The Treatment of Chronic Constipation in Adults

A Systematic Review

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OBJECTIVE: **To evaluate whether laxatives and fiber therapies improve symptoms and bowel movement frequency in adults with chronic constipation.**

DATA SOURCES: **English language studies were identified from computerized MEDLINE (1966–1995), *Biological Abstracts* (1990–1995), and Micromedex searches; bibliographies; textbooks; laxative manufacturers; and experts.**

STUDY SELECTION: **Randomized trials of laxative or fiber therapies lasting more than 1 week that evaluated clinical outcomes in adults with chronic constipation.**

MEASUREMENTS AND MAIN RESULTS: **Two independent reviewers appraised each trial's characteristics including methodologic quality. There were 36 trials involving 1,815 persons from a variety of settings including clinics, hospitals and nursing homes. Twenty-three trials were 1 month or less in duration. Several laxative and fiber preparations were evaluated. Twenty trials had a placebo, usual care, or discontinuation of laxative control group, and 16 directly compared different agents. Laxatives and fiber increased bowel movement frequency by an overall weighted average of 1.4 (95% confidence interval [CI] 1.1–1.8) bowel movements per week. Fiber and bulk laxatives decreased abdominal pain and improved stool consistency compared with placebo. Most nonbulk laxative data concerning abdominal pain and stool consistency were inconclusive, though cisapride, lactulose, and lactitol improved consistency. Data concerning superiority of various treatments were inconclusive. No severe side effects for any of the therapies were reported.**

CONCLUSIONS: **Both fiber and laxatives modestly improved bowel movement frequency in adults with chronic constipation. There was inadequate evidence to establish whether fiber was superior to laxatives or one laxative class was superior to another.**

KEY WORDS: **constipation, treatment; laxatives; dietary fiber; bowel movement, frequency; meta-analysis.**
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Constipation is one of the most prevalent gastrointestinal complaints of Americans. It affects 1 in 50 persons and is more prevalent in elders, women, persons from lower socioeconomic levels, and African Americans. Annually, more than 2.5 million physician visits are for constipation and more than $500 million is expended for prescription and nonprescription laxatives.[1,2]

The actual indications and benefits of laxative therapies are poorly characterized. Part of this difficulty stems from varying definitions of constipation. The diagnosis is often arbitrary and is largely dependent on the patient's perception of normal bowel function. One third of patients complaining of constipation define the condition as infrequent defecation. More often, their definition involves straining at stool (52%), passing hard stools (44%), and inability to defecate when desired (34%).[1]

Whereas patients chiefly identify constipation on the basis of symptoms, health care professionals often define constipation in terms of bowel movement frequency. Surveys in the western world show that bowel movement patterns follow a Gaussian distribution with more than 90% of persons having between three bowel movements per day and three per week.[3–6] As this is an objective measure that is easy to determine, health care providers often define constipation as fewer than three bowel movements per week.

Compounding the difficulty in defining constipation is the fact that its underlying pathophysiology is complicated. In the past, it was thought that constipation was due solely to the slowing of the gut in passing fecal material. Transit studies using radiopaque markers demonstrated that transit times in patients complaining of constipation may actually be slow, normal, or fast.[1] Growing evidence suggests that constipated patients with normal or fast transit times may suffer from discoordinated pelvic muscle activity. Anorectal manometric studies in such patients show a paradoxical contraction of pelvic muscles during the defecatory process and alterations of the anorectal inhibitory reflex.[1]

Regardless of the ambiguity of defining constipation, patients frequently perceive a need for treatment. The use of purgatives and enemas dates back to antiquity when the ancient Egyptians, Sumerians, Chinese, Hindus, Greeks, and Romans used prophylactic treatments to cleanse themselves of impurities and disease. Many people still espouse the notion that periodic bowel cleansing to remove toxins that might be absorbed into the body is part of good health. This notion is perpetuated by advertising portraying "regularity" as the secret to health and well-being.[7,8] Others may believe that their symptoms of straining, abdominal pain, and inability to defecate when

desired are likely to be ameliorated by laxatives and that laxatives have no serious adverse effects.

Given that constipation is a symptom and its presence and severity are often a matter of perception, how can patients and their health care providers determine rational therapy? The purpose of this systematic review is to provide patients and their clinicians with accurate information to aid their therapeutic decisions. Specifically, the following question is addressed: Do laxatives or dietary fiber improve symptoms and bowel movement frequency in adult persons with chronic constipation?

