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Title:

Same-day bowel cleansing regimen is superior to a split-dose regimen over two days for afternoon colonoscopy - results from a large prospective series

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Same-day Bowel Cleansing Regimen is Superior to a Split-dose Regimen Over Two Days for Afternoon Colonoscopy

Results From a Large Prospective Series

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Goals and Background: Conventional bowel preparation for afternoon colonoscopy requires an oral agent the day before the procedure. Bowel cleansing given only on the day of the colonoscopy has never been attempted. The aims of this study were to compare the efficacy of bowel cleansing, impact on activities of daily living (ADLs), side effects, and patient preference of a same-day regimen with a 2-day regimen.

Study: A single-blinded, prospective cohort study. Patients were block recruited into 2 groups with the endoscopist blinded to the regimen. Group A: 3 sachets of sodium picosulphate given at 12:00 noon and at 05:00 PM the day before and at 8:00 AM on the morning of the procedure. Group B: 2 sachets of sodium picosulphate on the morning of the procedure at 07:00 and 10:00 AM. Patients completed a quality-of-life questionnaire investigating the side effects, impact on ADLs, and regimen preference. The main outcome measures were mucosal cleansing, impact on ADLs, side effects, and patient preference of the regimen.

Results: A total of 227 patients underwent screening colonoscopy. There were 95 patients in group A and 132 in group B, all of whom were age and sex matched. Same-day preparation produced better mucosal cleansing ($P = 0.0046$) with fewer side effects ($P = 0.002$). Impact on ADLs was less with the same-day regimen ($P < 0.0001$). Significantly more number of patients preferred the same-day preparation compared with the 2-day regimen ($P = 0.0147$).

Conclusions: Same-day bowel preparation is feasible, safe, and more effective than a split-dose regimen. It has fewer adverse events and is preferred by patients.

Key Words: colonoscopy, bowel cancer screening program, bowel preparation, quality of life

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Bowel cancer is a major cause of morbidity and mortality in the western world. There are 1.4 million new cases each year, accounting for an estimated 550,000 deaths worldwide.¹ Despite advances in treatment, there is no cure for advanced disease. It is well recognized that colorectal cancer develops in a series of well-defined steps, from normal mucosa to adenomatous polyp through varying

degrees of dysplasia and finally to adenocarcinoma. As a result, there has been a drive toward early detection through screening, with established bowel cancer screening programs in the UK and US. This has been developed in parallel with ambitious targets for improving the quality of colonoscopy, and mandatory targets have been set for completion rates and adenoma detection rates.²

It is widely accepted that poor-quality bowel preparation leads to significant lesions being missed.^{3,4} Unfortunately, poor mucosal cleansing is not uncommon. A recent large retrospective study of 12,787 colonoscopies found that preparation was suboptimal in 24% of procedures.⁵ Among 216 repeat procedures in which preparation had been optimized, 198 adenomas were identified, of which 83 had not been seen on the original colonoscopy in which the preparation had been poor. This represents a miss rate of 42% on first inspection. The investigators concluded that suboptimal bowel preparation substantially decreases colonoscopy effectiveness. Endoscopists are often concerned about afternoon colonoscopy cases for fear of encountering colons that have been poorly prepared. Conventional practice for bowel cleansing for an afternoon colonoscopy case involves the use of an oral agent the day before the procedure, with further preparation on the morning of the procedure. This split-dose regime has been widely adopted. However, although superior to a single dose the previous day,⁶ it still leads to a significant time gap between the bowel preparation and colonoscopy, leading, in many cases, to the accumulation of intestinal secretions and deterioration in mucosal visibility, especially for patients scheduled toward the end of the list.

A further significant, often overlooked, factor in current bowel preparation is the impact on patient quality of life. It is generally recognized that bowel preparation is unpleasant. Current regimes require patients to take the preparation from the afternoon of the preceding day. This effectively prevents the patient from working or going out during this period, effectively making colonoscopy a 2-day procedure. Although this problem could be minimized by taking the preparation in the late afternoon or evening, there would still be interruption to sleep and a risk for nocturnal incontinence, which is generally considered to be unacceptable. With the development of bowel cancer screening programs, we are conducting investigations on patients who are asymptomatic. If we are to achieve a good uptake (and compliance with follow-up colonoscopy) with these programs, it is important to minimize disruption to the patient's life as far as possible. This is even more important for the younger working population.

