

The Comparison of Efficacy and Tolerability of Two Bowel Preparation Agents in Children: Polyethylene Glycol vs Sodium Phosphate

Çocuklarda İki Bağırsak Hazırlık İlacının Etkinlik ve Kullanılabilirliğinin Karşılaştırılması: Polietilen Glikol ve Sodyum Fosfat

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Abstract: Adequate bowel cleansing with a good patient tolerability is important for high-quality and safe colonoscopy. We aimed to compare the efficacy and tolerability of an osmotic agent, polyethylene glycol (PEG) and a less frequently used stimulant agent, sodium phosphate (NP) for pediatric patients. We analyzed the records of pediatric patients who underwent colonoscopy and used either PEG or NP for bowel cleansing between January 2016 and December 2019. The patient tolerability of bowel preparation was assessed using a patient questionnaire that consisted of acceptance and adverse events, recording abdominal pain, nausea, vomiting, dizziness and severity of these symptoms. The quality of bowel preparation was assessed according to the Ottawa scale, including cleanliness and fluid quantity. The colonoscopic video records were retrospectively and blindly evaluated for Ottawa scale. There were a total of 145 patients (65 boys, 44.8%) with a mean age of 12.3±4.2 years. PEG was used in 93 patients (64.1%), while NP was used in 52 patients (35.9%). The mean age of the patients was significantly lower in PEG group (11.2±4.6 years) when compared to NP group (14.2±2.7 years) ($p<0.0001$). The patients who used PEG had significantly better tolerance without any complaints when compared to the patients who used NP (49/93 patients (52.7%) vs 14/52 patients (26.9%), respectively, $p=0.003$). Regarding the severity of symptoms in patients who had adverse events, the NP group had significantly more frequent moderate-severe side effects when compared to PEG group (15/52 patients (28.8%) vs 15/93 patients (16.1%), respectively, $p=0.014$). One of the children in NP group had severe hyperphosphatemia, which required fluid resuscitation. Regarding the efficacy of the preparations, 39/93 (41.9%) of the patients in PEG group had required wash and suctioning in any segments of the colon, this ratio was significantly lower in NP group (12/52 (23%)), ($p=0.029$). The Ottawa bowel preparation quality score in right colon and total Ottawa scale rating was significantly better in NP group when compared to PEG group ($p=0.009$ and 0.034 , respectively). The Ottawa scores in mid and rectosigmoid colons were not significantly different between two groups. As conclusion, NP is more efficient in bowel cleansing when compared to PEG. But PEG had less frequent moderate-severe side effects compared to NP. Additionally, NP should be carefully used in selected cases where other bowel cleansing methods cannot be used, because of the severe side effects like hyperphosphatemia in children.

