



# The timing of bowel preparation before colonoscopy determines the quality of cleansing, and is a significant factor contributing to the detection of flat lesions: A randomized study

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## Abstract

**AIM:** To compare the cleansing quality of polyethylene glycol electrolyte solution and sodium phosphate with different schedules of administration, and to evaluate whether the timing of the administration of bowel preparation affects the detection of polyps.

**METHODS:** One hundred and seventy-seven consecutive outpatients scheduled for colonoscopy were randomized in one of four groups to receive polyethylene glycol electrolyte solution or oral sodium phosphate with two different timing schedules. Quality of cleansing, polyp detection, and tolerance were evaluated.

**RESULTS:** Patients receiving polyethylene glycol or sodium phosphate on the same day as the colonoscopy, obtained good to excellent global cleansing scores more frequently than patients who received polyethylene glycol or sodium phosphate on the day prior to the procedure ( $P < 0.001$ ). Flat lesions, but not flat adenomas, were more frequent in patients prepared on the same day ( $P = 0.02$ ).

**CONCLUSION:** The quality of colonic cleansing and the detection of flat lesions are significantly improved when the preparation is taken on the day of the colonoscopy.

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**Key words:** Colonoscopy; Preparation; Polyp; Flat lesion; Sodium phosphate; Polyethylene glycol

## INTRODUCTION

The aim of bowel preparation before colonoscopy is to obtain a clean bowel allowing for examination of the whole mucosal surface. This preparation method should be safe and well tolerated by the patient. However, the ideal colonic lavage solution is not yet available. The two most widely employed cleansing methods are sodium phosphate (NaP) and polyethylene glycol electrolyte solution (PEG-ELS). Available data suggest that NaP achieves excellent cleansing when the first dose is administered the day before the examination and the second one a few hours before the colonoscopy<sup>[1]</sup>. On the other hand PEG-ELS administered the same day as the colonoscopy renders a better preparation quality than when given the day before<sup>[2]</sup>. For both preparation methods, the cecum and ascending colon seem especially susceptible to a worse preparation when the whole agent is given the day before<sup>[1,2]</sup>. To date, no studies have been designed to compare the efficacy of NaP and PEG-ELS at their respective best administration schedules.

In the majority of available studies, the quality of bowel preparation is evaluated according to the endoscopist's impression, using pre-established scales<sup>[1-4]</sup>. These scales only take into consideration the features and amount of remaining material. Although the detection of polyps is one of the main aims of colonoscopy, the impact of colonoscopy preparation quality on the detection of polyps has only been investigated in two recently published studies<sup>[5,6]</sup>. Flat lesions are hard to detect due to their limited endoscopic expression. However they show a higher rate of high grade dysplasia and cancer than protruding polyps of similar sizes<sup>[7-9]</sup>, and for that reason they have become a recent field of interest and research. Although it is generally assumed by most experts in the

field that a good preparation is essential for the detection of flat lesions<sup>[10]</sup> no prospective studies have addressed that issue. Therefore it is important to determine the influence of bowel preparation quality in the detection of flat lesions and protruding polyps, as it may have important implications in the screening of colorectal neoplasia.

The aim of the present study was to investigate whether the timing of lavage solutions before colonoscopy determines the quality of colonic cleansing and facilitates the endoscopic recognition of polyps.

## MATERIALS AND METHODS

### Subjects

One hundred and ninety-seven consecutive outpatients, aged between 18 and 85 years, scheduled for elective colonoscopy with morning or afternoon appointments were initially included in the study. Exclusion criteria were: pregnancy, partial or total colectomy, and inflammatory bowel disease (known or suspected). The reason for excluding patients with suspected inflammatory bowel disease was that sodium phosphate can produce mucosal changes similar to those found in Crohn's disease, which may lead to misdiagnosis. Twenty patients were not eligible for the following reasons: impossibility of reaching the cecum due to loop formation ( $n = 5$ ), neoplastic stricture ( $n = 2$ ), abdominal pain during colonoscopy ( $n = 2$ ), bradycardia during colonoscopy ( $n = 1$ ), protocol deviation due to incorrect administration of study medication ( $n = 3$ ), incomplete data ( $n = 6$ ), or breakdown of the endoscope during examination ( $n = 1$ ). Therefore, one hundred and seventy-seven patients were finally included.

