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Osmotic laxative versus stimulant laxative in the management of childhood functional constipation

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Abstract

Background and objectives: Constipation within children is an extremely common problem. The objective of this study is to evaluate and compare the efficacy and safety of osmotic and stimulant laxative used to treat functional constipation in children. **Methods:** This interventional clinical study was conducted between August 2018 till February 2019; at Rapareen Pediatrics Teaching Hospital, in Erbil governorate. One hundred cases, between one to five years of age, were collected. All patients were suffering from functional constipation and fulfilled 2-3 ROME IV criteria. Patients were randomly divided into two groups: one group received osmotic laxatives and the other group received stimulant laxatives. Patients were followed up after 8 weeks and 12 weeks from initial visit. Patient`s medication and response to treatment was reported. **Results:** The mean age + SD of the stimulant group was 1.98 + 0.90 years, and that of the osmotic group was 2.92 + 1.23 years. Eight weeks after starting treatment, 58% of the patients in the osmotic group had abdominal pain, which was significantly higher than that (36%) of the stimulant group. Significantly higher proportion of patients in the osmotic group had increased the dosage of their medications than the stimulant group (40% vs. 20%, respectively). Twelve weeks after the start of the study, the rate of abdominal pain was 34% in the stimulant group and 24% in the osmotic group, but the difference was not significant **Conclusions:** Our current study showed no significant differences between stimulant and osmotic laxatives.

Key words: Abdominal pain,Functional constipation, Osmotic laxative, Stimulant laxative.

Introduction

Constipation is an underrated but a classic health issue globally, reducing life quality. Children with constipation will consistently visit a pediatrician or general practitioner. Constipation may be defined as delay or difficulty in defecation that persists for longer than two weeks[1-3]. The prevalence rates range from 0.7% to 29.6% world-wide. It is commonly diagnosed during the toddler period, with a median age of 2.8 years[4,5].

Most children with constipation have functional constipation, accounting for 95% of patients2. Whereas, an organic cause, such as structural, endocrine or metabolic disease, can be found in a small minority of cases[6].

During neonatal period, constipation is usually associated with distention and vomiting; functional, anatomical or mechanical causes should never be suspected. During infancy, constipation is often started after dietary manipulation or solid food establishment[7,8].

The pathophysiology underlying functional constipation is currently not fully known and tends to be multifactorial. In young children, it usually begins after a painful and frightening bowel motion; whereas, in older children, it is owing to the school system and very active lifestyle, where children do not have enough time for a proper bowel movement[9].

In the rectum, stools stay and more water reabsorption from retained stools occur by the rectal mucosa leading to more difficult evacuation. Fecal impaction occurs as a result of this vicious circle, occasionally with fecal overflow incontinence, rectal sensation loss and ultimately, loss of normal urge to defecate. In a subgroup of children, functional constipation may result from slow transit[1,10].

However, since 1999, Rome criteria have been used to define functional constipation in children. Rome definition of functional constipation is a developing process and two repetitions of Rome criteria have been in the field up to

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now. Rome criteria used multiple clinical features to define functional constipation rather than a single clinical sign, for example low defecation frequency or difficulty in passing stools[11,12].

The present guideline provides recommendations for diagnostic evaluation and the treatment of children with functional constipation. It is aimed to serve as a general protocol and should not be regarded a replacement for clinical evaluation or used as a guideline applicable to all cases. The protocol is also not intended for the treatment of cases with ongoing medical illnesses causing constipation, but rather just for functional constipation[13,14].

Laxative treatments, together with adjuvant therapies such as behavioral and dietary modification, are often the mainstay of medical management used in children complaining of functional constipation. Osmotic laxatives, for example, polyethylene glycol (PEG), milk of magnesia and lactulose, are often supplied as powder tubes dissolved in water or solutions and are thus relatively easy to be given to young children. Stimulant laxatives, such as Bisacodyl and Senna, come in a variety of forms, including suppositories, tablets and liquids[15-17].

In the gut, osmotic laxatives are poorly absorbed[15,18]. They behave as hyperosmolar agents, raising water content of stool and making them softer, as well as raising colonic peristalsis, thus making it easier to pass stool. Stimulant laxatives work on the intestinal mucosa, raising water and electrolyte secretion. They also stimulate peristaltic motion[15,18,19].

The aim of this study is to evaluate and compare the efficacy and safety of osmotic and stimulant laxative used to treat functional constipation in children.

Patients and methods

This interventional clinical trial was accomplished at Rapareen pediatrics teaching hospital from August 2018 till February 2019. One hundred cases were collected with ages ranging between one and five years. Patients were divided into two age groups: one group below three years old and the other above three years old. All patients suffered from functional constipation and fulfilled 2-3 ROME IV criteria (new criteria for diagnosing functional gastrointestinal disorders)[11]. Patients with organic constipation and children on medications that interfere with gastrointestinal function had been excluded. Patients were randomly divided into two groups. One group received osmotic laxatives (lactulose), while the other group received stimulant laxatives (sodium picosulfate).