Poor bowel preparation can also have cost implications. Poor cleansing is an indication for repeat colonoscopy. This

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can prove disruptive to patients and increases demand on already overstretched endoscopy units.

Some work has been conducted that has demonstrated that bowel prep administered on the day of the procedure is associated with a better outcome.⁷ In this study, only patients receiving polyethylene glycol were allocated to take all of the polyethylene glycol preparation on the same day. Patients randomized to sodium phosphate received the preparation over 2 days. There have been no studies published in the literature using sodium picosulphate (Picolax) as a same-day agent, nor has there been a study exploring patient preferences for bowel cleansing regimens and the impact of this on activities of daily living (ADLs).

We hypothesize that, for afternoon colonoscopy, same-day (morning only) preparation with 2 sachets of sodium picosulphate will provide better bowel cleansing than a 2-day split-dose preparation with 3 sachets of sodium picosulphate. The aim of the study was to prove the feasibility, safety, and effectiveness of same-day bowel cleansing for afternoon colonoscopy and to compare it with the more traditional split-dose regimen over 2 days. We also evaluated the effect of the 2 different regimens on the patients' ADLs and finally sought to determine the patients' preferred regimen.

MATERIALS AND METHODS

Inclusion Criteria

Patients receiving colonoscopy under the National Bowel Cancer Screening Programme (BCSP) aged 59 to 70 years.

Exclusion Criteria

Known renal impairment (CKD grade 3 Creatinine > 150 eGFR < 40).

Congestive Cardiac Failure.

Sodium < 130.

Patients were evaluated between May 2009 and May 2010. Data were recorded prospectively into the national BCSP database of procedure outcome. Bowel cleansing was graded by the following criteria recommended by the BCSP UK.²

Excellent: no or minimal solid stool and only clear fluid requiring suction.

Adequate: collections of semisolid debris that are cleared with washing/suction.

Poor prep: solid or semisolid debris that cannot be cleared effectively.

All assessments of the quality of bowel preparation were made by 2 nurses trained in the assessment criteria described above and blinded to the type of bowel cleansing regimen that the patient had undergone. All patients were seen by the endoscopy nurse in a dedicated preassessment clinic 2 weeks before taking the medication and were given written instructions on how to take the preparation. All procedures were performed by a single endoscopist (P.B.) on an afternoon list.

All consecutive patients were block recruited into 1 of the bowel cleansing regimens for 6 months. The regimen was then changed, and all subsequent patients were recruited into it for the next 6 months. The endoscopist and screening nurse practitioners were blinded to the regimen used. Assignment therefore was not randomized but allocated on the basis of date of procedure. However,

patients were not selected for a particular date and represented unfiltered referrals for screening.

In both groups, patients were instructed to consume a light diet only the day before the procedure, with no vegetables or fruit. They were also advised to increase fluid intake for 24 hours leading up to the procedure.

Group A (2-day regimen) consisted of patients prepared with 3 sachets of sodium picosulphate, given at 12:00 noon and at 05:00 PM the day before the procedure, and 1 sachet at 8:00 AM on the morning of the procedure, for an afternoon colonoscopy.

Group B (same-day regimen) consisted of patients given 2 sachets of sodium picosulphate at 07:00 and 10:00 AM, administered on the morning of the procedure for an afternoon colonoscopy. The patients were instructed to be at home for at least 3 hours after the last dose of sodium picosulphate before traveling to the hospital.

The endoscopist and the nurse practitioners (scoring the quality of bowel cleansing) were blinded to this information. The study was powered on the assumption that a difference in mucosal visibility of 30% would be observed, with a 1.0:1.5 recruitment ratio between groups A and B. The χ^2 test with the Fisher exact test was performed to test for any significant difference in mucosal visibility between the 2 regimens. A minimum of 150 patients would be required to demonstrate this difference.