Keywords: Bowel preparation, colonoscopy, polyethylene glycol, sodium phosphate

Özet: Hastalar tarafından iyi tolere edilebilen, yeterli bir bağırsak temizliğinin uygulanabilmesi, iyi kalitede ve güvenilir bir kolonoskopi yapılabilmesi açısından önem taşımaktadır. Çalışmamızda, çocuk hastalarda polietilen glikol (PEG) gibi ozmotik bir bağırsak temizleyici ile daha az kullanılan sodyum fosfat (SF) gibi uyarıcı bir ajanın etkinliğini ve kullanılabilirliğini karşılaştırmayı amaçladık. Hastanemizde, Ocak 2016 ve Aralık 2019 yılları arasında kolonoskopi yapılmış ve kolonoskopi hazırlık rejimi olarak PEG veya SF kullanılmış olan çocuk hastalarımızın kayıtlarını geriye dönük olarak değerlendirdik. Bağırsak temizliğinin kullanılabilirliği (tolerabilite), ilacın kullanım kolaylığı ve karın ağrısı, bulantı, kusma, baş dönmesi gibi yan etkileri ve bunların şiddetini sorgulayan bir anket ile değerlendirildi. Bağırsak temizliğinin kalitesi, temizliği ve sıvı miktarını değerlendiren Ottawa ölçeği ile belirlendi. Ottawa ölçeği, kolonoskopi video kayıtlarından kör bir şekilde ve geriye dönük olarak ölçüldü. Ortalama yaşları 12,3±4,2 yaş olan toplam 145 hasta (65 erkek, %44,8) çalışmaya alındı. Doksan üç (%64,1) hastada PEG, 52 hastada (%35,9) SF kullanılmıştı. Hastaların ortalama yaşları PEG grubunda (11,2±4,6 yaş) SF grubuna (14,2±2,7 yaş) göre anlamlı olarak düşüktü ($p<0,0001$). Bağırsak temizliğinin kullanılabilirliği değerlendirildiğinde, PEG'nin, SF kullanan hastalara göre anlamlı olarak daha iyi tolere edildiği görüldü (sırasıyla, 49/93 hasta (%52,7) ve 14/52 hasta (%26,9), $p=0,003$). Yan etki oluşan hastalarda semptom şiddeti değerlendirildiğinde, SF grubunda, PEG grubuna kıyasla orta-ağır şiddetli etkilerin daha sık oluştuğu gözlemlendi (sırasıyla, 15/52 hasta (%28,8) ve 15/93 hasta (%16,1), $p=0,014$). Sodyum fosfat kullanan çocukların birinde sıvı tedavisini gerektiren ağır hiperfosfatemi geliştiği görüldü. Kullanılan ilaçların etkinliği değerlendirildiğinde, PEG grubundaki 39/93 (%41,9) hastanın işlem sırasında aspirasyon gerektirdiği veya kolonun herhangi bir bölümünde katı kıvamlı dışkı izlendiği görüldü, bu oran SF grubunda anlamlı olarak daha düşüktü (12/52 (%23)), ($p=0,029$). Ottawa ölçeğine göre değerlendirildiğinde, NP grubu, PEG grubuna göre sağ kolon ve toplam Ottawa skorlarında daha etkin bulundu (sırasıyla, $p=0,009$ ve $p=0,034$). Her iki gruptaki orta kolon ve rektosigmoid kolon Ottawa skorları arasında anlamlı fark bulunmadı. Sonuç olarak, bağırsak temizliğinde SF, PEG'e göre daha etkindir. Fakat orta-ağır yan etkiler PEG kullanan hastalarda, SF kullanan hastalara göre daha az görüldü. Ek olarak SF'nin çocuklarda hiperfosfatemi gibi ağır yan etkiler nedeniyle dikkatli kullanılması gerektiği görüldü.

Anahtar Kelimeler: Bağırsak temizliği, kolonoskopi, polietilen glikol, sodyum fosfat

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1. Introduction

Colonoscopy is an essential tool in diagnosing many gastrointestinal diseases in children. It is a criterion standard for diagnosis of inflammatory bowel diseases and provides therapeutic options in colonic polyps or gastrointestinal bleeding. Adequate bowel cleansing with a good patient tolerability is important for high-quality and safe colonoscopy. Bowel preparation is suboptimal in one third of colonoscopies (1). Residual fluid or stool in the colon may hamper proper evaluation of the mucosa, assessment for pathologic lesions and sometimes lead to incomplete procedures (2). Besides, safety of the procedure is related with the quality of bowel preparation (2). There are numerous bowel preparation protocols for pediatric bowel cleansing, but no identified standard regimen exists currently (2).

We aimed to compare the efficacy and tolerability of an osmotic agent, polyethylene glycol (PEG) and a less frequently used stimulant agent, (NP) for pediatric patients.

2. Materials and Methods

We retrospectively analyzed the records of pediatric patients between 0-18 years of age, who underwent colonoscopy in our department and used either PEG or NP for bowel cleansing between January 2015 and December 2019. Children who completed less than 3/4 of the bowel preparation protocol or received a different bowel preparation protocol and those who have no video record or incomplete tolerance survey data were excluded from the study. The colonoscopic video records were reviewed blindly to evaluate bowel cleansing. The study was approved by the University Institutional Review Board.

