

DRUG UPDATE

No. 64

March 2009

LAXATIVE USE IN PALLIATIVE CARE

Constipation is a common and often debilitating problem in palliative care and laxative treatment is frequently required. A fully optimised combination of stimulant and softening laxative agents is often the most appropriate option for chronic constipation in palliative care, while macrogols and dantron may be less suitable, and bulk-forming laxatives should be avoided. Regular laxative therapy should always be prescribed for patients receiving strong opioid analgesics. Methylnaltrexone should be restricted to palliative care specialists for exceptional use when maximal conventional laxative therapy is ineffective.

Background

Chronic constipation is very common in patients with advanced illness and can markedly impair quality of life. It is usually caused by a variety of compounding factors relating to lifestyle (e.g. immobility), disease (e.g. sub-acute obstruction, ileus) or medication (e.g. opioids).¹⁻³ Increasing dietary fibre and exercise are rarely appropriate options in palliative care,^{2,3} and constipation usually requires treatment with laxatives.

What is the rationale for laxative use?

Constipation can cause significant pain and discomfort, and may lead to complications, such as faecal impaction or incontinence.² Appropriate laxative therapy can be highly effective for treating the symptoms of constipation and maintaining satisfactory bowel movements, defined as regular bowel action without straining, every 1-3 days.³

Although not all suitable for palliative care use, a wide range of laxatives are available, classified according to their mode of action:

- *Stimulant laxatives*, e.g. senna, bisacodyl and dantron, cause peristalsis by stimulating intestinal nerves.^{1,3,4} In palliative care, they are usually combined with softening agents.^{1,2}
- *Stool-softening agents*, e.g. docusate sodium, allow water to penetrate and soften stools.¹ Docusate also acts as a mild stimulant agent.^{1,5}
- *Osmotic laxatives*, e.g. lactulose and macrogols such as Movicol®, act by increasing the amount of fluid in the large bowel, thus promoting peristalsis.^{1,5} Some osmotic laxatives also possess stool-softening properties.¹
- *Bulk-forming laxatives*, e.g. ispaghula husk, act by retaining fluid within the stool to increase faecal mass and promote peristalsis.^{1,5} The full effect may take some days to develop.⁵ Some bulk-forming laxatives also possess stool-softening properties.¹

Why does laxative therapy fail?

Due to the wide variety of laxatives available and the lack of defined treatment regimens, therapy can be complex, costly and sometimes sub-optimal. Unsuccessful treatment for constipation in palliative care can be due to:

- Failure to fully optimise treatment, or maximally titrate the laxative dose, as required.⁶
- Failure to use a combination of laxatives.⁶
- Failure to allow sufficient time e.g. 72 hours, for some laxatives to become effective.

- Failure to administer laxatives regularly, rather than 'as required'.
- Failure to recognise progression of underlying disease, ileus or faecal obstruction.⁶

Is there any clinical evidence to facilitate laxative choice in palliative care?

Laxatives should be prescribed following guidelines^{1-3,7} and adjusted according to individual patient need. There are minimal data available from clinical trials to suggest that one laxative treatment is superior to another in palliative care, and the majority of studies available only compare laxatives with placebo.

A Cochrane systematic review evaluated the use of laxative therapy in palliative care and found an insufficient number of suitable studies to reach a conclusion.⁸ One trial (n = 75) found no difference between the efficacy of senna and lactulose on the mean number of defecation days.⁹ Another study (n = 51) reported a significantly higher stool frequency in patients using the combination of lactulose plus senna, compared with co-danthramer.¹⁰

Which laxatives are suitable in palliative care?

Although there are no nationally agreed guidelines, expert consensus is that a combination of laxatives can effectively treat constipation in palliative care.^{1,2,6} Typical regimens are shown in the table below. Doses should be titrated upwards every few days, and optimised according to individual patient response, to achieve comfortable defecation. It may be necessary to exceed the licensed dose and frequency of administration to achieve the required efficacy.

| Palliative care laxative combinations ^{1,2,6} (doses divided per day according to individual patient response) | | | |
|--|---------------|----------------------------------|------------------------------------|
| | Starting dose | Maintenance dose | Maximum dose |
| SENNA (tablets or syrup) | 7.5 mg | 7.5-15 mg | 15-45 mg (>30mg daily)* |
| OR | | | |
| BISACODYL (tablets) | 5 mg o.n | 5-10 mg b.d (>10mg daily)* | 10-15 mg t.d.s* |
| PLUS | | | |
| DOCUSATE (capsules) | 100 mg | 100-200 mg | 200-300 mg |
| OR | | | |
| LACTULOSE | 10 mls o.n | 10-20 mls b.d (>30 ml daily)* | 10-20 mls t.d.s (>30 ml daily)* |

* off licence dose

Macrogols may be less suitable in palliative care as patients need to drink a specified volume of liquid after reconstitution, which some patients find difficult.² In addition, care must be taken to ensure they are reconstituted with the correct volume of liquid (exactly 125 ml/sachet for Movicol®), or they are likely to be ineffective.⁶ There is no evidence that macrogols are superior to typical laxative combinations; however they may be suitable for a limited number of patients.

