Bowel Preparation Quality before Colonoscopy with Split-Dose vs Same-Day Dose of Polyethylene Glycol (PEG) in Northern Iran: A Randomized Clinical Trial on the Role of Opium Addiction

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ABSTRACT

Background: Colorectal cancer (CRC) is the third most prevalent cancer in the world. Preparation for a colonoscopy, the gold standard in screening for CRC, has been done with different methods. The use of opioids may cause inadequate colonic preparation. This study's aim was to compare the quality of bowel preparation using split doses versus the same-day dose of polyethylene glycol (PEG) in opiate-dependent non-addicted patients in a tertiary care center, Northeast of Iran.

Methods: The present study is a randomized double-blind controlled trial study (IRCT20180103038196N6). Two groups of 100 opiate-dependent patients each referred for screening colonoscopy were enrolled in the study during 2017. Subjects were randomized to receive split-dose or the same-day dose of PEG. The quality of bowel preparation was assessed using the Ottawa Bowel Preparation Scale.

Results: In this clinical trial, opiate-dependent patients that were candidates for colonoscopy were enrolled with mean age of 56.21 (12.34) years in split-dose group and 53.85 (13.45) years in same-day dose group. Results showed that the Ottawa score was significantly lower (better results) in the split-dose group than the same-day dose group and the preparedness was better in right and mid-colon areas (3.05 vs. 3.83, P = 0.022, 0.72 vs. 1.12, P=0.003, 0.52 vs. 0.79, P=0.035 respectively). But in the rectosigmoid colon, the Ottawa score was lower (better results) in the same-day dose group than in the split-dose group (P = 0.020). The total Ottawa score was also lower in the split-dose (P = 0.022), which means better preparation in the split-dose group

Conclusion: The split-dose preparation is better than the conventional previous evening preparation in terms of bowel preparation quality and patient compliance.

Keywords: Bowel preparation; Colonoscopy; Opioid; Iran

INTRODUCTION

Colonoscopy is the gold standard for the investigation of abnormalities within the colon and is an integral part of all colorectal cancer screening programs **[1]**. The quality of this procedure is critically dependent on the quality of colon-cleansing preparation **[2]**. Poor bowel preparation results in longer procedures, a need for a repeat colonoscopy, and missed lesions. The incidence of poor bowel preparation is between 9%-67% **[1, 3]**. Despite advances in bowel preparation, the procedure remains difficult for patients to tolerate **[4-8]**. Polyethylene glycol (PEG) is a commonly used bowel preparation substance for bowel-cleansing preparation and is typically associated with fewer fluid shifts and electrolyte abnormalities as compared with low volume osmotic agents **[9, 10]**. However, the standard large-volume solution and the special taste of it may reduce patient compliance **[9]**. Since its introduction in 1980, PEG remains one

of the safest and most efficacious bowel regimens **[11]**. PEG is a non-absorbable, large polymer that remains in the gut lumen resulting in a lavage effect through osmosis **[12]**. It is a balanced isotonic electrolyte solution that minimizes fluid shifts across the colon, as well as the potential of mucosal damage **[13]**. The traditional single 4-liter regimen of PEG bowel preparation may result in low-quality bowel preparation **[14]**. However, a split dose of PEG (2 liters the day before the procedure and 2 liters in the morning of the procedure) may alleviate some of the shortcomings of a single 4-liter preparation **[15]**. Previous studies evaluated the efficacy of patient education to improve the quality of bowel preparation as an important factor to achieve better colonoscopy results **[16]**, although the confounding factors are widely different in various studies.

Opium, traditionally used in many south-central Asian countries, especially Iran, Pakistan, Afghanistan, and India, as well as in some areas of South-East Asia **[17]**, could also affect the quality of bowel preparation. In an opium study in Golestan province, Northeast of Iran, 17% of participants older than 40 years used opioids routinely **[17, 18]**. Consumption of opium (in form of chewing) and its derivatives increase the risk of upper gastrointestinal gastric, and bladder cancers **[19-21]**. Opioids also decrease gastric emptying and stimulate pyloric tone **[22-25]**. Delayed colonic transit due to opioids, causes prolonged contract time of the colon, which in turn enhances liquid absorption **[24, 26]**. Patients with a history of opioid use have an approximately two-fold increase in inadequate bowel preparation **[27]**. In this study, we aimed to compare the quality of bowel preparation for colonoscopy with split-dose and the same-day dose of PEG in opiate-dependent individuals in a tertiary center.

METHODS

Study design: In this randomized double-blind controlled trial study, 200 patients referred for screening colonoscopy were randomly allocated into two groups; group 1 received a dose of PEG, 4 liters on the day of the colonoscopy, and group 2 received two split-doses, one in the night before the colonoscopy and another in the morning before colonoscopy. All patients had a history of daily consumption of opium products. We excluded patients under 18 years, women who were pregnant or were breastfeeding, and those with contraindications for colonoscopy (severe congestive heart failure (NYHA III or IV)). We also excluded patients with a history of bowel obstruction or resection, severe mental illness, neurological diseases such as Parkinson's and stroke, or who did not consent for the study.

