A review of current issues underlying colon cleansing before colonoscopy

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The present review examines four current issues related to the efficacy, patient tolerance and safety of the following bowel cleansing agents: oral sodium phosphate (NaP), polyethylene glycol (PEG) and magnesium citrate (Pico-Salax, Ferring Pharmaceuticals Inc, Canada), an agent recently made available in Canada. MedLine and PubMed databases were systematically searched to identify studies related to the efficacy of altered PEG solutions combined with adjunct treatments; the efficacy, tolerability and safety of Pico-Salax; the association between nephrocalcinosis, and chronic renal failure and oral NaP use; and the role of diet. Although lower volume PEG solutions combined with adjuvant agents were generally associated with better patient tolerance, their efficacy was varied and interpretation of this end point is complicated by study design issues. There are very few reported studies of Pico-Salax, and as a result, there are insufficient data to draw conclusions about the efficacy of this agent. The available data suggest that Pico-Salax may be better tolerated by patients, than oral NaP and PEG solutions. There is a paucity of hemodynamic monitoring data pre- and postadministration, but the available data suggests that this small-volume osmotic agent could cause subclinical contraction of the intravascular space. Recent case reports suggest an association between nephrocalcinosis and oral NaP ingestion, but to date, these reports have been confined to a single centre. Preliminary studies suggest that this is not a widespread problem, but more studies are needed. There are only a few studies examining diet and patient tolerability, but they do suggest that diet may be liberalized with some cleansing regimens to enhance tolerability without decreasing efficacy. The present review highlights current controversies and advances in colon cleansing before colonoscopy, and also identifies areas for further study.

Key Words: *Colon cleansing; Colonoscopy; Oral sodium phosphate; Pico-Salax; Polyethylene glycol*

Une analyse des enjeux courants reliés à la vidange colique avant une coloscopie

La présente analyse porte sur quatre enjeux d'actualité reliés à l'efficacité, à la tolérance par le patient et à l'innocuité des agents de vidange intestinaux suivants : phosphate de sodium par voie orale (NaP), polyéthylèneglycol (PEG) et citrate de magnésium (Pico-Salax, Ferring Pharmaceuticals Inc., Canada), un agent disponible depuis peu au Canada. Une recherche systématique a été effectuée dans les bases de données MedLine et PubMed pour repérer les études reliées à l'efficacité de solutions PEG modifiées associées à un traitement d'appoint, à l'efficacité, à la tolérabilité et à l'innocuité du Pico-Salax, à l'association entre la néphrocalcinose, l'insuffisance rénale chronique avec l'usage de NaP par voie orale, et aux rôle du régime alimentaire. Bien que des volumes plus faibles de solutions PEG associées à des traitements adjuvants aient généralement favorisé une meilleure tolérance de la part des patients, leur efficacité variait, et l'interprétation de cette valeur était compliquée par des problèmes de conception de l'étude. Relativement peu d'études portent sur le Pico-Salax, et par conséquent, les données sont insuffisantes pour qu'il soit possible de tirer des conclusions au sujet de son efficacité. D'après les données disponibles, le Pico-Salax serait mieux toléré par les patients que le NaP par voie orale et les solutions de PEG. Il existe peu de données de surveillance hémodynamique avant et après l'administration du médicament, mais celles qui sont disponibles indiquent que cet agent osmotique à faible volume pourrait causer une contraction subclinique de l'espace intravasculaire. Selon les rapports de cas récents, il y aurait un lien entre la néphrocalcinose et l'ingestion de NaP par voie orale, mais jusqu'à présent, ces comptes rendus sont confinés à un seul centre. Les données préliminaires indiquent qu'il ne s'agit pas d'un trouble généralisé, mais d'autres d'études s'imposent pour le confirmer. Seulement quelques études s'intéressent au régime et à la tolérabilité du patient, mais d'après leurs conclusions, le régime pourrait être libéralisé grâce à certaines posologies de vidange qui en amélioreraient la tolérabilité sans en réduire l'efficacité. La présente analyse souligne les controverses actuelles et les progrès en matière de vidange colique avant la coloscopie et expose des domaines qui méritent des études plus approfondies.

