A RANDOMISED TRIAL OF LIQUID PARAFFIN VERSUS LACTULOSE IN THE TREATMENT OF CHRONIC FUNCTIONAL CONSTIPATION IN CHILDREN

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Abstract- Liquid paraffin has been suggested as a good laxative comparing to lactulose as a treatment option in pediatric constipation. This study was performed to compare liquid paraffin with lactulose in pediatric constipation. A total of 247 patients (127 males and 120 females) aged 2-12 years (mean 4.1 ± 2.7 years) with chronic functional constipation were included in an 8 week, randomized, controlled trial. After faecal disimpaction, patients received oral liquid paraffin (1-2 cc/kg/day) or lactulose (1-2 cc/kg/day). Primary outcome measures were: defecation and encopresis frequency per week and successful treatment after 8 weeks. Success was defined as a defecation frequency ≥ 3 per week and encopresis ≤ 1 every two weeks. Secondary outcome measures were side effects during 8 weeks of treatment. A significant increase in defecation frequency, liquid paraffin group, 3 pre, versus, 12 post treatment per week and lactulose group: 3 pre, versus 8 post, per week was found. A significant decrease in encopresis frequency, liquid paraffin: 10 pre, versus 1 post per week; lactulose: 9 pre, versus 3 post per week, was found in both groups. However success was significantly higher in the liquid paraffin group (85%) compared with the lactulose group (29%). Liquid paraffin patients reported less abdominal pain, straining and pain at defecation than children using lactulose. Liquid paraffin is more effective than lactulose in the treatment of chronic functional constipation of childhood. It provided a higher success rate with fewer side effects. Liquid paraffin should be the laxative of first choice in childhood functional constipation.

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Key words: Childhood, Constipation, Lactulose, Liquid paraffin

INTRODUCTION

Childhood constipation is a common problem, accounting for 3% of visits to general pediatric clinics and as many as 10-25% of visits to pediatric gastroenterologist (1, 2). Childhood constipation has been defined as, stool frequency less than 3 per week for the last three months. Encopresis or fecal soiling is the involuntary passage of stool and is associated with fecal impaction (1, 3).

The most common cause of constipation in children is functional or idiopathic. That may be due to diet low in fiber-rich foods, insufficient time or routine for regular toileting and painful stool passage (2, 4, 5). Symptoms and signs associated with chronic constipation include abdominal pain, anorexia, flatulence and blood streaked stools. Presentation of abdominal distention and failure to thrive accompanied with constipation are suggestive of organic cause (1, 2, 6). Despite the fact that childhood constipation is the most common

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complaint in pediatric gastrointestinal disease, no large, randomized trial are available (7).

There is no information concerning the maximum dose, duration, or long term side effects of any compound used in the treatment of childhood constipation (8). Therefore, treatment of these children is symptomatic and based mainly on clinical experience. It consist oral and sometimes rectal lubricant or laxatives and behavioral component includes structured toilet training and increased fiber intake in regimens. Liquid paraffin one of the most agent was used as a treatment for Chronic Constipation and encopresis, stems from its tolerability and fewer side effect (2, 9). In contrast, lactulose is an osmotic laxative and it is fermented by colonic bacteria and results in expansion of faecal volume and acceleration of colonic transit (10).

The aim of this study was to compare the clinical, efficacy and safety of liquid paraffin and lactulose in the treatment of functional childhood constipation.

MATERIALS AND METHODS

The study was performed at the Children's Hospital Medical Center, from April 2000 to July 2003. 300 children with constipation were referred to the Pediatric gastroenterology clinic for evaluation and treatment of constipation. From total of these patients, 247 children (2-12) years old (mean 4.1 ± 2.1 years) with chronic functional constipation were enrolled in this study. The diagnosis of chronic constipation was based on: having at least two out of four of the following symptoms, for the last 3 months: less than 3 bowel movements per week; fecal soiling, more than once a week, large amounts of stool every 7-30 days and palpable abdominal or rectal fecal mass on physical examination.

Children with organic causes for defecation disorders; including, Hirschsprung's disease, spina bifida occulta, hypothyroidism, cystic fibrosis, neurologic abnormalities, intestinal pseudo–obstruction were excluded from the study. An open–label randomized study was designed to compare the effect of lactulose or liquid paraffin for 8 weeks. At enrollment, a careful history and physical examination was done. Stool frequency, fecal soiling (encopresis), stool consistency, and abdominal pain or rectal bleeding was recorded. At the first, patients received one or two enema daily for two days to clear any rectal fecal impaction. (30 cc / 10 kg weight of paraffin oil for enema).

Medications were administered orally as 1-2 ml/kg at, twice daily for each drug, for 8 weeks. For determination of the best dose for each child, parents were asked to increase or decrease the volume of each drug by 25% every 3 days as required, to yield, 1 or 2, firm– loose, stools. They also, were given instructions to increase their daily fiber intake to an amount of grams equal to their age plus 10 (9). Clinical efficacy and tolerability were recorded in a diary using scores for defecation and encopresis frequency, nausea, vomiting and diarrhea. Patient assessment of the taste of drug was also recorded. Toilet training after each meal (five minutes) was advised were used to enhance compliance.

