

## How to cleanse the colon after the colon cancer awareness month?

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We have already passed March that has been the National Colon Cancer Awareness Month, organized by the Colorectal Cancer (CRC) Alliance, in the United States (US) since 2000 (1). Its European counterpart, European Colon Cancer Awareness Month, was launched in 2008 by the EuropaColon that expanded into Digestive Cancers Europe, which is a patient organization dedicated to being the voice of patients with digestive cancer in Europe (2). Unfortunately, awareness of this month has not captured attention in Turkey until a couple of years ago, despite CRC being the third most common cancer in both genders, according to the 2017 report of Turkey Cancer Statistics, with an incidence of 22.8 and 13.8 per 100,000 persons in males and females, respectively (3).

National and international guidelines have implemented the CRC screening into the clinical practice more than a decade ago; however, nationwide screening programs have not been available in many countries even in Europe. The Ministry of Health has formally initiated the National CRC Screening Program in Turkey since September 1, 2014. According to the national screening program, it is recommended to offer fecal occult blood test (FOBT) every two years for every individual starting at the age of 50. Regardless of the initial FOBT result, the program mandates colonoscopy at the age of 51 and a follow-up colonoscopy 10 years after the initial negative colonoscopy (4). Although the CRC screening protocols vary around the world, colonoscopy is inarguably accepted with consensus as the gold standard and optimal method of screening for CRC regardless of the risk of individual patient (5). Nevertheless, colonoscopy is not perfect. Although it is considered safe compared with other more complicated endoscopic procedures, there are some risks associated with the sedation required and the procedure itself.

Other more relevant problem with colonoscopy is the risk of missing a polyp or even cancer during the procedure

because of multiple reasons. American (ASGE) and European (ESGE) Gastrointestinal Endoscopy Societies issued guidelines and updated them regularly to improve the quality of colonoscopy screening in the general population. According to these guidelines, evidence-based quality indicators for a colonoscopy screening are as follows: (i) the adenoma detection rate (ADR) should be  $\geq 25\%$  overall or  $\geq 30\%$  for male patients and  $\geq 20\%$  for female patients, and (ii) cecal intubation rate should be  $\geq 95\%$  (5,6). These two quality indicators of colonoscopy are significantly associated with the quality of bowel cleansing (7); therefore, ASGE recommends if bowel cleansing is inadequate to identify polyps  $>5$  mm in size, the procedure should be repeated in a year (8). An inadequate level of cleansing therefore results in increased costs because of repeated examinations or alternative investigations. Moreover, this may affect the acceptability and preferability of colonoscopy procedure in screening programs. Hence, the ESGE Quality Improvement Committee has recommended more than 90% minimum standard of adequate bowel preparation as a quality indicator (6).

The risk factors associated with poor bowel preparation have been studied in multiple studies showing that previous inadequate bowel preparation, linguistic barriers, health-care insurance, inpatient status, obesity, advanced age, and male gender are among the most important predictors (9). Also, patient comorbidities with polypharmacy that affects gastrointestinal motility significantly impair colonoscopy preparation. Other factors associated with colonoscopy preparation include poor adherence to preparation instructions, mistakes in timing of purgative administration, and longer appointment wait times for colonoscopy (10,11).

There two guidelines regarding bowel preparation before colonoscopy were issued by ESGE and ASGE in 2013 and 2015, respectively (12,13). Despite the slight variations in the guidelines, the general concept is the same. An ideal

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preparation for colonoscopy should empty the colon of all fecal material with no gross or histologic alteration of the mucosa. The preparation should be tolerated well with no fluid or electrolyte disturbances. The main components of the bowel cleansing include combination of dietary restriction and cathartics that has proven to be safe and effective. One common recommendation that should be highlighted is the split regimen of 4 L polyethylene glycol (PEG) solution or a same-day PEG regimen in the case of afternoon colonoscopy for routine bowel preparation. Split-dose regimen is strongly recommended because multiple studies and meta-analyses showed that effective bowel preparation requires at least half the preparation to be ingested on the day of the colonoscopy (14).