METHODS

Trial Identification

Trials examining laxative or dietary fiber treatment of chronic constipation from 1966 to 1995 were identified by a computerized search using MEDLINE. Search terms included constipation or defecation or feces-impacted or fecal incontinence and dietary fiber or laxative. The following search headings for generic names were used to identify trials using laxatives: acrylic resins, bisacodyl, cascara, castor oil, cathartics, cisapride, dioctyl sulfosuccinates, enema, glycerin, lactulose, magnesium citrate, magnesium compounds, magnesium hydroxide, magnesium sulfate, methylcellulose, mineral oil, phenolphthaleins, phosphates, polyethylene glycols, psyllium, senna, sodium phosphate, and sorbitol. Trade names of laxatives identified from *Drug Facts and Comparisons*,[9] *Martindale's*,[10] and *Index Nominum*[11] were also used as search terms.

The above search was supplemented by computerized searching of *Biological Abstracts*[12] and a drug information service.[13] Bibliographies from identified articles and textbooks on medical therapeutics and gastroenterology were searched. Laxative manufacturers in North America and experts (authors of journal articles and textbook chapters) were contacted. Searches were limited to English language articles on adult humans.

Trial Selection

Titles and abstracts of 733 articles identified by all of the search methods were reviewed by at least two independent reviewers. At the initial screen, 620 were excluded because they were not controlled trials of therapeutic interventions of chronic constipation in adults, involved surgical interventions, or were limited to special populations such as peripartum or tube-fed patients. The full text of the remaining 113 articles was read by two independent reviewers. Of these, 77 were excluded because they were not randomized controlled trials (n = 57); did not meet a minimum 2-week duration for chronic constipation (n = 2); did not evaluate treatment for at least 1 week (n = 3); did not assess clinical outcomes such as bowel movement frequency, consistency, or symptoms (n = 5); were duplicate reports (n = 5)[14–18]; or were available only in abstract form (n = 4). The latter four studies, which involved a total of 68 patients, were not obtainable as full reports,[19–22] and it was unclear whether one was randomized.[22] Finally, one unpublished trial that was identified from a bibliographic reference was not released by the sponsoring pharmaceutical company; it was unclear whether this trial was randomized.[23]

Data Abstraction

The 36 trials that met eligibility criteria were abstracted by two independent reviewers for information relevant to study populations, interventions, outcomes, and design.[24–59] Methodologic quality was assessed using a six-item scale addressing reported inclusion and exclusion criteria, randomization method, standardized assessment of adverse effects, double-blind design, description of withdrawals, and statistical analysis.[60] Each item was ranked as met or not met, except randomization and double-blind design were ranked as met and appropriately described, only stated, or not met. Total quality scores ranged from 1 to 8 with higher scores denoting higher quality. Reviewers disagreed on 6% of the quality assessment items (interrater reliability coefficient, 0.88). Disagreements were resolved by consensus.

Analysis

When authors did not report tests of significance for between-group comparisons, significance values were calculated with a χ^2 test for proportional data and Student's t-test for continuous data. Data concerning differences in bowel movement frequency and standard error (SE) of the difference between group means were combined across studies by weighting each study's reported values by sample size.[61] The composite SE for the weighted difference between group means was computed by taking the square root of the sum of the weighted standard variances for each study.[62] If the SE of the difference between group means for a trial was not reported, it was calculated from the standard deviations of the group means. If the standard deviations were not reported, the SE was back-calculated from reported significance values. Computations were not weighted by quality scores of studies.

RESULTS

Laxative Therapies

Twenty-five different laxative or dietary fiber therapies for chronic constipation were evaluated in the 36 randomized trials. Multiple types of therapies were studied: osmotically active agents such as lactulose and magnesium salts, irritants or stimulants such as bisacodyl, bulk-producing agents such as psyllium and dietary bran supplementation, surfactants such as docusate, combination preparations, and other agents such as cisapride. The mechanisms and sites of action of the different therapy classifications are listed in Table 1. Most are available

as oral preparations, though some rectal preparations are also available. In the 21 trials evaluating bulk-forming laxative or dietary bran supplementation, the amount supplemented ranged from 0.5 to 24 g per day. The equivalent amount of fruits, vegetables, or cereal would range from a one-fourth serving to 12 servings per day. Generally, a single dose of a commercially available fiber supplement is equivalent to one serving of fruit, vegetable, or cereal.

