Effectiveness of laxatives in adults

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This paper summarises the research evidence presented in a recent issue of *Effective Health Care* on the effectiveness of the four main types of laxatives used in the treatment of constipation in adults.¹ The bulletin was based on two systematic reviews^{2–3} (table 1) and on the additional randomised controlled trials (RCTs) identified since the publication (1997) of these reviews (tables 2 and 3).

Constipation is a common reason for GP consultations in adults. The UK National Survey of Morbidity in General Practice in England and Wales found consultations for constipation were particularly common among the very young and the very old.⁴ The prevalence is less than 10% in the UK general population,⁵ about 20% among older people living in the community,² and higher still among those living in nursing homes.⁶ About half of all patients admitted to specialist palliative care units report constipation, but about 75% of such patients will require laxatives.⁷ Laxatives are required by about 87% of terminally ill patients taking strong oral opioids, 74% of those on weak opioids, and 64% of those not receiving opioid analgesia.⁸ There also appear to be socioeconomic, sex, regional, and national differences in the prevalence of constipation.^{2–9} Constipation adversely affects the quality of life of the sufferer¹⁰ and accounts for a significant proportion of the NHS drug bill.¹¹ At over £46 million per year in England, expenditure on the four main types of laxative (bulk, osmotic, stimulant, and softener) is higher than on hypnotics and anxiolytics such as benzodiazepines.¹²

Defining constipation

A frequency of defaecation of less than three times a week has been widely used as an objective criterion for defining constipation.^{13–14}

although patients' definitions emphasise symptoms such as pain and straining rather than frequency.¹⁵ The "Rome II" diagnostic criteria for constipation, which tend to be used as inclusion criteria for laxative trials, require two or more criteria to be present for at least 12 weeks in the last 12 months in the absence of a structural or biochemical explanation.¹⁶

Risk factors for constipation

The prevalence of constipation may be increasing because modern food processing methods have produced a refined roughage-free diet.^{17–18} Dietary fibre intake is positively associated with increases in bowel movement frequency and faecal mass and reductions in bowel transit time and symptoms (for overviews see Spiller,¹⁹ Bennett and Cerda²⁰). Studies also show a lower incidence of constipation in vegetarians.^{21–22} One large population survey carried out in the USA has found that constipated adults report lower consumption of beans, peas, fruit and vegetables.²³ Frequency of consumption of fruit, vegetables, and bread declines significantly with age in UK adults.²⁴ Low calorie intake in older people (adjusted for fibre consumption) has also been implicated in the aetiology of constipation.²⁵

A meta-analysis of the effects of wheat bran which incorporated 20 comparative studies (non-randomised controlled trials) of the association between stool weight and gastrointestinal transit time found that bran supplementation resulted in increased stool weight and decreased transit time in both healthy and constipated adults.²⁶ However, in constipated patients receiving bran, stool weight remained lower than in controls, suggesting that low dietary fibre intake may not be the only factor influencing constipation.

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Table 1 Systematic reviews of effectiveness of laxatives in adult patients

Author	Inclusion criteria	Main results
NHS HTA review ²	RCTs in any language were included if all participants were 55 years or older, and were treated for chronic constipation with any oral laxative	Laxatives improve bowel movement frequency, consistency and symptoms in older adults. There is little evidence of differences in effectiveness between laxatives, and no good research evidence to support current NHS trends towards prescribing the more expensive stimulant laxatives
Tramonte <i>et al</i> ³	English language RCTs of laxative or fibre therapies in constipated adults (all ages)	Laxatives and fibre increased frequency by overall weighted mean of 1.4 (95% CI 1.1 to 1.8) bowel movements per week, decreased abdominal pain and improved consistency. No clear evidence found as to superiority of various treatments

