A prospective, observational study of colonic mucosal abnormalities associated with orally administered sodium phosphate for colon cleansing before colonoscopy

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Background: **Colonic mucosal abnormalities associated with sodium phosphate colonic preparations have been described. The aim of this prospective study was to determine the frequency at which these occur and to define the endoscopic and histopathologic patterns of these changes.**

Methods: **Within a 16-month period, 730 of patients referred for elective colonoscopy entered the study. Patients with known inflammatory bowel disease and those taking non-steroidal anti-inflammatory drugs were excluded. A sodium phosphate solution was ingested orally 14 and 8 hours before endoscopy. After standard colonoscopy, a 3-year clinical follow-up program was conducted.**

Results: **Endoscopically, mucosal lesions, possibly associated with sodium phosphate ingestion, were visible in 24 patients (3.3%). Erosions were found in 3 patients, aphthoid lesions in 21 patients, and an ulcer in one patient. Lesions often were multiple. Histopathologically, findings included focal active inflammation in 14 of 24 patients, mucosal disruption and erosion (7/24), edema of the lamina propria (5/24), mucosal hyperemia or focal hemorrhage (5/24), lymphoid nodules (5/24), and ulceration (1/24).**

Conclusions: **Orally administered sodium phosphate-associated colonic mucosal abnormalities are infrequent but can mimic an non-steroidal anti-inflammatory drug-induced injury or inflammatory bowel disease, and in particular must be differentiated from Crohn's disease. (Gastrointest Endosc 2004;59:651-4.)**

Sodium phosphate solutions have been widely used for colon cleansing before colonoscopy. Sodium phosphate appears to act through an osmotic effect. It must be diluted before administration to prevent vomiting, and, after ingestion, a sufficient volume of fluid must be taken to prevent dehydration. Sodium phosphate solutions are well accepted by patients and are highly effective for cleansing the colon.[1-3] Colon preparation with sodium phosphate is safe in the majority of patients, but its use should be avoided by patients with severe renal, cardiac, metabolic, or hepatic diseases.[3-5] Colonic mucosal abnormalities associated with sodium phosphate colonic preparations have been described.[6-12] These changes are thought to be clinically insignificant but can mimic inflammatory bowel disease (IBD) and must be distinguished from Crohn's disease in particular.[6,11,12] The aim of this prospective study was to determine the frequency of colonic mucosal abnormalities associated with the use of an orally administered sodium phosphate solution and to define the endoscopic and histopathologic patterns of these changes.

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PATIENTS AND METHODS

Within a 16-month period at a single center, 730 patients referred for elective colonoscopy entered the study. During the study period, a total of 1159 colonoscopies were performed. Indications for colonoscopy were the following: hematochezia (197 patients), iron-deficiency anemia (58), follow-up after polypectomy (139), irritable bowel syndrome (88), change in bowel habit and diarrhea (80), excision of colonic polyps (51), screening for cancer (37), and miscellaneous (80). Patients with known IBD (209) and those taking non-steroidal anti-inflammatory drugs (NSAID) (70) were excluded. Written informed consent for participation in the study was obtained from all patients. For all data obtained, all personal identification information was deleted in compliance with the laws for protection of confidentiality of the Czech Republic.

A sodium phosphate solution was ingested twice (14 and 8 hours before endoscopy). The solution consisted of

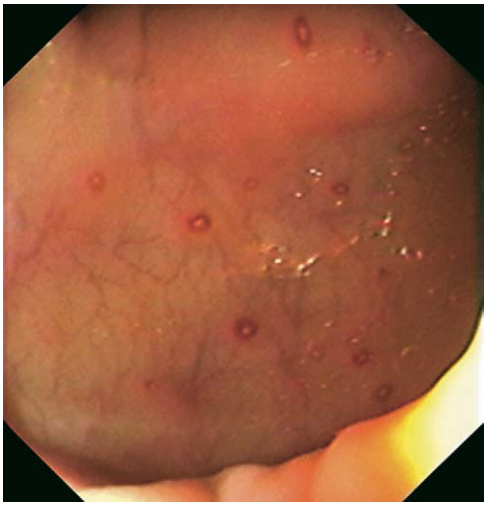

Figure 1. Endoscopic view, showing multiple aphthous lesions in sigmoid colon.

