Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline

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Bibliography
DOI http://dx.doi.org/10.1055/s-0032-1326186
Published online: 0.0.
Endoscopy 2013; 45: 142–150

ISSN 0013-726X

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Background and aim: This Guideline is an official statement of the European Society of Gastrointestinal Endoscopy (ESGE). It addresses the choice amongst regimens available for cleansing the colon in preparation for colonoscopy.

Methods: This Guideline is based on a targeted literature search to evaluate the evidence supporting the use of bowel preparation for colonoscopy. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was adopted to define the strength of recommendation and the quality of evidence.

Results: The main recommendations are as follows. (1) The ESGE recommends a low-fiber diet on the day preceding colonoscopy (weak recommendation, moderate quality evidence). (2) The ESGE recommends a split regimen of 4 L of polyethylene glycol (PEG) solution (or a same-day regimen in the case of afternoon colonoscopy) for routine bowel preparation. A split regimen (or same-day regimen in the case of afternoon colonoscopy) of 2 L PEG plus ascorbate or of sodium picosulphate plus magnesium citrate may be valid alternatives, in particular for elective outpatient colonoscopy (strong recommendation, high quality evidence). In patients with renal failure, PEG is the only recommended bowel preparation. The delay between the last dose of bowel preparation and colonoscopy should be minimized and no longer than 4 hours (strong recommendation, moderate quality evidence). (3) The ESGE advises against the routine use of sodium phosphate for bowel preparation because of safety concerns (strong recommendation, low quality evidence).

TF1

Non-laxative measures

Statement #1

The ESGE recommends a low-fiber diet on the day preceding colonoscopy
(weak recommendation, moderate quality evidence).

The ESGE does not make any recommendations regarding the use of low-fiber diet for more than 24 hours prior to the examination
(insufficient evidence to make a recommendation).

Statement #1: Rationale

- Efficacy of dietary modifications supported only by poorly controlled pre-PEG data (i.e. radiological)

- Dietary modifications included in most of PEG-based studies, leaving uncertainty on their exclusion

- RCT with bias showed a superiority of low-fiber diet over liquid diet, in the efficacy (1 of 2 RCT) or in the tolerability (2 of 2 RCT)

Study	Patient N°	Comparison	Outcome
Delegge	506	Low-fiber+MgCi vs liquid diet with NaP	Low-fiber+MgCi more effective

Statement #2: Rationale

- Some centers prescribe low-fiber diet for 3 days because some patients have slow transit time; no evidence is available to recommend 1 or 3 days

Statement #3

The ESGE recommends against the routine use of enemas in addition to oral bowel preparation (strong recommendation, moderate quality evidence).

Statement #3: Rationale

- Two RCT showed the lack of any benefit in adding enemas to oral BP.

- The addition of enemas reduced the acceptability of BP.

