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Can partially hydrolyzed guar gum be an alternative to lactulose in treatment of childhood constipation?

Çocuklarda kabızlık tedavisinde parsiyel hidrolize guar gum laktuloza alternatif olabilir mi?

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Background/aims: *In the present study, we aimed to investigate if partially hydrolyzed guar gum (PHGG) can be used safely as a fiber source for treatment of constipation in children and to compare its success with the most commonly used osmotic laxative, lactulose.* ***Methods:*** *A randomized prospective controlled study on 61 patients (partially hydrolyzed guar gum group, n: 31; lactulose group, n: 30) was performed. Patients were given lactulose or partially hydrolyzed guar gum for four weeks. Using a standardized bowel diary, defecation frequency, stool consistency, and presence of flatulence and abdominal pain were recorded. Family questionnaires about the success, safety and side effect profile of both treatment arms were also obtained.* ***Results:*** *No significant differences were found in the baseline daily fiber (fruits and vegetables) intake between the two groups. Bowel movement frequency per week and stool consistency improved significantly in both treatment groups ($p<0.05$). The percent of children with abdominal pain and stool withholding also decreased eminently in both groups ($p<0.05$). Weekly defecation frequency increased from 4±0.7 to 6±1.06 and from 4±0.7 to 5±1.7 in the lactulose and partially hydrolyzed guar gum treated groups, respectively ($p<0.05$). According to the family questionnaire, the parents complained of bad taste, flatulence and necessity to ingest a high amount of drug in the lactulose treatment group. In the partially hydrolyzed guar gum treatment group, parents were satisfied with the defecation frequency of their children.* ***Conclusions:*** *Treatment with partially hydrolyzed guar gum is as effective as lactulose treatment in relieving stool withholding and constipation-associated abdominal pain, and its use improves stool consistency. Lactulose seemed to have more side effects, including flatulence and sensation of bad taste.*

Key words: Partially hydrolyzed guar gum, lactulose, childhood, constipation

Amaç: *Bu çalışmada, çocuklarda kabızlığın tedavisinde, lif kaynağı olarak kısmi hidrolize guar gumun kullanımının güvenliği ve başarısının, en sık kullanılan ozmotik laksatif olan laktuloz ile karşılaştırılması amaçlanmıştır.* ***Yöntem:*** *61 hastada (31 kısmi hidrolize guar gum, 30 laktuloz) randomize prospektif kontrollü çalışma yapıldı. Hastalara 4 hafta boyunca laktuloz veya kısmi hidrolize guar gum verildi. Standardize edilmiş bir form verilerek dışkılama sıklığı, dışkı kıvamı, aşırı gaz çıkarma ve karın ağrısının kayıt edilmesi istendi. Her iki tedavi grubunda başarı, güvenilirlik ve yan etki profili aile anketi ile elde olundu.* ***Bulgular:*** *Günlük bazal lif (meyve ve sebze) tüketiminde her 2 grup arasında fark saptanmadı. Karın ağrısı olan ve dışkı tutan çocukların yüzdesi her 2 tedavi grubunda belirgin olarak azaldı ($p<0.05$). Laktuloz grubunda haftalık dışkılama sıklığında 4+0.7'den 6+1.06'ya, kısmi hidrolize guar gum alan hasta grubunda ise 4+0.7'den 5+1.7'ye artış oldu ($p<0.05$). Aile anketinde, laktuloz tedavi grubunda ebeveynler kötü tad, aşırı gaz çıkarma ve fazla miktarda ilaç tüketim zorunluğundan yakındılar. Kısmi hidrolize guar gum tedavi grubunda ise ebeveynler çocuklarının dışkılama sıklığından memnundular.* ***Sonuç:*** *Dışkı tutma ve karın ağrısı ile beraber olan kabızlığın giderilmesinde kısmi hidrolize guar gum tedavisi, laktuloz tedavisi kadar etkin bulunmuştur. Laktulozun aşırı gaz hissi ve kötü tad gibi yan etkileri daha çok bulunmaktadır.*