Both guidelines recommend the implementation of some dietary changes. It is a common practice among endoscopists to incorporate dietary restrictions before starting bowel preparation with purgatives. Usually, a clear-liquid diet is advised the day before colonoscopy to reduce solid residue in colon, especially starting 4-6 hours before administration of purgatives, and patients are allowed to have a low-residue diet for 2-3 days before starting a clear-liquid diet. However, we must admit that this is an empirical approach, and it does not have sufficient evidence to recommend universally. The evidence lacks to confirm a clear-liquid diet the day before colonoscopy improves colon cleansing over a low-residue diet that avoids only foods containing seeds and other indigestible substances. In fact, multiple studies show it to be at least as effective as a clear-liquid diet and associated with increased patient satisfaction (15-17). Therefore, both European and US guidelines suggest low-residue diet before colonoscopy preparation. The US guideline does not mention the duration of the diet before the procedure, while the ESGE guideline specifically addresses that it does not recommend the use of low-residue diet for more than 24 hours because of the lack of evidence. However, this aspect is less likely to be important than split-dose administration of PEG. A randomized-controlled study showed that split-dose 4 liters of PEG with no dietary restriction provided better colon preparation than single-dose 4 liters of PEG with a clear-liquid diet on the day before colonoscopy (18). Still many endoscopists, including the author of this editorial, routinely prescribe a low-residue diet during the 3 days preceding colonoscopy rather than on a single-day because of personal experiences, slow transit time in some patients with comorbidities, or because of potential patient or physician stress that can be caused by cancellation of colonoscopy due to poor preparation.

In a very recent randomized-controlled trial (RCT) published in April 2019 issue of *Endoscopy* by Gimeno-Garcia et al (19), the authors evaluated this unanswered question. The investigators included consecutive unselected patients older than 18 years scheduled for outpatient colonoscopy and randomized them to the 1-day or 3-day low-residue diet arms. They excluded patients with significant comorbidities and history of inadequate bowel preparation. The participants needed to complete a food record sheet for the duration of low-residue diet that depends on their group of assignment. All patients were administered low-volume (2-liters) split-dose PEG plus ascorbic acid, and procedures were scheduled during the morning endoscopy session. The investigators randomized 404 patients with 202 patients at each colonoscopy preparation arm; and after exclusions, 372 patients were included in the intention-to-treat analysis. The Boston Bowel Preparation Scale (BBPS) was used to evaluate efficacy of preparation in each arm. The adequate bowel cleansing was defined as BBPS  $\geq 2$  for each segment of colon. The investigators reported that both 1-day and 3-day low-residue diet arms were comparable in terms of adequate bowel cleansing (82.7% vs 85.6%, 95% CI 0.72-2.15, respectively), adherence to the diet (79.1% vs 72.4%, 95% CI 0.43-1.12, respectively), and willingness to repeat the diet (96.3% vs 95.1, 95% CI 0.28-2.09, respectively).

The results of this study provide high-quality evidence showing there is no need to prolong duration of diet in patients undergoing colonoscopy. I believe it is time to change our clinical practice accordingly. Of course, before jumping into conclusions, one may think that these results should be reproduced by other studies, especially in the other settings including afternoon colonoscopies, different bowel cleansing protocols, and more importantly in patients with comorbidities and previous history of poor preparation that were not addressed in this study. Another limitation that should be highlighted is that the study could not achieve the recommended threshold for a more than 90% minimum standard of adequate bowel preparation. It would be interesting to see if these results would be improved using a standard-volume (4-liters of PEG) split-dose regimen.

Overall, CRC screening is important, but implementing those quality indicators, guideline recommendations, and RCT evidence in our daily clinical practice is more important than the screening program itself. Those quality indicators including ADR, cecal intubation, and adequate bowel preparation rates should be implemented into

the clinical practice by the regulatory bodies. The split-dose regimen is underutilized in Turkey, which should be emphasized at every opportunity. As the accumulated data showing 1-day low-residue diet with subsequent low-volume split-dose preparation can be successful, we may increase the number of individuals who will accept colonoscopy for CRC screening.

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