiometer EML-100, Copenhagen, Denmark). The following concentrations (mmol/l) of electrolytes in venous blood serum were considered to be normal: sodium, 136–146; potassium, 3.5–5.0; chloride, 95–110; calcium (ionized), 1.15–1.29. Stool specimens were obtained shortly after admission for microbiological studies. Bacterial enteropathogens were identified by standard laboratory methods. Rotavirus antigen was detected by latex agglutination (Virotect-Rota, Omega Diagnostics Ltd, Alloa, UK). Faecal smears were also used for microscopic examinations for parasites.

All studies were performed at the laboratories of Vilnius University Children's Hospital and Kaunas Hospital of Infectious Diseases.

Statistical analysis

Qualitative variables were compared by the chi-squared test (or Fisher's test, where suitable). Quantitative variables were compared using Student's *t* test. A difference was considered statistically significant with a *P* value of less than 0.05.

Ethical considerations

This study protocol was approved by the National Drug Control Service and Ethics Committee of Lithuania. Written informed consent was obtained from the parents of enrolled children on admission to the hospital.

Results

Fifty-six children were enrolled in the study. Two patients had received intravenous fluid therapy before the diarrhoea had stopped for an intercurrent illness (one patient from control group) and uncontrollable vomiting not dissociated with Smecta (one patient from study group) and were excluded from the analysis of the study. Fifty-four non-breast-fed children were available for the final analysis; 26 received ORS alone (control group) and 28 received Smecta and ORS (study group).

Before and after admission, none of the children was given antibiotics. Only acetaminophen or ibuprofen was given if high fever occurred. No child was administered the solutions through a nasogastric tube.

Selected characteristics of all patients are shown in Table 1. The groups were similar at admission with regard to the patients' age, sex, weight, duration of diarrhoea before hospitalization, and indicators of severity of diarrhoea and dehydration. Bacteriological stool examination was positive in 10.7% of patients in the study group and 11.5% in the control group. Rotavirus antigen was found in 64.3% of patients in the study group and 76.9% in the control group; the difference was not significant. No difference in the range of duration of initial rehydration was seen between the control group and the study group (Table 2). The mean duration of treatment with Smecta in the study group was 62.7 ± 18.0 h (range 32–96 h). Mean times of obtaining the second blood for electrolytes were similar: 83.4 ± 23.6 h in the study group and 92.9 ± 29.0 h in the control group (Table 2). After the initiation of treatment, the mean duration of diarrhoea in the group receiving Smecta was significantly shorter (42.3 ± 24.7 h) than in the control group (61.8 ± 33.9 h) ($P = 0.019$). The mean duration of fever, body weight at the time of discharge from hospital, and number of vomiting episodes from initial therapy were not statistically different in the two groups (Table 3).

The values of serum electrolytes at admission before treatment (time 1) and at the time of discharge from the hospital after treatment (time 2) of both groups are

Table 1 **Characteristics of the patients on admission. Values are mean ± SD or numbers with % in parentheses**

Characteristic	Study group	Control group	*P*
Patients (*n*)	28	26	
Age (months)	19.2 ± 10.5	20.5 ± 10.4	0.645
Duration of diarrhoea before admission (h)	30.6 ± 19.5	30.7 ± 16.0	0.98
Admission body weight (kg)	11.1 ± 2.7	11.2 ± 3.0	0.863
Sex			
Male	15 (57.1)	14 (53.9)	0.812
Female	13 (42.9)	12 (46.1)	
Number of stools in 24 h before admission	5.4 ± 3.0	4.2 ± 2.1	0.09
Number of episodes of vomiting in 24 h before admission	3.1 ± 2.6	2.8 ± 1.9	0.588
Aetiological agents			
Rotavirus	18 (64.3)	20 (76.9)	0.316
Pathogenic *E. coli*	1 (3.6)	1 (3.8)	
Campylobacter	2 (7.1)	2 (7.7)	
No agent recovered	7 (25.0)	3 (11.5)	0.206
Degree of dehydration			
Mild	22 (78.6)	20 (76.9)	0.887
Moderate	6 (21.4)	6 (23.1)	0.98

Table 2 **Duration of treatment and time for obtaining blood**

	Study group				Control group				
Parameter	Minimum	Maximum	Median	Mean ± SD	Minimum	Maximum	Median	Mean ± SD	*P*
Duration of initial rehydration (h)	3	6	4	4.3 ± 0.8	2	6	4	3.9 ± 0.9	0.183
Duration of treatment of Smecta (h)	32	96	61	62.7 ± 18.0					
Time of second blood (h)	38	134	87.5	83.4 ± 23.6	45	160	91.5	92.9 ± 29.0	0.195