Anahtar kelimeler: Kısmi hidrolize guar gum, laktuloz, çocukluk, kabızlık

INTRODUCTION

Constipation in childhood is common, with a reported prevalence ranging from 0.8-28%. Nearly half of the children relapse after being successfully treated for constipation. The current treatment advice for cases of functional constipation consists of toilet training, high fiber diet and oral

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laxatives for an extended period of time (1). Dietary fiber has important health benefits in childhood, especially in promoting normal laxation. Two small randomized controlled trials showed a beneficial effect of glucomannan, a nonabsorbable fiber gel polysaccharide, on defecation frequency and stool consistency in children with constipation (2, 3). Recently, a double-blind randomized controlled trial was published comparing the efficacy of a dietary mixture versus lactulose, and it concluded that fiber mixture and lactulose give comparable results (4).

In regard to which fiber sources are most effective, there are insufficient literature data available to make evidence-based recommendations (5). Indeed, one of the most promising fiber sources is partially hydrolyzed guar gum (PHGG) because of its low viscosity and complete fermentation in the colon (6). As far as we know from the English literature, there has been no study that investigated the use of PHGG in childhood constipation. The purpose of our study was to evaluate the therapeutic role of PHGG in children with chronic constipation and to compare its effects with lactulose treatment.

MATERIALS AND METHODS

Constipated children admitted to the outpatient pediatric gastroenterology clinic of the Ankara Medical Faculty were eligible for this study. Constipation was confirmed by Rome III criteria (7). All of the children had to fulfill at least two or more criteria for constipation: stool frequency of two or fewer per week, at least one episode of fecal incontinence per week, history of retentive posturing or excessive volitional stool retention, history of painful or hard bowel movements, presence of large fecal mass in the rectum, and history of large diameter stool that may obstruct the toilet. These criteria should be met at least once per week for at minimum of two months before diagnosis. Children aged between 4 to 16 years were included. Children with organic causes of defecation disorders, including Hirschsprung disease, spina bifida, hypothyroidism or other metabolic or renal abnormalities, and mental retardation were excluded from the study. Children using drugs that can influence gastrointestinal function other than laxatives, prebiotics or probiotics, or antibiotics in the previous four weeks before the visit were also excluded. Written informed consent was obtained before the start of the study. The study protocol was approved by the local medical ethics committee of the hospital.

The study had a randomized prospective parallel group design. Randomization was performed by the use of sequential numbers allocated to the patients at the study entry. Patients were screened during their first visit to the hospital. A detailed medical history using a standard questionnaire was obtained, and a complete physical examination, including abdominal and rectal examination, was performed. In case of rectal impaction, an enema was given at the first visit. During the baseline period, defecation frequency, consistency of stool, and frequency of fecal incontinence and abdominal pain were recorded regularly. If persistent diarrhea was reported, the original dose was reduced by 50%. Finally, all adverse reactions encountered during the study were recorded. One group was given lactulose (1 ml/kg/day, in divided doses) and the other group was given PHGG (for children between 4-6 years: 3 g/day; 6-12 years: 4 g/day; and 12-16 years: 5 g/day). As PHGG can cause hypoglycemia, we recommended that our patients take PHGG mixed with fruit juice during meals or between meals. Patients were seen in the outpatient clinic four weeks after inclusion. In addition, data were recorded daily in the bowel diary by the parents or the patient. Bristol Stool Form (stools are rated based on water content of the feces, with 1 meaning hard stool and 7 meaning liquid stool) was given to parents and information was given (8). As lack of consistency in methodology for measurement of dietary fiber is a problem, the two groups were given an equal diet with fiber. However, as dietary fiber can bind fluid, the group given PHGG was recommended to increase their fluid intake.