Trial Participants and Settings

Most of the 1,815 subjects in the 36 identified trials were entered into the trials because they had "chronic constipation requiring laxative agents."[24–59] The actual duration of chronic constipation was not given in 20 trials, was longer than 1 month in eight trials,[36,37,39,41,42,48,51,55] and was longer than 1 year in eight trials.[28,31,33,38,40,53,58,59] Thirty-seven percent of the participants were described as having fewer than three bowel movements per week, which was a stated entry criterion in 15 trials.[24,32,35–37,40,43,45,48,51,53–56,59] Specific symptoms of constipation such as straining, passing hard stools, abdominal pain, and inability to defecate when desired were used as part of the entry criteria in nine trials involving 277 persons.[24,32,33,35,38,41,42,53,59] Whether the constipation was secondary to motility dysfunction or pelvic floor dysfunction was only stated in three trials.[31,32,38] One small trial involved 10 persons with pelvic floor dysfunction,[32] and two others involved 37 persons with motility dysfunction.[31,38]

Approximately 40% of trial participants were more than 60 years of age and 70% were women. The socioeconomic background and race were rarely given. Fifty-eight percent of participants were outpatients, 33% were nursing home residents, and 8% were hospitalized. Three of the outpatient studies were limited to special populations: two involved 35 persons with irritable bowel syndrome,[28,42] and the other studied 10 persons with diverticular disease.[24] Trials were conducted in Great Britain and western continental Europe (n = 16), the United States and Canada (n = 12), Scandinavia (n = 5), Australia (n = 1), Israel (n = 1), and Mexico (n = 1).

Design Characteristics of Trials

Of 36 trials, 20 compared single active agents such as laxatives or fiber to a placebo, controlled diet, or discontinued therapy (Table 2). Sixteen trials were direct comparisons between active agents (Table 3). In 20 trials, laxatives or enemas other than those being evaluated were allowed according to the patients' or providers' discretion (Tables 4 and 5). Twenty-three trials followed participants for 1 month or less; six followed them for 3 months or longer. Dropout rates ranged from 0% to 60%, with 19 trials having less than 20%. Quality scores ranged from 1 to 7, with 12 trials having scores of 5 or higher. Most studies with lower quality scores failed to use standardized methods for assessing adverse effects and inadequately described inclusion criteria, dropouts, and statistical methodology.

Bowel Movement Frequency Results

Thirteen of 20 studies evaluating single agents showed that those agents caused increases in bowel movement frequency that were statistically significant compared with control groups (Table 4). These studies were conducted in multiple settings including nursing homes, hospitals, and outpatient clinics. Four studies

Table 1. Classification of Laxative Therapies

Class	Examples	Site of Action	Mechanism of Action
Osmotic	Magnesium hydroxide (saline osmotic) Lactulose Sorbitol	Small and large intestine	Attract/retain water in intestinal lumen increasing intraluminal pressure
Irritant or peristaltic stimulant	Senna Bisacodyl Danthron Cascara	Colon	Direct action on mucosa, stimulates myenteric plexus, and alters water and electrolyte secretion
Bulk or hydrophilic	Plantain derivatives Methylcellulose Psyllium Ispaghula Dietary bran Celandin Alovera	Small and large intestine	Holds water in stool and mechanical distention
Surfactant or softener or wetting agents	Docusate Poloxalkol	Small and large intestine	Softens stool by facilitating admixture of fat and water to soften stool
Other	Cisapride	Small and large intestine	(Prokinetic) Stimulates motility of the lower gastrointestinal tract

