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Editorial

Polyethylene glycol in chronic constipation

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DEFINITION AND THERAPEUTIC MANAGEMENT OF CONSTIPATION

Constipation is one of the most common medical conditions affecting the general population, with a prevalence of up to 30%, depending on demographic factors and the criteria used for diagnosis. It is usually a frustrating problem for both patient and physician. Prevalence of constipation increases with age, and women are more likely to report the symptom than men. It can be due to a variety of causes, ranging from endocrine abnormalities, medication inducement and anatomical anomalies, but can also be functional in origin. A careful and thorough history, coupled with appropriate laboratory, radiographic and possibly manometric evaluation may yield an etiology that allows medical treatment.

The term constipation is used primarily to refer to difficulty in defecation (straining) and infrequent bowel movement, not secondary to an underlying cause. Rome II diagnostic criteria[1] are a standard clinical measure to assess chronic constipation. The criteria are defined as 12 weeks (which need not be consecutive) of problematic defecation during the past 12 months, when at least two of the following occurred; straining in more than 25 percent of defecatory attempts, lumpy or hard stools in more than 25 percent of defecatory attempts, sensation of incomplete evacuation in more than 25 percent of defecatory attempts, sensation of anorectal obstruction/blockage in more than 25 percent of defecatory attempts, manual maneuvers to facilitate defecation in more than 25 percent of attempts (e.g. digital evacuation, manual support of pelvic floor), and/or less than three bowel movements per week. Diagnosis, however, is frequently made by patients themselves or by a pharmacist. Recently, a panel of experts agreed on an alternative set of criteria that may be more easily applied in general practice, namely low frequency of stools (less than 3 per week), hard stools and/or difficulties in evacuation[2].

The objective of treatment of constipation is safe and effective symptom relief. Chronic constipation requires long-term treatment, and the options available to the general population include osmotic laxatives [polyethylene glycol (PEG)–based laxatives, saccharated osmotics, saline preparations], bulk-forming laxatives (non-soluble and soluble fibres), stimulant laxatives (anthranoid compounds, diphenylmethane derivatives, ricinoleic acid), fecal softeners, suppositories and enemas. Consistency of outcome, stool frequency and patient satisfaction are considered to be the excellent indicators of medical treatment effectiveness.

Mainstays of treatment also include supplementary dietary fiber, increased fluid intake and increased physical exercise, although relative evidence of benefit is lacking. Most clinicians try to avoid stimulant laxatives, as they can lead to "dependence" and preservation of the problem. This is the main reason for which most physicians prescribe osmotic laxatives, as first-line therapy for chronic constipation. PEG is an osmotic laxative that inhibits the dehydration of bowel contents, leading to modification of stool consistency and increased fecal bulk. This, in turn, stretches muscle fibers in the bowel wall and probably triggers myogenic peristalsis. Increased retention of water in the colon lubricates and softens stools, allowing comfortable bowel action. PEG passes virtually unchanged through the whole gastrointestinal tract, including the colon. It is not metabolized, and its effect is not dependent on the state of colonic microflora.

Despite the excellent safety and efficacy profile of PEG-based laxatives, there has been very little evidence

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in the recent past, in setting double-blind, randomized, controlled clinical trials. Available evidence resulting from these studies will be further discussed.

EFFICACY OF PEG IN FUNCTIONAL CHRONIC CONSTIPATION

Andorsky et al[3] studied, for the first time, the efficacy of PEG as a treatment for patients with chronic constipation. Even though the criteria used for definition of constipation were somewhat subjective, it was shown that PEG-electrolyte lavage solution (ELS) is more effective than placebo for the treatment of chronic refractory constipation. In the same study, it was also shown that efficacy of PEG-ELS is dose-dependent. However, the therapeutic effectiveness of PEG was assessed for only 5 days. The aforementioned results were confirmed by a study of Corazziari et al[4], who evaluated the safety and efficacy of PEG-ELS for longer period (8 weeks). In the same study, it was also shown that PEG-ELS induces an acceleration of colonic transit through the left colon and the rectum. In a subsequent study[5] however, it was found that PEG-ELS has no effect on left colonic and recto-sigmoid motor activity, despite its clinical effectiveness.