Table 2 Additional trials evaluating single laxative treatments in adults

Author (country)	Population	Intervention and length of follow up	Results	Comments and funding details
Parallel RCTs				
Ashraf <i>et al</i> (USA) ⁴¹	Ambulant patients, mean age 51 years, 64% female (n=14)	Bulk v placebo I: Metamucil (n=11) 5 g/day, C: placebo (n=11), 8 weeks	<i>Frequency</i> : I: increase in BM/week from 2.9 (0.1) to 3.8 (0.4) (p<0.05); C: no data given, estimated from graph: 2.7 v 2.9 <i>Pain score (range 1-7)</i> : I: Decreased from 2.6 (0.5) to 2.0 (0.4), p<0.05; C: slight increase (from Fig 3c): 2.7 v 2.8. No significant group differences in consistency, straining, evacuation, or side effects	Quality score: 3 Randomisation: stated Double blind Description of dropouts Funding: Proctor and Gamble
Howard <i>et al</i> (USA) ⁴²	Institutionalised men from a single care centre; mean age intervention group 73 years, mean age comparator group 74 years	Bulk v usual care I: Bran mixture: (n=6) 3 cups apple sauce, 2 cups coarse wheat bran, 1.5 cups prune juice, C: Usual care (n=6) normal diet, laxatives and enemas as needed, 4 months	<i>Frequency (BM/week)</i> : end of treatment: I=2.3 (0.39), C=2.7 (0.79) (NS) <i>Number of bowel medications/week</i> : end of treatment: I=1.39 (1.08), C=13.28 (5.68) (p=0.03). Reduction of bowel medication with bran at maximum dose (p=0.03)	Quality score: 1 Randomisation: not stated Open study Funding: not stated
Sculatti and Giampiccoli (Italy) ³¹	Ambulant patients, mean age 67.4 years, 83% female	Bulk v water I: Fibriform (n=20) 7 g/day+400 ml water, C: water (n=20) 400 ml, 30 days	<i>Overall effectiveness</i> : % non-constipated at 15 days: I=30%, C=5% p=0.09; at 30 days: I=74%, C=15% p=0.001. <i>Consistency</i> : % with soft faeces at 15 days: I=25%, C=20% p=0.9; at 30 days: I=84%, C=25% p=0.0001 <i>Painful defaecation</i> : % pain free at 15 days: I=73%, C=64% p=0.5; at 30 days: I=90%, C=67% p=0.13.	Quality score: 2 Randomisation: not stated Not blind Description of dropouts Funding: not stated
Corazziari <i>et al</i> (Italy) ⁴⁷	Outpatients, mean age 41.8 years, 77% female	Osmotic v placebo I: PMF-100 (Normopeg) (n=25) 14.6 g PEG 4000, 1.42 g anhydrous sodium sulphate, 0.42 g sodium bicarbonate, 0.18 g potassium chloride, 0.01 simethicone, flavoured, C: placebo (flavoured maltodextrine) (n=23), 4 week run in, then 8 weeks PMF-100 or placebo twice daily in 250 ml of water	<i>Frequency (BM/week)</i> : end of 4 week run in: I=2.2 (0.5), C=1.9 (0.8); end of 8 week treatment period: I=4.8 (2.3), C=2.8 (1.6). <i>Bowel frequency normalised</i> : I=64%, C=22% (p<0.008; per ITT analysis p<0.04) <i>Consistency</i> : % with hard stools: I=12%, C=50% (per ITT analysis p<0.07) <i>Use of laxatives</i> : I=16%, C=48% (p<0.03; per ITT analysis p<0.1) <i>Straining</i> : I=8%, C=41% (p<0.03). No group differences in occurrence or severity of other symptoms	Quality score: 4 Randomisation: stated Double blind Description of dropouts ITT Funding: not stated
Corazziari <i>et al</i> (Italy) ⁴⁸	Outpatients, mean age intervention group 42.4 years, mean age comparator group 43.2 years, 82.9% female	Osmotic v placebo I: PMF-100 (Normopeg) (n=33) as in Corazziari <i>et al</i> , ⁴⁷ C: placebo (flavoured maltodextrine) (n=37), 4 week run in, then 20 weeks of PMF or placebo as above	<i>Frequency (BM/week)</i> : week 4 (end of run in): I=8.3 (4.0), C=7.7 (4.3); week 12: I=7.4 (3.1), C=4.3 (2.5); week 24: I=7.4 (3.2), C=5.4 (2.1) <i>Mean consumption of non-study laxatives, previous 4 weeks</i> : week 4: I=1.1 (2.8), C=0.31 (0.74); week 12: I=0.7 (2.7), C=2.2 (3.3); week 24: I=0.2 (0.8), C=1.4 (2) <i>Mean number of drug sachets, previous 4 weeks</i> : week 4: I=38 (12) C=38 (15), week 12: I=33 (13), C=43 (12); week 24: I=33 (13), C=44 (12) <i>Number of adverse events</i> : I=57, C=41	Quality score: 4 Randomisation: stated Double blind Description of dropouts Funding: not stated