Table 2. Characteristics of Trials Evaluating Single Active Agents

Source	*n*	Age (years)	Population	Treatment	Agent Class	Comparison	Duration (weeks)	Dropouts* (%)	Quality Score	Double-Blind
Ewerth et al.[24]	10	68	Diverticuli	Psyllium husks 6 g BID	Bulk	Placebo	8	10	3	Only stated
Fenn et al.[25]	201	49	Outpatient	Ispaghula 3.6 g TID	Bulk	Placebo	2	9	5	No
Rajala et al.[26]	51	>60	Hospital	Yogurt + bran 150 ml BID	Bulk	Yogurt	2	33	4	Described
Finlay[27]	12	80	Nursing home	Bran 1.5 g QD	Bulk	Regular diet	6	33	3	No
Odes and Madar[28]	35	55	Irritable bowel	†Kal-Keva 500 mg QD	Bulk	Placebo	4	9	6	Described
Capra and Hannan-Jones[29]	37	40	Mental unit	Fiber 7 g QD	Bulk	Regular diet	6	Not given	1	No
Mantle[30]	50	>60	Nursing home	Bran 0.5–1.5 g QD	Bulk	Regular diet	13	26	1	No
Badiali et al.[31]	29	37	Outpatient	Bran 6.6 g TID	Bulk	Placebo	4	34	7	Described
Cheskin et al.[32]	10	>60	Outpatient	Psyllium 6 gm QID	Bulk	Placebo	4	30	4	No
Stern[33]	25	71	Nursing home	‡Prucara 2 tabs BID	Irritant	Placebo	3	Not given	3	Described
Wesselius-de Caparis et al.[34]	103	>60	Not given	Lactulose 15 ml QD	Osmotic	Placebo	3	Not given	3	Described
Sanders[35]	45	85	Nursing home	Lactulose 30 ml QD	Osmotic	Placebo	12	22	3	Only stated
Bass and Dennis[36]	24	28	Outpatient	Lactulose 60 ml QD	Osmotic	Placebo	1	0	4	Only stated
Vanderdonckt et al.[37]	43	84	Nursing home	Lactitol 20 gm QD	Osmotic	Placebo	4	2	6	Only stated
Klauser et al.[38]	8	46	Outpatient	Propylethylene glycol 4000	Osmotic	Placebo	6	Not given	2	No
Hyland and Foran[39]	40	>60	Hospital	Docusate sodium 100 mg TID	Surfactant	Placebo	4	60	4	Described
Muller-Lissner[40]	126	51	Outpatient	Cisapride 20 mg BID	Other	Placebo	8	8	6	Described
Verheyen et al.[41]	47	50	Outpatient	Cisapride 5 mg TID Cisapride 10 mg TID	Other	Placebo	12	4	5	Only stated
Van Outryve et al.[42]	72	48	Irritable bowel	Cisapride 5 mg TID	Other	Placebo	12	4	7	Described
Muller-Lissner[43]	119	43	Outpatient	Cisapride 20 mg BID	Other	No treatment	12	Not given	2	Only stated

**No significant difference between any groups in dropouts.*
†*Kal-Keva is celandin + alovera + psyllium.*
‡*Prucara is prune concentrate 162 mg + Cascarin 162 mg/tablet.*

showed active agents led to increased frequency that was not statistically significant,[27,29,32,41] while one showed a nonsignificantly decreased frequency with active agent,[24] and two did not assess bowel movement frequency.[33,34] Combining the 13 single-agent trials with available mean frequency data showed the average weighted increase in bowel frequency per week with laxatives or fiber was 1.4 (95% CI 1.1–1.8). Average bowel movement frequencies per week for treatment and control groups were 5.0 and 3.5, respectively. The six trials with data on mean frequency that evaluated bulk laxatives or dietary fiber showed an average weighted increase of 1.4 (95% CI 0.6–2.2) bowel movements per week, whereas the seven trials with data on mean frequency that evaluated laxative agents other than bulk showed an increase of 1.5 (95% CI 1.1–1.8) bowel movements per week.

Three studies directly compared fiber with nonbulk laxatives (Table 3). A multicenter trial involving 112 patients attending general practitioner clinics showed fiber (ispaghula) increased bowel movement frequency nonsig-