### Methods

Having provided written informed consent, patients were assigned to one of the following four groups using a computer generated random number list. The numbers were assigned consecutively by the endoscopy assistant when the appointment for endoscopy was given. Group 1: PEG-ELS (Solución Evacuante Bohm, Laboratorios Bohm S.A, Fuenlabrada, Madrid, Spain) 3 Liters starting at 06:00 the same day of colonoscopy ( $n = 43$ ); Group 2: NaP (Fosfosoda, Casen Fleet, Utebo, Zaragoza, Spain) 45 mL the day before (20:00) and 45 mL at 06:00 the same day of colonoscopy ( $n = 45$ ); Group 3: PEG-ELS 3 L starting at 20:00 the day before ( $n = 45$ ); Group 4: NaP 45 mL at 15:00 and 20:00 the day before colonoscopy ( $n = 44$ ). Patients in groups 2 and 4 were encouraged to drink fluids liberally (at least 2 L) during the period of colonic cleansing. PEG-ELS and NaP were supplied by the manufacturers. Every patient in the study received Bysacodyl (Dulcolaxo, Boehringer Ingelheim S.A., San Cugat del Vallés, Barcelona, Spain), 15 mg. the day before colonoscopy, as it reduces the volume of PEG-ELS required for bowel preparation<sup>[11]</sup>. A low-fibre diet (mainly avoidance of fruits and vegetables) was recommended for the day before colonoscopy to all subjects. Having completed bowel preparation, the patients were allowed to drink only clear fluids. Patients with co-morbid conditions (chronic renal failure, symptomatic ischemic heart disease, congestive heart failure, hypertension with poor pharmacological control) allocated to the groups receiving

NaP were given PEG-ELS instead (those allocated to group 2 and 4 were given preparation for groups 1 and 3 respectively), and evaluated on an intention-to-treat analysis. The study was approved by the ethical committee of the University Hospital of the Canary Islands.

Colonoscopic examinations were performed between 09:00 and 15:00 by four experienced endoscopists on staff, one of whom had received additional training in flat polyp detection. Standard colonoscopies (CF140L, Olympus Optical España S.A., Barcelona, Spain) performed the colonoscopic examinations. Indigo carmine (2-5 g/L) was applied with a spraying catheter or a syringe to the polyp at the will of each endoscopist, usually whenever a flat lesion was suspected, or to help clarify the margin or the surface features of any type of polyp. However indigo carmine was not applied in a routine way onto normal appearing mucosa to increase polyp detection yield. Flat elevated lesions were defined according to Sawada *et al*<sup>[12]</sup> as those with a height of less than half their diameter. Flat depressed lesions were those with a central distinct depression<sup>[9]</sup>. Protruding polyps were resected by cold or hot biopsy when  $\leq 3$  mm, and those larger were resected by snare polypectomy. Some sessile polyps were resected by saline-assisted polypectomy to enable complete resection. Flat elevated lesions  $\leq 5$  mm were resected by hot biopsy or mucosectomy, and larger lesions with mucosectomy. Flat depressed lesions amenable to endoscopic treatment were resected by mucosectomy.

The quality of bowel preparation was determined during colonoscopy by two observers (the endoscopist performing the examination, and the attending nurse) both unaware of the preparation method employed, according to the following scale: 5 excellent, (no material or liquid material covering  $< 10\%$  of the mucosal surface in each location), 4 good, (liquid material or mucus covering  $> 10\%$  of the mucosal surface), 3 acceptable, (small particles easy to suction), 2 fair, (solid material impossible to suction, covering  $< 10\%$  of the mucosal surface), 1 poor, (solid material covering  $> 10\%$  of the mucosal surface). Global quality was calculated, as the arithmetic mean of the quality in the different locations. Whenever there was a discrepancy in the evaluation, consensus was reached after discussion. The following variables were evaluated: gender, age, chronic constipation (defined as inability to pass stools at least 3 times weekly without laxatives), indication for colonoscopy, nausea, vomiting, abdominal pain, thirst, consideration of the preparation as moderately to very disgusting, procedure time (AM or PM), quality of cleansing (globally and in the different large bowel locations), polyp status (existence or absence), protruding polyp status, flat lesion status, polyp histology, and endoscopist.