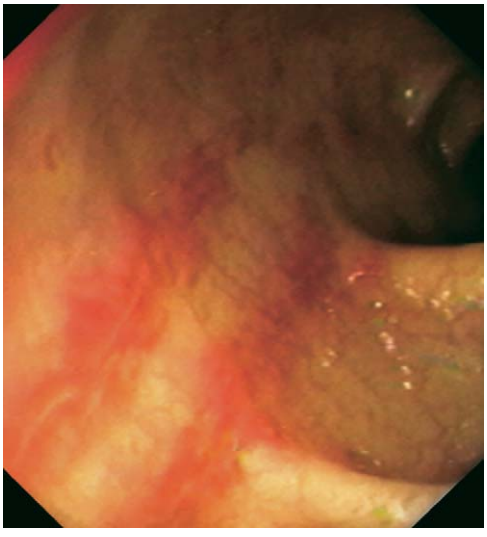

Figure 2. Colonoscopic view of linear erosions in rectum.

$Na_2HPO_4 \cdot 12H_2O$ (21.6 gm) and $NaH_2PO_4 \cdot 2H_2O$ (8.1 gm) diluted in 100 mL of water. Each dose was given as a hot drink (about 50°C; 122°F).

Standard colonoscopy was performed and included a careful search for visible mucosal abnormalities. Biopsy specimens were taken when any mucosal abnormality was found. All positive findings were recorded on videotape and as digital images that were stored in a personal computer for later review.

The colonoscopic findings in the 730 patients were as follows: colorectal cancer (44 patients), adenomatous polyps (117), newly recognized IBD (22), severe diverticular disease (bleeding or diverticulitis; 29), bleeding angiodysplasias (7), minor findings (e.g., a single diverticulum, hemorrhoids; 110), miscellaneous (36), and normal (341). Mucosal abnormalities thought to be caused by sodium phosphate were noted in 24 patients.

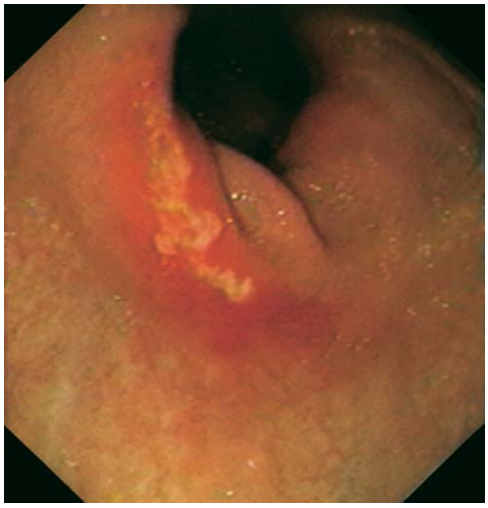

Figure 3. Colonoscopic view of sodium phosphate-associated rectal ulcer.

A 3-year clinical follow-up was conducted subsequent to colonoscopy to preclude progression to IBD in the patients with sodium phosphate-associated mucosal abnormalities. No patient had clinical symptoms or signs of IBD at study entry.

Statistical analysis

Data were analyzed statistically with both a Mann-Whitney test and a Spearman rank correlation. Statistical software was used for these analyses (SigmaStat; Jandel Corp., Erkrath, Germany).

RESULTS

No major clinical (dehydration, heart failure, severe vomiting) or metabolic (serum electrolyte concentrations) side effect from the sodium phosphate solution was recorded.