The importance of colon cleansing before colonoscopy continues to heighten with the rapid expansion of colon screening. The adequacy of cleansing is essential to ensure that lesions are not missed and that procedures are not cancelled due to poor mucosal visualization. The latter effect delays diagnosis and decreases the efficiency of already overstretched endoscopy resources. Patient tolerability is also extremely important, because inability to complete the preparation contributes to poor cleansing and impacts on patient compliance in screening programs (1). These issues must also be balanced against the safety of the preparation.

Over the past 10 years, two bowel preparations have been used predominately in North America and many parts of Europe: large-volume lavage with osmotically balanced polyethylene glycol (PEG) solutions and small-volume lavage with osmotically active oral sodium phosphate (NaP). Numerous studies (2-7) have shown that oral NaP is better tolerated by patients and provides a good or better cleansing than PEG. Although both preparations can result in serious adverse events, including death, safety issues related to the use of oral NaP have received the greatest attention (8).

Given the importance of colon cleansing before colonoscopy, studies continue to address issues of efficacy, safety and patient tolerability in an effort to optimize cleansing. The aim of the present review is to examine important issues that are currently unresolved and may negatively impact patient care. Four questions are addressed: Can a lower volume of PEG solution be administered with adjuncts to increase tolerability without

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TABLE 1
Studies aimed at increasing patient tolerance of polyethylene glycol (PEG)

	Cleansing agents evaluated		Modified regimen versus control group	Results compared with control with respect to		
Reference, year	Modified regimen	Control	(n versus n)	Efficacy	Tolerability	Comments and conclusions
Hookey et al (9), 2006	Senna and 2 L PEG	4 L PEG	79 versus 81	Decreased	Improved	Decreased quality of preparation with the low-volume group, timing of senna may affect quality of preparation
Adams et al (11), 1994	Bisacodyl and 2 L PEG	4 L PEG	191 versus 191	No difference	Increased tolerance	
Di Palma et al (12), 2003	Bisacodyl and 2 L PEG	4 L PEG	93 versus 93	No difference	Improved	Although no difference was seen in the overall efficacy scores, a significantly higher proportion of patients in the reduced volume group had inadequate preparations
Borkje et al (14), 1991	Pico-Salax* and 1.5 L PEG	4 L PEG	93 versus 90	No difference	Improved	A liberated diet in the Pico-Salax group may have negated a difference in efficacy
Hangartner et al (15), 1989	1.5 L cascara and 1.5 L PEG	4 L PEG	102 versus 100	Decreased	Decreased	
Iida et al (16), 1992	Senna and 2 L PEG	Historical control of Brown's method	297	Improved	Improved	There are several methodological concerns with this study (see text); group may have negated a difference in efficacy
Ziegenhagen et al (17), 1991	Senna and PEG	PEG	60 versus 60	Increased	No difference	PEG administered as a titration until clear rectal effluent; senna decreased the volume
Sharma et al (18), 1998	4 L PEG	2 L PEG and magnesium citrate; 2 L PEG and bisacodyl	59 versus 45 versus 46	No difference	Improved tolerance of low-volume preparations	
El Sayed et al (19), 2003	Split dose PEG and bisacodyl	3 L PEG	91 versus 96	Improved	Improved	Liberated diet in both groups; nontraditional control group with 3 L PEG
Clarkston and Smith (20), 1993	Biscodyl and 4 L PEG	4 L PEG	59 versus 55	Improved	Not reported	There was some suggestion of increased fluid loss with the addition of bisacodyl to PEG
Sharma et al (21), 1997	Magnesium citrate and 4 L PEG	4 L PEG alone	40 versus 40	Improved	Improved with addition of magnesium citrate	

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sacrificing efficacy of cleansing? Is the combined low-volume osmotic agent and stimulant laxative, oral picosulphate and magnesium citrate (Pico-Salax, Ferring Pharmaceuticals Inc, Canada), recently introduced in Canada, a safe alternative agent? What is the current status of renal function impairment, nephrocalcinosis and oral NaP? Can diet be liberalized on the day of cleansing to enhance tolerability without compromising efficacy?