Bulk-forming laxatives are not usually recommended in palliative care as patients may not maintain adequate fluid intake to avoid intestinal obstruction/faecal impaction. They may cause abdominal distension and flatulence.^{1,3,5} Although only licensed for palliative care, dantron-containing laxatives are less suitable for use, as dantron can colour the urine red,^{2,3,5,6} which can be mistaken for bleeding. It can also cause severe peri-anal irritation.^{2,3,5,6} Combination preparations are generally less suitable for palliative care, as it is not possible to titrate the individual components for optimal efficacy.⁶

Opioid-induced constipation is common in palliative care;^{1,3} and patients receiving strong opioids should receive concurrent prophylactic laxative therapy.³ Methylnaltrexone was recently licensed for opioid-induced constipation in palliative care. It requires concomitant laxative therapy, causes more side effects than laxatives alone and its long term safety has not been established.¹¹ It is relatively expensive, and has not been compared with fully optimised and maximal combination laxative regimens.¹¹ Methylnaltrexone was reviewed in a previous New Drug Evaluation which recommended that it should only be prescribed by palliative care specialists, for exceptional use.¹¹

How safe are they?

With correct laxative use, adverse effects are usually minor.

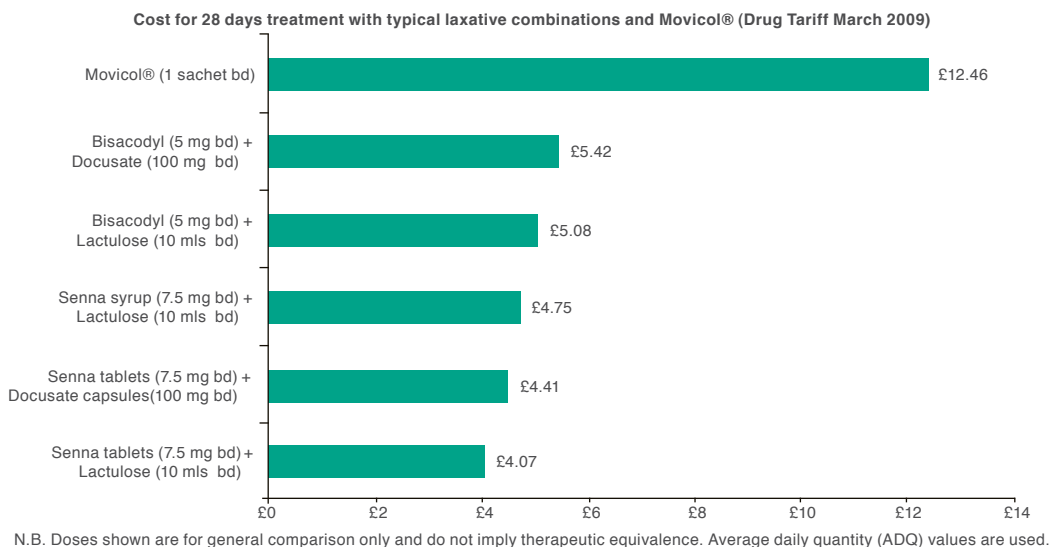
- Stimulant laxatives may cause abdominal cramps and should be avoided in cases of intestinal obstruction.⁵ Excessive use of stimulant laxatives can cause diarrhoea^{1,3,5} and hypokalaemia.⁵ Powerful stimulant laxatives such as cascara and castor oil are obsolete.⁵
- Stool-softening agents may cause diarrhoea, nausea and abdominal cramps.³ Use of the faecal softener liquid paraffin is not supported due to the potential risk of lipid pneumonia, anal irritation, granulomatous reactions and interference with fat-soluble vitamin absorption.⁵
- The Palliative Care Formulary discourages the use of lactulose as the sole laxative due to its tendency to cause gastro-intestinal discomfort when used in large doses.³ However, when combined with a stimulant laxative, doses can be kept to levels that tend to avoid these effects.⁶
- Macrogols may cause abdominal distension, pain and nausea.^{1,3,5} Excessive macrogol use can also cause electrolyte disturbances.^{3,5}

When should they be used?

Laxatives should only be used to treat constipation once bowel obstruction, faecal impaction, painful haemorrhoids and/or local tumour have been addressed. The causes of constipation, symptom type and severity should direct treatment, and combination treatment with stimulant and softening laxatives is recommended in palliative care. Doses should be fully optimised and titrated to maximal levels to provide the required efficacy according to individual patient response.

How much does it cost?

Costs for maintenance doses of typical laxative regimens are shown in the graph below.



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KEY: G - Guidelines, RCT - randomised controlled trial, R - review

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