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Improved health and wellbeing through collaborative working across
Cheshire, Merseyside, Lancashire & South Cumbria

Guidelines for the Management of Constipation in Palliative Care

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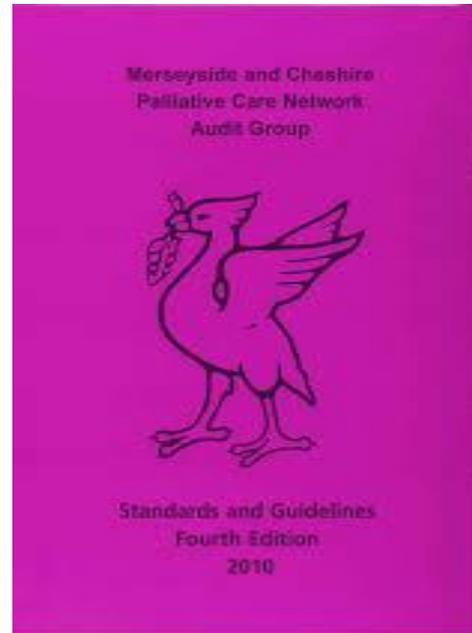
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WITH SPECIAL THANKS TO

- Patient, Carer and Public Representative
 - Angela Fell
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CURRENT STANDARDS AND GUIDELINES- LAST REVIEWED 2009



Guidelines for the Management of Constipation in Palliative care

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Guidelines for the management of constipation in palliative care

General Principles

- Constipation is defined by the patient and is a symptom not a disease
- Patients with ECOG performance status 3 or 4 are at high risk of developing constipation (ie confined to bed or chair for more than 50 % of waking hours)
- Patients on weak or strong opioids are at high risk of developing constipation
- There is no evidence to suggest the superiority of any one laxative in resolving constipation

Common causes of constipation in advanced cancer

Bowel obstruction	Depression	Immobility
Concurrent disease	Drugs	Poor food intake
Confusion	Environmental	Spinal cord compression
Dehydration	Hypercalcaemia	Weakness

GUIDELINES

- To identify patients at risk of constipation, an assessment of performance status should be undertaken [Level 4]
- A digital rectal examination should be carried out on first assessment, if appropriate [Level 4]
- Bowel obstruction should be excluded (see Guidelines on Management of Bowel Obstruction) [Level 4]
- General management includes encouraging fluid intake, particularly fruit juices [level 4]

- Oral laxatives should be reviewed every 3 to 4 days using stool consistency (e.g Bristol Stool Chart) and ease of defecation as guides to dose titration [Level 4]
- The laxative dose should be titrated upwards until constipation is controlled. Oral laxatives should initially be given at night [Level 4]
- If strong opiate induced constipation is severe, then consider substitution to transdermal Fentanyl (see Guidelines for Opioid Substitution) [Level 2+]