METHODS

MedLine and PubMed databases were searched to address each of the four questions mentioned above. Search terms were: Question 1 = polyethylene glycol and colonoscopy, Question 2 = sodium picosulphate, picolax, Pico-Salax (with only studies related to colonoscopy, air contrast barium enema [ACBE] cleansing or safety-specific studies), Question 3 = nephrocalcinosis and sodium phosphate, and Question 4 = diet and colonoscopy. In addition, the reference lists for the articles, as well as major review articles over the past five years, were examined, and relevant references for each question not already detected in the above search were added. Pharmaceutical data on Pico-Salax provided by Ferring Pharmaceuticals Inc, Canada, were also reviewed.

RESULTS

Question 1: Can a lower volume of PEG solution be administered with adjuncts to increase tolerability without sacrificing efficacy of cleansing?

The ability of patients to tolerate the ingestion of the standard 4 L volume of PEG has been a significant problem (2,3,9-13). One strategy to overcome this problem has been to reduce the volume (eg, from 4 L to 2 L) but combine this with a stimulant laxative in an effort to sustain or possibly enhance efficacy (Table 1) (9,11,12,14-21). The two stimulants most widely studied are bisacodyl and senna (9,11,12,14).

Bisacodyl combined with 2 L of PEG has been studied in three trials. Recently, DiPalma et al (12) compared this

TABLE 2
Studies comparing cleansing efficacy of Pico-Salax (PCSLX)* with oral sodium phosphate (NaP) or polyethylene glycol solution (PEG)

	Cleansing agent, n					
Reference, year	PCSLX patients	NaP patients	PEG patients	Procedure	Efficacy	Comments
Hamilton et al (13), 1996	35	–	20	Colonoscopy	PCSLX=PEG	Trend favoured PEG, small numbers
Schmidt et al (23), 2004	182	190	–	Colonoscopy	PCSLX=NaP	Trend favoured NaP, three doses PCSLX
Yoshioka et al (24), 2000	52	51	–	Colonoscopy	NaP>PCSLX	Fecal residue score = 2.0 versus 3.2, P<0.05
Macleod et al (25), 1998	83	111	–	ACBE	NaP=PCSLX	Fecal residue score, bowel coating
Lai et al (26), 1996	50	–	50	ACBE	PCSLX=PEG	Fecal residue score, bowel coating
Hawkins et al (27), 1996	45	–	47	ACBE	PCSLX>PEG	Fecal clearance score, descending colon only

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combination with the standard 4 L volume of PEG and found that mean scores of preparation quality were not different, but there was a significantly higher proportion of poor preparations in the low-volume group. In the second study, Adams et al (11) also compared these same combinations and found improved tolerance with the lower volume preparation, with no significant differences in efficacy between these preparations. In the third study, Sharma et al (18) also found that the reduced volume preparation was better tolerated with no apparent reduction in efficacy of cleansing. Based on the results of these studies, the combination of bisacodyl and 2 L of PEG has now been packaged together and is commercially available as Half Lytely (Braintree Laboratories, USA). However, a recent study (22) that compared this combination with two doses of oral NaP found that the combined low-volume preparation was less efficacious than oral NaP.

Senna has also been investigated in combination with low-volume PEG solutions in three trials (9,16,17). Although Iida et al (16) reported increased efficacy with 2 L of PEG combined with sennosides (36 mg), this trial was nonrandomized, used a historical control group, and data collection from both patients and endoscopists was incomplete. Another approach was reported by Ziegenhagen et al (17), in which PEG was administered by mouth or nasogastric tube the morning of colonoscopy until rectal effluent was clear. The addition of senna the night before significantly reduced the amount of PEG required for an adequate preparation. Recently, 2 L of PEG and 120 mg of sennosides syrup were compared with 4 L of PEG, and results showed that although the lower volume preparation was better tolerated, it was less efficacious (9). In the present review, the sennosides were given just before the ingestion of PEG and altering the timing of the sennosides from 30 min to 60 min before the PEG may be more beneficial.