### Statistical analysis

In advance of the study, a statistical sample size calculation was performed based on previously published data, indicating a good to excellent preparation in 90% of patients receiving PEG-ELS or NaP on the same day of colonoscopy, and in 70% of patients receiving those preparations the day before. To achieve an absolute difference of 20% in the frequency of good to excellent quality of cleansing in the cecum and ascending colon (score  $\geq 4$ ) (with a statistical type I error of 5% and a

Table 1 Basal features of patients in the four preparation groups

|                          | Group 1         | Group 2         | Group 3         | Group 4         | P  |
|--------------------------|-----------------|-----------------|-----------------|-----------------|----|
| Patients (n)             | 43              | 45              | 45              | 44              |    |
| Gender ratio (M/F)       | 21:22           | 24:21           | 19:26           | 21:23           | NS |
| Age (yr) (mean $\pm$ SD) | 58.0 $\pm$ 15.9 | 52.4 $\pm$ 16.7 | 53.6 $\pm$ 15.2 | 54.0 $\pm$ 16.5 | NS |
| Chronic constipation (%) | 17.1            | 26.3            | 24.4            | 27.2            | NS |
| Polyp surveillance (%)   | 23.3            | 12.5            | 6.6             | 13.6            | NS |

Table 2 Comparison of rate of patients with cleansing quality  $\geq 4$ , between different treatment groups (mean  $\pm$  SD, %)

| Group | Global                      | Cecum                       | Ascending                   | Transverse                  | Descending-sigmoid          | Rectum                      |
|-------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| 1     | 78.6 $\pm$ 0.2              | 72.1 $\pm$ 0.2              | 79.1 $\pm$ 0.2              | 81.0 $\pm$ 0.1              | 76.7 $\pm$ 0.2              | 79.1 $\pm$ 0.2              |
| 2     | 80.0 $\pm$ 0.2              | 84.4 $\pm$ 0.1              | 77.8 $\pm$ 0.2              | 82.2 $\pm$ 0.1              | 86.7 $\pm$ 0.1              | 86.7 $\pm$ 0.1              |
| 3     | 26.7 $\pm$ 0.2 <sup>b</sup> | 38.6 $\pm$ 0.2 <sup>b</sup> | 22.2 $\pm$ 0.2 <sup>b</sup> | 35.6 $\pm$ 0.2 <sup>b</sup> | 60.0 $\pm$ 0.2 <sup>d</sup> | 57.8 $\pm$ 0.2 <sup>d</sup> |
| 4     | 6.8 $\pm$ 0.1 <sup>b</sup>  | 14.6 $\pm$ 0.1 <sup>b</sup> | 9.8 $\pm$ 0.1 <sup>b</sup>  | 32.6 $\pm$ 0.2 <sup>b</sup> | 45.5 $\pm$ 0.2 <sup>b</sup> | 50.0 $\pm$ 0.2 <sup>b</sup> |

<sup>b</sup> $P < 0.01$  vs Group 1, 2. (Bonferroni's correction); <sup>d</sup> $P < 0.01$  vs Group 2.

statistical power of 80%) at least 124 patients (62 patients per group) was calculated as required.

A global chi-square test and singly ordered Kruskal Wallis test were used to compare qualitative data. The comparison of the proportion of patients with good-excellent and those with worse preparation quality in the four groups, was initially analysed with the Chi-square test, and then group to group comparisons were done. For the adjustment of multiple contrasts, the Bonferroni correction was employed.

Continuous variables were compared with the Student's *t* test, and means and standard deviations (SD) were reported. Calculated  $P < 0.05$  was considered to indicate statistical significance.