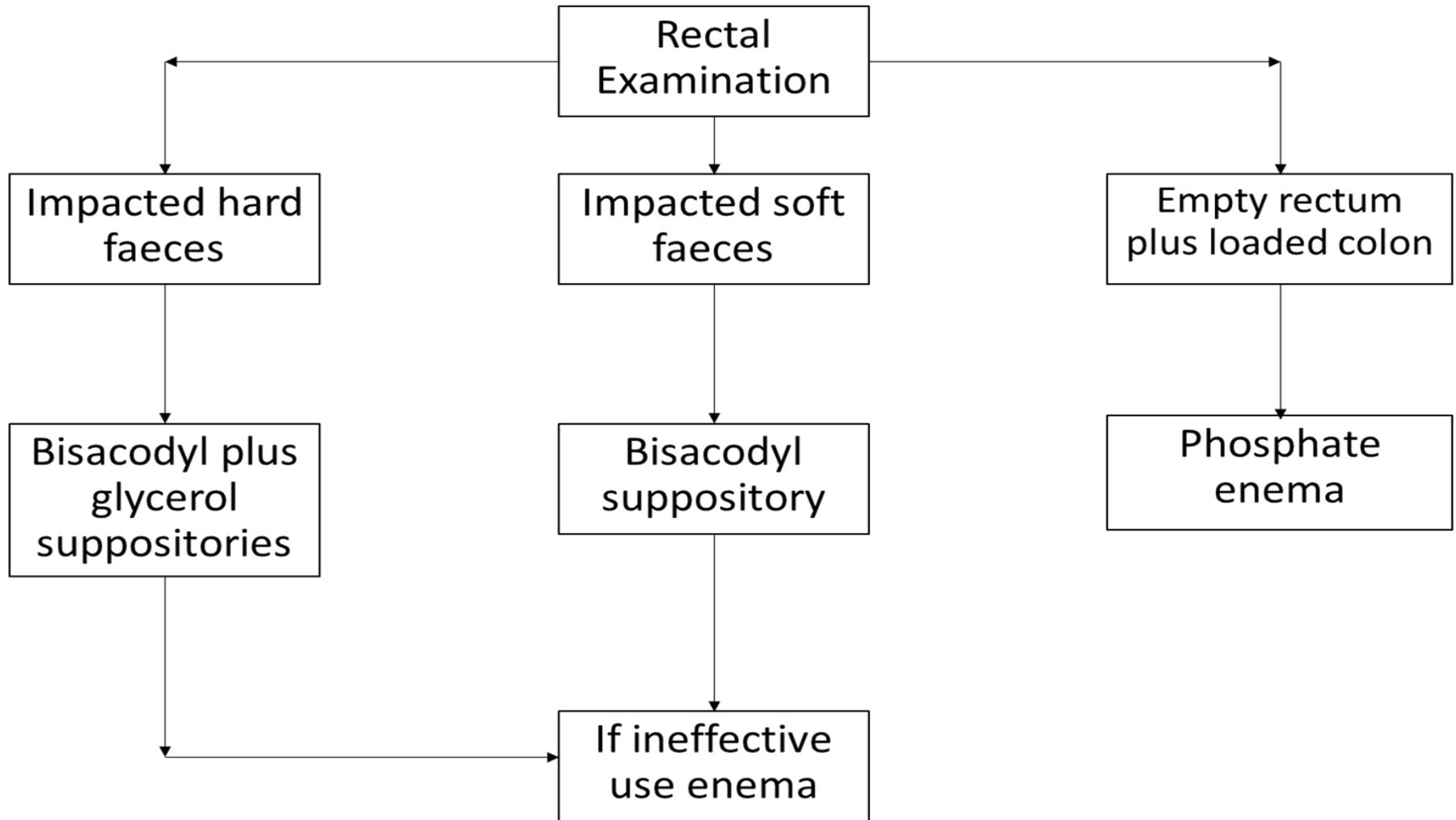
- Oral laxatives may be subdivided into different groups according to their mode of action :-
 - combination laxatives eg Codanthramer
 - stimulant laxatives eg Senna
 - osmotic laxatives eg Lactulose

[Level 4]

- Guidance offered in steps for increasing Codanthramer (figure 12.1) [Level 4]

- The use of rectal interventions will be guided by the findings on rectal examination (see figure 12.2) [Level 4]
- If rectal intervention is required for the management of constipation, the oral laxative dose should also be increased [Level 4]
- In patients with spinal cord compression or cauda equina syndrome, alternate day suppositories should be considered, in addition to a review of the current oral laxative therapy [Level 4]

Figure 12.2 Rectal interventions for constipation [Level 4]



- Methylnaltrexone (Relistor) is licensed for the treatment of opioid induced constipation in patients with advanced disease receiving palliative care, when response to the usual laxative therapy has not been sufficient.
- It is a peripheral μ -opioid antagonist which is given subcutaneously. It is supplied in 12 mg / 0.6 ml single use vials.
- It must not be used in patients with known or suspected mechanical bowel obstruction, or patients with acute surgical abdomen.
- The onset of action is 30-60 minutes.
- Side-effects include bloating, flatulence, cramps and nausea. Guidance to doses offered (Table 12.3) [Level 1+]
- If constipation remains a significant problem, consider the use of further investigations e.g abdominal x-ray [Level 4]