Table 3. Characteristics of Trials Comparing Active Agents

Source	*n*	Age (years)	Population	Treatment 1	Agent Class	Treatment 2	Agent Class	Duration (weeks)	Dropouts* (%)	Quality Score	Double-Blind
McCallum et al.[44]	27	50	Psychiatric hospital	Unrefined bran 10 g QD Bran biscuits 10 g QD	Bulk	Senna syrup 10 ml QD	Irritant	3	15	2	No
Graham et al.[45]	10	26	Outpatient	Corn bran 10 g BID	Bulk	Wheat bran 10 g BID	Bulk	2	Not given	2	No
Pers and Pers[46]	20	83	Hospital	†Agiolax 1 sachet QD	Bulk + irritant	†Lunelax 1 sachet QD	Bulk + Irritant	2	5	3	No
Borgia et al.[47]	26	52	Not given	Ispaghula 5.5 g BID	Bulk	†Herb mixture BID	Other	2	23	1	No
Marlett et al.[48]	42	26	Outpatient	Psyllium 7.2 g QD	Bulk	Psyllium 6.5 g + senna 1.5 g QD	Bulk + irritant	1	5	3	No
Bass et al.[49]	72	18–76	Outpatient	Calcium polycarbophil 2 g QD	Bulk	Psyllium 6.8 g QD	Bulk	3	6	2	No
Chokhavatia et al.[50]	42	55–81	Outpatient	Calcium polycarbophil 2 g QD	Bulk	Psyllium 9.5 g QD	Bulk	3	7	3	No
Hamilton et al.[51]	59	27	Outpatient	Methylcellulose 1–4 g QD	Bulk	Psyllium 3.4 g QD	Bulk	1.5	Not given	5	Described
Kinnunen and Salokannel[52]	64	81	Nursing home	Magnesium hydroxide 20 ml QD	Osmotic	†Laxamucil 9 g QD	Bulk + osmotic	8	5	3	No
Lederle et al.[53]	31	72	Nursing home, outpatient	Lactulose 30 ml QHS	Osmotic	Sorbitol 30 ml QHS	Osmotic	4	3	6	Described
Rouse et al.[54]	112	50	Outpatient	Lactulose 15 ml BID	Osmotic	Ispaghula 3.5 g BID	Bulk	4	18	5	No
Kinnunen et al.[55]	30	82	Nursing home	Lactulose 30 ml QD	Osmotic	†Agiolax 20 ml QD	Bulk + irritant	5	20	4	No
Passmore et al.[56]	77	83	Nursing home	Lactulose 15 ml BID	Osmotic	†Agiolax 10 ml QD	Bulk + irritant	2	Not given	6	Described
Williamson et al.[57]	40	76	Nursing home	†Dorbanex 10 ml QD	Surfactant + irritant	Sodium picosulphate 20 ml QD	Irritant	2	5	2	No
Fain et al.[58]	47	82	Nursing home	Docusate sodium 100 mg QD Docusate sodium 100 mg BID	Surfactant	Docusate calcium 240 mg QD	Surfactant	3	2	3	No
Hernandez et al.[59]	29	35	Outpatient	Cisapride 5 mg TID	Other	Cisapride 10 mg TID	Other	16	13	5	Only stated

**No significant difference between any groups in dropouts.*

†*Combination therapies: Agiolax is plantaginis ovata 2.6 g + ispaghula 0.11 g + senna 0.62 g; Lunelax is ispaghula 3.3 g + senna 25 mg; herb mixture is Boldo 125 mg + Alder buckthorn 125 mg; Laxamucil is plantain 800 mg/g + sorbitol 190 mg/g; Dorbanex is danthron + poloxalkol.*

nificantly compared with an osmotic laxative (lactulose).[54] One study involving 26 patients showed a nonsignificant increase in frequency with ispaghula compared with an herb mixture; and another study of 27 hospitalized psychiatric patients showed no differences between two preparations of bran and an irritant laxative (senna).[44,47]

Five of 16 direct comparisons demonstrated that one agent was significantly superior to another in improving