Another approach with combination treatments has been to examine whether stimulant laxatives can enhance the efficacy and possibly the tolerability of standard volume PEG solutions (20,21). Unfortunately, although these modifications may improve the quality of colon cleansing, they typically have no effect on patient tolerability.

Other combinations have been investigated but have not been widely accepted. For example, one dose of Pico-Salax was added with 1.5 L of PEG in a trial by Borkje et al (14) and compared with the standard 4 L volume of PEG. Although no differences in efficacy were observed, one possible confounding variable was that the group receiving the low-volume preparation also had their diet liberalized whereas the PEG group did not.

Question 2: Is the combined low-volume osmotic agent and stimulant laxative, oral picosulphate and magnesium citrate (Pico-Salax), recently introduced in Canada, a safe alternative agent?

Pico-Salax was introduced in the United Kingdom in 1983 and in Canada in 2005 as a colonic cleansing agent. This cleansing agent is administered in two sachets at a recommended dosing interval of approximately 6 h to 8 h apart on the day before colonoscopy. Each sachet contains sodium picosulphate (10 mg) which hydrolyzes with water and is suggested to decrease water and electrolyte absorption, as well as increase motility and doses of magnesium citrate (magnesium oxide 3.5 g and citric acid 12 g), an osmotic laxative.

Efficacy: Table 2 lists the available studies comparing Pico-Salax and oral NaP or PEG. There is only one large study (23) (more than 180 patients in each group) comparing Pico-Salax and oral NaP as cleansing agents before colonoscopy. There was no detectable difference in the quality of the cleansing between the two groups, although there was a trend in favour of NaP, which may be noteworthy, given that three sachets of Pico-Salax were administered (as opposed to the recommended two sachets). In a smaller study (24), NaP was superior to Pico-Salax when retained fecal residue was scored. Pico-Salax and PEG efficacies for cleansing before colonoscopy have only been compared in one study (13), which was too underpowered to draw meaningful conclusions. Pico-Salax and NaP or PEG have also been compared in several studies (25-27) examining cleansing efficacy for ACBE. While the end points were sufficiently different from colonoscopy to limit meaningful comparisons, there was no obvious advantage with Pico-Salax. One additional study (28) was identified that compared oral NaP with modified

TABLE 3
Studies comparing overall taste, tolerability and symptoms of Pico-Salax (PCSLX)* compared with oral sodium phosphate (NaP) or polethylene glycol solution (PEG)

Reference, year	Cleansing agent: PCSLX patients, n	NaP patients, n	PEG patients, n	Procedure	Taste	Tolerability	Symptoms: Nausea/vomiting	Discomfort	Dizziness	Thirst
Hamilton et al (13), 1996	25	–	27	Colonoscopy/ ACBE	Not tested	Not tested	PEG>PCSLX	–	–	–
Schmidt et al (23), 2004†	182	190	–	Colonoscopy	PCSLX>NaP	PCSLX>NaP	NaP>PCSLX	NaP>PCSLX	NaP>PCSLX	NaP>PCSLX
Yoshioka et al (24), 2000	77	76	–	Colonoscopy	Not tested	Not tested	No difference‡	No difference‡	Not tested	Not tested
Macleod et al (25), 1998	83	111	–	ACBE	PCSLX>NaP	PCSLX>NaP	NaP>PCSLX	No difference‡	Not tested	Not tested
Hawkins et al (27), 1996	45	–	47	ACBE	Not tested	Not tested	PEG>PCSLX	PEG>PCSLX	Not tested	Not tested

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TABLE 4
Studies aimed at patient safety after taking doses of Pico-Salax (PCSLX)* and oral sodium phosphate (NaP) or polethylene glycol solution (PEG)

Reference, year	Cleansing agent: PCSLX patients, n	NaP patients, n	PEG patients, n	Procedure	Weight	Hemoglobin	Biochemistry	Hemodynamic	Comments
Hamilton et al (13), 1996	28	–	21	Colonoscopy or ACBE	–	–	Mg^{2+} mean increase of 0.15 mmol/L	–	Significant difference compared with PEG
Yoshioka et al (24), 2000	51	54	–	Colonoscopy or colon surgery	–	No difference	No difference (electrolytes)	–	Mg^{2+} not measured
Barker et al (29), 1992	10 versus controls	–	–	Colon surgery	2.3 kg increase	Mean increase of 0.65 g/100 mL	–	Increase in pulse 10% to 20%	Significant differences compared with controls
Ryan et al (31), 2005	144	–	–	ACBE	–	–	Urea mean decrease of 0.56 mmol/L	–	Significant differences compared with baseline
							K^+ mean decrease of 1.6 mmol/L	–	–
							Na^+ mean increase of 1.3 mmol/L	–	–

