0021-7557/11/87-01/24
Jornal de Pediatria

Comparison of the effectiveness of polyethylene glycol 4000 without electrolytes and magnesium hydroxide in the treatment of chronic functional constipation in children

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Abstract

Objective: To compare the effectiveness of two drugs, polyethylene glycol 4000 without electrolytes and magnesium hydroxide, in the treatment of chronic functional constipation in children.

Methods: Thirty-eight children were randomly assigned to either of two groups, polyethylene glycol 4000 without electrolytes or magnesium hydroxide. The children were followed through periodic appointments until they reached 6 months of treatment. In each medical appointment the following aspects were evaluated: stool consistency, frequency of bowel movements, fecal incontinence, abdominal pain, straining and acceptance of the drugs.

Results: Seventeen children made use of polyethylene glycol and twenty-one received magnesium hydroxide. All variables analyzed improved for both groups, with no statistically significant differences. All children accepted polyethylene glycol, while 42.9% refused magnesium hydroxide.

Conclusion: The two laxatives showed no difference in effectiveness for the treatment of constipation. However, due to its better acceptance, because it is odorless and tasteless, polyethylene glycol proved to be a better option for treating chronic functional constipation.

J Pediatr (Rio J). 2011;87(1):24-28: Treatment, children, constipation.

Introduction

Chronic functional constipation (CFC) has high rates among children[1-3] and a very difficult treatment course,[1] including biopsychosocial changes and prolonged use of medications.[1,4-7] Success rates are low, while symptoms relapse often.[1,5,7] Many children suffer from the condition into early adolescence.[2,8] The pediatric approach to CFC is based primarily on consensus[1] and specialist experience.[4,6,7,9] The treatment has been the focus of controversies due to the prolonged use of laxatives, with no evidence supporting its routine use.[1,10,11] Too few randomized controlled clinical trials using placebos have studied the subject.[11]

The major laxatives used in treating CFC are magnesium hydroxide, lactulose and mineral oil.[1] Recently, polyethylene glycol (PEG) has been cited as a therapeutic alternative for pediatric CFC.[12-27]

PEG is an osmotic laxative, minimally absorbed, available in molar masses of 3,350 and 4,000 Daltons, with or without the addition of electrolytes.[12,13,23] PEG without electrolytes stands out from other laxatives because it's tasteless and odorless.[16,19,23-26]

Several randomized studies compare PEG to other laxatives (magnesium hydroxide and lactulose) or

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No conflicts of interest declared concerning the publication of this article.

Suggested citation: Gomes PB, Duarte MA, de Melo MC. Comparison of the effectiveness of polyethylene glycol 4000 without electrolytes and magnesium hydroxide in the treatment of chronic functional constipation in children. J Pediatr (Rio J). 2011;87(1):24-28.

Manuscript submitted Jul 23 2010, accepted for publication Oct 06 2010.

doi:10.2223/JPED.2051

placebos.[12-19] Candy & Belsey[22] performed a systematic review of those studies and concluded that this particular medication has the highest rate of acceptance. Some studies show it's also the first drug of choice.[12,16,20,21] Loening-Baucke & Pashankar[14] showed acceptance rates of 95 and 65 percent, respectively, comparing PEG to magnesium hydroxide during a period of 12 months for the treatment of CFC.

The objective of this study was to compare the effectiveness of PEG 4000 without electrolytes and magnesium hydroxide in treating CFC in children.

Methods

The data were collected between July 2007 and November 2008 at the Universidade Federal de Minas Gerais (UFMG) School of Medicine's Hospital das Clínicas. All children included in this study were referred to the pediatric gastroenterology department. The inclusion criteria were: ages 1 to 15 years old; history of CFC according to Rome III criteria: presence of at least two of the following criteria before diagnosis (for at least a month for children younger than 4 years old,[28] or 2 months for children older than 4 years old[29]): two bowel movements or less per week; at least one episode of fecal incontinence per week, history of retentive posturing (children older than 4 years old); abdominal pain; presence of large fecal masses in rectum; and history of large-diameter stools that may obstruct the toilet. Children were excluded if constipation had organic causes, if they had neurological problems or previous surgery to the digestive system.