A total of 130 consecutive patients were asked to complete a questionnaire on the tolerability of bowel preparation, impact on ADLs, and patient preference for future bowel cleansing agent. This was completed by the patients after they had taken the bowel preparation. Level of impairment of each activity was measured on a 5-point Likert scale, with 0 being completely unimpaired, 1 being a minimal impairment to activity, 2 being moderate impairment, 3 being significant impairment, and 4 being a major impact effectively preventing activity completely. Data were categorical, and therefore the Fisher exact test was used to compare the outcomes between the 2 groups.

RESULTS

Demographics

A total of 227 patients were recruited into the study. Ninety-five patients were recruited into group A and 132 into group B. Seventy percent of the patients were male. The median age was 65 years with a range of 60 to 71 years. The groups were matched for age, sex, and comorbidities. There was no difference in the level of sedation and comfort scores between the groups (Table 1).

Mucosal Cleansing

The mucosal cleansing effect of each regimen is summarized in Table 2. There were fewer cases with poor cleansing in patients receiving same-day preparation (group B) compared with those receiving the split-dose 2-day regimen (group A). A χ^2 test was performed, which showed a statistically significant difference between the 2 regimens with better cleansing achieved by the novel same-day regimen ($P = 0.0046$).

Adenoma Detection Rate

A numerical trend was observed for superior adenoma detection rate in patients receiving same-day cleansing compared with patients receiving split-dose preparation, 71% in group B versus 62% in group A, but this failed to

TABLE 1. Level of Sedation by Patient Group

	Group A	Group B
No. Patients	95	132
Age (SD)	66 (3.4)	66 (3.2)
Male patients	63%	72%
Female patients	37%	28%
Mean sedation levels (1 = awake, 2 = drowsy, 3 = asleep)	1.27	1.20
Mean midazolam used (mg) (range)	0.60 (0-2.5)	0.89 (0-2.5)
Mean pethidine used (mg) (range)	18.4 (0-50)	35 (0-50)

Group A = 3 sachets split-dose preparation. Group B = 2 sachets same-day preparation.

reach statistical significance ($P = 0.2$). A high adenoma detection rate was expected as all patients were screened as part of the UK Bowel Cancer Screening Program and all had positive fecal occult blood before colonoscopy.

Adverse Events

Quality-of-life questionnaires were completed by 105 patients. Fifty-eight patients were from group A, and 47 patients were from group B. In group A, 14% of patients had difficulty taking the bowel prep compared with 8.5% of patients in group B. Ninety-five percent of patients completed the bowel prep in group A compared with 98% of patients in group B. These differences failed to reach statistical significance. The symptoms experienced by each group are shown in Table 3. There were significantly fewer adverse events in group B compared with group A ($P < 0.0002$). The major differences were in interruption to sleep (29.3% vs. 10.6%), headaches (36.2% vs. 10.6%), fecal incontinence (7.0% vs. 2.1%), and vomiting (7.0% vs. 2.1%).

Impact on ADLs

This study was conducted in a bowel cancer screening population between 60 to 70 years of age, and the level of daily activities was assessed. The 2 groups were comparable in age, sex, and activity profile with no significant differences between the groups. In group A, 55% of patients were working in paid work or as a full time care provider compared with 59% of patients in group B. In group A, 62% enjoyed gardening, 83% shopping, 71% performed daily house work, 67% engaged in regular social activity, and 93% watched television. In group B, 57% enjoyed gardening, 87% shopping, 79% performed daily house work, 75% engaged in regular social activity, and 92% watched television. The impact on ADLs is described in Table 4. This shows that both bowel cleansing regimens have an effect on ADLs, but the split-dose regimen had a significantly higher impact on ADLs compared with the same-day regimen ($P = 0.0001$). The main differences seen between the 2 regimens were in interruption to work

TABLE 3. Adverse Events by Bowel Preparation Regimen

	Group A n = 58	Group B n = 47
Fecal incontinence	4 7%	1 2.1%
Interruption to sleep	17 29.3%	5 10.6%
Headaches	21 36.2%	5 10.6%
Bloating	8 13.8%	3 6.4%
Vomiting	4 7.0%	1 2.1%
Abdominal pain or cramps	21 36.2%	8 17.0%

$P = 0.002$

Group A = 3 sachets split-dose preparation. Group B = 2 sachets same-day preparation.