Four week later, we evaluated the symptoms, duration of constipation and their relationship to treatment and outcome. Successful treatment was defined as soft to formed stool consistency, absence of pain, stool withholding and blood in the stool, and no palpable rectal or abdominal mass. At the end of the treatment period, each parent was given a questionnaire to obtain their observation on the compliance and tolerance to fiber or lactulose treatment by their children and the success of the treatment.

Statistics

All data are expressed as mean and standard error of mean. For comparison of group results, $p<0.05$

was considered statistically significant. Comparison between the two treatments groups was performed using Student t testing. Statistical analysis was performed using SPSS-PC version 13 (SPSS, Inc, Chicago, IL) software.

RESULTS

Between January 2008 and December 2008, 68 patients with constipation were enrolled in the study. During the treatment period, 7 patients dropped out (4 from the PHGG group, 3 from the lactulose group). The final data set consisted of a total of 61 patients (31 in the PHGG group and 30 in the lactulose group). Age, gender and duration of constipation (PHGG group: 8.9±0.7 weeks; Lactulose group: 9.2±1.1 weeks) were not different between the two groups.

Significant improvements in all parameters as compared with initial data were achieved (Table 1). The bowel movement frequency per week increased from 4±0.7 to 5±1.7 and from 4±0.7 to 6±1.06 in the PHGG and lactulose groups, respectively ($p<0.05$). The stool consistency improved from 2.1 to 3.9 and from 2.8 to 4.3 in the fiber and lactulose groups, respectively ($p<0.05$). The percent of children with abdominal pain decreased from 49.2% to 16% and from 50.8% to 10% in the fiber and lactulose groups, respectively ($p<0.05$). The stool withholding percentage decreased from 38% to 3% and 20% to 3% in the fiber and lactulose groups, respectively ($p<0.05$). No bloody defecation was seen after the treatment with both fiber and lactulose.

Other parameters, including stool consistency, stool withholding and abdominal pain, were also compared between the two groups. There was no statistical difference between the two groups ($p>0.05$). During the four-week study period, adverse effects of fiber and lactulose were recorded. There was no important difference between the two treatment arms with respect to abdominal pain, abdominal distension and emesis in our patients ($p>0.05$). Although the statistical difference was insignificant, flatulence was recorded more often in the lactulose group than in the fiber group.

The family questionnaire showed that parents were satisfied with the success of the treatment in both groups. However, they complained of adverse side effects, especially regarding flatulence, in the lactulose group. Moreover, the necessity of using a large amount of lactulose in children between 12 and 16 years of age was another problem emphasized by parents in the questionnaire.

DISCUSSION

In the present study, we noted that bowel movements per week were statistically significantly increased in both treatment arm groups. Statistical analysis between the two groups showed that lactulose-treated patients had higher defecation frequency per week compared with the fiber group. However, our family questionnaire indicated that bad taste, flatulence and high amounts of lactulose ingestion were the main complaints about the lactulose treatment. Moreover, parents and children in the fiber group were satisfied with the defecation frequency, decreased abdominal pain and stool withholding. Remembering the fact that both treatment groups had nearly the same amount of daily fiber consumption, additional fiber supplementation with PHGG was responsible for the treatment of constipation in our study group. The side effect profile was similar in both treatment groups, including abdominal pain, abdominal distention and emesis. The frequency of these side effects seen during the treatment period was also comparable and not different significantly between the two treatment arms. Although statistically insignificant, flatulence was more commonly observed in the lactulose treatment group than in the PHGG treatment group. However, in our country, the first-line compound for treatment of constipation during childhood is usually an osmotic laxative such as lactulose. The action of lactu-

Table 1. Baseline characteristics of groups

	PHGG			LACTULOSE		
	Before treatment	**After treatment**	**p**	**Before treatment**	**After treatment**	**p**
BM frequency/week	4.0±0.7	5.0±1.7	0.005	4.0±0.7	6.0±1.1	<0.001
BM consistency	2.1±0.6	3.9±0.7	<0.001	2.8±0.6	4.3±0.6	<0.001
Abdominal pain (%)	49.2	16	0.01	50.8	10	0.013
Stool withholding (%)	38	3	0.012	20	3	0.01
Rectal bleeding (%)	24	0	0.001	20	0	<0.001

BM: Bowel movements.

lose is dependent on the colonic microflora, and a large amount of gas is produced as a result of this fermentation, causing bloating and abdominal pain. Lactulose is also associated with changes in bacterial colonic flora and a subsequent decrease in efficacy with long-term use. Thus, early discontinuation is frequent in this age group (9, 10).