DiPalma <i>et al</i> (USA) ⁴⁹	Participants recruited from gastroenterology practices and local advertising, mean age intervention group 46.7 years, mean age comparator group 45.8 years, overall mean age 45 years, 87% female	Osmotic v placebo I: Braintree PEG 3350 (Miralax) (n=80) 17 g/day in approx 8 oz water or juice, C: dextrose powder placebo (n=71) same size scoop/day as I in 8 oz water or juice, 14 days	<i>Frequency (BM/week)</i> : week 1: I=4.2 (2.8), C=2.9 (1.9); week 2: I=4.5 (3.0), C=2.7 (1.8) <i>Treatment success (>3 BM/week)</i> : weeks 1 and 2: I=72.2%, C=49.6% (p<0.001; p<0.05 on ITT analysis). <i>Patient rated effectiveness</i> : I=68%, C=40% (p<0.001) <i>Investigator rated effectiveness</i> : I=71.4%, C=47.1% (p<0.005) <i>Other</i> : wignificant improvements in self-reported consistency, straining passage, cramping and flatus (all p=0.001)	Quality score: 3 Randomisation: stated Single blind Description of dropouts ITT Funding: Braintree Laboratories
Huys and Van Vaerenbergh (Belgium) ³³	Hospital inpatients, mean age not stated, M:F ratio not stated	Softener/stimulant v placebo I: Softener (n=15) 60 mg DSS, 50 mg 1.8-dioxanthraquinone, C: placebo (n=15), 10 days "preparation" then 20 days treatment	<i>Frequency</i> : % patients with daily stools: I: pre: 32%; post: 72%. C: pre: 33%; post: 47%. Significant group difference, no alpha stated. No difference in diarrhoea incidence	Quality score: 2 Randomisation: not stated Double blind Description of dropouts Funding: not stated
Crossover RCTs				
Marsicano (Venezuela) ⁴³	Hospital cardiology patients, mean age 40.1 years, all female	Bulk v placebo I: Glucomannan fibre 3 g/day and 4 g/day, C: placebo (n=60), 5 weeks (2 weeks washout)	<i>Frequency</i> : I: 3 g: increase of 0.47 BM/day compared with 4 g: increase of 0.83 BM/day; C: change of -0.2 to 0.1 <i>Straining</i> : 9 cases with placebo (15%), 5 (8.3%) with 3 g and 6 (10%) with 4 g glucomannan <i>Diarrhoea</i> : I: glucomannan 3 g: 6 (10%), 4 g: 5 (8.3%), placebo: 1 (2%) <i>Flatulence</i> : Glucomannan 3 g: 10 (17%), 4 g: 13 (22%), placebo: 11 (18%)	Quality score: 3 Randomisation: stated Double blind Description of dropouts Funding: not stated
Andorsky (USA) ³²	Outpatients, mean age 62 years, 76% female	Osmotic v placebo I: PEG 8 or 16 oz daily, C: placebo (n=37), 5 days (2 day washout)	<i>Frequency (BM/5 day period)</i> : I (8oz)=5.81 (3.92), C=4.36 (2.8); I (16oz): 9.56 (4.41), C=5.38 (2.44). Overall, PEG significantly more effective than placebo and 2 glasses more effective than 1. <i>Consistency score (range 1-4)</i> : PEG significantly more effective than placebo (2.6 v 1.2; p<0.05) and 2 glasses more effective than 1 (2.7 v 0.8; p<0.05). <i>Side effects</i> : Problems with cramps, gas, nausea, loose stools and taste with PEG but none resulted in termination of trial. 9/37 (24%) had transient gas/cramps.	Quality score: 2 Randomisation: stated Double blind No ITT Authors note that greater effect of 16 oz may be due to fluid intake Funding: drugs donated by Reed and Carnrick Pharmaceuticals
Castillo (Argentina) ⁶¹	Ambulant, mean age not stated, M/F ratio unclear	Osmotic v placebo I: Lactulose 30 ml/day, C: placebo, 4 weeks (2 weeks washout)	<i>Overall effectiveness</i> : Number of satisfactory or partially satisfactory treatments at 1 week: I=23, C=17 (p<0.01) at 1 week: I=22, C=8 (p<0.01) at 4 weeks <i>Adverse effects</i> : number of patients with meteorism: I=3, C=6, p not stated; flatulence: I=5, C=3, p not stated	Quality score: 1 Randomisation: not stated Double blind No ITT analysis Funding: not stated
Lemann <i>et al</i> (France) ⁵⁰	Patients with chronic constipation, mean age 48 years, 85% female	Osmotic v placebo I: PEG 3350 13-39 g/day; C: placebo (n=32)	<i>Frequency (BM/week)</i> : I: 9.4 (4.3), C:4.7 (3.4) (p<0.001) <i>Straining score (range not stated)</i> : Lower with PEG (0.7 (0.7) v 1.6 (0.7), p<0.001). <i>Overall improvement</i> : greater with PEG (score 6.4 v 1.6, p<0.001; score range not stated)	Quality score: 2 Randomisation: not stated Double blind No dropouts reported Funding: Norgine Pharma