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regimens of low-dose Pico-Salax, PEG and senna syrup before colonoscopy, and it found an advantage with this triple regimen.

Tolerability: When studies examining colon cleansing before either colonoscopy or ACBE are taken together (Table 3), Pico-Salax generally shows an advantage in overall tolerability, taste, and symptoms of nausea and vomiting compared with oral NaP. There are less available comparative data with PEG, but the smaller volume is preferred over PEG solutions, and there is also less nausea and vomiting compared with PEG (Table 3).

Safety: Pico-Salax is a small-volume, osmotically active agent, and therefore has the potential to contract the intravascular space and alter electrolytes. It also contains magnesium and could result in hypermagnesemia. There is a paucity of hemodynamic monitoring data pre- and postadministration of Pico-Salax, but the available data suggest that this agent could cause intravascular volume contraction (Table 4). In a small study (29) of 10 patients scheduled for colorectal surgery (two sachets before day of surgery and oral fluids ad libitum until midnight) there was a significant reduction in postural systolic blood pressure (13%) and an increase in resting (9 beats/min) and postural (15 beats/min) pulse rates. These data were supported by measurements of weight and hematocrit changes (29,30) that also suggested a minor contraction in intravascular volume (Table 4).

Magnesium levels have been shown in several studies (Table 4) to be increased the day after ingestion, but the magnitude of the change is relatively small. Although serious adverse events have been reported related to hyponatremia

(see below), measurements in clinical studies demonstrate little or no decrease in mean values (Table 4). Similarly, measurements of serum potassium in these studies do not suggest that there are changes that would lead to clinical problems (13,31).

Hyponatremia associated with seizures has been described in a case report (32) and in reporting to the Australian Adverse Drug Reactions Bulletin (five cases) (23). Other adverse events reported to this agency have included four reports of syncope and dehydration.

Question 3: What is the current status of renal function impairment, nephrocalcinosis and oral NaP?

Oral NaP is a small-volume osmotic agent that causes a subclinical contraction of intravascular volume and transient hyperphosphatemia. Until recently, only a few isolated cases (8) of renal failure had been reported, and these appeared to have resulted from inappropriate dosing and/or hydration. Nephrocalcinosis and chronic renal failure associated with the ingestion of oral NaP was first reported in 2003 (33) in a single case report and subsequently in a series of 21 cases from a single centre (34,35). These cases were identified from screening 7349 renal biopsy specimens and obtaining a history of temporally related ingestion of oral NaP. The biopsies were reviewed at Columbia University (USA) but were received from a wide referral base covering at least four states in the United States. The pathophysiology linking nephrocalcinosis and oral NaP is not clear. Most patients were hypertensive (16 of 21), 14 of 21 patients were either on an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB), and four were on diuretics. The hydration status of the patients was unknown. These reports have not been described by other centres to date, but raise the concern that renal damage may not be restricted to a handful of cases and reflects wider spread renal damage that has gone undetected.

This possibility has been examined in two preliminary studies (22,36) published in abstract form. Both studies evaluated changes in serum creatinine levels and estimated creatinine clearance using the Cockcroft-Gault formula or the Modified Diet in Renal Disease Study formula. In one study (22), creatinine was prospectively measured pre- and postingestion of oral NaP before colonoscopy in 191 subjects. The data suggested that oral NaP ingestion was not associated with clinically significant changes in renal function, including in patients who used ACEIs, ARBs or diuretics concurrently. The other study (36) examined 770 patients receiving oral NaP (81%) or PEG (19%) and compared renal function measured before colonoscopies one to five years apart. A small proportion of patients had creatinine levels outside the normal range at subsequent testing over this time interval (7% of NaP patients, maximum 160 µmol/L; 9% of PEG patients, maximum 160 µmol/L), but the bowel preparation agent used was not a predictive factor. Independent of bowel preparation, age and hypertension were predictors of renal failure. Patients in both studies had been advised to hydrate throughout the cleansing period up until several hours before the time of colonoscopy, as currently recommended by the manufacturer (CB Fleet Inc, USA).

