Polymeric hydroxy-alkyl starches (e.g. partially hydrolysed guar gum) have been shown to be efficacious in the treatment of persistent diarrhoea. This is likely related to their physicochemical properties, which include the ability to form a gel in the intestinal lumen, which can help to control diarrhoea by reducing the osmotic load and improving water and electrolyte absorption. These properties are thought to be mediated by the production of short chain fatty acids (SCFAs) by colonic microflora. SCFAs are fermentation products of dietary fibres and have been shown to have a number of beneficial effects on colonic function, including improving colonic water and electrolyte absorption.

Patients and Methods

This study was conducted at the Dhaka Hospital of ICDDR, B, from February 1999 to December 2000. Patients were eligible if they were male children between the ages of 5 and 24 months, with a history of watery diarrhoea lasting for more than 14 days. Children were excluded if they had signs of associated diseases (e.g. pneumonia, septicaemia, meningitis), presence of malnutrition, or if they had received antimicrobial treatment in the previous 10 days.

Results

The study showed that children receiving the test diet had a significantly shorter duration of diarrhoea compared to those receiving the control diet. The median duration of diarrhoea was 4 days for children receiving the test diet, compared to 7 days for those receiving the control diet (p=0.001). There was also a trend towards a greater number of children receiving the test diet who had a complete recovery of their diarrhoea compared to those receiving the control diet (42/55 vs 29/58, p=0.06).

Conclusion

The results of this study suggest that partially hydrolysed guar gum supplemented comminuted chicken diet may be an effective treatment for persistent diarrhoea in children. Further studies are needed to confirm these findings and to evaluate the long-term effects of this treatment.

Abbreviations: ICDDR, International Centre for Diarrhoeal Disease Research; ORS, oral rehydration solution; PHGG, partially hydrolysed guar gum; SCFA, short chain fatty acid

ORIGINAL ARTICLE

Partially hydrolysed guar gum supplemented comminuted chicken diet in persistent diarrhoea: a randomised controlled trial

N H Alam, R Meier, S A Sarker, P K Bardhan, H Schneider, N Gyr


Background: Partially hydrolysed guar gum (Benefiber) added to a diet is fermented in the colon, producing short chain fatty acids, which improve intestinal function, including colonic salt and water absorption.

Aims: To evaluate the effect of Benefiber supplemented comminuted chicken diet in the treatment of persistent diarrhoea.

Methods: One hundred and sixteen children (aged 5–24 months), presenting to Dhaka Hospital with a history of watery diarrhoea for more than 14 days (persistent diarrhoea), were randomised to receive either: (1) comminuted chicken diet with Benefiber (study diet); or (2) comminuted chicken diet without Benefiber (control diet). The study period was seven days.

Results: Of 116 children, 57 received the study diet and 59 received the control diet. Diarrhoea resolved in a greater number of children with the study than with the control diet (46/55 (84%) v 36/58 (62%); odds ratio 3.12, 95% CI 1.19 to 8.4). Survival analysis for the duration of diarrhoea also showed a reduced duration of diarrhoea in children receiving the study diet. There was also a trend in daily stool reduction in children receiving the study diet, significant on days 4–7.

Conclusion: Results show that Benefiber supplemented comminuted chicken diet enhances recovery of children with persistent diarrhoea, indicating its therapeutic potential.

Patients and methods

The study was carried out at the Dhaka Hospital of ICDDR, B, from February 1999 to December 2000. The protocol was approved by the ICDDR’s Research Review and Ethical Review Committees. Patients eligible for the study were male children between the ages of 5 and 24 months, with a history of watery diarrhoea lasting for more than 14 days. Children excluded from the study were those with signs of associated diseases (e.g. pneumonia, septicaemia, meningitis), presence of malnutrition, or if they had received antimicrobial treatment in the previous 10 days.

Results

The study showed that children receiving the test diet had a significantly shorter duration of diarrhoea compared to those receiving the control diet. The median duration of diarrhoea was 4 days for children receiving the test diet, compared to 7 days for those receiving the control diet (p=0.001). There was also a trend towards a greater number of children receiving the test diet who had a complete recovery of their diarrhoea compared to those receiving the control diet (42/55 vs 29/58, p=0.06).

Conclusion

The results of this study suggest that partially hydrolysed guar gum supplemented comminuted chicken diet may be an effective treatment for persistent diarrhoea in children. Further studies are needed to confirm these findings and to evaluate the long-term effects of this treatment.