After explaining the goals of the study and taking informed consent, a demographic questionnaire (including age, sex, body mass index, and any underlying disease) was completed by all participants. Colonoscopies were performed by three expert gastroenterologists with at least 5 years of experience. Gastroenterologists were unaware of the patients' allocation to the study groups. The quality of patients' bowel preparation was recorded by the gastroenterologist during the procedure based on the Ottawa Preparation Scale **[3]**. This scale assesses cleanliness and the amount of fluid in different parts of the colon (right colon (cecum, ascending), mid colon (transverse, descending), and the recto-sigmoid colon). Each colon section was individually rated from 0 to 4 (0= no liquid, 1=minimal liquid, no suctioning required, 2=suction required to see mucosa, 3=wash, and suction, 4=solid stool, not washable). The amount of the remaining fluid was rated from 0 to 2 for the entire colon (0=minimal, 1=moderate, 2=large). The Ottawa Scale scores range from 0 (perfect) to 14 (solid stool in each colon segment and lots of fluid) **[3]**.

Statistical analysis: To analyze the results, the chi-square test was used for qualitative variables and a t-test for quantitative variables. All statistical analyzes were performed using SPSS-V16 software. A value of $P < 0.05$ was considered statistically significant.

Ethical considerations: The trial protocol was registered on the Iranian website (www.irct.ir) for registration of clinical trial (IRCT20180103038196N6) and approved by the local ethical committee of the Golestan University of Medical Sciences (IR.goums.REC.1394.41). After a comprehensive explanation of the study design and goal, written informed consent was obtained from all candidates.

RESULTS

The mean (SD) age of patients was 56.21 (12.34) years in the split-dose group and 53.85 (13.45) years in the same-day dose group (Table 1). The Ottawa Score was significantly lower in the split-dose group than the same-day dose group (3.05 vs. 3.83, $P = 0.022$) and the preparedness was

Table 1: Basic characteristics of opium-addicted candidates of colonoscopy in split-dose and same-day dose PEG

	Same-day dose N= 100	**Split dose N=100**	**P-value**
Mean age (SD), years	56.21 (12.34)	53.85 (13.45)	0.44
Female, N(%)	43 (43)	20 (20)	<0.001
BMI, mean (SD), kg/m2	26.04 (4.80)	24.32 (2.47)	0.00
Underlying disease, N (%)	27 (27)	21 (21)	0.32
Ottawa scoring system scores			
Right colon (cecum and ascending colon)	1.12(0.98)	0.72(0.87)	0.003
Mid colon (transverse and descending colon)	0.79(0.85)	0.52(0.93)	0.035
Recto sigmoid colon	1.12(1.00)	1.47(1.10)	0.020
Total fluid score	0.80(0.66)	0.55(0.51)	0.003
Total score	3.83(2.67)	3.05(2.05)	0.022

better in right and mid-colon areas, (0.72 vs. 1.12, P=0.003, and 0.52 vs. 0.79, P=0.035; respectively). But in the rectosigmoid colon, the Ottawa Score was lower (better) in the same-day dose group than in the split-dose group (1.12 vs. 1.47, = 0.020). The total fluid was lower in the split-dose (0.55 v. 0.80, P = 0.003) (Table 1).

DISCUSSION

This study aimed to compare the quality of bowel preparation for colonoscopy with the split-dose and same-day dose of PEG in opiate-dependent patients. The results of this study showed that the group that received split-dose PEG, had a better result in the right colon (cecum and ascendant colon) and mid colon (transverse and descending colon) than the single-dose group.

Traditionally, the entire bowel-cleansing preparation solution is given in the evening before colonoscopy. Previous studies showed that the split-dose preparation is better than the conventional single-dose preparation in terms of bowel preparation quality and patient compliance **[28-30]**. Optimal colon cleansing requires a purgative administration close to the time of colonoscopy. Seo et al, evaluated 366 consecutive outpatients undergoing colonoscopy using the split-dose preparation; colonoscopies within the 3 to 5 hours had the best bowel preparation quality **[3]**. In a study by Marmo et al., a split-dose PEG lavage outperformed a single-dose PEG for colonoscopy **[31]**. The improved bowel preparations were associated with a 5-fold increase in cecal intubation and a 2-fold increase in adenoma detection **[31]**. The superiority of the split-dose lavage in the right colon has also been shown in this study and others **[32]**. In another study conducted by Martel et al., the two-day regimen was superior for achieving adequate bowel preparation for colonoscopy **[33]**. On the contrary, Kotwal et al. found that morning-only PEG is not inferior to split-dose preparation regarding bowel cleansing efficacy for colonoscopy in hospitalized patients. However, split-dose preparation was preferred by patients because of fewer side effects which may be due to differences in the study group **[34]**. In another study by Chan et al., to compare the same-day dose vs split-dose of 2-liter PEG-electrolyte lavage solution (PEG-ELS) plus bisacodyl for colon cleansing for morning colonoscopy, splitting reduced-volume PEG-ELS for morning colonoscopy was as effective as taking the whole dose on the same morning but was better tolerated and preferred by patients **[35]**.

CONCLUSION

The results of the present study demonstrated that bowel preparation quality can be optimized through the use of split doses of PEG in opium-addicted patients

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