Colorectal cancer (CRC) is the most common newly-diagnosed cancer and the second most common cause of cancer deaths in Europe. In the European Union, CRC ranks second in incidence and mortality in both sexes, with approximately 330,000 new cases and 149,000 deaths estimated for men and women combined in 2008 (1). However, CRC can be considered a preventable and curable disease. On the one hand, preventable because most CRCs develop from adenomas. In fact, endoscopic removal of adenomas has been shown to reduce the incidence and mortality of CRC by stopping their progression to cancer (2-6). On the other hand, curable because the 5-year survival rate of CRC in early stages is up to 90 % (7). Thus, CRC screening is widely recommended by most health systems. The 2013 European guidelines for CRC screening suggest fecal occult blood testing initially at age 50-74, and recommend that colonoscopy remain the gold standard procedure (8,9). One of the main limitations of CRC screening programs is the low uptake rate by the target population –up to 50 % in the best clinical scenario (10). Some studies have demonstrated that acceptability is partly determined by the practicalities of stool collection, transport, and storage, together with perceptions about the endoscopic procedure (11-13). These are some of the reasons that have encouraged medical devices manufacturers to develop new technologies for colon examination, including capsule endoscopy and CT-colonography. Since its introduction by Iddan et al. in 2001 (14) wireless capsule endoscopy has proven to be an accurate, painless and safe procedure for small-bowel examination. In fact, more than 2,000,000 capsule procedures have been performed worldwide. Due to its excellent acceptance by both patients and physicians, Given Imaging Ltd. (Yoqneam, Israel) decided in 2006 and 2007 to develop two new capsule prototypes for esophageal and colon examination, namely the PillCam® ESO and PillCam® COLON capsules. The first generation of the capsule intended for colon examination, the PillCam® COLON, was 31 x 11 mm in size and had two optical heads taking 2 images per second, a field of view of 140°, and a battery life of 10 hours approximately (15). The largest study that evaluated its accuracy for the detection of polyps and cancers was published in The New England Journal of Medicine in 2009 (16). It included more than 300 patients and demonstrated that the PillCam® COLON capsules was feasible for colon examination in most of the cases, safe for patients, and moderately effective for polyps and cancers –72 % and 78 % for sensitivity and specificity, respectively—. Some of the main limitations of first-generation colon capsules that resulted in missed lesions included blind angles, capsule progression rate in some segments, and inadequate cleansing for some procedures. To overcome these limitations, a second-generation colon capsule, the PillCam® COLON-2 was developed in 2009, which captures up to 35 images per second with a field of view of 172° (17). In addition, some changes in the patients’ preparation regimen were done. Different studies to date have evaluated the accuracy of the PillCam® COLON-2 device for polyps and
cancers, showing an overall sensitivity and specificity of 86 % and 71 %, respectively (18). These results were better than those obtained with first-generation capsules for colon examination. However, the optimal regimen for colon cleansing remains a controversial issue. The impact of colon cleansing on the quality and diagnostic yield of capsule endoscopy is well known: Sensitivity for polyp detection (> 6 mm) increases from 42 %-54 % to 75 %-100 % in patients with inadequate and adequate cleansing, respectively (16,19). Since capsules cannot irrigate, aspirate or insufflate, colon cleanliness becomes a critical issue, and every effort should be made in order to achieve an adequate level. In most published studies (16,17,19-26), the regimen used for colon cleansing consisted mainly of a combination of 4-L split-dose polyethylene glycol (PEG) the afternoon and 2-3 hours before capsule ingestion, and 1-2 sodium phosphate (NaP) boosters after capsule ingestion. PEG is used to obtain an adequate cleansing level, and NaP boosters are used to maintain cleanliness and to promote capsule propulsion until excretion. The two main studies that used this regimen showed an adequate cleansing level in 72 % and 81 % of cases, and an excretion rate of 93 % and 88 % (16,19). These results are acceptable, but the large amount of laxatives used during the procedure may be inconvenient and deter patients from undergoing colon capsule endoscopy. On the other hand, patient adherence to large-volume regimens is scarce and results in poorer cleansing levels with a clear impact on success (16,19). Other studies using the same regimen showed highly variable results, with adequate colon cleansing ranging from 52 % to 84.4 % of patients (20-26). These are the main reasons that encouraged physicians to evaluate new regimens for bowel cleansing including low-volume solutions such as PEG plus ascorbic acid. In the present issue of The Spanish Journal of Gastroenterology, Argüelles et al. publish the results of an innovative study where a