Statement #3: Rationale

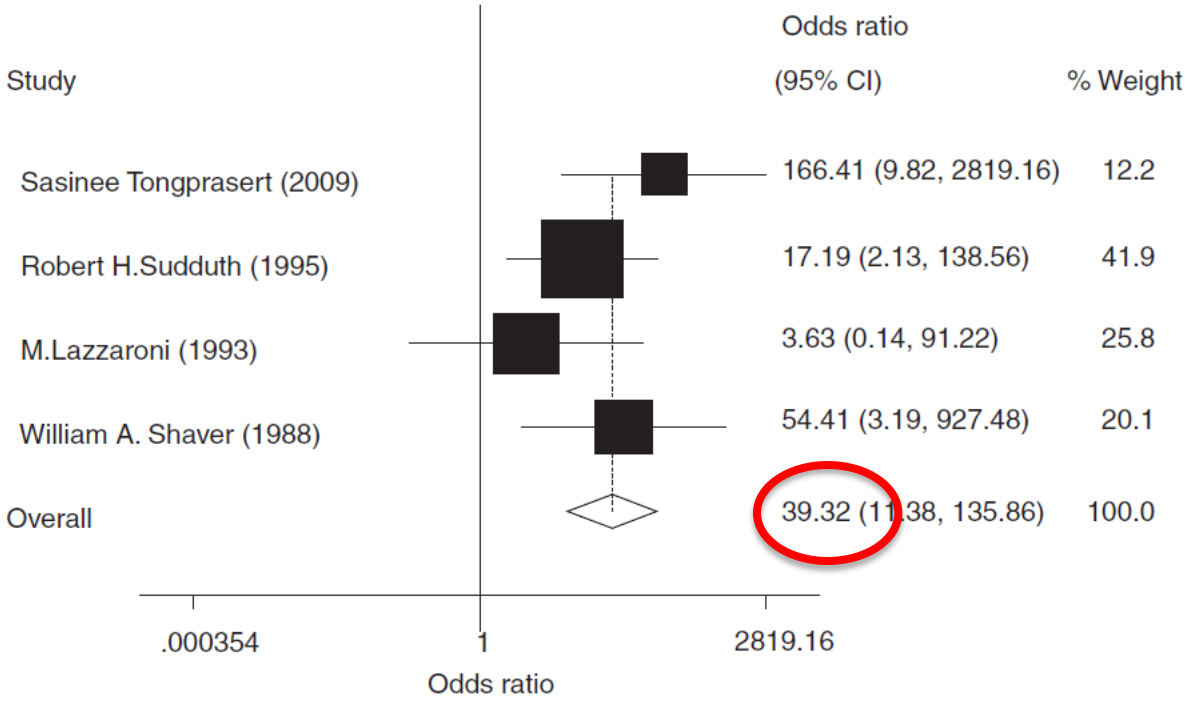
Study	Patient N°	Comparison	Outcome
Lever*	82	Oral lavage vs oral lavage+enemas	Cleanliness equal Pts would refuse further prep: 12% vs 22%
Borkje	271	Oral senna+enema vs PEG vs Picosalax	PEG superior

Statement #4-5

The ESGE recommends adding simethicone to standard bowel preparation
(weak recommendation, high quality evidence).

The ESGE does not recommend the routine use of prokinetic agents as adjunct to bowel preparation
(weak recommendation, moderate quality evidence).

Systematic review



Simeticone has been shown to significantly decrease air bubbles at colonoscopy (OR = 39.32, 95% CI: 11.38–135.86, p = 0.00), with no significant heterogeneity (p = 0.29, I2 = 20.0%).

Wu L et al. Scand J Gastroenterol 2011;46(2):227-35

TF2/TF5

PEG/Mg Ci

Statement #6

The ESGE recommends a split regimen of 4-L PEG solution (or same-day in the case of afternoon colonoscopy) for routine bowel preparation. A split (or same-day in the case of afternoon colonoscopy) regimen of 2-L PEG plus ascorbate or of sodium picosulphate/magnesium citrate may be valid alternatives, in particular for elective outpatient colonoscopy.

(strong recommendation, high quality evidence).

In patients with renal failure, PEG is the single recommended bowel preparation. The delay between the last dose of bowel preparation and colonoscopy should be minimized and no longer than 4 hours

(strong recommendation, moderate quality evidence).

Statement #6:PEG Rationale

- 5 meta-analysis showed comparable or lower efficacy of PEG vs NaP, as well as comparable efficacy with Mg Ci/SPS.

Statement #6: Rationale

Author	Study	Intervention	Conclusions
Hsu CW	8 RCT	2x45mL NaP vs. 4L PEG	Equivalence for adequate; NaP superior for excellent
Tan JJY,	29 RCT	2x45mL NaP vs. 3-4L PEG vs. 10-30mg SPS	PEG less efficacious than NaP and equal to SPS
Belsey	82 RCT	2x45mL or 90mL NaP solution or NaP tablets vs. 3-4L PEG	Equivalence
Juluri R	18 RCT	2x45mL NaP vs. 4L PEG	NaP more effective
Juluri R	71 RCT	4L PEG alone +/- adjunctive medications, 2L PEG + adjunctive medication, split-dose PEG (2L+2L or 2L+1L), 2x45mL NaP solution +/- adjunctive medications, NaP tablets	NaP tablets superior to PEG

Statement #6: Split- Rationale

- 18 RCT (3256 pts. split , 2919 non-split), including PEG (high or low dose) and NaP or Mg Ci

- Pooling of data independently of the type of comparison shows an improved degree of bowel cleansing good/excellent of 20% [95% CI 0.14 - 0.26], ($p<.0000$, I^2 91.1%) favoring the split regimen.