I=intervention; C=comparator; BM=bowel movements; ITT=intention to treat; NS=not significant.

Table 3 Additional trials comparing laxative treatments in adults

Author (country)	Population	Intervention and length of follow up	Results	Comments and funding
Parallel RCTs				
Attar (France and Scotland) ⁵¹	Recruited from general and geriatric hospitals, mean age 55 years, 82% female	Osmotic <i>v</i> osmotic I: PEG 3350 low dose (n=60), mean=1.6 × 13 g sachets/day; C: lactulose (n=55), mean=2.1 sachets × 10 g /day, 4 weeks	<i>Frequency</i> (BM/day): I=1.3 (0.7), C=0.9 (0.6), p=0.005. Proportion passing <3 BM/week: I=10%, C=14% <i>Straining</i> (median score; range 0 (absence)–3 (severe)): I=0.5 (0.7), C=1.2 (0.9), p=0.0001 <i>Overall improvement</i> (VAS, range 0 (no change)–10 (excellent)): I=7.4 (2.5), C=5.2 (3.3), p<0.001 <i>Adverse events</i> : 2 in PEG group, 1 in lactulose group <i>Use of suppositories/enemas</i> : I=16%, C=34%, p=0.04 <i>Symptoms</i> : no difference in % with liquid stools, pain, bloating, flatulence, rumbling. More days with flatulence with lactulose (I=9.2 (10.1), C=3.8 (6.8)). Mean no of liquid stools higher with PEG (I=2.4 (3.5), C=0.6 (1.2), p=0.001)	Quality score: 2 Randomisation: stated Single blind No ITT analysis Funding not stated
Bobbio (Italy) ⁶²	Patients with chronic constipation, mean age 63.5 years, 63% female (n=25)	Osmotic+bulk <i>v</i> osmotic I: lactulose+glucomannan (n=20), 12 g/day (24% glucomannan, 70% lactulose); C: lactulose (n=20), 8.4 g/day, 4 weeks	<i>Frequency</i> (BM/week): I: 5.75 (0.29); C: 6.55 (0.18), p<0.05 <i>Flatulence</i> : mean change in score; range 0 (symptom absent)–2 (intense): I=–0.2, C=+0.7, p<0.01 <i>Meteorism score</i> : I=–0.1, C=0.8, p<0.001 <i>Pain score</i> : no difference between groups. <i>Tolerance score</i> (range 0 (low tolerability)–3 (optimum tolerability)): I=2.2, C=1.9, p<0.05	Quality score: 2 Randomisation: not stated Double blind No dropouts reported Funding not stated
Norgine Ltd unpublished data (China, 2001)	Hospital population, mean age intervention group 51 years, 64% female, mean age comparator group 50 years, 56% female	Osmotic <i>v</i> bulk I: PEG 3350 plus electrolytes (n=60), 13.7 g/bag twice/day; C: Konsyl (ispaghula) (n=60), 3.5 g/bag twice/day, 14 days	<i>Frequency</i> (BM/week): increase in BM at 1 week <i>baseline</i> : I=6.95 (3.46), p=0.0001, C=3.98 (2.68), p<0.0001. At 2 weeks <i>baseline</i> : I=7.48 (3.54), C=4.33 (2.40), p<0.0001. <i>Consistency</i> : % normal stools: week 1: I: 84%, C: 52%, p=0.001. Similar results for 2nd week <i>Overall efficacy</i> I: overall effectiveness rate 92.07%, C: 73%, p=0.005 <i>Adverse events</i> : I: 12%, C: 8%, p=0.5 (NS)	Quality score: 3 Randomisation: stated Unclear whether blinded Description of dropouts Funding: Norgine Ltd