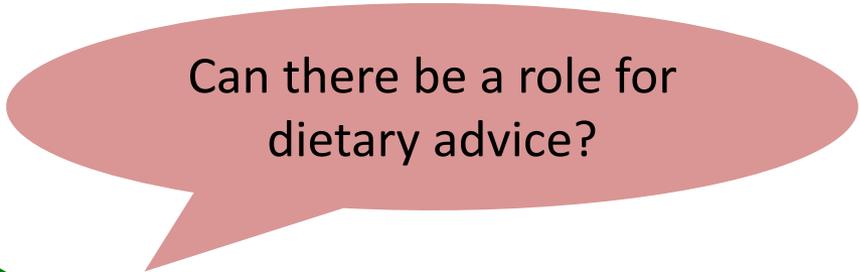
Standards

1. Identify the cause of constipation, treating reversible causes and managing bowel obstruction where appropriate (see Guidelines on the Management of Bowel Obstruction) [Grade D]
2. Patients commencing opioid therapy should also be offered a combination laxatives [Grade D]
3. Changes in laxatives should be documented in the patients' case notes [Grade D]

People's Voice Feedback



Useful topic to review



Can there be a role for dietary advice?



Dignity is a key message, particularly when considering rectal interventions

SYSTEMATIC LITERATURE REVIEW

May-July 2017

OUR QUESTIONS USING PICO

1- In patients receiving palliative care and suffering from medication-induced constipation (P), is one method of management (I) superior to other methods or no formal method (C) in relieving constipation (O).

2- In patients receiving palliative care and suffering from non-medication-induced constipation (P), is one method of management (I) superior to other methods or no formal method (C) in relieving constipation (O).

3- In patients receiving palliative care and suffering from constipation secondary to spinal injury (P), is one method of management (I) superior to other methods or no formal method (C) in relieving constipation (O).

LITERATURE REVIEW

Palliat AND constipation AND (manag* OR treat*)*

Medline, EMBASE, CINAHL and Cochrane databases:

1131 articles

124 abstracts

16 articles

11 Full texts included

NICE: No palliative care guideline. Opioid induced constipation guidance exists but only appraises naloxegol.

ARTICLES



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Tarumi Y, Wilson MP, Szafran O & Richard Spooner G. (2013). Randomized, double-blind placebo-controlled trial of oral docusate in the management of constipation in hospice patients. *J Pain Symptom Manage*, **45(1)**: 2-13

Placebo-controlled RCT

No difference from adding docusate to senna noted during 10 day prospective trial. QoL implications from being able to reduce a tablet and therefore minimise tablet burden for patients [Level 1-]

Tack J, Lappalainen J, Diva U, Tummala R, & Sostek M. (2015). Efficacy and safety of naloxegol in patients with opioid-induced constipation and laxative-inadequate response. *United European Gastroenterology Journal*, **3(5)**: 471-480.

RCT

Naloxegol is more effective than placebo in treating OIC and is more effective at greater doses. Frequency of laxation is greatly improved and satisfaction is also greater with higher dose naloxegol. However adverse events including abdominal pain, diarrhoea and nausea are also statistically significantly increased.

Miles C, Fellowes D, Goodman ML, & Wilkinson SSM. Laxatives for the management of constipation in palliative care patients (Review). 2006. *The Cochrane Library of Systematic reviews*, 4: 1-20.

Systematic review of RCTs

Unable to pool data so no ability to recommend any particular laxatives. HOWEVER, among the RCTs there are some interesting findings:

- There is no difference between lactulose and senna in terms of efficacy (both are effective). [Level 1]
- Lactulose and senna combination is more effective than dantron and poloxamer combination in treating constipation. [Level 1]

UPDATED GUIDELINE RECOMMENDATIONS AND STANDARDS

INTRODUCTION

- Constipation is a very common symptom that causes significant suffering in patients receiving palliative care. Constipation has been shown to result in significant physical, psychological, social and existential problems affecting quality of life.
- Due to the difficulties defining constipation, incidence is difficult to determine, however this has been estimated as between 18 and 90% of patients receiving palliative care, with prevalence of contributory factors between 25 and 90%.
- In addition, the difficulty defining constipation can contribute to difficulties and delays in reaching a diagnosis of this condition, and no tools or criteria have been consistently demonstrated to be effective in reaching an accurate diagnosis of constipation in this patient group.