The demographic features of the patients including age, sex and indications for colonoscopy were recorded. The patient tolerability of bowel preparation was assessed using a patient questionnaire that evaluates difficulty in drinking and experience of adverse events, recording abdominal pain, nausea, vomiting, dizziness and severity of these symptoms (3). Difficulty in drinking the

given agent was scored as easily accepted, mild-moderate and very difficult to drink. The severity of the symptoms was scored as none, mild, moderate and severe. Sodium phosphate was given to patients with ≥ 15 kg weight in a dose of 45 ml (that contains 21.6 g monobasic and 8.1 gr dibasic NP) in two doses, 6 and 18 hours before procedure. Polyethylene glycol (that contains 236g PEG 3350, in addition to 22.74 g sodium sulphate, 6.74 g sodium bicarbonate, 5 c .86 g sodium chloride and 2.97 g potassium chloride in 4 L solution) was given in a dose of 100ml/kg, at a rate of 20 ml/kg/hr, 12 hours before procedure. Both groups received a clear liquid diet the day before the procedure and were given a 66 ml pediatric rectal enema which contains 9.5 g monobasic and 3.5 g dibasic NP, 2 hours before procedure. Renal function tests and serum electrolytes were checked and reported normal in all of the patients before colonoscopy.

The quality of bowel preparation was assessed according to the Ottawa bowel preparation quality scale, including cleanliness and fluid quantity (4). Cleanliness was evaluated for right (cecum and ascending), mid (transverse and descending) and rectosigmoid colon separately, rated from 0 to 4 (no liquid=0, minimal liquid, no suctioning needed=1, suction required to see mucosa=2, wash and suction=3, solid stool=4). Fluid quantity was rated from 0 to 2 for the entire colon (minimal=0, moderate=1, large=3). The Ottawa scale ranges from 0 (perfect cleansing) to 14 (unprepared colon); a high level cleansing is identified with a score of ≤ 5 (4, 5). The colonoscopic video records were retrospectively and blindly evaluated for Ottawa scale by a pediatric gastroenterologist. The amount of fluid suctioned during colonoscopy and time to reach the terminal ileum was also recorded.

The data were analyzed using SPSS 16.0 statistical software (SPSS Inc., Chicago, IL, USA). Data are presented as mean \pm SD unless otherwise indicated. Chi square test was used to compare nominal data and Mann-Whitney U test was used to compare

continuous data. Chi-square analysis was used for comparison of discrete data and Spearman test was used for correlations. A p value of < 0.05 was considered statistically significant.

3. Results

A total of 316 patients had colonoscopy during the study period. Thirty-two patients who completed less than 3/4 of the bowel preparation protocol, 62 patients who used a different bowel preparation protocol, 51 patients who had no video record, and 26 patients with incomplete tolerance survey data were excluded from the study. A total of 145 pediatric patients (65 boys, 44.8%) with a mean age of 12.3±4.2 years (min-max: 2-18 years) were included in the study. Indications for colonoscopy were abdominal pain in 56 patients (38.6%), inflammatory bowel disease in 31 patients (21.4%), diarrhea in 18 (12.4%), rectal bleeding in 17 (11.7%), polyps in 7 (4.85%) and other in 16 (11%) patients. Polyethylene glycol was used in 93 patients (64.1%), while NP was used in 52 patients (35.9%).