Table 4. Outcomes of Trials Evaluating Single Active Agents

Source	Treatment	Comparison	Mean Bowel Movement Frequency Per Week		Intergroup Comparison†	Overall Symptom Improvement†	Break-through Laxatives†	Stool Consistency†	Less Abdominal Pain†
			Treatment	Comparison					
Ewerth et al.[24]	Psyllium	Placebo	6.9	7.1	−				+
Fenn et al.[25]	Ispaghula	Placebo	7.0 [median]	4.5 [median]	+*	+*		+*	+
Rajala et al.[26]	Yogurt + bran	Yogurt	5.8	4.5	+*	+	+		+
Finlay[27]	Bran	Regular diet			+		+*	+	
Odes and Madar[28]	‡Kal-Keva	Placebo	7.9	4.3	+*	+*	+	+*	+
Capra and Hannan-Jones[29]	Fiber	Regular diet	3.8	3.6	+		+	+*	
Mantle[30]	Bran	Regular diet			+*		+		
Badiali et al.[31]	Bran	Placebo	6.4	5.1	+*		+		+
Cheskin et al.[32]	Psyllium	Placebo	9.1	5.6	+			+	
Stern[33]	‡Prucara	Placebo				+			
Wesselius-de Caparis et al.[34]	Lactulose	Placebo					+*		
Sanders[35]	Lactulose	Placebo	4.9	3.6	+*		+		+
Bass and Dennis[36]	Lactulose	Placebo	4.5	2.8	+*			+*	−*
Vanderdonckt et al.[37]	Lactitol	Placebo	6.9	3.6	+*		+	+*	+
Klauser et al.[38]	Propyl-ethylene glycol	Placebo	11 [median]	3 [median]	+*	+*	+*		
Hyland and Foran[39]	Docusate sodium	Placebo	3.3	2.5	+*	+*			
Muller-Lissner[40]	Cisapride	Placebo	3.0	1.5	+*	+*	+*	+*	
Verheyen et al.[41]	Cisapride 5 mg	Placebo	3.9§	3.0	+	+*	+	+*	−
Verheyen et al.[41]	Cisapride 10 mg	Placebo	3.7	3.0	+	+*	+	+	−
Van Outryve et al.[42]	Cisapride	Placebo			+*‖	+*		+*	+*
Muller-Lissner[43]	Cisapride	No treatment	5.2	4.1	+*	+*	+*		

**Significant at* $p < .05$ *level.*

†*A "+" indicates treatment superior to comparison; "−" indicates treatment inferior to comparison.*

‡*Combination therapies: Kal-Keva is celandin + alovera + psyllium; Prucara is prune concentrate 162 mg + cascarin 162 mg/tablet.*

§*5-mg arm not included in the summary results of mean bowel movement (BM) frequency.*

‖*Compared number of days with BM (as opposed to BM frequency per time period).*

bowel movement frequency. One showed magnesium hydroxide, an osmotic laxative, increased frequency compared with a combination laxative containing a very small dose of sorbitol (osmotic) plus fiber.[52] This trial involved 64 nursing home patients and was not double-blind. Another single-blind trial among outpatients showed an irritant laxative (senna) combined with fiber (psyllium) increased bowel movement frequency more than fiber alone.[48] Two trials,[55,56] one of which was double-blind,[56] showed a combination of irritant (senna) plus bulk increased stool frequency more than an osmotic agent (lactulose). Finally, an unblinded trial of 42 outpatients comparing two bulk laxatives reported psyllium increased frequency more than calcium polycarbophil.[50]

Seven trials evaluated bowel frequency for 1 to 4 weeks after discontinuation of interventions.[26,29,34,35,40,41,43] All showed decreased frequency with discontinuation of therapy.

Breakthrough Laxative Use

Several trials allowed use of nonstudy laxatives (i.e., breakthrough laxatives) when study regimens were not successful. The 13 trials evaluating single agents that gave data on breakthrough laxatives showed less non-

Table 5. Outcomes of Trials Comparing Active Agents

Source	Treatment 1	Treatment 2	Mean Bowel Movement Frequency Per Week			Overall Symptom Improvement†	Break-through Laxatives†	Stool Consistency†	Less Abdominal Pain†
			Treatment 1	Treatment 2	Intergroup Comparison†				
McCallum et al.[44]	Bran	Senna	2.4	2.7	2		1	0	
McCallum et al.[44]	Bran biscuits	Senna	2.2	2.7	2		2	0	
Graham et al.[45]	Corn bran	Wheat bran	4.6	3.2	1	1*			
Pers and Pers[46]	‡Agiolax	‡Lunelax			2				
Borgia et al.[47]	Ispaghula	‡Herb	5.1	4.7	1				
Marlett et al.[48]	Psyllium	Psyllium + senna	3.6	6.8	2*	2		2*	
Bass et al.[49]	Calcium poly-carbophil	Psyllium	8.3	8.7	2			1	
Chokhavatia et al.[50]	Calcium poly-carbophil	Psyllium	8.3	9.1	2*			2	
Hamilton et al.[51]	Methyl-cellulose 1 g	Psyllium	4.1§	4.1§	0				
Hamilton et al.[51]	Methyl-cellulose 2 g	Psyllium	3.6§	4.1§	2				
Hamilton et al.[51]	Methyl-cellulose 4 g	Psyllium	4.8§	4.1§	1				
Kinnunen and Salokannel[52]	Magnesium hydroxide	‡Laxamucil	3.3	2.6	1*		1*	1*	
Lederle et al.[53]	Lactulose	Sorbitol	7.0	6.7	1	1	1	1	2
Rouse et al.[54]	Lactulose	Ispaghula	6.6§	7.8§	2	1		2	1
Kinnunen et al.[55]	Lactulose	‡Agiolax	2.2	4.5	2*		2	2	
Passmore et al.[56]	Lactulose	‡Agiolax	4.2	5.6	2*			2*	0
Williamson et al.[57]	‡Dorbanax	Sodium pico-sulfate	6.0	6.7	2	2	2	1*	0
Fain et al.[58]	Docusate sodium QD	Docusate calcium	2.0	2.8	2		2	0	
Fain et al.[58]	Docusate sodium BID	Docusate calcium	2.3	2.8	2		2	0	
Hernandez et al.[59]	Cisapride 5 mg	Cisapride 10 mg	4.4§	5.5	2		2	0	2