Parents were received a chart to record stool frequency, encopresis frequency, and associated symptoms. Patients were seen 4 weeks later and the end of 8 weeks, and their charts were reviewed.

Treatment success was defined as three or more bowel movements a week and encopresis episode less every two weeks. The incidence and severity of gastrointestinal adverse event were recorded in the diary and assessed at weeks 2, 4 and 8 weeks period of the trial.

Comparisons between the two treatment groups were performed using Student's *t* test, and chi-square tests. A P value of < 0.05 was considered significant.

RESULTS

Between April 2000 and July 2003, 300 children aged 1 month to 12 years with constipation were studied. The majority of patients (n = 280) were seen in the outpatient clinic of Children's Medical Center, and 20 patients were admitted in this hospital. From total of 300 patients with constipation, 247 cases (82.30%) had functional or idiopathic and 53 cases (17.70%) had organic constipation. The most common cause of organic constipation was Hirschsprung's disease (6.60%) (Table 1). 247 patients (aged 2-12 years) with childhood functional constipation were considered for enrollment in the study. As shown in table 2, no significant differences

Table 1. The causes of constipation in children (300 cases)

Cause	No	Percent
Functional	247	82.30%
Hirschsprung	20	6.60 %
CP	5	1.60 %
Pseudoobstruction	5	1.60 %
Anus anomalies	4	1.30 %
Spinal cord lesion	4	1.30 %
Systemic disorder		
Cystic fibrosis	3	1%
Hypothyroidism	3	1%
Renal (RTA, DI)	3	1%
Muscular disease	2	0.70 %
Celiac disease	2	0.70 %
Hyperparathyroidism	1	0.33 %
Drug	1	0.33 %
Total	300	100

Table 2. Baseline Characteristics

Characteristic	Liquid paraffin	Lactulose
No of patients at randomization	127	120
Age (y) mean, SD	4.1 ± 2.1	4.2 ± 2
Sex, M/F	66.61	61.59
Duration of constipation (months)	24 ± 5	22 ± 3
Defecation frequency < 3/ weeks	120	97
Number of patients with history of encopresis	45	40
Large amount of stool	97	90
Faecal impaction in the rectum	50	38
Rectal bleeding	9	5
Lost to follow-up after 8 weeks	20	17
Bad palatability of study medication	5	8

were found with respect to demographic data and recorded baseline characteristics between the two treatment groups. Compared with intake a significant increase in mean defecation frequency per week and a significant decrease in mean encopresis frequency per week were found at first 4 weeks in both group (Table 3). But a significantly higher number of patients in the liquid paraffin group (85%) were successfully treated after 8 weeks of treatment compared with the lactulose group (29%, $P < 0.001$). Success rates did not change in the liquid paraffin treatment group during the follow up period 12 weeks. In the group of children on lactulose, switched to liquid paraffin at the end of the eight weeks study period a significant increase in success rate was found (29% to 51%, $P < 0.001$) after 12 weeks of follow up. During the eight weeks study period, there were no serious or significant adverse events recorded. Figure 1 shows that significantly more adverse events were reported by patients using lactulose compared with patients on liquid paraffin.

The mean liquid paraffin dosage at 4-8 weeks for children who clinically improved was 1.72 ± 0.13 ml/kg/day and 2.08 ± 0.21 kg/day, respectively.

In the liquid paraffin group, stool frequency increased 1.6 ± 1 to 12.1 ± 3.2 per week during first 4 weeks, and increased to 13.1 ± 2.3/ week during the last 4 week.

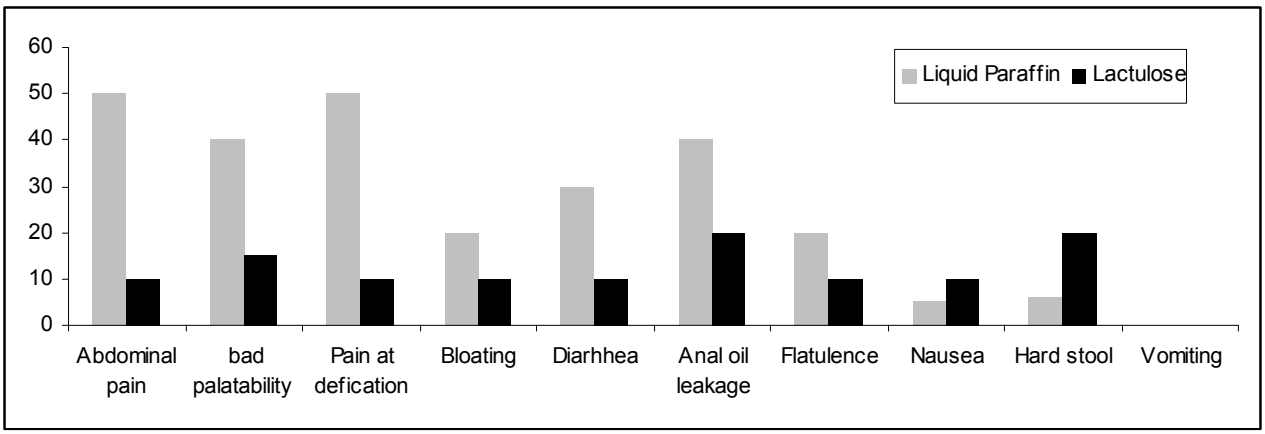

Fig. 1. Side effects during 4-12 week intervention of study in the liquid paraffin group and lactulose group