Currently, children consume low amounts of dietary fiber, which appears to be inadequate for optimal health promotion and disease prevention (11, 12). Inadequate intake of dietary fiber has been linked to constipation, a common clinical problem in childhood (13). One study of 52 young children with chronic constipation found that their intake of dietary fiber was significantly lower than that of comparable children with normal intestinal habits (14). Some other authors reported that approximately half of the children from families who were health conscious enough to request dietary evaluation still fell below the age + 5 guidelines for grams of dietary fiber intake per day. Those constipated patients were consuming less than one-fourth of the recommended fiber intake. Thus, dietary fiber supplementation carries great importance in reducing the fiber gap in children, especially those complaining of constipation (15-16).

Partially hydrolyzed guar gum (PHGG) is a natural, water-soluble dietary fiber (17). The guar plant, *Cyamopsis tetragonolobus,* has been grown in India and Pakistan since ancient times. Guar gum is a water-soluble fiber derived from the seed of the cluster bean. In the food industry, guar gum is used as a thickening and stabilizing agent in a wide variety of foods. Although guar gum has positive physiologic benefits, its high viscosity makes it difficult to incorporate into food products and enteral solutions. PHGG has smaller molecular weight and less viscosity than native guar gum. PHGG is stable, does not hold much water and has a bland flavor. In 1993, the Life Sciences Research Organization of the Federation of American Societies for Experimental Biology commissioned a panel of six experts to assess the use of PFGG in consumer food. PHGG has undergone extensive toxicity testing, and the experts concluded that a daily consumption of PHGG at levels up to 20 g/day was safe. As a result, PHGG was produced to provide a dietary fiber source that could be added easily to the diet and would be acceptable to consume. PHGG, similar to other dietary fibers, increases the concentration of Bifidobacterium in feces from 14.7% to 31.7%. The ability of dietary fiber to alter the gut microflora is considered as a prebiotic type effect that may improve colonic immunologic status (18). In the literature, there is only one report investigating the benefit of PHGG treatment for constipation in an adult population. The beneficial effects of PHGG in 15 women were clearly indicated in that report. PHGG treatment in these patients resulted in soft feces, thus increasing the defecation frequency of severely constipated patients (19). As far as we know from the English literature, our study is the first to clearly show the success and safety of short-term PHGG treatment in children. However, there are some limitations to the present study. One is that the sample size is too small to draw firm conclusions. The second is that we only had data about the safety and success of short-term use of PHGG treatment.

In conclusion, treatment with PHGG is as effective as lactulose treatment in relieving stool withholding and constipation-associated abdominal pain, and its use improves stool consistency. Although lactulose provides higher bowel movements than PHGG treatment, PHGG provides satisfaction for the relief of constipation in children. Children complained more about the bad taste, flatulence and amount of ingested dose during lactulose treatment. PHGG appeared to be safe and showed no serious side effects. Moreover, PHGG, like the other dietary fiber supplements, might have other important health benefits in childhood, including prevention and treatment of childhood obesity, maintenance of normal blood glucose and lipid values and blood pressure, and risk reduction for future chronic disease, such as cancer, cardiovascular disease and type 2 diabetes. Although we did not investigate it, PHGG might be used as an adjunct to osmotic laxatives to decrease the side effects associated with ingestion of a high volume of lactulose. Further studies with larger patient numbers are warranted to obtain more information about the long-term safety profile and success of PHGG alone or in combined use with lactulose.

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