Dettmar and Sykes (UK) ⁴⁵	Participants recruited by 65 GPs, mean age unclear, 63.4% female, 35.3% male, 1.3% not recorded	Osmotic <i>v</i> bulk <i>v</i> other I: ispaghula husk (Fybogel) (n=224) 3.5 g twice/day with water; C1: lactulose (n=91); C2: other prescribed laxatives (n=79) (bisacodyl (n=24), softener (n=21), senna (n=18), docusate sodium (n=13), magnesium sulphate (n=3)), 4 weeks	<i>Overall effectiveness</i> : self-reported overall effectiveness (77% excellent or good with ispaghula versus 61% lactulose, 49% other), palatability (62%, 49%, 50%), acceptability (73%, 49%, 50%), all higher with ispaghula with fewer adverse effects (all p<0.01). <i>Consistency</i> (% normal): 55% <i>v</i> 43% <i>v</i> 39% (p<0.05) <i>Speed of action</i> : no difference in onset time of first bowel movement. <i>Other symptoms</i> : lower incidence of pain and diarrhoea with ispaghula husk	Quality score: 2 Randomisation: not stated Open study Description of dropouts Funding: Reckitt and Colman
Gordin (France) ⁶³	Ambulant patients, mean age not stated, M:F ratio not stated	Osmotic+stimulant <i>v</i> osmotic I: lactulose and paraffin (n=36) 15 ml/day; C: lactulose 50% (n=36) 15 ml/day, 2 weeks	<i>Frequency</i> : patients with 1 or 2 BM/day: I=88%, C=81% (NS) <i>Overall effectiveness</i> : % patients self-reporting good or very good improvement: I=76%, C=54%, p=0.05 <i>Tolerability</i> : % patients reporting good or very good: I=70%, C=40% (p=0.01) <i>Consistency</i> : % "soft": I=61%, C=55%	Quality score: 1 Randomisation: not stated No blinding No ITT analysis Funding not stated
Hammer and Ravelli (Germany) ⁵²	Ambulant patients, mean age 54 years, 81% female	Osmotic <i>v</i> osmotic I: lactitol (Importal) (n=31), 20 g/day for 3 days, then 10 g/day for 25 days (maintenance dose); C: lactulose (Dulphalac) (n=26), initial dose 20.1 g for 3 days, then 13.4 g for 25 days, 4 weeks	<i>Frequency</i> (BM/week): I=6.7 (4.39) C=7.4 (4.48) % patients with ≥3.5 BM/week at end of study: I=82%, C=81% <i>Consistency</i> : % patients reporting "normal" or "soft" at end of trial: I=19/25 (76%), C=16/24 (67%) p=0.50 <i>Overall effectiveness and tolerability</i> : no significant difference between in I and C in terms of patients' or physicians' ratings <i>Adverse effects</i> : % reporting adverse effects: I=10/32 C=16/26 p=0.02	Quality score: 2 Randomisation: not stated Open study Description of dropouts Funding not stated