**Significant at* $p < .05$ *level.*

†0 indicates no difference between groups or direction not reported; 1 indicates treatment 1 superior to treatment 2; 2 indicates treatment 2 superior to treatment 1.

‡Combination therapies: Agiolax is plantaginis ovata 2.6 g + ispaghula 0.11 g + senna 0.62 g; Lunelax is ispaghula 3.3 g + senna 25 mg; herb mixture is Boldo 125 mg + alder buckthorn 125 mg; Laxamucil is plantain 800 mg/g + sorbitol 190 mg/g; Dorbanex is danthron + poloxalkol.

§Values estimated from graphical presentation of data.

study laxative use by participants assigned to active therapy (Table 4). One direct comparison showed significantly less breakthrough laxative use with magnesium hydroxide compared with the combination of sorbitol and fiber.[52]

Symptoms

Eight of 10 trials of single active agents that assessed overall improvement in symptoms showed fiber or laxatives significantly improved symptoms compared with pla-

cebo (Table 4). The other two trials showed nonsignificant benefits with treatment, with one trial bordering on statistical significance ($p = .09$).[26] Symptom improvement was assessed differently in the trials. Two used scales that assessed multiple dimensions such as stool consistency and pain,[33,42] and eight used either a visual analogue scale or a single question to subjectively assess whether constipation was improved.

Stool consistency was most often evaluated in trials that involved fiber, bulk laxatives, or cisapride. Consistency was improved with treatment in 10 of these trials, though two of the comparisons were nonsignificant. Most trials evaluating fiber or bulk laxatives showed decreased abdominal pain with active therapy, although none of these comparisons was significant. Of four trials that assessed abdominal pain with nonbulk laxatives, two showed significant differences. One showed lactulose increased abdominal pain compared with placebo,[36] while one showed cisapride decreased abdominal pain.[42]

Two trials comparing bulk plus senna showed the combination improved stool consistency significantly better than either lactulose or bulk alone.[48,56] One unblinded trial showed magnesium hydroxide improved consistency more than the combination of bulk plus osmotic.[52] Another trial showed dorbanex (surfactant plus irritant) resulted in improved consistency compared with laxoberal (irritant).[57] Only one trial showed a significant decrease in the number of fecal impactions among nursing home residents with lactulose compared with placebo,[35] but most trials ($n = 34$) did not evaluate this outcome.

General Well-being

Two trials comparing lactulose with either sorbitol or ispaghula (fiber) evaluated general well-being outcomes.[53,54] Neither showed significant differences between groups. No studies evaluated depression outcomes.

Adverse Effects

Few studies used standardized techniques for assessing adverse effects. As stated above, most that assessed symptoms such as abdominal pain did not suggest that fiber or laxatives increased pain. The studies of nursing home residents that assessed electrolytes did not demonstrate any marked abnormalities. Megacolon and pseudoobstruction were not reported.

DISCUSSION

Available data regarding the efficacy of laxatives and fiber in treating chronic constipation are limited. Many of the randomized trials are limited by relatively short study durations, methodologic flaws, and lack of comprehensive, clinically relevant outcomes. Studies have used varying criteria for chronic constipation reflecting general ambiguity in its definition. Most study participants perceived their chronic constipation severe enough to require laxatives. Different types of patients in a variety of settings with a variety of complaints have been studied. Although studies did not evaluate whether particular therapies are better in certain situations than others, both laxatives and fiber have been shown beneficial in multiple patient groups and settings. Thus, results are most likely generalizable to many of the patients complaining of constipation seen by clinicians.