- In 23 out of the 24 comparisons the split schedule provided the best degree of bowel cleansing.

Statement #6: Rationale

Comparison	N. pts.	Rate difference (95% CI)	P<	I^2
Peg low vs Peg low	917	0.180 (0.014- 0.346)	0.034	91.2%
Fosfo vs Fosfo	1519	0.244 (0.108 - 0.380)	0.000	92.9%
*Peg High vs Peg Low	172	0.04 (-0.042 - 0.131)	.314	.
Peg Hi vs Peg High	1305	0.306 (0.192 - 0.421)	0.000	81.5%
*Peg Hi vs sodium citrate+Peg Low	152	0.247 (0.099 - 0.395)	0.001	.
Fosfo soda vs Peg High	1021	0.136 (0.067 - 0.204)	0.000	67.9%
Fosfo soda vs Peg Low	652	0.155 (0.098- 0.212)	0.000	0.0%
Pospho soda vs Mg citrate	437	-0.094 (-0.150 to -0.038)	0.001	.

Statement #6: delay-Rationale

Time (hours) to colonoscopy	N. comparison	N. pts.	Rate difference (95% CI)	P=	I^2
1.3	1	141	0.203 (0.051 - 0.355)	0.009	.
2 Hours	11	3120	0.293 (0.200- 0.387)	0.000	92.9%
3 hours	8	1051	0.137 (0.082 - 0.193)	0.000	44.9%
4 hours	2	894	0.009 (-0.198 to 0.217)	0.929	94.5%
6 hours	1	107	0.032 (-0.078 to 0.142)	0.565	.

Statement #6: low-volume Rationale

- Overall, 11 studies, including over 7,000 randomized subjects, have generally shown a similar efficacy between high- and low-volume PEG regimens.

- As expected, low-volume PEG preparation were not associated with a higher rate of adverse events as compared with the high-volume PEG regimens, whilst it was generally associated with a better tolerability.

Statement #6:Low-PEG Rationale

Cohen	216	peg 2l+asc vs peg 2l+bys	peg asc better	equal	mono
Ell	359	peg 2l+asc vs 4l	equal	peg 2l better	multi
Corporaal	350	2 l asc acidvs 4l	equally	equal	mono
Marmo	1763	peg 2l asc acid vs 4l	equal	more palatable	multi
Bitoun	352	2l+asc vs nap	equal	more tolerable	mono
Hookey	2688	peg 2l+sennosides vs 4l	4 peg better	2 l more better tolerated	mono
Di Palma	200	peg 2l sulfate free+ bys vs 4-l peg	equal	2 l better tolerated	multi
Ker	912	nap vs 2l+bys vs 4l	equal	worse for 4l	mono
Ker	300	2l + bys vs 4l	equal	better with 2 l	mono
Adams	382	2l + bys vs 4l	equal	better with 2l	mono
Park	232	2l+mag vs 4l	2l more efficient	more tolerable	mono
Sharma	150	peg 2l+mag citrate or bys vs 4l peg	equal	2l better tolerated	mono

Statement #6:Low-Mg/SPS Rationale

Author	Regime	Pt no	Cleansing	Tolerability
Berkel-hammer	NaP 45ml vs Mg 300ml	300	Mg>NaP overall	NaP > Mg
Schmidt	NaP 90 ml vs Mg & SPS	400	Equal	Mg>NaP
Tjandra	NaP 90 ml vs Mg & SPS	225	NaP>Mg	Mg>
Yoshioka	NaP 90 ml vs Mg & SPS	103	NaP>Mg	NSD
Hamilton	4l PEG vs Mg & SPS	69	Equal	Mg & SPS>PEG
Renaut	NaP vs Mg & SPS	73	Equal	Mg & SPS>NaP
Rapier	PEG with clear liquid diet vs Mg & bisacodyl with low residue or clear liquid diet.	114	Equal	Equal
Regev	PEG 3l vs Mg & SPS	68	Mg>PEG	Mg & SPS>PEG
Worthington	PEG & ascorbic acid vs Mg & SPS	65	PEG > Mg	Mg & SPS>PEG & ascorbic acid ($p<0.001$)