large-volume regimen (PEG 4L and NaP) is compared to a low-volume regimen (PEG plus ascorbic acid 2 L and NaP) in terms of colon cleansing level and capsule excretion rate (27). To our knowledge, this is the first study using a combination of PEG plus ascorbic acid and NaP. The authors of the present study report an adequate overall cleansing level in 78.3 % of patients receiving the PEG plus ascorbic acid regimen (2 L) —similar to the results obtained with PEG 4 L— and 64.5 % of patients receiving the PEG regimen (4 L), but differences were not statistically significant. However, when taking colon segments into account, they found that the cecum and transverse colon were significantly cleaner in patients with the PEG plus ascorbic acid regimen. Based on these findings, it seems there is a positive trend for PEG plus ascorbic acid (2 L) versus PEG (4 L). However, a recent meta-analysis demonstrates that low-volume PEG plus ascorbic acid regimens are as effective as large-volume PEG regimens in patients undergoing optical colonoscopy (28). Therefore, the differences found in the study by Argüelles et al. may be related to poor patient compliance with the PEG (4 L) regimen or simply to the small sample size used. Of note, the percentage of patients with adequate cleansing levels in the PEG (4 L) group is significantly lower than reported in larger series where similar regimens were used (16,19). Two additional studies have used PEG plus ascorbic acid as primary laxative for the colon capsule endoscopy cleansing process (29,30). Their results were quite similar to those obtained by Argüelles et al., achieving adequate bowel cleansing levels in approximately 80 % of patients. Anyway, the overall colon cleansing level obtained with PEG plus ascorbic acid is consistent with the findings of previous studies using both “classic” and “low-volume” regimens, and this is the first relevant conclusion from this study. However, it has to be noted that there is a lack of objective cleansing scales for colon capsule endoscopy. Thus, one should be cautious when interpreting conclusions from cleanliness evaluation studies. As stated before, the primary goals of these regimens during colon capsule endoscopy are: a) To achieve an adequate colon cleansing level;
and b) to promote capsule propulsion until excretion before battery life is over. In general, colon cleansing is done during the initial phase of the procedure—before capsule ingestion—and capsule propulsion is generated during the second phase of the procedure—after capsule ingestion. The aforementioned “classic” regimens use 1-2 NaP boosters with doses ranging from 30 to 40 ml (first booster) and from 25 to 30 ml (second booster) in order to facilitate capsule excretion. The efficacy of NaP is very high as it allows complete procedures in 88% and 93% of cases in the largest series (16,19). Argüelles et al. used in their study a combination of PEG and NaP (2 30-ml boosters) with a capsule excretion rate of 92.9% for the PEG plus ascorbic acid group—consistent with most studies—and of 70% for the PEG group—quite lower than values obtained in other studies. Surprisingly, capsule transit times in the colon were shorter in the PEG group than in the PEG plus ascorbic acid group. This probably means that such significant differences may again result from small sample size, which is the main limitation of this study. Due to the safety profile of NaP, other solutions for capsule propulsion are being proposed. Hartmann et al. used 2 PEG plus ascorbic acid boosters (0.5 L and 0.25 L) with a rate of complete procedures of 76% (30). Of note, there is no consensus on a definition of complete procedure. While in most papers complete procedures are determined by capsule excretion before battery life expiration, other papers define complete procedures as the detection of the haemorrhoidal plexus. Surely, the rate of complete examinations would be higher if the second definition—the correct one—was taken into account. Kakugawa et al. used a magnesium citrate booster in patients undergoing colon capsule endoscopy. The rate of complete examinations was very low, 55% in patients following the “classic” regimen (PEG 4 L) and 71% in patients following a new reduced-volume regimen (PEG 2 L) (31). Two recent studies compared the rate of complete examinations using NaP versus PEG (32) and NaP versus sodium picosulfate (33), with significantly better results for NaP -100% versus 75% and 88% versus 70%, respectively. Therefore, it seems that the best method to promote capsule propulsion until excretion is still the administration of 2 NaP boosters. In summary, the study by Argüelles et al. demonstrates that a combination of low-volume solutions and NaP could be the answer to the million-dollar question. It is feasible and as effective as “classic” regimens in terms of colon cleansing level and capsule excretion rate. However, future studies are needed in order to: a) Develop an objective cleansing level scale and confirm these results; and b) demonstrate whether patient compliance with low-volume cleansing regimens may have any impact on colon capsule endoscopy procedures.

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REFERENCES

Editorial