The mean age of the patients was significantly lower in PEG group (11.2±4.6 years) when compared to NP group (14.2±2.7 years) (p<0.0001). The patient characteristics in two bowel cleansing groups were shown in Table 1. Boy/girl ratio, colonoscopy indications, difficulty in drinking and type of adverse events were not significantly different

between groups. However, the patients who used PEG had significantly better tolerance without any side effects when compared to the patients who used NP (49/93 patients (52.7%) vs 14/52 patients (26.9%), respectively, p=0.003). Regarding the severity of symptoms in patients who had adverse events, the NP group had significantly more frequent moderate or severe side effects when compared to PEG group (15/52 (28.8%) patients vs 15/93 (16.1%) patients respectively, p=0.014). Besides the above described symptoms, one of the children in NP group had severe hyperphosphatemia, which required fluid resuscitation. She was a 12-year-old girl who applied with the symptoms of abdominal pain, loss of appetite and weight loss. She had malnutrition with a weight for height at 73rd percentile. Her serum phosphate, calcium levels and renal function tests were normal before colonoscopy. She had tetany in her hands and numbness of her face after using NP. Her serum phosphate level was measured as 20.4 mg/dL, calcium was 7.8 mg/dl and vitamin D level was 7.28 ng/ml. Her renal function tests did not deteriorate. She was treated with intravenous (iv) hydration, and iv calcium and oral vitamin D replacement. It was learned that she could not provide adequate oral hydration while using the bowel preparation. She was diagnosed with pulmonary and gastrointestinal tuberculosis after colonoscopy.

Table 1. The patient characteristics in two bowel cleansing groups.

Patient characteristics	Bowel preparation		p value
	Polyethylene glycol (n=93) (%)	Sodium phosphate (n=52) (%)	
Age, mean ±SD (min-max), years	11.2±4.6 (2-18)	14.2±2.7 (4.5-18)	<0.0001
Sex Male/Female	46/47 (49.5/50.5)	19/33 (36.5/63.5)	0.164
Acceptance/tolerability (Difficulty in drinking)			0.651
No difficulty	35 (37.6)	15 (28.8)	
Mild difficulty	28 (30.2)	23 (44.2)	
Moderate difficulty	14 (15)	12 (23.1)	
Very difficult to drink	15 (16.2)	2 (3.9)	
Acceptance/tolerability without any side effects	49/93 (52.7)	14/52 (26.9)	0.003
Type of side effects (Patient number)			0.779
Nausea	3 (3.2)	4 (7.7)	
Vomiting	4 (4.3)	2 (3.8)	
Abdominal pain	4 (4.3)	4 (7.7)	
Nausea+abdominal pain	9 (9.7)	10 (19.2)	
Nausea+vomiting	7 (7.5)	6 (11.5)	
Nausea+abdominal pain+vomiting	12 (12.9)	12 (23.1)	

Nausea+abdominal pain+dizziness	5 (5.4)	-	
Severity of symptoms			0.048
None	49/93 (52.7)	14/52 (26.9)	0.003
Mild	29 (31.2)	23 (44.2)	0.228
Moderate	12 (12.9)	13 (25)	0.065
Severe	3 (3.2)	2 (3.8)	0.845

SD: Standard deviation, min: minimum, max: maximum

The efficacy of the colonoscopy and Ottawa scores in two bowel cleansing groups were shown in Table 2. The number of patients who had an intubation of terminal ileum were similar in both groups. It took 19.7±10.9 min to reach terminal ileum during colonoscopy in PEG group, while this time was 17.3±9.7 min in NP group, and this difference was not statistically significant. Regarding the efficacy of the preparations, 39/93 (41.9%) of the patients in PEG group had required wash and suctioning in any segments of the colon, this ratio was significantly lower in NP group (12/52, 23%), (p=0.029). The amount of fluid suctioned during colonoscopy were similar between PEG and NP groups, 187.4±130.9 ml and 188.3±125.1 ml, respectively.

Table 2. The efficacy of the colonoscopy and Ottawa scores in two bowel cleansing groups.