## RESULTS

Basal features of the patients are shown in Table 1; there were no differences among the four groups in terms of gender, age, chronic constipation or indication for colonoscopy. Two patients allocated to group 2 and two to group 4 received PEG-ELS due to chronic renal failure ( $n = 2$ ), congestive heart failure ( $n = 1$ ) and hypertension ( $n = 1$ ), and were analyzed on an intention-to-treat fashion. There was no significant difference in the number of examinations performed by each endoscopist on patients prepared the same day or the day before. Endoscopist number 1 performed 84 (47.5%) of the 177 colonoscopies, 42 corresponding to preparation the same day and the remaining 42 to preparation the day before. Colonoscopy was performed in the morning (from 08:30 to 12:00) in 39.5%, 53.3%, 68.9%, 77.3% patients in groups 1 to 4 respectively ( $P < 0.01$ ).

### Quality of cleansing

When the four groups were compared, the quality of cleansing was different among all the segments and globally ( $P < 0.001$ ). Per segments, in patients who received the preparation the same day (group 1, 2, Table 2) as the colonoscopy, quality was superior compared to

those prepared the day before (group 3, 4, Table 2). The global score was  $\geq 4$  in 78.6%  $\pm$  0.2 %, 80.0%  $\pm$  0.2%, 26.7%  $\pm$  0.2%, and 6.8%  $\pm$  0.1% patients in groups 1 to 4 respectively. Groups receiving preparation the same day had significantly better global scores ( $P < 0.001$ ) than groups prepared the previous day. Fewer patients in group 4, compared to group 3, had global scores  $\geq 4$ , but the difference was not significant after the application of Bonferroni's correction. In general, in groups 3 and 4 a cleansing score  $\geq 4$  was more frequent in distal than in proximal colonic locations.

Poor preparation (global quality score  $< 2$ ), theoretically requiring a repeat colonoscopy, was found in 12.4% (11/89) of the patients prepared the previous day but only in 2.2% (2/88) of those prepared the same day as the colonoscopy ( $P = 0.02$ ). Poor preparation precluded insertion to cecum in two patients in group 4 and one in group 3 respectively.

### Polyp detection (Tables 3 and 4)

One-hundred and eighty three polyps were detected in eighty-six (48.6%) patients. Thirty-seven (20.2%) were flat (36 flat elevated, 1 flat depressed); the total number of flat lesions detected in patients who received some preparation the same day as the colonoscopy (groups 1, 2) was significantly higher ( $P = 0.002$ ) than in those prepared the day before (Table 3). However, no significant difference was found between groups prepared the same day or the day before in the total number of polyps, the number of protruding polyps, or the number of small ( $\leq 3$  mm) polyps. Indigo carmine was employed in 39 (44.3%) patients in groups 1 and 2, and in 22 (24.7%) in groups 3 and 4 ( $P = 0.005$ ). There was a histological confirmation for 152/183 (83.1%) polyps, for 79.1% and 86.6% of those detected in patients receiving preparation the day before (group 3, 4) or the same day as the colonoscopy (group 1, 2) respectively. There was one (0.6%) submucosally invasive cancer, 107 (70.4%) adenomas, and 44 (28.9%) non-neoplastic polyps. Among flat lesions, 23/31 (74.2%) were neoplastic, whereas 75/121 (70.2%) protruding polyps were neoplastic. The rate of neoplastic polyps

**Table 3** Distribution by size and shape of all polyps detected in the patients who received bowel preparation the same day and the day before

| Lesion                                     | Preparation same day (group 1, 2) | Preparation day before (group 3, 4) | P      |
|--|-----------------------------------|-------------------------------------|--------|
| Polyp size (mean ± SD)                     | 5.6 ± 3.8                         | 5.3 ± 5.1                           | NS     |
| Polyp size ≤ 5 mm (n = 121)                | 59                                | 62                                  | NS     |
| Flat lesions (n = 37)                      | 28                                | 9                                   | < 0.01 |
| Flat lesions size (mean ± SD)              | 4.8 ± 3.7                         | 9.0 ± 12.0                          | NS     |
| Protruding polyps (n = 146)                | 69                                | 77                                  | NS     |
| Protruding polyps size (mean ± SD)         | 5.9 ± 3.8                         | 4.9 ± 3.6                           | NS     |
| Total polyps (flat + protruding) (n = 183) | 97                                | 86                                  | NS     |

Bonferroni's correction.