Table 3 **Clinical data of patients in the two treatment groups**

	Study group		Control group		
Clinical data	Median	Mean ± SD	Median	Mean ± SD	*P*
Duration of diarrhoea (h)	48	42.3 ± 24.7	71	61.8 ± 33.9	0.019
Duration of fever (h)	12	21.1 ± 23.4	24	22.3 ± 22.7	0.854
Number of vomiting episodes from initial therapy	0	1.4 ± 2.2	1	1.0 ± 1.0	0.355
Body weight (kg) at discharge from hospital	11.0	11.5 ± 2.8	11.0	11.5 ± 2.2	0.941

shown in Tables 4 and 5. Before treatment, mean values of concentrations of sodium, potassium, chloride and calcium were in the normal range in the two groups of children, but mean potassium levels were significantly lower in the control group than in the study group ($P = 0.044$). Six (23.1%) children in the control group and five (17.9%) children in the study group had hypocalcaemia on admission. Hyponatraemic dehydration on admission was established in 12 (46.2%) children in the control group and nine (32.1%) children in the study group (Table 5). Hypernatraemic dehydration was not detected in any child. At the time of discharge from hospital, the mean sodium concentration had increased in the control and study groups, but it remained in the normal range. The difference between basal and post-treatment mean values was more significant in the control group ($P = 0.001$ *v.* $P = 0.058$, respectively) (Table 4). In children with hyponatraemic dehydration, plasma sodium levels became normal after treatment, except in one child in the control group (134 mmol/l before *v.* 135 mmol/l after treatment). In one child from the study group who presented with an

Table 4 **Serum electrolytes depending on time in the two treatment groups**

		Study group			Control group			*P* (difference between control and study groups)
Electrolyte (mmol/l)	Time*	Median	Mean ± SD (range)	*P* (difference between first and second blood)	Median	Mean ± SD (range)	*P* (difference between first and second blood)	
Sodium	1	136.6	136.4 ± 2.3 (131–142)	0.058	136.0	135.8 ± 2.1 (131–139)	0.001	0.347
	2	138.0	137.7 ± 2.9 (124–141)		139.0	139.2 ± 2.0 (135–144)		0.032
Potassium	1	4.4	4.5 ± 0.6 (3.8–6.0)	0.03	4.2	4.2 ± 0.4 (3.5–5.4)	0.955	0.044
	2	4.2	4.2 ± 0.7 (3.1–5.4)		4.1	4.2 ± 0.5 (3.6–5.4)		0.871
Chloride	1	104.0	104.0 ± 3.3 (99–112)	0.82	104.5	105.3 ± 4.3 (98–110)	0.142	0.205
	2	105.0	103.8 ± 5.5 (85–110)		106.5	106.6 ± 3.1 (99–115)		0.025
Calcium	1	1.3	1.2 ± 0.2 (0.9–1.4)	0.143	1.2	1.2 ± 0.1 (0.7–1.4)	0.788	0.704
	2	1.2	1.2 ± 0.1 (0.9–1.4)		1.2	1.2 ± 0.1 (1.0–1.3)		0.669

*1, first blood; 2, second blood.

Table 5 **Characteristics and evolution of serum electrolytes in the two treatment groups**

	Study group: number of patients (%)				Control group: number of patients (%)			
Characteristic	Na	K	Cl	Ca	Na	K	Cl	Ca
Normal levels at time 1	19 (67.9)	26 (92.9)	26 (92.9)	14 (50.0)	14 (53.8)	25 (96.2)	24 (92.3)	14 (53.8)
Unchanged at time 2	3 (15.8)	1 (3.8)	2 (7.7)	0	3 (21.4)	1 (4.0)	2 (8.3)	2 (14.3)
Increased at time 2	11 (57.9)	10 (38.5)	17 (65.4)	4 (28.6)	9 (64.3)	12 (48.0)	17 (70.8)	5 (35.7)
Decreased at time 2	5 (26.3)	15 (57.7)	7 (26.9)	10 (71.4)	2 (14.3)	12 (48.0)	5 (20.8)	7 (50.0)
Decreased levels at time 1	9 (32.1)	0	0	5 (17.9)	12 (100)	0	0	6 (23.1)
Unchanged at time 2	0	0	0	0	0	0	0	1 (16.7)
Increased at time 2	9 (100)	0	0	3 (60)	12 (100)	0	0	4 (66.7)
Decreased at time 2	0	0	0	2 (40)	0	0	0	1 (16.7)
Increased levels at time 1	0	2 (7.1)	2 (7.1)	9 (32.1)	0	1 (3.8)	2 (7.7)	6 (23.1)
Unchanged at time 2	0	0	0	0	0	0	0	0
Increased at time 2	0	0	0	1 (11.1)	0	0	1 (50.0)	0
Decreased at time 2	0	2 (100)	2 (100)	8 (88.9)	0	1 (100)	1 (50.0)	6 (100)
Normal levels at time 2	27 (96.4)	21 (75.0)	26 (92.9)	21 (75.0)	25 (96.2)	24 (92.3)	25 (96.2)	20 (76.9)
Increased levels at time 2	0	4 (14.3)	0	1 (3.6)	0	2 (7.7)	1 (3.8)	1 (3.8)
Decreased levels at time 2	1 (3.6)	3 (10.7)	2 (7.1)	6 (21.4)	1 (3.8)	0	0	5 (19.2)