Abbreviations: ICDDR, International Centre for Diarrhoeal Disease Research; ORS, oral rehydration solution; PHGG, partially hydrolysed guar gum; SCFA, short chain fatty acid

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history and thorough physical examination, including anthropometry. Dehydration was assessed according to the WHO guideline. Laboratory investigations included stool microscopic examination for leucocytes, red blood cells, and parasites (including *Giardia lamblia*, *Entamoeba histolytica*, and *Cryptosporidium*); stool was cultured for *Shigella*, *Salmonella*, *Vibrio cholerae*, *Aeromonas*, and *Campylobacter jejuni* by standard methods, and detection of rotavirus by enzyme linked immunosorbent assay (ELISA) as a part of routine laboratory tests for management of persistent diarrhoea patients.

### Sample size

The sample size was estimated based on a recently conducted study (PK Bardhan et al, personal communication) at the ICDDR in which 65% of children receiving the comminuted chicken diet recovered within seven days. A sample size of 60 children per group was selected with the expectation of a 90% recovery within seven days with comminuted chicken diet supplemented with Benefiber, assuming a 20% withdrawal rate, at a 5% level of significance and 80% power.

### Treatment allocation/randomisation

After enrolment, children were randomly assigned to one of the two dietary treatment groups: (1) Benefiber supplemented comminuted chicken diet (study diet), defined in the next section under “Diet”; or (2) comminuted chicken diet (control diet). A randomisation list was prepared for an intervention to control ratio 1:1 using a random number table with permuted blocks of 20 and compiled by a statistician not involved in the study. Serially numbered sealed identical envelopes were also prepared by the statistician containing the allotted diet. The envelopes were supplied to the dietician of the hospital who prepared the diets according to the list. The two diets were identical in appearance, smell, and taste. For analysis a code (group A or B) was provided to the investigators, without disclosing the patients’ identities. After extensive analysis and preparation of tables, group identity was disclosed for preparation of the final report.

### Case management

#### Fluid treatment

After admission, the children were rehydrated with the standard WHO oral rehydration solution (ORS) (10–12 ml/kg body weight per hour) during a period of 4–6 hours. Ongoing stool losses were replaced with the same ORS with a volume at least equal to the loss of watery stool until diarrhoea ceased. The prepared ORS was discarded after 12 hours if the whole amount (0.5 l) was not consumed within this period.

### Diet

Breast milk was allowed as desired. Supplementary feeding was given in the form of comminuted chicken diet (minced chicken, soy oil, glucose mixture, 60 kcal/100 g). The study group received comminuted chicken diet with 20 g/l of Benefiber, and the control group received comminuted chicken diet without Benefiber.

### Micronutrients

All children received 10 multivitamin drops twice daily, zinc acetate 5 mg three times daily, and folic acid 1.2 mg daily orally for at least two weeks as standard hospital practice. In addition, children above 1 year of age and children 6–12 months of age were given 200 000 IU and 100 000 IU respectively of vitamin A on admission.

### Measurements

The children were placed on a “cholera cot”, and a paediatric urine collector was applied to collect urine separately. Stool weight, supplemented food (comminuted chicken diet), and body weight were measured with an electronic scale (Sartorius, Gottingen, Germany) with a precision of 1 g. ORS, plain water, and urine were measured with a calibrated cylinder. All intake (ORS, plain water, and food) and output

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**Table 1** Admission characteristics of the study children

<table>
<thead>
<tr>
<th>Variables</th>
<th>Study diet</th>
<th>Control diet</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (mth)</strong></td>
<td>9.0 (2.9)</td>
<td>8.4 (3.0)</td>
</tr>
<tr>
<td><strong>Duration of diarrhoea before admission (days)</strong></td>
<td>20.2 (5.6)</td>
<td>20.7 (10.7)</td>
</tr>
<tr>
<td><strong>Frequency of stool in previous 24 h before admission</strong></td>
<td>10.9 (4.0)</td>
<td>10.2 (3.9)</td>
</tr>
<tr>
<td><strong>Frequency of vomiting in previous 24 h before admission</strong></td>
<td>2.0 (2.1)</td>
<td>1.6 (2.0)</td>
</tr>
<tr>
<td><strong>Wt for age Z score</strong></td>
<td>−1.9 (0.9)</td>
<td>−2.0 (1.0)</td>
</tr>
<tr>
<td><strong>Breast fed (no.)</strong></td>
<td>54/57</td>
<td>55/59</td>
</tr>
<tr>
<td><strong>Dehydration status (no.), no sign:some</strong></td>
<td>35/22/57</td>
<td>34/25/59</td>
</tr>
<tr>
<td><strong>Stool pathogen (no.)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Shigella</em></td>
<td>0/57</td>
<td>2/59</td>
</tr>
<tr>
<td><em>Salmonella</em></td>
<td>1/57</td>
<td>1/59</td>
</tr>
<tr>
<td><em>Campylobacter jejuni</em></td>
<td>8/57</td>
<td>11/59</td>
</tr>
<tr>
<td><em>Vibrio cholerae</em></td>
<td>0/57</td>
<td>0/59</td>
</tr>
<tr>
<td><em>Aeromonas sobria</em></td>
<td>4/57</td>
<td>6/59</td>
</tr>
<tr>
<td><em>Aeromonas hydrophila</em></td>
<td>3/57</td>
<td>2/59</td>
</tr>
<tr>
<td>No bacterial pathogen identified</td>
<td>41/57</td>
<td>33/59</td>
</tr>
<tr>
<td><strong>Rotavirus</strong></td>
<td>25/57</td>
<td>15/59</td>
</tr>
</tbody>
</table>