Heitland and Mauersberger (Germany) ⁶⁴	Participants were laxative users, mean age intervention group male 52 years, female 64 years, mean age comparator group male 58 years, female 65 years	Osmotic <i>v</i> osmotic I: lactitol (Importal) (n=30) mean dose 20 g/day as single dose; C: lactulose (Dulphalac) (n=30) mean dose 20 g/day as single dose (30 ml Dulphalac syrup), 2 weeks	<i>Frequency</i> (BM/day): after 2 weeks treatment: I=0.87 C=0.79 (0.05<p<0.1, NS). No significant difference in no of patient days with 1 or more bowel movements. No significant differences in consistency, side effects or other symptoms (bloating, flatulence, nausea, cramping, diarrhoea)	Quality score: 0 Quasi-randomised: (alternation) Open study Funding not stated
McRorie (USA) ⁴⁴	Ambulant patients, mean age 37 years, 92% female	Bulk <i>v</i> stimulant/softener I: psyllium (n=88) 5.1 g twice/day; C: docusate sodium (n=82) 100 mg twice/day, 2 weeks	<i>Frequency</i> (BM/week): by week 2: I=3.5 (0.22), C=2.87 (0.22), p=0.02 <i>Consistency</i> : Score on 7 point scale for each symptom (1=normal, 7=constipated, or extreme symptoms): I=3.1 (0.14), C=3.2 (0.15), p=0.29 <i>Straining score</i> : I=2.8 (0.15), C=3.1 (0.16), p=0.15 <i>Stool water content</i> : I=74%, C=72%, p=0.004 <i>Pain score</i> : I=2.04 (0.13), C=2.3 (0.14), p=0.12 <i>Evacuation incompleteness score</i> : I=2.9 (0.15), C=3.2 (0.17), p=0.04	Quality score: 3 Randomisation: stated Double blind ITT analysis Funding: Proctor & Gamble
Crossover RCTs				
Lugli <i>et al</i> (Italy) ⁶⁵	Ambulant patients, age range 26–70 years, 53% female	Bulk <i>v</i> bulk I1: methylcellulose (MC) 1 g/day; I2: wheat bran (WB) 24 g/day; I3: ispaghula (IH) 7 g/day (n=30), 7 days (with 1 week washout)	<i>Frequency</i> (mean BM/day) : IH and WB higher than MC (p<0.001); actual data not reported. IH <i>v</i> WB: no difference <i>Adverse effects</i> : no adverse events for any preparation and all well tolerated; no data on other symptoms	Quality score: 1 Randomisation: not stated Not blinded No dropouts reported Funding: not stated
Michetti (Italy) ⁵⁴	Unclear, mean age 52.4 years, 66% female	Softener+stimulant <i>v</i> softener+stimulant <i>v</i> placebo I: Drocil (50 mg DSS softener + 25 mg danthron) 100mg × 2 caps/day, C1: DSS (0.075 g)+cascara (0.05 g) + herbal ingredients, C2: placebo (n=35)	<i>Frequency</i> (BM/day): I=1.05, C1=1.26, C2=0.83 (both treatments significantly different from placebo at p<0.05) <i>Use of laxatives</i> (mean number of days): I=1.76, C1=1.73, C2=1.68 (NS) <i>Mean no of days with liquid stools</i> : highest with C1 (DSS+cascara): 0.29 <i>v</i> 1.88 <i>v</i> 0.59 (p<0.05) <i>Pain</i> : mean number of days with abdominal pain highest with C1 (DSS+cascara): 0.59 <i>v</i> 1.88 <i>v</i> 0.77 (p<0.05) <i>Meteorism</i> : most common with I1 (Drocil): 1.94 <i>v</i> 3.06 <i>v</i> 2.39 (p<0.05)	Quality score: 2 Randomisation: stated Not blinded No dropouts reported Funding: not stated