**Table 4** Polyp status in patients who received bowel preparation the same day or the day before (group 3, 4), n (%)

|                                | Preparation same day (group 1, 2) | Preparation day Before (group 3, 4) | P      |
|--------------------------------|-----------------------------------|-------------------------------------|--------|
| Patients (n)                   | (88)                              | (89)                                |        |
| Any polyp                      | 46 (52.3)                         | 40 (44.9)                           | NS     |
| Flat lesions <sup>1</sup>      | 19 (21.6)                         | 8 (9.0)                             | < 0.05 |
| Protruding polyps <sup>2</sup> | 35 (39.7)                         | 37 (41.6)                           | NS     |
| Multiple (≥ 3) polyps          | 16 (18.1)                         | 14 (15.7)                           | NS     |
| Small (≤ 5 mm) polyps          | 39 (44.3)                         | 33 (37.0)                           | NS     |

<sup>1</sup>Irrespective of the existence of protruding polyps; <sup>2</sup>Irrespective of the existence of flat polyps.

between patients prepared the same day (61/84: 72.6 %) and those prepared the day before (47/68: 69.1%) was not statistically different. A histological diagnosis was lacking in 31/183 (16.9%) of the lesions; the most frequent reasons being inadequate preparation that precluded polyp sampling, resection or recovery, or patients on whom polypectomy was not performed at that moment, but who required a repeat colonoscopy for that purpose.

Among patients with polyps, fifty-nine (68.6%) had protruding polyps, thirteen (15.2%) had flat lesions, and fourteen (16.2%) had both protruding polyps and flat lesions. Altogether in 27 (31.4%) patients who had any kind of polyp, flat lesions were detected.

For the patient-based analysis, polyp status was evaluated: polyp status positive (patients with polyps), protruding-polyp status positive (patients with protruding polyps irrespective of presence or absence of flat lesions), flat-lesion status positive (patients with flat lesions, irrespective of presence or absence of protruding polyps), multiple-polyps (≥ 3 polyps) status, and minute-polyp (≤ 3mm) status (Table 4). There was no difference in the polyp status, protruding-polyp status, or the minute or multiple polyp status; however flat-lesion status positive was more frequent in groups 1 and 2 compared to groups 3 and 4 (21.6% *vs* 9.0%, respectively, *P* = 0.02).

The following factors were significantly associated with the diagnosis of flat lesions in the univariate analysis: male

**Table 5** Comparison of the tolerance variables in the four groups n (%)

| Side effect                 | Group 1   | Group 2   | Group 3   | Group 4   | P  |
|-----------------------------|-----------|-----------|-----------|-----------|----|
| Nausea                      | 17 (39.5) | 24 (53.3) | 24 (53.3) | 15 (34.1) | NS |
| Vomiting                    | 4 (9.3)   | 10 (22.2) | 10 (22.2) | 8 (18.2)  | NS |
| Disgusting <sup>1</sup>     | 10 (23.3) | 12 (26.7) | 12 (26.7) | 12 (27.3) | NS |
| Thirst <sup>1</sup>         | 6 (13.9)  | 9 (20.0)  | 9 (20)    | 12 (27.2) | NS |
| Abdominal pain <sup>1</sup> | 4 (9.3)   | 4 (8.9)   | 3 (6.6)   | 5 (11.4)  | NS |
| Anal pain <sup>1</sup>      | 1 (2.3)   | 4 (8.9)   | 1 (2.2)   | 2 (4.5)   | NS |

<sup>1</sup>As moderate or severe.

gender, endoscopist number 1, and “same day” preparation.

### Tolerance and side effects (Table 5)

There was no difference regarding the occurrence of nausea, vomiting, thirst, abdominal pain or anal pain among patients in the four groups. A similar proportion of the patients in the different groups rated the preparation as moderately to very disgusting. The proportion of patients in the different groups who had bowel activity on their way to the hospital was: 16.3%, 7.7%, 9.1% and 9.5% for groups 1, 2, 3, and 4 respectively (not statistically significant).

