**Review: Good evidence supports polyethylene glycol and tegaserod for constipation**


**Clinical impact ratings:** GIM/FP/GP ★★★★★✩✩  Hospitalists ★★★★★✩✩  Gastroenterology ★★★★★✩✩

**Question**
How effective and safe are various medical therapies in patients with chronic constipation?

**Methods**
Data sources: MEDLINE (1966 to 2004) and bibliographies of relevant studies and reviews.

Study selection and assessment: Randomized controlled trials (RCTs) that compared medical therapies with placebo or compared 2 separate agents in adults with constipation. Quality assessment of individual studies was done using a 5-point scale (5 = highest quality) and included randomization procedure, allocation concealment, blinding, and completeness of follow-up.

Outcomes: Stool frequency, stool consistency, straining, use of additional laxatives, ease of defecation, and side effects.

**Main results**
The agents evaluated were osmotic laxatives (e.g., polyethylene glycol [PEG], lactulose, milk of magnesia, and sorbitol), irritant and stimulant laxatives (e.g., senna and bisacodyl), bulk laxatives (e.g., psyllium [ispaghula], methylcellulose, bran, celadine, and aloe vera), softening or wetting agents (e.g., docusate and poloxalkol), and other agents (e.g., misoprostol, cisapride, colchicine, and tegaserod). Levels of evidence (good, fair, and poor) and classifications of recommendations (A [good evidence supports], B [moderate evidence supports], C [poor evidence supports], D [moderate evidence against], and E [good evidence against]) were assigned to each drug or drug class. The Table summarizes the results of the trials that had sufficient evidence to make a recommendation. Good evidence supports the use of PEG and tegaserod, and moderate evidence supports the use of lactulose and psyllium. Most side effects did not preclude use of the agents.

**Conclusion**
In patients with constipation, good evidence exists to support the use of polyethylene glycol and tegaserod and moderate evidence supports the use of lactulose and psyllium.

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For correspondence: Dr. S.S. Rao, University of Iowa Carver College of Medicine, Iowa City, IA, USA. E-mail satish-rao@uiowa.edu.

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**Randomized controlled trials (RCTs) of medical therapies for constipation**

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Drug</th>
<th>Number of RCTs</th>
<th>Level of evidence and recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmotic laxatives</td>
<td>Polyethylene glycol</td>
<td>8 (5 placebo-controlled)</td>
<td>Good evidence supports use; better than lactulose</td>
</tr>
<tr>
<td></td>
<td>Lactulose</td>
<td>11 (3 placebo-controlled)</td>
<td>Moderate evidence supports use</td>
</tr>
<tr>
<td>Bulk agents</td>
<td>Psyllium</td>
<td>9 (3 placebo-controlled)</td>
<td>Moderate evidence supports use</td>
</tr>
<tr>
<td></td>
<td>Calcium polycarbophil</td>
<td>1 (vs psyllium)</td>
<td>Poor evidence for or against use</td>
</tr>
<tr>
<td></td>
<td>Bran</td>
<td>4 (1 placebo-controlled)</td>
<td>Poor evidence for or against use</td>
</tr>
<tr>
<td></td>
<td>Methylcellulose</td>
<td>1 (vs psyllium)</td>
<td>Poor evidence for or against use</td>
</tr>
<tr>
<td>Softening or wetting agents</td>
<td>Dicyt (docusate) calcium, dicyt sodium</td>
<td>4 (1 placebo-controlled)</td>
<td>Poor evidence for or against use; psyllium better</td>
</tr>
<tr>
<td>Stimulant laxatives</td>
<td>Senna</td>
<td>1 vs sodium picosulfate, 1 vs bran</td>
<td>Poor evidence for or against use</td>
</tr>
<tr>
<td></td>
<td>Bisacodyl</td>
<td>1 vs bisacatinate</td>
<td>Poor evidence for or against use</td>
</tr>
<tr>
<td>Other agents</td>
<td>Tegaserod</td>
<td>1 placebo-controlled</td>
<td>Good evidence supports use</td>
</tr>
</tbody>
</table>

**Commentary**
A plethora of prescription and over-the-counter agents are used to treat constipation. The systematic review by Ramkumar and Rao used rigorous methods to identify studies, extract data, weigh the scientific evidence, and grade the studies.

We agree with the conclusions, subject to certain caveats. First, a major shortcoming of therapeutic trials for chronic constipation is that patients were not subclassified by the underlying pathophysiologic mechanism (i.e., pelvic floor dysfunction, colonic motor dysfunction, or “simple” constipation). The effects of therapy may vary depending on the subtype (1), and biofeedback therapy may be more appropriate for patients with pelvic floor dysfunction. Second, none of these trials evaluated a “stepped-care” approach, which is frequently used to manage “simple” constipation in clinical practice (e.g., beginning with fiber supplementation and switching to or adding other agents if necessary [2]). Third, these studies primarily relied on subjective endpoints, not colonic transit. Some studies suggesting that dietary fiber increases stool weight and colonic transit were excluded from this review since they did not meet the authors’ definition of an efficacy endpoint (3). Lastly, clinicians and patients also need to consider the cost of medications, which varies widely even among grade A and B agents.

The review was inclusive with a handful of exceptions: a controlled crossover study showing that bran fiber accelerated colonic transit (4) and an original article on colchicine in constipation (5). Although the use of these agents is not generally limited by side effects, long-term use of colchicine may be associated with neuromyopathy (6).

In summary, while the evidence to support use of certain agents is strong, lack of evidence is not necessarily synonymous with no effect. It would be regrettable to throw the baby out with the bath water!

**References**