This non-blind randomized clinical trial studied 38 children, randomly assigned to either of two groups. Sample size was estimated by considering acceptance ratios between PEG and magnesium hydroxide for the first 10 patients.[30]

The first appointment determined as follows: frequency of bowel movements, fecal incontinence, straining, abdominal pain, and stool characteristics according to the Bristol stool scale.[5] In that scale, feces are classified visually according to seven drawings, which vary by consistency and presentation.

The following initial doses were prescribed: 1 mL/kg/day for magnesium hydroxide (maximum dose 3 mL/kg/day, up to 60 mL/day) and 0.5 g/kg/day for PEG (maximum dose 1.5 g/kg/day, up to 48 g/day).

The second assessment, made 15 days later, focused on: period between beginning of medication and bowel movements more frequent than three times per week and period between beginning of medication and occurrence of soft stools (Bristol 4 and 5).[5] The three other assessments were made in 60-day intervals, focusing on: stool characteristics (Bristol),[5] frequency of bowel movements (number of movements per week), abdominal pain, straining, fecal incontinence, and acceptance of medication. To every appointment, caregivers brought a journal with information about frequency of bowel movements, doses administered, and occurrence of soiling. Acceptance of medication was assessed by the number of envelopes containing PEG and the volume of magnesium hydroxide prescribed compared to the number of doses consumed. All assessments were made by the same researcher.

Therapeutic interventions were considered failures when there was lack of acceptance, vomiting upon administration or absence of improvement in frequency of bowel movements and/or ongoing Bristol types 1, 2 or 3[5] with use of maximum doses of the medication from the moment of the first return appointment.

The project was approved by the UFMG Research Ethics Committee (Protocol 240/07), registered with Comissão Nacional de Ética em Pesquisa (CONEP, National Research Ethics Committee) under number 0240.0.203.000.07. Free and informed consent was obtained from caregivers and/or patients.

The Fisher and chi-square tests were used to compare frequencies between variables, while Student's *t* was used for means.[30] Differences were considered not statistically significant when comparisons found two-tailed $\alpha \geq 0.05$. Sample size was calculating using ratio comparisons.[30]

Table 1 shows sample characteristics at the beginning of treatment.

Results

Twenty-seven children completed the 6 months of treatment. Among those using PEG, 15 reached the final stage of the study (2 losses). Three showed improvements on the 4th month of intervention and were followed up to the 6th month without the use of medication. In the magnesium hydroxide group, 9 children were considered treatment failures (5 for vomiting, 4 for persistent refusal of medication).

Table 2 shows the outcomes in appointments 15 days after the beginning of treatment.

Table 3 describes a comparison of stool consistency, frequency of bowel movements, soiling, abdominal pain and straining, as well as acceptance of medication, considering patients at 2, 4 and 6 months. PEG acceptance was much better, at statistically significant levels on months 2, 4 and 6. Children using PEG also had better stools on the fourth month than the children in the other group.

The mean dose was 0.6±0.2 g/kg/day for PEG and 1.3±0.7 mL/kg/day for magnesium hydroxide; coefficient of variations were 33 and 54%, respectively.

Table 1 - Comparison between groups of children in study

Variable	PEG (n = 17)	Mg(OH)2 (n = 21)	p
Age (mean ± SD)	4.37±2.78	5.05±3.11	0.478
Male (%)	58.8	61.9	0.847
Frequency of bowel movements in days/week (mean ± DP)	2±1.58	1.33±0.77	0.125
Bristol stool scale type 1, 2 or 3[5] (%)	88.2	95.2	0.577
Abdominal pain (%)	64.7	85.7	0.249
Straining (%)	94.1	100	0.447
Fecal incontinence (%)	52.9	38	0.360

Mg(OH)2 = magnesium hydroxide; PEG = polyethylene glycol 4000 without electrolytes; SD = standard deviation.