I=intervention; C=comparator; BM=bowel movements; DSS=diocetyl sodium sulphosuccinate; ITT=intention to treat; NS=not significant.

Low fluid intake has also been cited as a risk factor for constipation.²⁷⁻²⁸ The elderly, in particular, may be at risk as they may drink less in an attempt to control incontinence.²⁷ There have been few studies that have examined the effects of low fluid intake on constipation while controlling adequately for other factors. However, studies have shown low fluid intake to be related to slow colonic transit²⁵ and low stool output in healthy adults.²⁹ A large USA survey also reported lower consumption of beverages (sweetened, carbonated and non-carbonated) in constipated adults.²³ A community survey in New Zealand, however, found no association with constipation.³⁰

No trials have systematically assessed the impact of fluid intake as a treatment, although one small trial included 400 ml/day water as a control intervention and found it to be less effective than fibre plus the same amount of water.³¹ The authors of another small laxative trial also suggested that the dose-response effect which they observed may have been partly due to the associated increased intake of fluid.³² However, the effectiveness of increased fluid intake as a treatment for constipation remains largely unknown at present.

Constipation has been found to be more prevalent in those who take little exercise or are relatively inactive,²³ and this association persists after controlling for age. The highest risks are associated with being chairbound or bedbound.³³ Several studies have described bowel management programmes in institutionalised patients which have recommended exercise in the treatment of constipation.³⁴⁻³⁵ Several reviews have also recommended exercise.¹⁵⁻³⁶ However, these interventions appear not to have been formally evaluated in constipated patients.³⁷

Use of drugs that can cause constipation is also important, in particular anticholinergic antidepressants, opioid analgesics, and non-steroidal anti-inflammatory drugs including aspirin.³⁶⁻³⁸

Other factors which have been implicated in the development of constipation include anxiety, depression, and impaired cognitive function. For a more extensive list of other risk factors associated with constipation the reader is referred to the 1997 NHS HTA review.² The validity of many suspected risk factors for constipation has been questioned by some researchers as they have not been systematically investigated.³⁸

Treatment of constipation

A number of different interventions have been used in the treatment of constipation. Non-pharmacological interventions include guar gum, bread, bran, lentils, aloe vera, and fruit. Some of these treatments may act by increasing dietary fibre, while others have a stimulant action. Aloe is a folk remedy which, like senna and rhubarb, contains anthraquinone derivatives with a stimulant effect. Fruit may work by increasing bulk and liquid in the diet and/or by fermentation in the colon. Other non-pharmacological treatments for constipation

include abdominal massage, biofeedback, hypnosis, and yogic breathing. None of these interventions are evaluated in this bulletin.

Laxatives are the most commonly prescribed pharmacological interventions, of which there are four main types (bulk, osmotic, stimulant, and softener). Prescribing of bulk-forming laxatives is decreasing yearly, while that of stimulant and osmotic laxatives is increasing.¹²

WHO SHOULD BE TREATED WITH LAXATIVES?

In general, there is much uncertainty over what constitutes effective management of constipation and laxatives may not be appropriate in all constipated patients. For mobile people (including older patients) it has been suggested that lifestyle changes involving changes in diet, increasing fluid intake, and increasing physical activity may be sufficient,³⁹ although treatment will ultimately depend on the underlying causes and severity of the constipation. It has also been suggested that mild constipation can be managed with increasing fibre in the diet, while more severe constipation may require treatment with pharmacological laxatives after exclusion of underlying pathology.⁴⁰ Only a small minority with intractable constipation will require referral for further investigations.³⁹

EFFECTIVENESS OF LAXATIVE TREATMENTS

The average weighted mean increase in bowel frequency associated with treatment with bulk laxatives is around 1.4 bowel movements per week in adults.³ The increase associated with treatment with other laxative agents is approximately 1.5 bowel movements per week, with no apparent differences between bulk and non-bulk laxatives.³ Four additional RCTs carried out in populations of ambulant and institutionalised patients that were identified (table 2) suggest an increase in frequency of up to one bowel movement per week with bulk laxatives compared with placebo. However, these trials are very small and/or have methodological problems.³¹⁻⁴¹⁻⁴³

A double blind comparative study of bulk laxatives found a significantly greater increase in frequency and feelings of complete evacuation with fibre than with docusate sodium.⁴⁴ Overall, the evidence from these new RCTs and previous systematic reviews suggests that bulk laxatives are associated with an increase in frequency of 1–2 bowel movements per week compared with placebo and may be better tolerated than other laxative products.

Most trials that have evaluated fibre or bulk laxatives have found an improvement in abdominal pain with treatment, although no comparisons were significant.³ Consistency of the stool was improved in laxatives compared with placebo. A recent unblinded RCT compared ispaghula (Fybogel) with lactulose in 473 patients recruited by 65 GPs in the UK. Ispaghula was found to be more effective overall than lactulose with greater tolerability and fewer adverse effects, although frequency data are not reported.⁴⁵

There is little comparative evidence of differences between bulk and other laxatives in terms of frequency or symptoms.