Patients data has been collected on initial visit and treatment were prescribed. All patients were followed up after eight weeks and twelve weeks from initial visit. Patient`s responses to the medication was reported, including stool frequency, consistency of stool, abdominal pain and any other medications used during this period. Also, the adverse effects of the drugs had been reported. Verbal consent was obtained from all of the patients' parents. This study was approved by the Ethics Committee of Kurdistan Board for Medical Specialties before the beginning of the study.

The initial dose of lactulose was 1ml/Kg/day and of sodium picosulfate was 2.5mg/day, which was increased to 2-3 mL/Kg/day and 5 mg/day, respectively, if the child had poor response.

Data were analyzed using Statistical Package for Social Sciences (SPSS version 22). Chi square test of association was used to compare proportions. Fisher's exact test was used when the expected count of more than 20% of the cells of the table was less than 5. A non-parametric test (Mann Whitney test) was used to compare the mean ranks of the grades of the stool characteristics. A p value of ≤ 0.05 was considered statistically significant.

Results

One hundred patients with constipation were included in the study, 50 received stimulant laxatives, and 50 received osmotic laxative. The mean age + SD of the stimulant group was 1.98 + 0.90 years, and that of the osmotic group was 2.92 + 1.23 years (p-value= 0.001). Half of the children in the osmotic group were aged ≥ 3 years which was significantly higher than that (24%) of the stimulant group (p-value= 0.007).

More than half (52%) of the children in the whole sample had constipation for more than three months, but the differences were not significant between the two groups (p-value= 0.230), as presented in Table 1. Results showed also that all the patients had abdominal pain at the start of the study.

Table (1): Basic characteristics of osmotic and stimulant groups.

	Stimulant laxative		Osmotic Laxative		Total		
	No.	(%)	No.	(%)	No.	(%)	p-value
Age							
< 3	38	(76.0)	25	(50.0)	63	(63.0)	
≥ 3	12	(24.0)	25	(50.0)	37	(37.0)	0.007
Mean (±SD)	1.98	(±0.90)	2.92	(±1.23)			<0.001
Duration of constipation							
Two weeks to three months	27	(54.0)	21	(42.0)	48	(48.0)	
More than three months	23	(46.0)	29	(58.0)	52	(52.0)	0.230
Total	50	(100.0)	50	(100.0)	100	(100.0)	

Table 2 shows that, at the start of the study, there were no significant differences between the two groups regarding the mean ranks of the stool frequency (one to two times per week), and the stool consistency were type one and two according to Bristol chart (p-value= 0.291 and p-value= 0.770, respectively). The mean rank of the fecal incontinence per week was significantly higher in the osmotic group than the stimulant group (p-value= 0.041).

Table (2): Stool characteristics at the start of the study.

Stool characteristic baseline	Stimulant laxative Mean rank	Osmotic laxative Mean rank	p-value
Stool frequency	48.55	52.45	0.291
Fecal incontinence / week	44.97	56.03	0.041
Consistency of stool	51.10	49.90	0.770

Table 3 shows no significant differences between the two groups regarding the stool characteristics, which include stool frequency (p-value= 0.066), stool incontinence (p-value= 0.960), and stool consistency (p-value= 0.981).

Table (2): Stool characteristics at the start of the study.

Stool characteristic after 8 weeks	Stimulant laxative	Osmotic laxative	p-value
Stool frequency	55.48	45.52	0.066
Fecal incontinence	50.61	50.39	0.960
Consistency of stool	50.44	50.56	0.981

Eight weeks after starting treatment, 58% of patients in the osmotic group had abdominal pain, which was significantly higher than that (36%) of the stimulant group (p-value= 0.028). Significantly (p-value= 0.029) higher proportion of patients in the osmotic group had increased the dosage of their medications than the stimulant group (40% vs. 20%, respectively). Table 4 also shows that 10% of each of the study groups developed diarrhea eight weeks after administration of the laxatives (p-value> 0.999). Twelve weeks after the start of the study, the rate of abdominal pain was 34% in the stimulant group and 24% in the osmotic group, but the difference was not significant (p-value= 0.271). The medication intake was increased in some patients in the stimulant group, and the rate of drug intake was 20% compared with 32% in the osmotic group (p-value= 0.171). The incidence of diarrhea was higher in the osmot-

ic group (16%) than in the stimulant group (10%), but the difference was not significant (p-value= 0.372), as shown in Table 5.

Table (4): Follow-up of patients after twelve weeks.