Table 2 - Comparison between stool consistency and frequency of bowel movements after 15 days

Variable	PEG (n = 17)	Mg(OH)2 (n = 21)	p
Time between onset of medication (days) and stool types 4 or 5 in Bristol stool scale[5] (mean ± SD)	3.0±2.2	5.4±3.18	0.013
Time between onset of medication (days) and frequency of bowel movements ≥ 3 times per week (mean ± SD)	3.71±2.44	3.5±3.11	0.830

Mg(OH)2 = magnesium hydroxide; PEG = polyethylene glycol 4000 without electrolytes; SD = standard deviation.

Table 3 - Outcomes presented as treatment evolved

Variable/time	PEG	Mg(OH)2	p
Stool type 4 or 5 in Bristol stool scale[5] (%)			
2 months	94.1	53.3	0.061
4 months	100	69.2	0.026
6 months	80	75	0.217
Frequency of bowel movements in days/week (mean ± DP)			
2 months	5±1.56	4.31±1.89	0.217
4 months	5.59±1.37	4.77±1.53	0.135
6 months	5.75±1.6	4.92±1.51	0.203
Fecal incontinence (%)			
2 months	23.5	13.3	0.461
4 months	23.5	15.33	0.850
6 months	6.6	0	0.362
Abdominal pain (%)			
2 months	47	40	0.688
4 months	35.2	30.7	0.794
6 months	20	16.6	0.825
Straining (%)			
2 months	11.7	26.6	0.281
4 months	5.8	7.6	0.844
6 months	0	8.3	0.255
Acceptance of medication (%)			
2 months	94.1	26.6	0.001
4 months	94.1	53.8	0.025
6 months	91.6	33.3	0.001

Mg(OH)2 = magnesium hydroxide; PEG = polyethylene glycol; SD = standard deviation.

Discussion

CFC treatment is multifactorial and involves various stages. Prolonged use of laxatives is one such stage, but therapeutic alternatives are restricted. Current medications attain poor acceptance rates.[1]

The study found no differences between groups in terms of stool consistency, frequency of bowel movements, straining, fewer episodes of fecal incontinence, and abdominal pain. Similar findings are cited in randomized studies comparing PEG with magnesium hydroxide or lactulose.[12-19] Pijpers et al.[11] question the influence of PEG on frequency of bowel movements.

In this study, PEG led to improved stool consistency faster than magnesium hydroxide, which might decrease parental anxiety and painful episodes of bowel movements. The authors found no similar reports in the literature.

The mean PEG dose found by the study was similar to that found by Loening-Baucke & Pashankar[14] in their study of PEG 3350. Dosage variability was lower than for the magnesium hydroxide group, allowing for better therapeutic response sooner than the alternative.

Two children using PEG were lost during the trial. The loss had no influence on the statistical objectivity of the comparison between ratios: sample size for assessing medication acceptance was estimated at 14 children per group.

This study used a convenience sample. Stool type, frequency of bowel movements, fecal incontinence, straining and abdominal pain presented very similar rates. Rejecting the null hypothesis would require, on average, 476 patients per group. Therefore, these results should be assessed as secondary data. The difference in acceptance between the two medications was significant. In that case, the use of 14 or more patients per group does not compromise statistical objectivity.[30]

The study found better acceptance for PEG than for magnesium hydroxide. In the magnesium hydroxide group, the treatment had to be interrupted in 42.9 percent of cases due to persistent refusal or vomiting. There was no refusal for children receiving PEG. The data are similar to the findings of randomized studies.[12-19]

In conclusion, magnesium hydroxide and PEG without electrolytes are effective, but the latter provides for better adherence to treatment. The mean dosage found reaffirms those found in randomized clinical trials,[12-19] with lower variability for PEG, making therapy easier and more feasible, since taste plays no factor in compliance.

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