INTRODUCTION

- The causes in this population are often multifactorial relating to poor dietary intake, physical inactivity, disease and treatment related. Prevention and treatment of constipation is therefore often related to the cause. However, given that constipation for the majority of people receiving palliative care has the potential to be drug-induced, management to promote satisfactory bowel movements commonly involves laxative administration.
- Balanced against the benefits of treatment, one also has to consider side effects. Many laxatives can contribute to the discomfort experienced by patients by exacerbating colic or causing diarrhoea. In addition, the use of rectal interventions for constipation has implications for dignity and acceptability of treatment to the patient, and this requires discussion with the patient and/or those important to them and taking full account of their views and preferences.

ASSESSMENT AND DIAGNOSIS

- Assessment of constipation is complicated by difference in perception and definition between clinicians and patients. Health professionals' assessment of whether a patient is constipated, often differs from that of the patient [Level 3]
- Therefore, when reaching a diagnosis of constipation, the views of the patient should be sought as to their experience with their bowels and whether they believe themselves to be constipated [Level 3]
- **An assessment of a patient with suspected constipation should include details of [Level 4]**
 - Frequency of bowel movement
 - Ease of defecation
 - Consistency and volume of stool
- **A Bristol Stool Chart may also be of benefit in reaching a diagnosis of constipation based on stool consistency [Level 4]**

ASSESSMENT AND DIAGNOSIS

- Other non-pharmacological contributory factors which should be asked about as part of the assessment include assessment of mobility, fluid and dietary intake and environmental factors such as equipment needs [Level 4].
- Health professionals should perform abdominal examination prior to making a diagnosis of constipation [Level 4]
- In cases where a diagnosis of constipation is suspected, consideration should be given to further investigations such as [Level 4]
 - Urea, electrolytes and adjusted calcium
 - Rectal examination
- An assessment should aim to exclude bowel obstruction prior to commencing treatment [Level 4]

PREVENTION OF CONSTIPATION

Table 1. Key risk factors for the development of constipation [Level 2+]

Being treated in a palliative care ward	Paracetamol
Poor appetite	No regular laxative use
Haemorrhoids	No laxatives available on request
No information given on constipation	Opioids
Heart disease	

NON-PHARMACOLOGICAL MANAGEMENT

- Where possible, non-pharmacological management of constipation should be tailored to any reversible causes detected on assessment of the patient [Level 4]
- Advice should be given in all instances regarding diet, fluid intake, mobility, and environmental factors such as having suitable and accessible toilet facilities and allowing ample time to use them. Privacy and dignity should be maintained at all times and changes to a persons care and regime should be minimised in order to control constipation. Maintaining a regular schedule for toileting can also be important in patients with constipation secondary to malignant spinal cord compression [Level 4]
- Medications should be reviewed regularly to ensure that those which contribute to constipation are minimised as much as possible [Level 4]
- Other related factors such as reduced mobility, poor food intake, weakness and dehydration should always be addressed as far as is practical [Level 4]

NON-PHARMACOLOGICAL MANAGEMENT

- For palliative patients that are able to maintain nutritional status through oral diet and fluids, it is advised that patients aim for 30g fibre per day, including wholegrains, fruit and vegetables [Level 4]
- **The prescription of fibre containing complete oral nutritional supplements may be considered, however, their nutritional value may not be equivalent to non fibre containing products [Level 4]**
- Although a minimum of 1.5 litres of fluid per day has been suggested, consumption of this volume may not be realistic. Palliative care patients that are able to manage some oral dietary intake can maximise fluid intake with foods containing higher water content, e.g. fruit , jelly , soups , sauces , mousses , ice cream , milky puddings and oral nutritional supplements where appropriate [Level 4].
- **Palliative patients that require a texture modified diet will potentially struggle to meet fluid requirements and optimise fibre intake. These should be referred to a dietetic service [Level 4]**

PHARMACOLOGICAL MANAGEMENT

- Combination docusate and senna has been shown to be no more effective than senna monotherapy [Level 1-]
- Using laxative monotherapy, where possible, arguably also avoids tablet burden and is better for the patients' quality of life [Level 4]
- Senna and lactulose monotherapy are equally effective [Level 1] however 40% of patients treated with monotherapy required senna and lactulose combination therapy in order to relieve constipation, suggesting greater efficacy with a combination regimen, although this was not statistically significant.
- Senna and Lactulose combination therapy has been demonstrated to be an effective combination and has demonstrated superiority against paraffin, magnesium hydroxide and co-danthramer [Level 1].
- Dose increases and addition of further laxatives should be undertaken gradually in order to avoid potentially unwanted side effects, i.e. colic and diarrhoea. Side effects are more common with higher doses and increasing numbers of laxatives [Level 1].
- **Consider trial of linclootide 290mcg once daily OR Lubiprostone 24mcg twice daily (in divided doses) in mobile non-opioid constipation patients if rectal examination normal [Level 4]¹⁶.**