(median, 4 vs. 0), shopping (median, 4 vs. 0), and social activities (median, 4 vs. 0.5).

Patient Preference for Bowel Cleansing Regimen

The patients were asked about the mode of preparation they would favor were they to undergo a future colonoscopy. Of the whole cohort, 29.5% of patients favored split dose and 61.9% of patients favored same-day prep, with 8.6% unsure ($P = 0.0147$).

Among group A patients (split-dose patients), 40% favored split dose and 47% favored same-day prep, with 12% unsure ($P = 0.5994$).

Among group B patients (same-day prep patients), 14.9% favored split dose and 80.9% favored same-day prep, with 4.33% unsure ($P = 0.0001$).

The difference between the groups was highly significant ($P = 0.0005$).

DISCUSSION

This is the first reported study demonstrating the feasibility, safety, and efficacy of sodium picosulphate given as 2 sachets 3 hours apart on the morning of an afternoon colonoscopy. This is a novel approach to bowel cleansing as it can significantly reduce the time spent in preparing for colonoscopy from 2 days to 1 day. This is also the first time that the effect of bowel preparation on patients' ADLs has been assessed. We have demonstrated a significantly better mucosal cleansing with a novel morning-only preparation using 2 sachets of sodium picosulphate as compared with a 3-sachet split-dose 2-day preparation regimen. Furthermore, the morning-only cleansing had fewer adverse events and less impact on ADLs compared with the split-dose regimen. Our study showed that same-day bowel preparation is superior to conventional split-dose regimens.

TABLE 2. Grade of Bowel Cleansing With 2 Different Regimens

	Group A (3 Sachets Over 2 d)	Group B (2 Sachets on the Morning of Colonoscopy)	P
Excellent (95% CI)	49.5% (39.6-59.4)	46.9% (38.7-55.5)	
Average (95% CI)	40.0% (30.7-50.1)	51.5% (43.1-59.9)	
Poor (95% CI)	10.5% (5.6-18.5)	1.5% (0.07-5.7)	0.0046

CI indicates confidence interval.

TABLE 4. Level of Impairment to Activities of Daily Living

	Mean Level of Impairment to Activity (Median)	
	Group A: Split-Dose Cleansing	Group B: Same-Day Cleansing
Work (paid or voluntary)	2.92 (4)	1.17 (0)
Caring for others	1.47 (1)	0.46 (0)
Gardening	1.49 (1)	1.03 (0)
Shopping	2.7 (4)	1.51 (0)
House work	1.71 (2)	1.16 (1)
Social activity	2.73 (4)	1.3 (0.5)
Watching television	1.27 (1)	0.52 (0)
		P = 0.0001

Higher scores reflect greater impairment of activities.

Until now, we have been unaware of patient choices and preferences, and preparations were prescribed as per the recommendations of the pharmaceutical manufacturers. For the first time, we have assessed patient preferences and have found that the patient preference is for a same-day regimen. This seems quite logical as the same-day regimen leaves the previous day and evening free for normal activities and does not interrupt sleep on the night before the colonoscopy. This is a significant finding and we believe that all the available bowel preparations should be tested as a same-day regimen to improve the patient experience of bowel cleansing.

The design of our study suggests that the outcome of bowel cleansing is not improved by increasing the dose of sodium picosulphate from 2 to 3 sachets but is linked to the time gap between the dosing of sodium picosulphate and the procedure. This is a new concept and we believe that our results are in keeping with the results of recent publications on bowel preparation, which demonstrate that receiving a dose of bowel preparation close to the time of the procedure is important in achieving adequate cleansing.⁸ We believe that our study takes this further and demonstrates that the sodium picosulphate dose given the previous day is not only unnecessary, as it does not improve mucosal cleansing, but also adversely affects the patient ADLs and is thus not preferred by the patients. This has significant implications. At present, the standard practice for patients undergoing colonoscopy is to receive preparation the day before the procedure. This regimen is not only suboptimal in terms of bowel cleansing but is also disruptive, having a major impact on patients' quality of life, and is associated with more adverse events. In effect, our novel regimen makes colonoscopy a 1-day event, freeing the patient for more productive activities the day before the procedure. It is important to emphasize that none of the patients experienced any difficulties in getting to the hospital because of fecal leakage, incontinence, or uncontrollable bowel movements after taking the same-day prep, which is a reason sometimes given for avoiding preparation close to the procedure.

