Laxatives or Methylnaltrexone for the Management of Constipation in Palliative Care Patients

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Objective

To assess the effectiveness of laxatives or methylnaltrexone for the management of constipation in palliative care patients.

Type of Review

A review of seven randomized, controlled trials (RCTs) with data extraction. Meta-analysis was used to provide a pool estimate effect where the data were of sufficient quality.

Relevance for Nursing

Constipation is common in palliative care because of the use of medications for pain control (particularly opioids) and because of disease-related, dietary, and mobility factors. Constipation causes considerable suffering because of the unpleasant physical symptoms. Therefore, nurses who are predominate caretakers of palliative care patients must have information relating to the most effective way to treat constipation.

Characteristics of the Evidence

The review included seven RCTs involving 616 participants. Studies were required to have investigated the effectiveness of laxatives or the opioid antagonist methylnaltrexone. No language restrictions existed, and published as well as unpublished studies were eligible for inclusion. Participants were adults receiving palliative care that were given a laxative or methylnaltrexone in any care setting either as a prophylactic or because they were constipated. Participants included patients with cancer and other long-term, progressive medical conditions. The average age of participants ranged from 61–72 years. All participants were in advanced stages of disease and were cared for in palliative care settings. Most participants had cancer with other diagnoses, including cardiovascular disease, AIDS, and dementia.

The outcome measures were reported in terms of relief from constipation, which could include:
- Change in frequency of defecation
- Ease of defecation
- Relief of systemic and abdominal symptoms related to constipation, such as improved appetite, reduction in abdominal pain and distension, and lessening of confusion
- Change in quality of life
- Use of rescue laxatives such as a rectal suppository or an enema.

Information also was collected on adverse effects including nausea and vomiting, pain, flatus, diarrhea, and fecal incontinence.

In four studies, lactulose, senna, co-danthramer, misrakasneham, and magnesium hydroxide with liquid paraffin were examined. In the remaining studies, methylnaltrexone was evaluated. None of the studies reported their results in full nor did they describe the methods to conceal random allocation.

Summary of Key Evidence

One crossover study of 51 participants evaluated the effectiveness of co-danthramer versus senna plus lactulose. The interventions were in liquid form; however, dosage information and details of data analysis were not reported in full. The study highlighted that participants receiving 80 mg or more of a strong opioid had a significantly higher stool frequency when taking lactulose plus senna than when receiving co-danthramer; however, no statistical difference existed if they were receiving a lower dose or no opioid. All participants required rescue laxatives. Diarrhea was reported in 20 of the participants (15 while on lactulose and five while on co-danthramer). Perianal soreness and burning were reported by two participants taking co-danthramer, and twice as many participants disliked the flavor of co-danthramer compared to senna and lactulose.

One unpublished crossover study of 118 participants evaluated the effectiveness of one week of magnesium hydroxide plus liquid paraffin versus one week of senna plus lactulose. Only 36% of participants completed the trial (reason not stated). A higher dose of magnesium hydroxide plus liquid paraffin was required to achieve the same frequency of bowel movements as the lactulose plus senna. All participants required rescue laxatives. In the intervention groups, one participant found the treatments intolerably nauseating and another participant taking lactulose and senna experienced gripping abdominal pain. More participants preferred lactulose plus senna.
One small study of 36 participants evaluated the effectiveness of up to 10 ml of misrakasnehem versus senna (24–72 mg) over a two-week period. No statistical difference existed among the groups in relation to satisfactory bowel movements. Participants in that trial were taking various dosages of morphine but results were not analyzed in terms of whether different opioid doses influenced the laxative results. Six participants required rescue laxatives, five of whom were in the senna group. Nausea, vomiting, and colicky pain were reported by two participants taking misrakasnehem.

One study of 75 participants evaluated the effectiveness of lactulose (10–40 mg) versus senna (12–48 mg) over four weeks. No statistical difference existed in any outcome measured between the two groups. Thirty-seven percent of participants who completed the study required combined lactulose and senna to relieve constipation.

Two studies (288 participants) evaluated subcutaneous methylnaltrexone versus a placebo. A statistically significant difference favored the intervention in rescue-free laxation four hours and 24 hours after the first dose of methylnaltrexone. No overall change occurred in baseline pain scores, although significantly more suffered from flatulence and dizziness in the intervention group. From the combined studies, 30 participants experienced adverse effects, possibly related to methylnaltrexone, such as abdominal pain, sweating, increased blood pressure, loss of consciousness, delirium, aneurysm, respiratory arrest, suicidal ideation, and hallucinations. However, the investigators considered all the adverse effects as either not related or unlikely to be related to the drug trial.

One study of 33 participants compared the effectiveness of 1 mg, 5 mg, and 12.5 mg of subcutaneous methylnaltrexone. The laxation effects were measured four hours and 24 hours after intervention dose at days 1, 3, and 5. Although the results were underpowered, statistical difference favored the higher dose for bowel movement in four hours at days 3 and 5, and at day 5 within 24 hours. No information was provided on the different opioid doses in regard to their influence on laxative results. Across all dose groups, adverse effects were similar, and the common adverse effect was abdominal pain. Two participants discontinued the trial because of an adverse effect.

Best Practice Recommendations

The review cannot provide any information on what may be the optimal laxative management of constipation in palliative care patients. No research has evaluated laxation response rate, patient tolerability, or acceptability. Some evidence exists regarding the effectiveness of methylnaltrexone compared to a placebo, but those evaluations only measured effects in the short term. In addition, safety concerns need to be investigated.

Research Recommendations

A need exists for rigorous and independent RCTs measuring standardized and clinically relevant outcomes in a clearly defined population to establish the effectiveness of laxatives and opioid antagonists in the management of constipation in palliative care patients.

Bibliography


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