Patient characteristics	Bowel preparation		p value
	Polyethylene glycol (n=93)	Sodium phosphate (n=52)	
Intubation of terminal ileum (patient no)	77/93 (82.8%)	49/52 (94.2%)	0.071
Time to reach terminal ileum (minutes)	19.7±10.9	17.3±9.7	0.198
Wash and suction needed during colonoscopy (patient no)	39/93 (41.9%)	12/52 (23%)	0.029
Ottawa scores			
Cleanliness			
Right colon (0-4), median (min-max)	3 (0-4)	1 (0-4)	0.009
Mid colon (0-4), median (min-max)	1 (0-4)	1 (0-4)	0.151
Rectosigmoid colon (0-4), median (min-max)	0 (0-4)	0 (0-4)	0.435
Fluid quantity (0-2), median (min-max)	1 (0-2)	1 (0-2)	0.024
Total Ottawa score (0-14), median (min-max)	5 (0-14)	3.5 (0-14)	0.034

min: minimum, max: maximum

According to the Ottawa bowel preparation quality scores, NP was significantly more efficient in right colon when compared to PEG (p=0.009). The fluid quantity was also significantly lower in NP group when compared to PEG group (p=0.024). The Ottawa bowel preparation quality scores in mid colon and rectosigmoid colon were comparable between two groups. However, total Ottawa scale rating was significantly better in NP group when compared to PEG group (p=0.034).

4. Discussion

The studies that compare the efficacy of PEG and NP in children are limited. A meta-analysis including two studies that compare PEG and NP in 63 participants found no difference in adequacy of bowel preparation (6-8). Similarly, colonoscopy time and

amount of suctioned fluid were not different between two groups in our study. However, total Ottawa scale was better in NP group and also regarding the right colon, NP was more efficient in cleaning.

According to the US. Multi-Society Task Force on Colon Cancer the ideal bowel preparation should achieve a bowel cleansing that is able to detect a lesion over 5mm (9). In order to objectively evaluate clinically acceptable bowel cleansing preparations, several bowel preparation rating scales were developed recently (10). However, hitherto these scales are rarely used to evaluate bowel cleansing regimes in children. There are several studies that evaluate different bowel preparations by using mainly Boston Bowel Preparation Scale, recently, however none of them compared PEG vs NP (11-14). Ottawa Bowel Preparation Quality Scale, which was

developed and published in 2004, evaluates the colon in three segments and also separately rates the fluid quantity (4). A recent systematic review, which evaluates the validated bowel preparation scales, reported that both Boston and Ottawa Bowel Preparation Scales satisfy a varying spectrum of optimal criteria for high quality measurement scale (10). Similarly, a recent study that compares two bowel preparations in children established an excellent correlation between Boston and Ottawa scales (12). Our study is the first one that use Ottawa scale to evaluate the efficacy of PEG and NP as bowel preparations in children.

The tolerability of PEG was usually reported as poor, because it requires consumption of large amount of fluid and necessitates the use of nasogastric (NG) tube (6). One disadvantage of our study is that we did not evaluate the use of NG tube in our patients. However, the rank in difficulty in drinking was not different between two groups. The dosage of PEG is adjusted in ml/kg, and it is used as 100 ml/kg in our department, which is similar with NASPGHAN recommendations (2). As the patient gets older the amount needed to clean the bowels increase greatly (up to 4L), this may decrease the tolerability in older patients. Oral NP may be an alternative in patients who refuse to drink large amounts of PEG or insertion of an NG tube.

Hirschsprung's disease, fecal retention, excessive doses and poor phosphate clearance in chronic kidney diseases and cardiac failure constitute the risk factors for complications of NP (15-18). Our patient who developed hyperphosphatemia after NP use had normal renal functions and serum electrolytes before colonoscopy and there was no renal involvement of tuberculosis. However, she had severe malnutrition, loss of appetite and probably mild dehydration before the procedure which made her prone to inadequate hydration and electrolyte imbalance during bowel preparation. Vitamin D deficiency may also facilitate the development of hyperphosphatemia and hypocalcemia. Kuehn et al (19), reported a patient with cystic fibrosis and vitamin D

deficiency, who developed hyperphosphatemia and hypocalcemia after NP enema use for bowel preparation. Therefore, serum electrolytes and renal function tests should be checked in every pediatric patient before NP use and we recommend to measure vitamin D levels as well, in patients with signs of severe malnutrition or with findings of rickets.