Time 1, first blood sampling; time 2, second blood sampling.

isotonic dehydration (137 mmol/l), sodium levels decreased below the normal range (124 mmol/l) after treatment (Table 5). The mean potassium concentration decreased significantly after treatment in the study group ($P = 0.03$), but it was still in the normal range. After treatment, chloride concentrations remained unchanged in the study group and increased slightly but not significantly in the control group. At the time of discharge, the mean chloride concentration in the control group was significantly higher than in the study group ($P = 0.025$). There was no significant change in the mean calcium concentration in either group (Table 4). Calcium levels increased in four patients in the control group and three patients in the study group who had hypocalcaemia at first. However, there was persistent hypocalcaemia in five children in the control group and six children in the study group.

Tolerance

No adverse effects of the treatment were reported from either group.

Discussion

Acute gastroenteritis represents a major cause of morbidity and mortality worldwide among children, and rehydration treatment has been one of the cornerstones in the management strategy. Oral rehydration is the preferred treatment for diarrhoea because it is simpler to administer and is less costly than intravenous rehydration. Glucose-based ORS effectively replaces diarrhoeal losses of water and salts, but it does not limit the duration or amount of diarrhoea [12,13]. It has been proven scientifically that a hypotonic ORS with an osmolarity of 200–250 mosmol/l prevents osmotic diarrhoea [14,15]. Infectious diarrhoea is always accompanied by an impairment of the structure and function of the intestinal barrier. Antimicrobial agents and antimotility drugs sometimes used during diarrhoea may be associated with major side effects [16]. In addition, parents are often not fully satisfied with oral rehydration therapy. Many want a prestigious drug that is expensive, even if its only effect is to reduce symptoms [17].

This relative drawback may foster the use of adjuvant treatment. *Lactobacillus* GG combined with ORS shortened the duration of diarrhoea [18]. Dioctahedral smectite in association with ORS has been used successfully in various countries in children and adults with acute diarrhoea and nonspecific chronic diarrhoea in human immunodeficiency virus (HIV)-infected patients [6–8,19,20]. Smecta has been shown to protect the intestinal mucosal barrier and adsorbs agents aggressing the intestinal mucosa [4,5]. Smecta combined with ORS significantly reduced the duration of acute diarrhoea compared with ORS alone [7,8,19]. It is important for decreasing the cost in children with diarrhoea. Smecta can decrease the percentage of children with persistent diarrhoea, and it has no bad side effects.

Our study including 54 children aged 6–48 months with acute gastroenteritis of mostly rotavirus aetiology confirms the results of previous studies [7,8,19], which showed that Smecta associated with ORS significantly shortens the course of the disease. The randomized double-blind, placebo-controlled trial conducted by Madkour *et al.* was in favour of a beneficial effect of dioctahedral smectite in shortening the duration of diarrhoea and reducing the frequency of liquid stools in children rehydrated with ORS [7]. In the study of Vivatvakin *et al.*, the mean duration of diarrhoea was reduced by half, and the number of infants with diarrhoea was significantly lower in the Smecta group [19]. Furthermore, 27% of infants receiving ORS alone and 3% of infants treated with Smecta and ORS still had diarrhoea on day 5. The stool frequency and weight changes were not statistically different in the two groups. In a case–control study conducted in acute infantile diarrhoea, Molocco *et al.* have estimated that treatment with ORS and Diosmectite shortened the mean duration of hospitalization by 0.4 days/child in the treatment group compared with the control group [21]. Gilbert *et al.* compared Smecta with placebo and loperamide in 56 infants aged 2 months–2 years [22]. They showed that diarrhoea resolved faster using Smectite than placebo, and at least as fast using Smectite as using loperamide. Furthermore, Smecta had the advantage over loperamide of having neither a direct effect on the intestinal motility nor adverse events such as dryness of the mouth and nausea. Dupont and co-workers measured the effect of Diosmectite on intestinal permeability changes in acute diarrhoea during a double-blind placebo-controlled trial carried out in 59 Gabonese children aged 5–35 months [23]. This study established that children with diarrhoea have a greater lactulose : mannitol ratio compared with children without diarrhoea. During gastroenteritis, Diosmectite appears to enhance the absorption of mannitol, a marker of intestinal absorptive area.