Statement #7-8

The ESGE advises against the routine use of oral sodium phosphate for bowel preparation because of safety concerns.
(strong recommendation, low quality evidence)

The ESGE suggests that oral sodium phosphate can only be advised in selected cases of specific needs that cannot be met by alternative products (e.g., patient unable to tolerate other agents) and only in subjects assessed by physicians to be at low risk of oral sodium phosphate-related side-effects. An evaluation of the kidney function should be available before prescribing oral sodium phosphate.
(weak recommendation, low quality evidence).

If oral sodium phosphate is used for bowel preparation, 90 mL (solution) or 32 tablets containing 1.5 gram NaP each in split-dose regimen is recommended.
(strong recommendation, high quality evidence).

Statement #7: Rationale

- Systematic review serious AE (n=109) (Belsey 2009)
  - (i) Electrolyte imbalance (n=46, 11 deaths)
  - (ii) delayed renal failure (APN, n=26);
  - (iii) colon aphtous ulcerations (n=37)

- Meta-analysis of 7 controlled trials (n=12,168) comparing kidney function after OSP vs. other BP: no significant association (Brunelli 2009).

- **Over a 2-year period, 171 cases of renal failure were reported to the FDA following the use of OSP and 10 following the use of PEG -> FDA warning.**

- A population-based national Icelandic retrospective analysis: biopsy-proven APN in 1/1000 sold doses of OSP (Pálmadóttir 2010).

Statement #8: Rationale

- Risk factors include age >55 years, hypovolemia, baseline kidney disease, bowel obstruction or active colitis, drugs affecting renal perfusion or function such as diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers and NSAIDs.

- Recommendations to prevent AE (Balaban 2008):
  - Proper dosing and hydratation
  - Adequate patient instructions (prescriber should ensure patient understanding)

Statement #9

In patients with inadequate bowel cleansing, the ESGE suggests the adoption of endoscopic irrigation pumps or repeating colonoscopy on the following day after additional bowel preparation (weak recommendation, low quality evidence).

For the first colonoscopy, the use of models to identify patients at increased risk of inadequate cleansing with the aim to adapt the bowel preparation is not recommended. (insufficient evidence to determine net benefits or risks)

Statement #9: Rationale

- Five studies including (20,000 patients) showed increased age, male sex, in-patient status and comorbidities to predict inadequate preparation.

- Sociodemographic variables – such as literacy and marital status – also resulted to be associated with an unfavourable outcome.

- No evidence on the efficacy of alternative regimens in those at higher risk of inadequate preparation.

Statement #9: Rationale

Author	Pts.	BP	Predictive factors
Borg	1815	PEG/NAP	Demographic, indication, inpatient, medical hx,race, weight, height, comorbid., drugs, alcohol, tobacco
Ness	732	PEG/NAP	Demographic, indication, inpatient, medical hx,race, weight, height, comorbid., drugs, regimen, compliance, bmi frequency, prevoius surgery
Chan	522	PEG 2L	Demographics, bmi, in-pt, timing oc, indication,hx med, hx oc, prev surger, compliance bp
Lebwohl	13498	PEG	demogr, in-pt, time oc, marital status, medicais status
Hassan	2811	PEG/PEG 2l/NaP	demographic data, indication and comorbidities
Chung	362	PEG	Age, comorbidity, surgery

Conclusions

- **1-day low-fiber diet** – new studies needed

- **Simethicone** highly effective in reducing bubbles - new studies on ADR needed

- **4 Liter as first-choice** – Low-volume PEG/PSP as valid alternatives

- **Split** essential **to close the interval** between BP and colonoscopy