

# The lower the volume of a cleansing product the higher its osmolarity and thus the risk of determining electrolyte imbalances in predisposed patients



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Because colorectal cancer (CRC) represents a significant cause of mortality worldwide and incidence is rising in younger people, particular importance is given to effective screening programs, including noninvasive and invasive modalities [1]. In particular, colonoscopy has a central role in detecting early-stage CRC and identifying and resecting precancerous lesions. A quality examination requires adequate bowel preparation, considering that poor colon cleansing negatively influences quality indicators for colonoscopy, such as adenoma detection rate and cecal intubation. The theme of ideal bowel preparation is still controversial, because it should meet criteria of tolerability and efficacy, but safety also is a concern, particularly in fragile patients [2].

The efficacy of low-volume and very-low-volume polyethylene glycol (PEG)-based bowel preparations is well-established. Several studies and meta-analyses comparing PEG-based preparations of different volumes and different characteristics have reported similar efficacy for overall colon cleansing. [3, 4] The recent trend toward the development of the lowest-volume bowel preparations, obtained with the adjunct of osmotically active substances such as ascorbic acid, has drawn attention to the safety of these solutions. Because of their high osmolarity, low-volume bowel preparations are likely more prone to influence fluid and electrolyte balance.

Because major concerns have been raised about the occurrence of electrolyte imbalance and dehydration following the ingestion of bowel preparation, large-volume, iso-osmotical, PEG-based bowel preparations have been developed and have

become the standard of care in the last decades. In general, electrolyte alterations and dehydration may be caused by different mechanisms induced by bowel preparations, such as diarrhea, but colonoscopy itself activated the renin-angiotensin-aldosterone system. Hypokalemia may present with a wide spectrum of clinical characteristics, ranging from absence of symptoms to constitutional symptoms such as fatigue, muscular weakness, arrhythmias, and cardiac arrest. The clinical implications are related not only to the severity of hypokalemia and the rapidity of onset, but also to the characteristics of patients, because the major incidence of hypokalemia in hospitalized and elderly patients or patients on thiazide therapy is well known [5, 6]. The use of sodium phosphate as bowel preparation, for example, has been associated with disruption in electrolytes homeostasis, including hypokalemia [7, 8]. High-volume PEG solutions are generally considered safe, even in patients who are at risk for serum electrolyte imbalance, and accordingly, European Society of Gastrointestinal Endoscopy guidelines suggest that in patients at risk for hydroelectrolyte disturbances, the choice of laxative should be individualized, with large-volume PEG products still playing an important role, while attention must be paid if low-volume hyperosmotic formulations are used [9].

In this issue of Endoscopy International Open, Reumkens et al. have published a prospective cohort study addressing the problem of the risk of developing hypokalemia following the ingestion of a low-volume PEG-ascorbic acid solution as bowel preparation for colonoscopy.

Although no serious adverse event occurred, about 5% of normokalemic individuals developed hypokalemia after bowel preparation and 1% of the initial population presented with a combination of both a “high cardiac risk” profile and hypokalemia. Female sex, thiazide use, and CRC diagnosis were found to be predictors of hypokalemia development. The authors conclude that additional screening for electrolyte imbalances may be needed in “high cardiac risk” patients and those on thiazide diuretics who are more prone to develop post-cleansing hypokalemia.

In a previous study, performed in patients considered at risk for hypokalemia, the authors of the current paper found that 23.6% of patients developed hypokalemia after bowel preparation with low-volume PEG plus ascorbic acid solution [6]. Similar results were observed by Ho et al in their retrospective chart review, which found a rate of 20.5% of hypokalemia after administration of high-volume PEG solution in hospitalized patients aged  $\geq 65$  years [10].

The data, thus, are still sparse and equivocal. In a randomized controlled trial (RCT) comparing 4-L PEG and 2-L PEG-ascorbic acid solutions, the levels of serum potassium decreased after intake of 4-L PEG compared to 2-L PEG [11]. Moreover, from the literature review, no univocal pattern emerges of electrolyte changes after bowel preparations; however, almost all of the studies agree that these changes are transient and of uncertain clinical significance [11–14].

Undoubtedly, the adjunct of osmotically active substances to bowel preparation solutions increases the risk of dehydration and impairs electrolyte balance. A recently published metanalysis that included 3 RCTs comparing a 1-L PEG-based preparation for colonoscopy (NER1006) to trisulfate, sodium picosulfate plus magnesium citrate, and 2-L PEG preparations, showed a higher incidence of dehydration in NER1006 [4].

At present, the market trend is extremely oriented toward the use of very-low (1L), hyperosmotic, PEG-based preparations because they are very effective and well accepted by patients; their use will likely increase in coming years. This fact prompts the need for further real-life studies to properly investigate the safety of low-volume bowel preparations, especially in at-risk populations; in particular, the real impact of the transient dehydration and electrolyte imbalances induced by bowel preparation should be explored. At the same time, availability of different products with different characteristics should push endoscopists to make an effort to individualize colon preparation to minimize the risk of adverse events, as suggested by the current guidelines [9].

## Competing interests

The authors declare that they have no conflict of interest.

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