There are controversial results in the literature regarding the changes of serum electrolytes in the treatment of children's acute diarrhoea with different ORS. Some authors have concluded that the concentration of sodium and potassium was not changed when World Health Organization-ORS was used [24]. Others established a moderate but significant decrease of the concentration of sodium [25,26] and an increase of potassium [26] after 48 treatment hours. Effects of Smectite on water–electrolyte movements have been studied in the rat and rabbit [9,10]. We have found no scientific data regarding the adsorption impact of Smecta on serum electrolytes in children with acute diar-

rhoea. In an open, multicentre, general practice study carried out in 80 adult patients with acute diarrhoea, Leber *et al*. compared the effectiveness and tolerability of treatment with a liquid formulation of smectite and loperamide [27]. During this trial, serum electrolytes were recorded on entry and after 1 week. All remained unchanged. These results are in accordance with ours: we have seen no important variations in the average electrolyte serum levels after treatment in either of the groups, except the statistically significant increase of sodium concentrations in the control group. A decrease of potassium was noticeable in both groups, but it was statistically significant only in the study group. The significant decrease of potassium concentration in the study group could be due to significantly higher potassium concentration on admission in the study group than in the control group.

All studies stressed the excellent tolerance of dioctahedral smectite. No side effects of Smecta were recorded during our study.

We conclude that dioctahedral smectite (Smecta) combined with hypotonic ORS Gastrolit was effective for children with acute diarrhoea and mild or moderate dehydration. Smecta significantly reduced the duration of diarrhoea, was safe and well tolerated, and had no impact on the adsorption of electrolytes. Smecta could be used together with ORS in children suffering from acute gastroenteritis (without uncontrollable vomiting) with mild and moderate dehydration.