In our study, the number of patients without any symptoms or patients with moderate/severe side effects were significantly lower in PEG group when compared to NP group. Two studies in the literature compared PEG and NP as bowel cleansing methods for colonoscopy in children and evaluated the side effects of NP. Gremse et al (7), used NP in 19 pediatric patients in a lower dose of 30mg/1.73m², and observed increased phosphate levels above 10mg/dl in 3 patients without any symptoms or hypocalcemia. Similarly, de Silva et al (8) used NP in pediatric patients >30kg in a dose similar to our patients' PEG dose and half the dose in patients <30kg and observed an increase in phosphate concentrations to upper limit of normal in all, but all levels returned to normal range by 10 hours post-fasting and none of the patients had clinical signs of hypocalcemia or hyperphosphatemia. As both of these studies reported a comparable efficacy of PEG and NP in above mentioned doses, using a lower dose of NP may provide both efficacy and less side effects.

It is crucial to state that US Food and Drug Administration and Health Canada do not recommend to use NP for any indication in children under the age of 5 years and for bowel preparation in children under 18 years. In addition to fluid and electrolyte disturbances, oral NP also may cause erosions and ulcers in colon (20-23). This side effect is especially important in pediatric colonoscopy, because most common indication of colonoscopy in children is diagnosis of inflammatory bowel disease and NP use may mimic the ulcers of inflammatory bowel diseases.

Currently, we prefer to use PEG or senna alkaloids and not to use oral NP for bowel

cleansing as a first choice in our department. Although NP is efficient and easily tolerable in bowel cleansing, we believe it should only be used with great caution in selected cases in whom adequate hydration can be provided and other preparations cannot be used.

5. Conclusions

Sodium phosphate is more efficient in bowel cleansing when compared to PEG. But PEG had less frequent moderate-severe side effects compared to NP. Additionally, NP should be carefully used for severe side effects like hyperphosphatemia in children. Our study is important in comparing a less frequently used bowel cleansing agent with a widely used one in a large pediatric population.