## DISCUSSION

It has been proven that a superior quality of cleansing is obtained when PEG-ELS is administered wholly or in part on the same day as the colonoscopy<sup>[2,13]</sup>. In fact, in many Japanese institutions patients take the PEG-ELS in the endoscopy waiting room and the examination is started when the excretions become liquid and transparent. Similarly, significantly better cleansing scores have been reported when the second dose of NaP is given on the same day as the colonoscopy<sup>[11,3]</sup>. Although many studies have compared the efficacy of cleansing between PEG-ELS and NaP, PEG-ELS was given in those studies on the day before the colonoscopy. To the best of our knowledge this is the first study ever to compare oral PEG-ELS and NaP administered at their respective best timing schedules, and our results confirm the importance of timing. In the current study, when the agent was administered the same day as the colonoscopy (the whole agent for PEG-ELS or partial for NaP), the quality of cleansing was significantly better globally and per segment than when the whole preparation was given the day before. In addition, the detection of flat lesions was markedly improved in patients with a better quality of cleansing, given that the number of flat lesions were significantly greater in patients receiving the bowel cleansing agents the same day than in those prepared the day before.

In our study the groups receiving preparation the same day as the colonoscopy reached a good to excellent quality of cleansing for all colonic segments. It is important to note that more than 75% of patients prepared the same day had a global score of ≥ 4 (good-excellent). However in groups prepared the day before, proximal bowel segments were especially poorly prepared. This



would indicate that having obtained a clean colon, material coming later from the small bowel could make the colon become dirty again, starting with the right colon. There are at least two possible explanations for that fact. Firstly, gastric, intestinal and biliary secretions could account for the material staining the colon. Secondly, although bowel preparation methods clean the colon efficiently, their effect on the small bowel might be more modest. In both instances, a longer time interval between the administration of the bowel preparation agent and the colonoscopy could account for a dirty colon. Videocapsule or enteroscopy studies could be useful to determine small and large bowel cleansing quality with different timing of administration of preparation agents.

In Spain both PEG-ELS and NaP are employed for colonoscopy. NaP is usually administered in the same way as in our study; however PEG-ELS is given by most institutions the day before colonoscopy, probably because of concern regarding the duration of diarrhoea after its ingestion. In the current study colonoscopies were scheduled from 09:00 to 14:00, and this is the rule for most public hospitals in our country. Although significant differences were not found among the different groups, we found that 16.3% of those in group 1 (PEG-ELS the same day) had bowel movements on their way to the hospital. Therefore, it might be reasonable to administer PEG-ELS at least one hour earlier than we did in our study. Although such an early administration will interfere with the patient's sleep, we believe that the effort is worthwhile, providing a good quality of cleansing and diagnostic yield, and preventing repeat examinations. Although it could be argued that from the patient's perspective it might be more difficult to ingest a large volume of fluids a few hours before the examination (same day), than the day before, no difference in tolerance variables was found between the groups. Conversely, it could be said that drinking the bowel prep a few hours before the examination, instead of the previous day, would impact on the patient's activities during a shorter period of time. Moreover, in the present study bisacodyl was used in order to reduce the total volume of PEG-ELS, as it has proven to be effective for that purpose<sup>[11]</sup>. In our opinion, the remarkably significantly superior preparation quality observed in patients prepared the same day seems to justify that choice. An alternative strategy could be to give the bowel preparation in the endoscopy unit, which is a common practice in many Japanese institutions.

One potential limitation of the present study is the use of a non-validated scale for assessing the adequacy of the bowel preparation. There is no standardized system for describing bowel preparation<sup>[14]</sup>, and in fact most studies comparing different methods of bowel cleansing have used non-validated scales. We used a scale similar to others employed in previous reports<sup>[4,15]</sup>, but including a numerical value (90%) to describe the average of the mucosal surface covered by liquid or faecal content. Moreover, quality assessment was done by two examiners. Therefore, although employing a validated scale would have provided more reliable data, we do not believe that this has affected our study significantly.