Values are mean (SD) or numbers, unless specified.

---

**Figure 1** Survival plot for recovery from diarrhoea.
(stool, urine, and vomit) measurements were summarised every eight hours. Body weight was also measured every eight hours until the children were discharged. Clinical evaluation was performed every morning and evening. Cessation of diarrhoea was defined as the passage of stool of normal consistency over a period of at least 48 hours. Therapeutic success was defined as the cessation of diarrhoea within seven days of inclusion in the study treatment. Duration of diarrhoea was calculated as the duration in hours from the time of randomisation to the last watery or loose stool within seven days. Children were withdrawn from the study if their parents or legal guardian withdrew consent, or if transferred to other units for treatment of severe underlying illness; data of such patients up to the point of withdrawal were included in the analysis. Data of the children who failed to recover within the study period (seven days) were also included in the analysis for a maximum of seven days; those were labelled as therapeutic failures and were treated in the hospital until recovery.

Clinical outcome
Main outcome measures were resolution of diarrhoea within seven days and daily stool output.

Data analysis
All data were analysed by means of a microcomputer using SPSS PC+ (version 10). Baseline characteristics of the study groups were compared using Student’s t test for continuous variables and the χ² test for categorical variables. Outcome data of continuous variables were compared between groups using Student’s t test, and a non-parametric test was used when data were not normally distributed. Categorical variables were compared using the χ² test. Also continuous data such as stool weight, urine output, vomit, ORS intake, and water intake were log transformed (because the distribution was not normal) before applying the Student’s t test. Kaplan-Meier survival curves were constructed to compare duration of diarrhoea; comparison was by the log rank test; a p value <0.05 was considered statistically significant. All analyses were performed on the “intent to treat” data set.

RESULTS
In total, 158 children were screened for the study, of whom 116 children were randomised; 57 received comminuted chicken diet with Benefiber (study diet) and 59 received comminuted chicken diet without Benefiber (control diet). Reasons for non-randomisation included failure to meet study inclusion criteria (n = 34) and refusal of consent (n = 8). Three children were withdrawn from the study by the parents before completion of the study—two from the study diet and one from the control diet.

Baseline clinical characteristics such as age, body weight, duration of diarrhoea before admission, breast feeding status, and pathogens isolated were comparable between the groups (table 1). Although rotavirus detection in stool was more

<table>
<thead>
<tr>
<th>Variables</th>
<th>Study diet n = 57</th>
<th>Control diet n = 59</th>
<th>Difference between means (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%) children stopped diarrhoea within 7 days</td>
<td>46/55 (84)</td>
<td>36/58 (62)</td>
<td>3.12 (1.19 to 8.4)†</td>
<td>0.02*</td>
</tr>
<tr>
<td>Total stool, g/kg†</td>
<td>525 (177)</td>
<td>615 (359)</td>
<td>-90.00 (–278 to 92.26)</td>
<td>0.456</td>
</tr>
<tr>
<td>Total urine, ml/kg†</td>
<td>298 (233)</td>
<td>416 (211)</td>
<td>-118.51 (–272.76 to 35.72)</td>
<td>0.111</td>
</tr>
<tr>
<td>Total ORS, ml/kg†</td>
<td>492 (195)</td>
<td>638 (403)</td>
<td>-146.69 (–356.65 to 63.27)</td>
<td>0.283</td>
</tr>
<tr>
<td>Total water, ml/kg†</td>
<td>330 (144)</td>
<td>353 (172)</td>
<td>-22.67 (–142.26 to 96.90)</td>
<td>0.716</td>
</tr>
<tr>
<td>Total calories, kcal/kg/day</td>
<td>47.0 (13.1)</td>
<td>49.5 (13.0)</td>
<td>-2.51 (–8.19 to 3.16)</td>
<td>0.381</td>
</tr>
</tbody>
</table>

Values are mean (SD) or number (%), unless specified.
*Statistically significant.
†Odds ratio (95% CI).
‡Cumulative data until recovery of diarrhoea or maximum 7 days.
frequent in the study group, the difference was not statistically significant. Tests for diarrhoeagenic E. coli were not performed.