Endoscopically, mucosal abnormalities considered to be associated with the orally ingested sodium phosphate solution, for which there was no other explanation, were observed in 24 patients (3.3%) (12 men, 12 women; mean age 52.5 years). These included aphthoid lesions (Fig. 1) in 21 patients (in one case, in combination with evident mucosal hemorrhage), erosions in 3 patients (Fig. 2), and a rectal ulcer in one patient (Fig. 3). The most frequently encountered endoscopic appearance was a minute aphthoid lesion, with a pale central area and reddish halo (Fig. 4). This appearance was noted in 21 of the 24 patients. Lesions often were multiple and were located in the rectum (18 patients); sigmoid colon alone (5); sigmoid and rectum (10); and in the rectum, sigmoid, and descending colon (1).

Histopathologic findings included focal active inflammation (14/24 patients), mucosal disruption

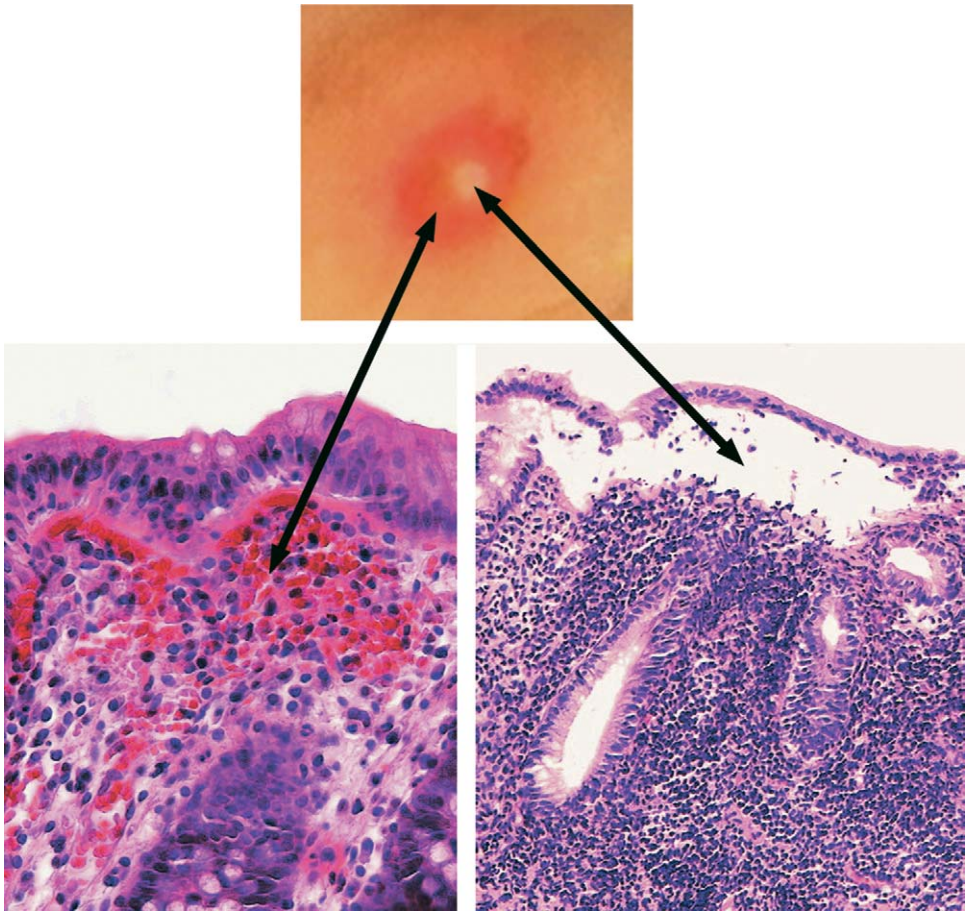

Figure 4. Photomicrograph showing sodium phosphate-associated aphthous lesion. The pale center is from a superficial mucosal disruption over a lymphoid follicle (lower right) (H&E, orig. mag. ×100), and the red ring is caused by focal hemorrhage (lower left) (H&E, orig. mag. ×400).

and erosion (7/24), edema of the lamina propria (5/24), mucosal hyperemia or focal hemorrhage (5/24), lymphatic nodules (5/24), and ulceration (1/24). Normal histologic findings were noted in two patients.