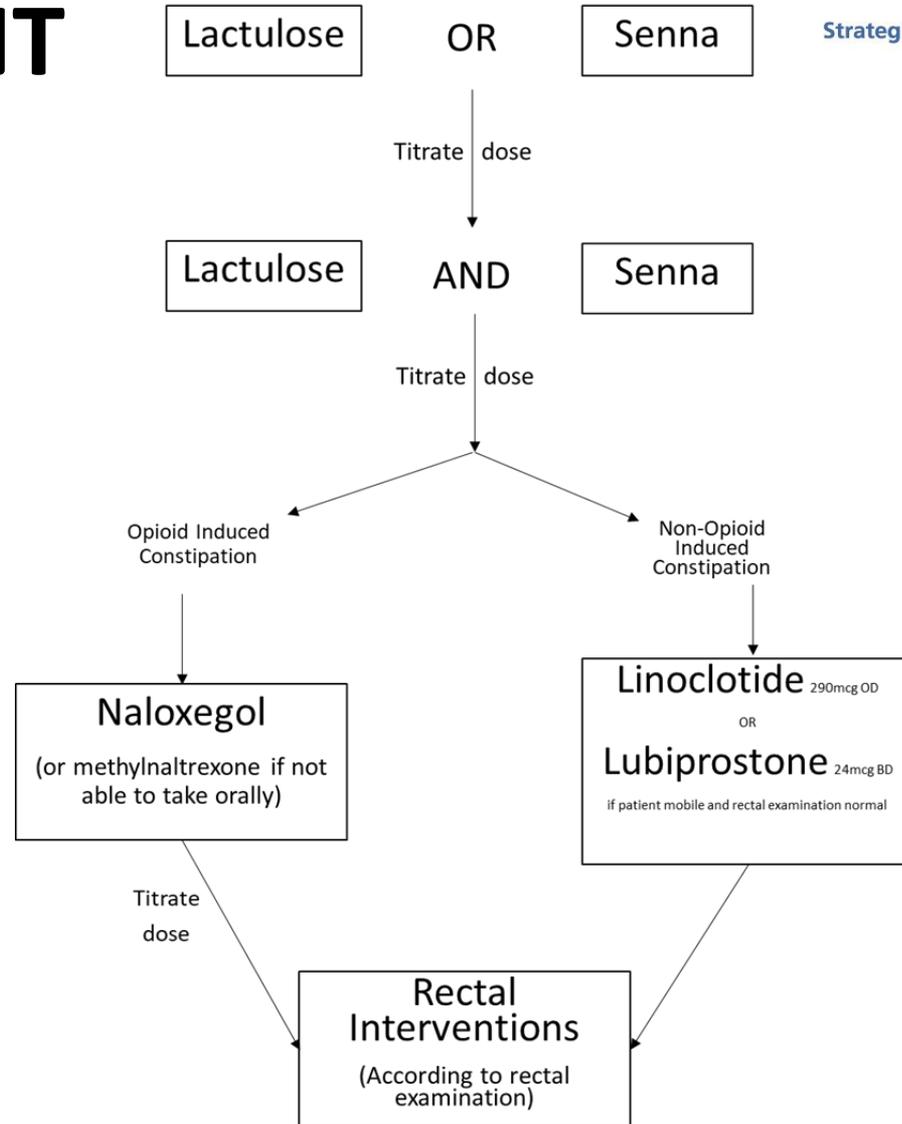
PHARMACOLOGICAL MANAGEMENT

- There is no evidence from this review that rotation of opioid is more effective than laxative use in the treatment of opioid induced constipation.
- Senna and lactulose combination therapy has also been shown to be more effective than co-danthramer monotherapy in the management of opioid induced constipation at morphine equivalent doses of $>80\text{mg}/24\text{h}$ [Level 1].
- In opioid induced constipation, for those patients who do not respond sufficiently to other laxatives (approximately 50% of one study), naloxegol is superior to placebo in relieving constipation [Level 1]
- Those efficacy of naloxegol is more effective at higher doses, but titration should be undertaken cautiously as side effects are also more common at higher doses [Level 1].
- In the absence of an oral route, methylnaltrexone has also been shown to be effective in treating opioid induced constipation [Level 1].