A significantly greater number of children on the study diet had resolution of diarrhoea within seven days than children on the control diet: 46/55 (84%) v 36/58 (62%) (odds ratio 3.12, 95% CI 1.19 to 8.4, p = 0.02) (table 2). The survival analysis for the duration of diarrhoea also showed a similar trend towards reduced duration of diarrhoea in children receiving the study diet (p = 0.0017, log rank test; fig 1). There was also a trend for reduction in daily stool weight in children receiving the study diet; however, the differences were statistically significant only from days 4–7 (p = 0.041, 0.045, 0.023, respectively; fig 2). Cumulative stool weight (g/kg body weight) from day 1 to day 7, although reduced in the study group, was not significantly different (table 2). Total ORS intake (ml/kg body weight) and energy intake (kcal/kg body weight per day) from supplemented diets were not significantly different between the groups. Total urine output (ml/kg body weight) and water intake (ml/kg body weight) were also similar in both groups (table 2).

**DISCUSSION**

The study shows that Benefiber, when added to comminuted chicken diet, enhances recovery of children suffering from persistent diarrhoea. Similar results were also reported when Benefiber supplemented, WHO recommended, glucose based oral rehydration solution was used in the treatment of acute diarrhoea in children compared with the treatment without Benefiber. In both studies, the subjects’ age and nutritional status were similar. Although persistent diarrhoea is recognised as a separate entity, it is thought to be initiated by an intestinal infection; however, isolation of pathogen is less frequent in persistent diarrhoea. The impact of Benefiber was modest with regard to reduction of stool output. Whether increasing the dose of Benefiber (50 g/l) could be beneficial, is beyond the scope of this study; however, further studies with different doses might be useful in determining the optimal dose for maximising the effect of Benefiber in the management of persistent diarrhoea. Consistent with our hypothesis, a recent study by Ramakrishna and colleagues has shown that amylase resistant starch, derived from maize, added to glucose based WHO ORS and used in the treatment of adult cholera patients, significantly reduced diarrhoeal stool volume and duration of illness. Although the mechanism of diarrhoea is different in cholera, colonic dysfunction has been described as a result of lack of luminal SCFAs in cholera.

In Bangladesh, fibre containing vegetables and fruits (for example, green plantain and semi-ripe wood apple) are traditionally used in diarrhoeal diseases; with an expectation of early recovery, however, there is a lack of randomised clinical trials to prove their efficacy. Recently, one clinical trial in the ICDDR examined the effect of cooked green banana and pectin in the treatment of persistent diarrhoea in children. Both green banana and pectin treatment were shown to be beneficial in terms of reducing the duration and stool output in children with persistent diarrhoea. The antidiarrhoeal effect of soluble fibres/unabsorbed carbohydrates is thought to be mediated through their bacterial fermentation, resulting in production of SCFAs. In the colon, SCFAs facilitate the absorption of sodium chloride and water, they also serve as an important source of energy for the colonocytes, and stimulate epithelial cell proliferation and exert a trophic effect on the colon as well as small bowel mucosa. In addition, Benefiber slows colonic transit, which might enhance absorption of salt and water.

Nutritional therapy is an important component in the management of persistent diarrhoea. An algorithmic approach, advised by the WHO, is followed at most centres, including the ICDDR. In this approach, the initial diet includes a simple, inexpensive, culturally acceptable, less modified (milk based) diet. If this diet fails, it is followed by a lactose and cows’ milk free diet, based on rice powder, egg white, and soy oil. If this is unsuccessful a comminuted chicken diet is given.

In our study, we used comminuted chicken diet because this diet is free of fibres and complex carbohydrates. This was intended to examine the effects of Benefiber supplementation. One limitation of this diet is low calorie content (60 kcal/100 ml), because glucose was the only carbohydrate present and the concentration of glucose was restricted given its effect in increasing the osmolality. Further studies may be useful to examine the effect of Benefiber added to first and second line diets in the management of persistent diarrhoea.

In conclusion, the present study shows that Benefiber supplemented comminuted chicken diet enhances recovery of children suffering from persistent diarrhoea, which indicates its therapeutic potential in the management of persistent diarrhoea in children.

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**Competing interests:** HS is an employee of Novartis Nutrition.

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