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References

1 Isolauri E, Vesikari T. Oral rehydration, rapid feeding, and cholestyramine for treatment of acute diarrhoea. *J Pediatr Gastroenterol Nutr* 1985; **4**:366–374.
2 Majamaa H, Isolauri E, Saxelin M, Vesikari T. Lactic acid bacteria in the treatment of acute rotavirus gastroenteritis. *J Pediatr Gastroenterol Nutr* 1995; **20**:333–338.
3 Booth I, Cunha Ferreira R, Desjeux JF, *et al*. Recommendations for composition of oral rehydration solutions for the children of Europe. Report of an ESPGHAN working group. *J Pediatr Gastroenterol Nutr* 1992; **14**:113–115.
4 Droix-Lefaix MT, Drouet Y, Schatz B. Sodium glycodeoxycholate and spinability of gastrointestinal mucus: protective effect of smectite. *Gastroenterology* 1985; **88**:1369.
5 Droy MT, Navetat H, Espinasse JL. Diarrhees neo-natales a rotavirus du veau: effect protecteur de la smectite. Congres Mondial de Gastro-Enterologie Sao Paulo, 5–13 September 1986.
6 Lachaux A, Danzon A, Collet JP, Descos B, Hermier M. Acute infantile diarrhoea: role of treatment with smectite as a component to rehydration. *International Review Pediatr* 1986; **163**:29–31.
7 Madkour AA, Madina EMH, El-Azzouni OEZ, Abbas T. Smectite in acute diarrhoea in children: a double-blind placebo-controlled clinical trial. *J Pediatr Gastroenterol Nutr* 1993; **17**:176–181.
8 Lexomboon U, Harikul S, Lortholary O. Control randomized study of rehydration/rehydration with dioctahedral smectite in ambulatory Thai infants with acute diarrhoea. *Southeast Asian J Trop Med Public Health* 1994; **25**:157–162.
9 Kheroua O, Jutteau J, Tome D, Desjeux JF. Action de la smectite en présence de la toxine cholérique et de la solution de réhydration sur les mouvements d'eau et des électrolytes dans l'intestin de rat, *in vivo*. *Gastroenterol Clin Biol* 1987; **11**:240A.
10 Rateau JG, Morgant G, Droy-Priot MT, Parier JL. A histological, enzymatic and water-electrolyte study of the action of smectite, a mucoprotective clay, on experimental infectious diarrhoea in the rabbit. *Curr Med Res Opin* 1982; **8**:233–241.
11 American Academy of Pediatrics. Practice parameter: the management of acute gastroenteritis in young children. *Pediatrics* 1996; **97**:424–435.
12 Mahalanabis D, Patra FC. In search of a super oral rehydration solution: can optimum use of organic solute-mediated sodium absorption lead to the development of an absorption promoting drug? *J Diarrhoeal Dis Res* 1983; **1**:76–81.
13 Dale CB, Northrup RS. Cereal-based rehydration therapy: theory and practice. *J Diarrhoeal Dis Res* 1989; **5**:245–305.
14 El-Mougi M, el-Akkad N, Hendawi A, Hassan M, Amer A, Fontaine O, Pierce NF. Is a low-osmolarity ORS solution more efficacious than standard WHO ORS solution? *J Pediatr Gastroenterol Nutr* 1994; **19**:83–86.
15 Rautanen T, Kurki S, Vesikari T. Randomized double blind study of hypotonic oral rehydration solution in diarrhoea. *Arch Dis Child* 1997; **76**:272–274.
16 Murtaza A. Paralytic ileus, a serious complication in acute diarrhoeal disease among infants in developing countries. *Acta Pediatr Scand* 1989; **78**:701–705.
17 Rhoads M. Oral rehydration therapy for viral enteritis. *J Pediatr Gastroenterol Nutr* 1996; **22**:114.
18 Rautanen T, Isolauri E, Salo E, Vesikari T. Management of acute diarrhoea with low osmolarity oral rehydration solutions and *Lactobacillus* strain GG. *Arch Dis Child* 1998; **79**:157–160.
19 Vivatvakin B, Jongpipatvanich S, Harikul S, Eksaengri P, Lortholary O. Control study of oral rehydration solution (ORS)/ORS + dioctahedral smectite in hospitalized Thai infants with acute secretory diarrhoea. *Southeast Asian J Trop Med Public Health* 1992; **23**:414–419.
20 Phanuphak P, Hanvarnick M, Lortholary O. Smectite in HIV-associated diarrhea: a preliminary study. *J Acquir Immune Defic Syndr* 1992; **5**:9.
21 Molocco C, Bolis A, Rizzo V, Suprani T, Cerasoli G, Marani M, Pocecco M. Evaluation of diosmectite in acute infantile diarrhoea. *Pediatr Med Chir* 1999; **21**:129–133.
22 Gilbert B, Lienhardt A, Palomera S, Barberis L, Borreda D. The efficacy of smectite in acute infantile diarrhoea, compared to a placebo and loperamide. *Ann Pediatr (Paris)* 1991; **38**:633–636.
23 Dupont C, Moreno JL, Barau E, Bargaoui K, Thiane E, Plique O. Effect of diosmectite on intestinal permeability changes in acute diarrhoea: a double-blind placebo-controlled trial. *J Pediatr Gastroenterol Nutr* 1992; **14**:413–419.
24 Dutta D, Bhattacharya MK, Deb A, Chowdhury AS, Nair GB, Ramakrishna BS, Bhattacharya SK. Uncooked rice powder in oral rehydration solution: an alternative to glucose or cooked rice powder. *Indian J Med Res* 1998; **107**:257–261.
25 Guiraldes E, Trivino X, Figueroa G, Parker M, Gutierrez C, Vasquez A, Harun A. Comparison of an oral rice-based electrolyte solution and a glucose-based electrolyte solution in hospitalized infants with diarrhoeal dehydration. *J Pediatr Gastroenterol Nutr* 1995; **20**:417–424.
26 Molina S, Vettorazzi C, Peerson JM, Solomons NW, Brown KH. Clinical trial of glucose–oral rehydration solution (ORS), rice dextrin–ORS, and rice flour–ORS for the management of children with acute diarrhoea and mild or moderate dehydration. *Pediatrics* 1995; **95**:191–197.
27 Leber W. A new suspension form of smectite (Liquid 'Diasorb') for the treatment of acute diarrhoea: a randomized comparative study. *Pharmatherapeutica* 1988; **5**:256–260.