Question 4: Can diet be liberalized on the day of cleansing to enhance tolerability without compromising efficacy?

Many endoscopy units advise only clear fluids on the day of colon cleansing, but this may decrease patient tolerability and, with it, the likelihood of undergoing repeat colonoscopies. Despite this, only a few studies (11,37-39) have specifically examined the effect of liberalizing the diet on the day of colon cleansing. Other studies (3,6,18,40-44) have examined various diet regimens, but these were not the primary focus of the study. The most widely studied dietary modification is the low-residue breakfast the day before colonoscopy, rather than clear liquids (3,6,11,18,40-44). Overall, the low-residue breakfast is better tolerated and did not result in poorer colon cleansing. Scott et al (37) also examined the effects of a light lunch the day before colonoscopy. In this randomized, controlled trial (37), patients having a light breakfast followed by clear fluids were compared with a group of patients who were permitted to have a light lunch in addition to breakfast, which was then followed by clear fluids. Both groups received oral NaP as the cleansing agent. One hundred patients were included in each group, and no significant difference was found in preparation quality between the groups (P=0.357). Aoun et al (38) studied lifting all dietary restrictions for the entire day before colonoscopy followed by a split dose of PEG (2 L the night before colonoscopy followed by 2 L the morning of the procedure), and found no significant difference in preparation quality compared with clear liquid diet and regular full-dose PEG. In contrast, Salwen and Basson (39) investigated the use of psyllium for four days before colon cleansing with 4 L of PEG, but this dramatically decreased the cleansing efficacy. One other study (11) reported a trial with a subgroup of patients having no dietary restrictions. However, recruitment to this arm was stopped early due to the high proportion of poor and unacceptable preparations.

DISCUSSION

The ideal colon cleansing regimen provides maximal efficacy and patient tolerability while maintaining patient safety. In the present review, we examined studies investigating whether low-volume PEG and stimulant laxatives enhance patient tolerability while maintaining adequate efficacy, whether the recently introduced Pico-Salax is a viable alternative to PEG or oral NaP, whether nephrocalcinosis associated with the use of oral NaP is a widespread concern and whether diet may alter patient tolerance. A common limitation of available studies is the lack of sufficient power to detect meaningful differences. Furthermore, it is important not to infer equivalence when no difference between preparations is found.

Our review of studies that examined reduced volumes of PEG combined with stimulant laxatives (Table 1) suggests that this combination is better tolerated than the standard 4 L volume of PEG, and that in most cases, differences in cleansing efficacy were not observed. However, there are several limitations to interpreting these results. First, as described above, the absence of difference does not demonstrate equivalence. Second, whether 4 L of PEG is the best gold standard for efficacy is debatable. A number of studies (2-5,7) suggest that oral NaP may be a superior cleansing agent, particularly when the doses are given the night before and early in the morning of the procedure (3,6). In the one study (43) that compared low-volume PEG combined with stimulant laxatives with oral NaP, oral NaP was more efficacious. Splitting the dose of PEG has been shown in one well-designed trial (19) to be feasible and perhaps better tolerated than regular PEG dosing, but these results may need to be confirmed in other trials before they are widely accepted.