No consistent evidence was found that stimulant laxatives are more effective than non-stimulant laxatives. In trials conducted in older adults (>55 years) there is also little evidence of differences in effectiveness between categories of laxatives, and no trial evidence to suggest that the more expensive stimulant dantron (danthron) based laxatives are more effective than cheaper alternatives.² (Note: the BNF now states that dantron should only be prescribed for constipation in terminally ill patients.⁴⁶) A combination of a bulk plus stimulant laxative (agiolax, available as Manevac in the UK) has been reported in two good quality trials of older adults to be more effective in improving consistency and frequency than an osmotic laxative (lactulose).²

Laxatives with an osmotic effect appear to be consistently associated with significant improvements in frequency, consistency, straining, and pain compared with placebo based on the results of two systematic reviews^{2,3} and additional small trials.^{47–50} There is little evidence for differences in effectiveness between osmotic laxatives and other treatments. Two small hospital based RCTs compared polyethylene glycol (PEG) 3350 with lactulose⁵¹ and ispaghula (Konsyl),⁵² respectively. Both of these trials suggest that PEG 3350 may produce a greater increase in frequency than either comparator, with no significant difference in the incidence of adverse effects. In addition, the use of PEG 3350 may result in a greater reduction in straining than lactulose (Norgine Ltd, unpublished data, 2001). Another small trial has reported lactitol and lactulose to be equally effective.⁵²

Laxatives with a softening action appear to be more effective than placebo in terms of increasing frequency and overall symptom improvement,^{2,3} but again there is little evidence available as to their comparative effectiveness. One additional parallel trial was identified which supports this conclusion.⁵³ A crossover trial combined a softener with a stimulant and found that this was associated with an increase in frequency compared with placebo.⁵⁴ Both these trials are very small.

Adverse effects and quality of life

Few studies have used standardised outcome measures to assess adverse effects and/or quality of life, although most studies did not report an increase in pain with fibre or non-bulk laxatives. Only two trials have examined improvements in general well being, neither of which showed any difference between fibre and other laxatives.³ Stimulant laxatives have previously been reported to cause abdominal cramping and diarrhoea with excessive use.⁵⁵ Adverse effects previously noted with the use of lactulose include cramping and nausea.^{56,57}

Cost effectiveness of laxatives

Two UK RCTs have examined the cost effectiveness of laxative treatment. One calculated the cost per stool associated with treatment with a senna fibre combination or with lactulose, giving a cost of 10.3p and 39.7p, respectively.^{58,59} The senna fibre combination

was concluded to be significantly more effective in older subjects than lactulose at a lower cost. Another RCT compared two osmotic agents—lactulose and sorbitol—and found them to be equally effective and similar in terms of adverse effects in the treatment of older patients.⁶⁰ The authors concluded that sorbitol is a cost effective alternative to lactulose. A review of cost containment strategies has noted that cost containment primarily rests on reduction in the use of unnecessary laxatives by promoting increased fibre intake in older people.³⁶ However, there has been no formal assessment of the cost effectiveness of this recommendation.

Prevention

Three RCTs of the prevention of constipation in older people were also reviewed.² Two of the trials evaluated the effectiveness of bran in preventing constipation and the third assessed the use of a bulking agent (sterculia). None of the three RCTs found any significant benefit for the prevention of constipation.

Conclusions

- Bulk (fibre based) laxatives and osmotic laxatives (including lactulose and PEG) are associated with increases in frequency and improvements in stool consistency and symptoms of constipation.
- Little evidence is available at present as to the comparative effectiveness of bulk and non-bulk laxatives.
- There is no good evidence that laxatives prevent constipation in older patients.
- A stepped approach to laxative treatment would seem justified, involving initial intervention with cheaper laxatives, before proceeding to the more expensive alternatives.
- There is a pressing need for large comparative trials of different strategies for the management of constipation in adults. This should include comparisons of the effectiveness of different classes of laxative.
- Research is also required into the effectiveness of overall dietary change (including increased fluid intake) in the treatment of constipation.

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