Follow up (8 weeks)	Stimulant laxative		Osmotic laxative		Total		
	No.	(%)	No.	(%)	No.	(%)	p-value
Abdominal pain							
Yes	18	(36.0)	29	(58.0)	47	(47.0)	
No	32	(64.0)	21	(42.0)	53	(53.0)	0.028
Medication dosage increased							
Yes	10	(20.0)	20	(40.0)	30	(30.0)	
No	40	(80.0)	30	(60.0)	70	(70.0)	0.029
Diarrhea							
Yes	5	(10.0)	5	(10.0)	10	(10.0)	
No	45	(90.0)	45	(90.0)	90	(90.0)	> 0.999
Total	50	(100.0)	50	(100.0)	100	(100.0)	

Table (4): Follow-up of patients after eight weeks.

Follow up (12 weeks)	Stimulant laxative		Osmotic laxative		Total		
	No.	(%)	No.	(%)	No.	(%)	
Abdominal pain							
Yes	17	(34.0)	12	(24.0)	29	(29.0)	
No	33	(66.0)	38	(76.0)	71	(71.0)	0.271
Medication dosage increased							
Yes	10	(20.0)	16	(32.0)	26	(26.0)	
No	40	(80.0)	34	(68.0)	74	(74.0)	0.171
Diarrhea							
Yes	5	(10.0)	8	(16.0)	13	(13.0)	
No	45	(90.0)	42	(84.0)	87	(87.0)	0.372
Total	50	(100.0)	50	(100.0)	100	(100.0)	

*By Fisher's exact test.

Discussion

Constipation remains a frequent problem in childhood. Functional type is the most common form of constipation. A small number may have an organic origin and proper laboratory investigation is necessary.

Despite the widespread use of these medications by pediatricians to manage constipation, there has been a long-standing scarcity of high-quality evidence to support this practice.

In the current study, one hundred patients with constipation were included, about 63% of the patients were younger than three years old while 37% were older than three years old. This agrees with Chanpong at al4 in which most of the patients (53%) were diagnosed before 3 years old. However, it is in contrast with Bischoff et al [20] in which

94% of cases were older than three years of age.

Analysis of both primary and secondary efficacy parameters indicated that both osmotic and stimulant laxatives are equally effective in the treatment of chronic constipation, over a treatment period of 3 months. The change in number of stools since baseline was slightly greater in stimulant group compared to osmotic, this result is same as in Chanpong et al.4 and Horn et al[7].

There was no significant difference in stool characteristics after eight and twelve weeks from treatment. The improvements in stool frequency in stimulant laxative group were 55.48% and 48.44%, and in osmotic laxative group were 45.52% and 52.56%. Regarding improvement in stool consistency, it was higher in osmotic laxative group (55.2%) in comparison to stimulant laxatives group (45.8%) after twelve weeks of treatment. This result is agreed with Pare et al21 and Koppen et al[22]. Comparative efficacy trials between stimulant and non-stimulant laxatives were appreciably lacking.

The incidence of fecal incontinence was not significantly different between children who were treated with osmotic and those treated with stimulant laxatives, which were 50.39% and 50.61%, respectively, after eight weeks of therapy. This indicates that stool incontinence needs longer time on medications in order to resolve, as reported by Koppen IJN et al[22] who showed a decrease in the incidence of fecal incontinence to 29% after two years of treatment. However, it has been reported that at times fecal incontinence can be exacerbated by the use of laxatives. In fact, studies have shown that fecal incontinence was a common side effect of the use of laxatives, as reported by Langseder et al [23].

After eight weeks of treatment, abdominal pain was more significant in patients treated with osmotic laxatives which were 58%, this decline to about 24% after twelve weeks of treatment. In stimulant group there were no such difference as the frequency were 36 % and 34% after eight and twelve weeks, respectively. Further studies are needed to assess the impact of long-term treatment and comparisons of efficacy and outcome among laxatives, particularly between osmotic and stimulant, as reported by pare et al[21].The incidence of diarrhea was higher among patients treated with osmotic laxatives (16%) than stimulant laxatives (10%) after 3 months of treatment. This agrees with most of the studies, such as Xinias et al[2]. However, diarrhea was a common adverse effect of stimulant laxatives in a report done by pare et al[21]. Stimulant laxatives differ in their action from osmotic laxatives which work by reducing absorption of fluid in the intestine and thereby increasing the amount of water in the stool. Thirty-two percent of the patients on osmotic laxative and 20% of those on stimulant laxative needed increase in the dose of medication, in order to get response more frequently, after 3 months of treatment. The advantage of using stimulant laxative is that treatment can be reduced to lowest effective dose to prevent diarrhea while still benefiting from functional constipation relief, as agreed with pare et al [21].

Conclusions

Functional constipation is a spectrum and in its extreme forms represents a therapeutic challenge. There is no significant difference between stimulant and osmotic laxatives in terms of efficacy and side effects. Based on the idea that every patient is different and that each one requires a different quantity and type of laxative, it is possible to improve the results of treatment.

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