PEG-ELS theoretically may lead to sodium overload, which could be deleterious in aging patients with co-existing illnesses. This is the main reason for which some authors evaluated, along with the efficacy, the safety of PEG electrolyte free solutions (PEG-EFS) for the treatment of chronic constipation. DiPalma et al[6] reported that PEG-EFS is as safe as it is effective for patients with chronic constipation. However, therapeutic effectiveness was studied for two weeks only. From a theoretical point of view, PEG-EFS may lead to plasma electrolyte loss, an adverse event not reported so far. Furthermore, in a very recent study[7], no significant differences were found between PEG-ELS and PEG-EFS in terms of safety.

Therapeutic effectiveness of PEG-EFS for the acute (within 24 hours) relief of chronic constipation has also been studied[8]. In this study, it was shown that 68g of PEG-EFS in 500 ml water is an effective dose for eliciting a rapid and limited action for the relief of chronic constipation within 24 hours. Even though the number of patients studied was too small for firm conclusions, there were no adverse reactions, and no patient reported incontinence or complained of abdominal cramps or diarrhea.

In a multicentric, randomized, comparative trial[9], the authors concluded that PEG-ELS was more effective and better tolerated than lactulose in patients with chronic constipation. After 4 weeks of treatment, patients randomized in the PEG group had a higher number of evacuations and a lower median daily score for straining at stool than patients in the lactulose group. Flatus was less frequently reported in the PEG group. However, the mean number of liquid stools was higher in the PEG group during the first two weeks of treatment, and this was attributed to the increased daily dose of PEG used at the beginning of the study. This finding was not observed during subsequent follow-up, as patients were allowed to make appropriate dose-adjustments. There were no significant adverse events in either group. The aforementioned data suggest that PEG-ELS may be more effective than other osmotic laxatives in the treatment of functional chronic constipation. Furthermore, a subsequent cost-effectiveness analysis[10] showed that PEG-ELS, as first-line therapy, may reduce overall costs in the management of patients with chronic constipation.

Long-term efficacy, safety and tolerability of PEG-ELS has also been studied with favourable outcome. In a relative study[11], it has been shown that, in contrast to treatment options based on traditional laxatives, the doses of which are usually increased over time, prolonged administration of PEG-ELS remained effective throughout a 6-month period, while the mean daily dose was progressively reduced from 340 ml to 288ml. Additionally, it was suggested that long-term therapy may have favourable effects on abdominal symptoms such as bloating, pain, flatulence and borborygmi.

Currently, there is growing evidence suggesting that PEG solutions are equally effective in children with functional constipation, but a systematic review of the relative literature is beyond the scope of this article. PEG solutions have been also used in some adults with fecal impaction or obstructed defecation (dyschesia) with promising results, but the number of patients enrolled in those studies has been rather low. These results must be confirmed by further studies.

According to the studies previously mentioned, there have been no significant adverse-effects related to PEG solutions. Sodium overload and excessive plasma electrolyte loss have been noted in a few patients after consumption of high doses (4 liters) for bowel cleansing before colonoscopy or intestinal surgery. In the setting of functional chronic constipation, administration of 250-500ml is usually effective and safe. The most frequent side-effects reported with this dose-regimen are nausea and vomiting. However, there has been an anecdotal report of PEG-induced acute pancreatitis, in an adult[12].

In conclusion, current data indicate that administration of small volumes of PEG, with or without electrolytes, are safe and effective for the long-term treatment of functional chronic constipation. Furthermore, it seems that PEG is superior to lactulose in terms of efficacy and tolerability. However, despite evidence favouring the use of PEG-based laxatives, lactulose is more widely used in clinical practice.

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