REFERENCES

1. Dahshan A, Lin CH, Peters J, Thomas R, Tolia V. A randomized, prospective study to evaluate the efficacy and acceptance of three bowel preparations for colonoscopy in children. *Am J Gastroenterol*. 1999;94:3497-501.
2. Pall H, Zacur GM, Kramer RE, et al. Bowel preparation for pediatric colonoscopy: report of the NASPGHAN endoscopy and procedures committee. *J Pediatr Gastroenterol Nutr*. 2014;59:409-16.
3. Seo EH, Kim TO, Kim TG, et al. Efficacy and tolerability of split-dose PEG compared with split-dose aqueous sodium phosphate for outpatient colonoscopy: a randomized, controlled trial. *Dig Dis Sci*. 2011;56:2963-71.
4. Rostom A, Jolicoeur E. Validation of a new scale for the assessment of bowel preparation quality [published correction appears in *Gastrointest Endosc*. 2004 Aug;60(2):326]. *Gastrointest Endosc*. 2004;59:482-6.
5. Rostom A, Jolicoeur E, Dubé C, et al. A randomized prospective trial comparing different regimens of oral sodium phosphate and polyethylene glycol-based lavage solution in the preparation of patients for colonoscopy. *Gastrointest Endosc*. 2006;64:544-52.
6. Gordon M, Karlsen F, Isaji S, Teck GO. Bowel preparation for elective procedures in children: a systematic review and meta-analysis. *BMJ Paediatr Open*. 2017;1:e000118.
7. Gremse DA, Sacks AI, Raines S. Comparison of oral sodium phosphate to polyethylene glycol-based solution for bowel preparation for colonoscopy in children. *J Pediatr Gastroenterol Nutr*. 1996;23:586-90.
8. da Silva MM, Briars GL, Patrick MK, Cleghorn GJ, Shepherd RW. Colonoscopy preparation in children: safety, efficacy, and tolerance of high-versus low-volume cleansing methods. *J Pediatr Gastroenterol Nutr*. 1997;24:33-7.
9. Johnson DA, Barkun AN, Cohen LB, et al. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the US multi-society task force on colorectal cancer. *Gastroenterology*. 2014;147:903-24.
10. Parmar R, Martel M, Rostom A, Barkun AN. Validated Scales for Colon Cleansing: A Systematic Review. *Am J Gastroenterol*. 2016;111:197-205.
11. Sriphongphankul H, Tanpowpong P, Lertudomphonwanit C, Treepongkaruna S. Split dose versus full single-dose regimen of polyethylene glycol for bowel preparation in pediatric colonoscopy: a pilot study of randomized controlled trial. *Eur J Gastroenterol Hepatol*. 2019;31:1382-6.
12. Tutar E, Bayrak NA, Volkan B, Ertem D. Bowel Preparation for Colonoscopy in Children: 1 Day PEG-3350 with Bisacodyl versus 3 Day Sennosides. *Dig Dis*. 2019;37:334-42.
13. Szaflarska-Popławska A, Tunowska D, Sobieska-Pozwa O, Krogulska A. The Effectiveness, Tolerability, and Safety of Different 1-Day Bowel Preparation Regimens for Pediatric Colonoscopy. *Gastroenterol Res Pract*. 2019;2019:3230654.
14. Cisarò F, Andrealli A, Calvo P, Guanà R, Pinon M, Barletti C. Bowel Preparation for Gastrointestinal Endoscopic Procedures With Sodium Picosulphate-Magnesium Citrate Is an Effective, Safe, and Well-Tolerated Option in Pediatric Patients: A Single-Center Experience. *Gastroenterol Nurs*. 2018;41:312-5.
15. Moseley PK, Segar WE. Fluid and serum electrolyte disturbances as a complication of enemas in Hirschsprung's disease. *Am J Dis Child* 1968;115:714.
16. Sotos JF, Cutler EA, Finkel MA, Doody D. Hypocalcemic coma following two pediatric phosphate enemas. *Pediatrics* 1977;60:305-7.
17. Oxnard SC, O'Bell J, Grupe WE. Severe tetany in an azotemic child related to a sodium phosphate enema. *Pediatrics* 1974;53:105-6.
18. Davis RF, Eichner JM, Bleyer A, Okamoto G. Hypocalcemia, hyperphosphatemia, and dehydration following a single hypertonic phosphate enema. *J Pediatr* 1977;90:484-5.

19. Kuehn D, May J, Bauer AJ. Phospho-soda-induced symptomatic hypocalcemia in a patient with cystic fibrosis and vitamin D malabsorption. *J Pediatr Gastroenterol Nutr.* 2008;47:514-6.
20. Hassall E, Lobe TE. Risky business: oral sodium phosphate for precolonoscopy bowel preparation in children. *J Pediatr Gastroenterol Nutr.* 2007;45:268-9.
21. Zwas FR, Cirillo NW, el-Serag HB, Eisen RN. Colonic mucosal abnormalities associated with oral sodium phosphate solution. *Gastrointest Endosc.* 1996;43:463-6.
22. Coskun A, Uzunkoy A, Duzgun SA, Bozer M, Ozardali I, Vural H. Experimental sodium phosphate and polyethylene glycol induce colonic tissue damage and oxidative stress. *Br J Surg.* 2001;88:85-9.
23. Atkinson RJ, Save V, Hunter JO. Colonic ulceration after sodium phosphate bowel preparation. *Am J Gastroenterol.* 2005;100:2603-5.