Laxatives and fiber consistently increased bowel movement frequency compared with placebo. The average increase was approximately one and a half bowel movements per week. Two trials showed bulk in combination with senna was superior to lactulose.[55,56] Other direct comparisons between different laxatives or laxatives and fiber were inconclusive because of the limited number of studies, small sample sizes, or methodologic flaws. There were no definitive data that suggested fiber increased frequency more than laxatives or vice versa. More randomized trials directly comparing these treatments are needed before reaching conclusions.

Fiber (dietary or bulk laxatives) consistently decreased abdominal pain and improved stool consistency compared with placebo, though many of these comparisons were not significant, perhaps owing to small sample size. There were few data regarding nonbulk laxatives and abdominal pain. Cisapride, lactulose, and lactitol improved stool consistency, but data regarding other laxatives were scant. Whether fiber or laxatives consistently prevented severe effects of constipation such as impaction was not established.

Whether fiber or laxatives improve quality of life or general well-being in persons with chronic constipation is not known. This is a particularly important outcome because “feeling constipated” is a perception that may contribute to a person’s overall assessment of general well-being. If therapies increase bowel movement frequency and improve stool consistency, but do not improve how people feel and their quality of life, some clinicians and patients may opt not to use them.

Clinical Implications

Whether clinicians and their patients decide to treat chronic constipation with laxatives or fiber should depend on several factors. First, the amount of discomfort, suffering, and impairment of well-being that patients perceive related to their constipation is important. Second, knowledge of risks of constipation and whether they vary depending on factors such as patient age and comorbidity is helpful. Third, physicians and their patients need to know which therapies are proved beneficial and their actual benefits. Fourth, they need reliable information about potential harms and costs of therapy. Fifth, the therapies proved beneficial must also be feasible.

This review addressed the benefits and harms of some of the available and commonly used therapies for chronic constipation: fiber and laxatives. A relative pau-

city of information was found. The available studies suggest that both fiber and laxatives are reasonable therapies if the main intent is to increase bowel movement frequency. If concerns about symptoms such as abdominal pain and stool consistency are paramount, clinicians and patients can be assured that fiber and bulk laxatives are likely to be beneficial. Information about nonbulk laxatives for these outcomes is scant and inconclusive, though cisapride, lactulose, and lactitol appear to improve stool consistency. Severe adverse effects of the therapies have not been noted, but more reliable long-term safety data for laxatives are needed. Some clinicians and patients may pause before spending money on laxatives until better information about their long-term benefits and harms is available. There are no data to help determine which specific laxatives or fiber preparations are most beneficial and least harmful for particular pathophysiologic etiologies of constipation or particular groups of patients such as nursing home residents.

Limitations of the Review

Although this review utilized an exhaustive searching strategy, it was limited to English language literature. Even though attempts were made to identify unpublished literature by contacting laxative manufacturers and experts, only one unpublished report was identified. This report was not obtainable, and other relevant unpublished data may exist. Numerous outcomes assessed in a variety of ways were used in the trials prohibiting quantitative analyses on outcomes other than bowel movement frequency. The scope of the review was limited to fiber and laxative therapies and did not evaluate other routinely recommended therapies such as exercise and education.

Future Directions

More and better information is needed in several areas relevant to laxative and fiber treatments for chronic constipation. Effects of treatments on a broader array of outcomes including general well-being and costs need to be assessed. Longer study durations are needed to determine whether treatment benefits are sustainable and potential harms such as electrolyte imbalances are avoidable. More detailed descriptions and categorizations of constipation are needed to help appropriately generalize and target results. More direct comparisons between therapies and combinations of therapies are needed. Some of these comparisons should be against other potential therapies for chronic constipation such as exercise, high fluid intake, and education about average ranges of bowel habits.

Summary Points

- Fiber and laxatives modestly increase bowel movement frequency.
- Fiber and bulk laxatives improve symptoms of constipation such as stool consistency and abdominal pain.
- Cisapride, lactulose, and lactitol improve stool consistency. There is inadequate evidence to establish whether other nonbulk laxatives improve symptoms such as consistency and abdominal pain.
- There is inadequate evidence to establish whether fiber is superior to laxatives or one laxative class is superior to another in treating constipation.
- Although there is no evidence that laxatives are unduly harmful, data are very limited and short-term.
- Whether fiber or laxative therapy for chronic constipation improves general well-being is not known.

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