Colonoscopy has been shown to be important in achieving a reduction in bowel cancer-related mortality.^{9–12} With the increasing availability of advanced imaging techniques, including high-resolution endoscopy, chromoendoscopy, and electronic imaging, it is often easy to overlook

the basics. Bowel preparation is fundamental to achieving high-quality colonoscopy. It is futile to contemplate electronic imaging or chromoendoscopy if the bowel is not clean and free of debris. Furthermore, screening a healthy, asymptomatic population poses new challenges related to patient acceptability. We have to acknowledge that if patients find a procedure disruptive or unpleasant to their life they will be less inclined to return for follow-up or to comply with a screening program, however effective the screening may have been. Therefore, it is necessary for us to proactively find methods to make bowel preparation as acceptable as possible, with minimal side effects and disruption in ADLs. Our same-day bowel cleansing regimen seems to achieve this goal better than the split-dose regimen.

Our study's key strength is its size. Our patient population was matched for age, sex, and indications. Furthermore, the quality of bowel cleansing was recorded by 2 trained and blinded bowel cancer screening nurse practitioners, reducing the likelihood of endoscopist bias or difficulties related to multiple individuals making different judgments on what constitutes a well-prepared bowel. In this study, a nationally accepted and widely used grading tool was used. All procedures were performed by a single endoscopist. This takes away a confounding factor for the neoplasia detection rate, patient comfort, sedation scores, and the way poor bowel cleansing was handled.

One of the limitations of our study is the lack of measurement of the impact of the 2 regimens on the renal profile and electrolytes. Little is currently known about the effects of bowel preparation on serum biochemistry. Given the established safety of colonoscopy, such changes are likely to be small and transitory. We believe that any such disturbances are less likely in the same-day regimen, as in our study we found significantly fewer clinical adverse events such as nausea, cramping pains, vomiting and so on in the same-day regimen compared with the split 2-day regimen. It could be argued that block allocation is not the optimal method of patient allocation, and a randomized trial would be the optimum way to study this. However, this does not detract from the underlying findings as both the endoscopist and screening nurse were blinded to the preparation regimen. Allocation was purely by date of procedure, eliminating any potential bias in the selection of patients for a given regimen.

The results of this study relate only to sodium picosulphate. However, these principles may well apply to other forms of bowel preparation. In particular, the benefits from a single-day approach could be reasonably expected to apply to most regimens as the key benefits are in preventing a day being lost to bowel cleansing.

The labor hours that could be saved should not be underestimated. Within the UK Bowel Cancer Screening program, 12,153 colonoscopies are performed every year.¹³ Given that 55% of the patients were either in fulltime paid work or working as a full time care provider, same-day preparation could potentially save 6600 working days a year within the BCSP. Furthermore, the BCSP targets individuals of 60 to 70 years of age. If this is applied to a general colonoscopy population, where the average age would be younger, the benefits may be even greater. A common concern raised by patients is how colonoscopy will impact work. This strategy could help significantly in this respect.

In summary, this study has demonstrated that our novel 2-sachet same-day bowel preparation regime offers superior bowel cleansing to standard split-day regimes. It has

an additional advantage that it avoids the “wasted day” normally associated with traditional regimes. It has fewer side effects, less impairment to ADLs, and is preferred by patients. Given the advantages and patient preference, same-day bowel preparation for afternoon colonoscopy should be the way forward but might require a multicenter, randomized, controlled trial to prove that it can be applied across the whole spectrum of patients undergoing colonoscopy.

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