Although Pico-Salax has been widely used in the United Kingdom, Europe and Australia for over 20 years, there are surprisingly little data available on its efficacy, tolerability and

safety, particularly in contrast to oral NaP and PEG (8). There are only two studies (23,24) that compared the efficacy of Pico-Salax with oral NaP before colonoscopy, and both have serious limitations. One study (23) used three rather than the two recommended doses of Pico-Salax, and the other (24) had very small numbers. Altogether, the data suggest that oral NaP may be as or more efficacious than Pico-Salax but more studies are needed to clarify this issue. Only one small study (13) exists comparing Pico-Salax with PEG, and the numbers were too small to draw meaningful conclusions. There is somewhat more data available concerning patient tolerability (Table 3), which suggest that Pico-Salax may have an advantage over oral NaP and/or PEG in overall tolerability, taste, and nausea and/or vomiting. Although Pico-Salax is a small-volume osmotic agent with the potential to contract the intravascular space, there are little hemodynamic data available (Table 4). A few small studies (29,31) indicate that intravascular volume contraction can occur, but whether this finding persists when patients are dosed the night before and the morning of the colonoscopy, and when these doses are combined with fluid replacement, remains to be determined. There are relatively few case reports in the literature of serious adverse events caused by Pico-Salax, but there have been several reports of hyponatremia associated with seizures or other adverse events. This paucity of reports may reflect a more advantageous safety profile than other small-volume osmotic agents such as oral NaP, but the magnitude of reporting bias is unknown.

There is currently no available colon cleansing agent that does not have the potential for serious adverse events (8), and recent reports linking nephrocalcinosis and ingestion of oral NaP (33,34) have raised concerns about the safety of oral NaP. These reports have been largely confined to a single centre that has a very large referral base. Over five million units of oral NaP are sold annually in the United States (CB Fleet, USA, personal communication). Together, these points may imply that the risk is low, but concerns about undetected cases have been raised. Preliminary reports (22,36) do not suggest this is a widespread phenomenon, but there have been other isolated case reports of renal failure in which renal biopsies were not performed, and further studies are needed. Most case reports of adverse events with oral NaP have resulted from either inappropriate dosing and/or selection of patients (8) (it is contraindicated in patients with congestive heart failure, renal failure, ascites, ischemic heart disease and pregnancy, and in debilitated patients who cannot maintain hydration), but these causes cannot be clearly traced to many of the cases in the Markowitz et al series (34). The pathophysiology underlying the diagnosis of nephrocalcinosis in this setting remains to be established. One possible explanation for the development of renal failure is the combination of poor hydration in the setting of a patient with a susceptible kidney due to subclinical disease and/or medications. In the Markowitz et al (34) series, most patients had hypertension and were on ACEIs, ARBs or diuretics, and no data are available on the status of individual patient hydration. It is well known that the osmotic action of oral NaP can lead to minor intravascular volume contraction and transient hyperphosphatemia (8). Therefore, the need for continued hydration with fluids, including rehydration solutions (45), up until a few hours before colonoscopy has been increasingly recognized.

There are few studies that have critically examined whether a liberalized diet on the day of colon cleansing adversely affects the quality of cleansing. Many centres restrict patients to clear liquids on the day of colon cleansing but a more liberal diet could enhance patients' ability to tolerate the cleansing and, hence, their likelihood to participate in long-term screening programs. Although limited, several studies (3,6,11,18,40-44) have suggested that a light breakfast the day before colonoscopy does not adversely affect colon cleansing quality. Unrestricted diets are not tenable, but one study (37) also suggest that a light lunch does not significantly reduce cleansing success. Interpretation of the studies addressing this topic is complicated by potential differences in efficacy of the cleansing agent and by varying the diet depending on the agent within a given trial.

Despite the large number of studies existing in the literature, numerous questions remain surrounding colonoscopy preparation. Varying methodology, regimen administration and patient selection make comparison of study results difficult and limit applicability of some studies to general gastroenterology practice. In addition, until recently (46), there was no reliable, validated scale for evaluation of efficacy of these preparations. One hopes that advances in research techniques as well as larger, well-designed studies will address these issues in a more definitive manner.

SUMMARY

The search for the optimum colon cleansing regimen continues to be a challenge. Each of the currently available regimens has limitations in efficacy, patient tolerance and/or safety. Although PEG has fewer contraindications than NaP or Pico-Salax, it has poorer patient tolerance. The introduction of Pico-Salax in Canada may provide a good alternative option to oral NaP and PEG for patients, but further data are needed with respect to safety, tolerance and efficacy. In addition to choice of cleansing agent, modified diets may be important in improving patient tolerance.

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