Colorectal cancer is the second leading cause of cancer

death in most western countries, and the detection and endoscopic removal of colonic polyps has been proven to reduce the incidence of colorectal cancer. The polyp 'miss' rate seems to be especially high for lesions < 10 mm, as determined by tandem colonoscopy studies<sup>[16]</sup>. Flat lesions represent about one fourth of all colonic polyps and may be hard to detect at colonoscopy. In the present study, flat lesions were more frequently detected in patients receiving PEG-ELS or oral NaP the same day as the colonoscopy, who reached higher rates of good to excellent bowel cleansing. The impact of colonic cleansing on polyp detection had been assessed only in two previous studies. Harewood *et al*<sup>[5]</sup>, in a retrospective study including more than 90000 colonoscopic procedures, found that an adequate preparation was associated with the detection of small ( $\leq 9$  mm) polyps, but not of larger polyps. In a prospective multicenter European study, the detection of polyps of any size, but not of cancer, was dependent on cleansing quality<sup>[6]</sup>. The present study represents the first evidence that flat lesion detection is associated with quality of cleansing. Although flat lesions were more frequent in patients prepared the same day, no significant difference was detected when flat neoplasia was evaluated; in fact the lack of histological diagnosis in 17% of the polyps is a potential limitation of our study. However, 74% of flat lesions with histological diagnosis available were neoplastic, which is similar to previously reported<sup>[7]</sup>. Although an increased detection of small flat hyperplastic lesions can be expected with a high quality of cleansing, it is well known that minute flat adenomas can bear high grade dysplasia and even invasive cancer; an excellent cleansing seems therefore desirable to improve the detection of such lesions.

The more frequent application of indigo carmine in the groups receiving preparation the same day might be interpreted as another limitation of our study, as it has been proven that pancolonial application of indigo carmine with a spraying catheter increases the detection rate of small polyps<sup>[17,18]</sup>. However, as explained in the materials and methods section, indigo carmine was applied only when a flat lesion was suspected, and only in a small amount on the suspect area. On the other hand, the more frequent application of indigo carmine in well-prepared patients (those in groups 1 and 2) is not surprising, as chromoendoscopy is used only when the colonic mucosa is sufficiently clean<sup>[19]</sup>. Therefore, we believe that the effect of indigo carmine did not play a significant role in the increased detection of flat lesions in groups 1 and 2 in our study.

Nevertheless the outcome of real interest would be the detection of flat adenomas, rather than of flat lesions in general. The impact of the timing of bowel preparation and colonic cleansing quality on flat neoplasia detection should be evaluated in future large-scale randomized studies, adequately powered for that purpose. The importance of other factors presumably involved in flat lesion detection, such as the expertise of the endoscopist and use of chromoendoscopy should be ascertained.

Apart from an excellent bowel preparation, flat lesion detection requires a high suspicion index by the endoscopist including specific training in their detection<sup>[20]</sup>.

In fact this contention was also proven in our study. Although the four participating endoscopists shared a similar number of explored patients in each study group, endoscopist 1, who had additional training in chromoendoscopy and flat lesion detection, identified significantly more flat lesions than the others. The basic techniques for flat lesion detection, interpretation and treatment should constitute a part of the training in colonoscopy. In the present study, both preparation methods were well tolerated, and we found no difference in this respect, although other studies indicated that NaP is tolerated better due to its smaller volume<sup>[1,3,4,15,21-24]</sup>. However in recent studies the amount of oral liquids with NaP has been increased (up to 3.8 liters) in order to prevent hydroelectrolytic disturbances<sup>[25]</sup>.

In conclusion, the present study demonstrates that the quality of colonic cleansing is significantly improved when the preparation (either PEG-ELS or NaP) is given a few hours before the colonoscopy. Although there was no overall difference in the number of polyps detected, flat lesions were more frequent in patients receiving preparation the same day. Training of the endoscopist in flat lesion detection seems to influence their detection. Larger prospective studies are needed to determine the impact of colonic preparation quality on the detection of flat and protruding neoplasia.

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