Table 3. Comparison of two groups

	Liquid paraffin group (n = 127)	Lactulose group (n = 120)	*P* V
Stool frequency			
Before treatment (per week)	1.6 ± 1	1.8 ± 1.2	0.155
During the first 4 weeks (per week)	12.1± 3.2	9.2 ± 2.1	<0.001
During the last 4 weeks (per week)	13.1 ± 2.3	8.1 ± 3.1	<0.001
Encopresis per week			
Before treatment	10 ± 4.7	9 ± 4.85	0.1
During the first 4 weeks / week	1 ± 4.3	2 ± 4.6	0.07
During the last 4 weeks / week	0 ± 0	3 ± 4.1	<0.001
Success rate (CI: 95%)			
During the first 4 weeks	90%	52%	<0.001
At the end of 8 weeks	85%	29%	<0.001
Optimal dose of drug			
Final effective dose (mean: ml/kg/day)	1.72 ± 0.13	2.08 ± 0.21	<0.001

Abbreviation: CI, confidence interval.

In the lactulose group, stool frequency increase from 1.8 ± 1.2 to 9.2 ± 2.1 per week, during first 4 weeks and decreased to 8.1 ± 3.1 per week during last 4 weeks. In the liquid paraffin group improvement in the number of stools per week was significantly higher during first and last 4 weeks of therapy (Table 3).

DISCUSSION

In this study we found that both liquid paraffin and lactulose resulted in significant increase in defecation frequency and decrease in encopresis frequency after first 4 weeks of treatment. During the intervention and follow up period of 8-12 weeks, we demonstrated the liquid paraffin was more effective than lactulose in the treatment of childhood's constipation. A similar study evaluating the efficacy of liquid paraffin and lactulose in management of chronic functional constipation showed that compliance rates were 90% in the liquid paraffin group and 60% in the lactulose group during 8 weeks of therapy (11).

Adverse effects related to lactulose were included, vomiting, bloating and abdominal cramping. However, liquid paraffin was better tolerated and compliance was higher compared with other laxative (12). In our study, during the 8-12 weeks of therapy, anal oil leakage in 15 cases of liquid paraffin group were complained, that with diminished dose of drug was subside. Liquid paraffin was also among the laxatives used in a randomized, controlled study showing the superior efficacy of laxative combined with behavioral modification (12). In a direct comparison of lubricant and stimulant laxatives as maintenance treatment for constipation, liquid paraffin fared better, with 11 of 19 children treated with liquid paraffin successfully discontinuing regular medications after 6 months compared to only 4 cases of 18 using sena. Poor symptom control was the reason for non–compliant patients (13). In the Netherlands, the first line compound is an osmotic laxative such as lactulose, but lactulose causing bloating and abdominal pain (1, 14). Lactulose is also associated with changes in bacterial colonic flora and a subsequent decrease in efficacy with long term use (1). Interestingly, despite the high prevalence of constipation in children, there have been very few well –designed therapeutic trials. A careful review of the literature of the 33 years identified less than a handful of controlled treatment trials of constipation in children (9).

The mean effective dose of liquid paraffin for treatment of constipation in children was 1.72 ± 0.13 ml/kg/day. The dose administered was equal of that used in other studies in children with constipation, comparable effect on clinical parameters were found

(11, 12). In both treatment groups, approximately 20% of patients needed additional stimulant laxatives during the intervention period, however significantly less patients with liquid paraffin needed stimulant laxative compared with lactulose. Recently, PEG (polyethylene glycol) has been suggested as alternative treatment for childhood constipation (15, 16). Unfortunately it is not yet available in the Iran.

In conclusions, the results of this study showed that liquid paraffin was more effective with fewer side effects than lactulose in the treatment of childhood constipation. NASPGN (North American Society For Pediatric Gastroenterology and Nutrition), also recommended liquid paraffin as a first step medication in childhood constipation (9). However, it is recommended that infants under the age of 1 year should not receive liquid paraffin, because increased risk of aspiration and development of lipoid pneumonia (9, 17). Therefore, parents are advised not to force– feed the liquid paraffin and it is never prescribed for children with underlying neurological condition or in those with disorders of swallowing. In addition, because of the theoretical possibility of aspiration, most children less than 12 months old are treated with lactulose in place of liquid paraffin. Also we recommended that the liquid paraffin was often drug of choice for maintenance therapy in the childhood functional constipation for many months too.

Conflict of interests

We have no conflict of interests.

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