PHARMACOLOGICAL MANAGEMENT

- There is no experimental evidence to support the use of rectal interventions for constipation, nor to direct the choice of rectal intervention. The following guidance is based on professional consensus and opinion.
- The choice of rectal intervention should be based on the results of a digital rectal examination, as detailed in figure 2 [Level 4]
- For patients with malignant spinal cord compression, a rectal intervention should be given on alternate days according to figure 2 and combined with an alternate day stimulant oral laxative i.e. senna [Level 4]

PHARMACOLOGICAL MANAGEMENT



PHARMACOLOGICAL MANAGEMENT

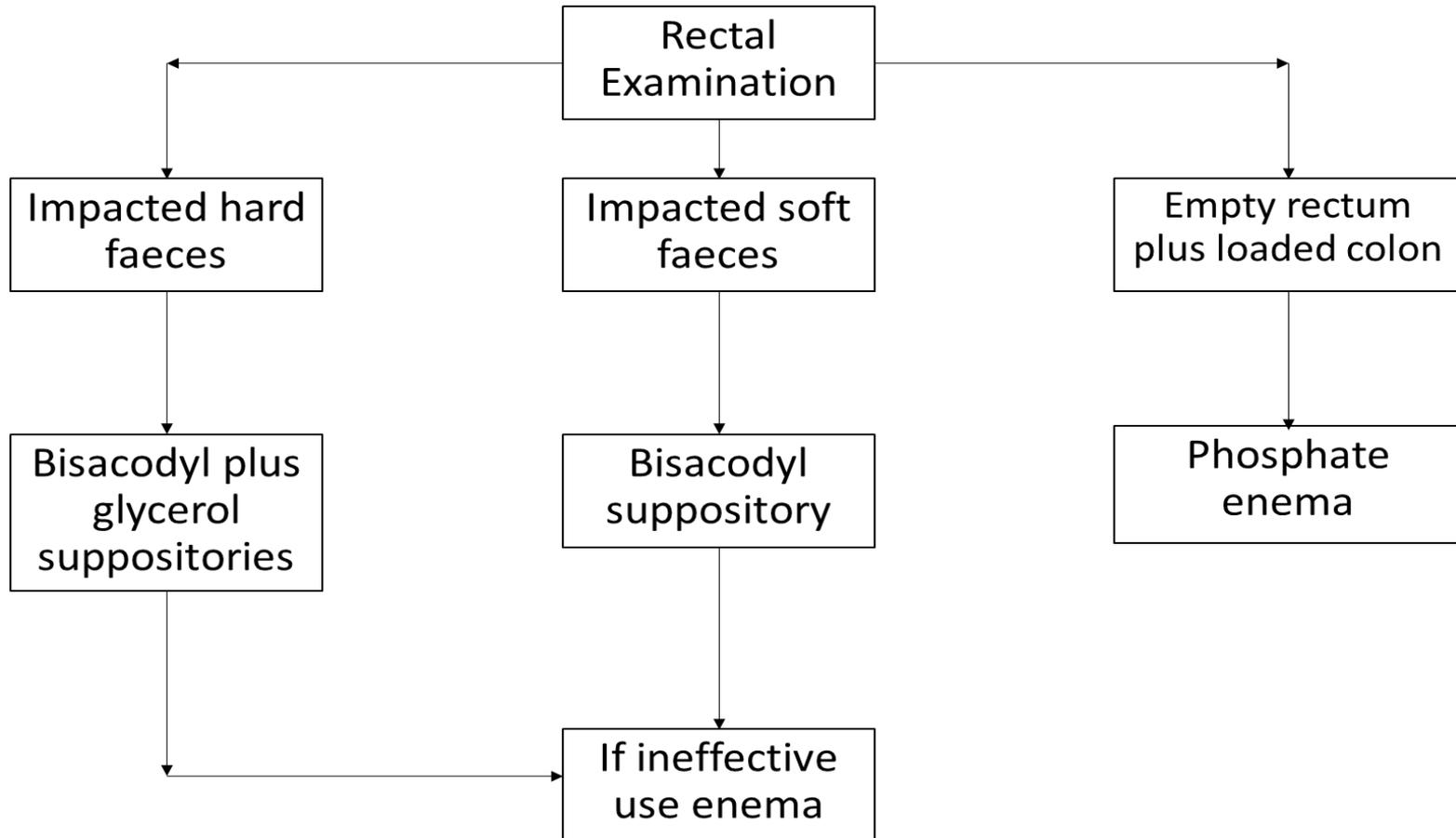


Table 1. Pharmacological Options for the Management of Constipation in Palliative Care^{27, 31}

	Senna [Level 1]	Lactulose [Level 1]	Sodium Docusate [Level 4]	Naloxegol (Moventig) [Level 1]	Glycerol Suppositories [Level 4]	Bisacodyl suppositories [Level 4]
Starting dose and titration advice	Start with 15mg bedtime. Increase to 15mg bd after 24-48h if no effect. If necessary increase to a maximum of 30mg tds	Starting dose is 15mls bd of 10g/15mL solution. Titrate according to result.	Start with 100mg bd. If necessary increase to a maximum of 200mg tds	Start with 25mg once daily. Maintenance dose is 25mg once daily.	One 4g suppository to be used when required.	One 10mg suppository to be used when required
Dosing in renal impairment	No dose adjustment required	No dose adjustment required	No dose adjustment required	If CrCl less than 60 mL/min: Reduce starting dose to 12.5 mg orally once a day; may increase to 25 mg orally once a day as needed for symptoms, if tolerated	No dose adjustment required	No dose adjustment required
Side effects	Intestinal colic, diarrhoea, hypokalaemia in cases of profuse diarrhoea.	Abdominal bloating, flatulence, nausea, intestinal colic	Diarrhoea, nausea, intestinal colic, rash.	Diarrhoea, intestinal colic, nausea.	Diarrhoea, faecal leakage	Diarrhoea, faecal leakage, local irritation
Contra-indications	Intestinal obstruction	Intestinal obstruction Use with caution in lactose intolerance Use in caution in diabetes due to sugar content	Complete intestinal obstruction	Intestinal obstruction. Concomitant use of potent CYP3A4 Inhibitors is contraindicated. Caution is advised if concomitant use with moderate CYP3A4 inhibitors .	Immediately post surgery involving pelvis	Immediately post surgery involving pelvis