There were no significant differences in findings between men and women. The proportion of patients with sodium phosphate-associated mucosal lesions was not higher in patients older than 60 years vs. those 60 years of age or younger.

During the clinical follow-up period (median 36 months, range 36-37 months), subsequent to colonoscopy, none of the 24 patients with sodium phosphate-associated mucosal abnormalities were found to have clinical evidence of IBD.

DISCUSSION

It is well established that sodium phosphate can cause colonic mucosal abnormalities when administrated as an oral solution[6-12] or as an enema.[13] The aim of the present study was to determine the frequency of colonic mucosal abnormalities associated with the oral administration of sodium phosphate and to assess the endoscopic and histologic patterns of such changes. The study has several limitations (observational, non-randomized, unblinded study), and, thus, the results must be interpreted with caution.

Colonic mucosal abnormalities thought to be associated with the orally administered sodium phosphate solution were observed in 3.3% (24/730) of the patients. Driman and Preiksaitis[7] noted mucosal abnormalities in 2.6% of patients (18/687). In the study of Zwas et al.,[12] mucosal abnormalities were present in 13 of 53 patients (24.5%) who received oral sodium phosphate vs. only one of 44 patients (2.3%) who had polyethylene glycol-based colon cleansing.

The endoscopic appearance of sodium phosphate-associated abnormalities is described as aphthoid-like erosion[12] or aphthoid ulcer.[7,9,11] In terminologic disagreement, Faigel et al.[8] described a patient in whom several lesions with the appearance of aphthous ulcerations were noted after colon cleansing by lavage with a polyethylene glycol-based solution.

However, it is our belief that these lesions were not aphthous ulcers but were lymphoid aggregates, a normal finding.[8] In a letter, Stark and Wolfe[10] supported this opinion, namely that a red ring lesion indicates the presence of prominent lymphoid tissue, a finding noted in 0.9% of colonoscopies. "Aphthous ulcer" is not a term used by us; when referring to aphthoid lesions, our preference is to use the term "aphtha". These aphthae were the most frequently found abnormality in the present study. The slightly prominent, pale center (1-2 mm in diameter) is caused by a superficial mucosal disruption over a lymphoid aggregate; the red ring (2-3 mm in diameter) is attributable to hyperemia or focal hemorrhage, as demonstrated by Fig. 4. In addition to these aphthoid lesions, true mucosal erosions were identified endoscopically in 3 patients and histopathologically in 7 other instances. One true rectal ulcer (confirmed histopathologically) also was noted.

Although the results of the present study are in agreement with those of other studies,[7,9,11,12] there are considerable differences with respect to the histopathologic findings. In our study, the major findings were edema within the lamina propria, with extravasation of erythrocytes; focal superficial mucosal disruption, often centered over lymphoid aggregates; mild inflammatory infiltration, plus true mucosal erosions; and one true rectal ulcer.

The sodium phosphate-associated lesions were predominantly located in the distal sigmoid colon and rectum, as noted in other studies.[9,11] The pathogenesis of these abnormalities has not been fully elucidated. Purportedly, they are metabolically mediated instead of caused by direct chemical injury.[11] In an experimental setting, sodium phosphate triggered an oxidative stress reaction in the colonic mucosa.[14]

Oral sodium phosphate-associated colonic mucosal abnormalities can mimic an NSAID-induced injury or IBD, and must be differentiated from Crohn's disease in particular.[6-12] During the subsequent 3-year clinical follow-up after colonoscopy, none of the 24 patients found to have sodium phosphate-associated colonic mucosal abnormalities in the present study developed clinically manifest IBD. This group of disorders might remain indolent and unchanged over long periods of time, but it seems improbable that IBD would not become evident over the 3-year follow-up period.

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