Notes	Nil	Can be used in those who experience colic with stimulant laxatives	Can be used in persistent partial bowel obstruction	Only to be used if constipation is felt to be due to opioids. To be taken on an empty stomach, 1 hour before or 2 hours after eating	15-30 minutes required to take effect	20-45 minutes required to take effect



COMMUNICATION AND INFORMATION

- Insufficient information about constipation and the risk of developing it is linked with a higher rate of patients developing constipation [Level 2+]
- **For this reason, patients should be offered information about constipation at the time of diagnosis, or the risk of developing constipation when medications which increase this risk (in particularly, opioids) are commenced [Level 4]**
- Currently, this information is lacking in UK practice, and in particular written information would be of benefit to give to patients about constipation [Level 3]
- **Verbal or written information on constipation should include; risk factors, advice regarding self-care, the role of laxatives in managing constipation and when to see a doctor [Level 4]**

STANDARDS

Identify and treat reversible causes of constipation where possible
[Grade D]

Patients commencing opioid therapy should be offered laxative
monotherapy [Grade D]

Bowel obstruction should be clinically excluded before treating
constipation [Grade D]

A PR examination should be undertaken before giving rectal interventions
for constipation [Grade D]

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INVITED EXPERT COMMENTS



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PATIENT/CARER REPRESENTATIVE COMMENTS

No concerns raised or suggested changes

DISCUSSION POINTS

- 1-Should it be a standard that a laxative should be started when an opioid is commenced even though there is no evidence?
- 2-Should we set a frequency of review in the guideline, i.e. “Oral laxatives should be reviewed every 3-4 days until constipation has resolved in an inpatient setting.”
- 3- Do we want macrogol or co-danthramer as level 4 evidence in the guideline and in the flow diagram- if so, where?