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Review

Gum chewing reduces postoperative ileus? A systematic review and meta-analysis

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ABSTRACT

Background: An important cause of delayed recovery from intestinal surgery is postoperative ileus. Gum chewing is a form of sham feeding, which could encourage gastrointestinal motility through cephalic-vagal stimulation.

Methods: We sought to identify all randomized controlled trials comparing gum chewing with standard care after elective intestinal surgery. We searched electronic databases (Cochrane, Embase, and PubMed), reference lists and contacted authors to obtain further data. We assessed the identified trials for quality and performed a meta-analysis and systematic review. The main outcome measures examined were time to flatus and stool postoperatively and length of hospital stay, which were analysed using random effect models. We also examined clinical complication rates.

Results: We identified nine eligible trials that had enrolled a total of 437 patients. The intervention was well tolerated and complication rates were low. There was statistical evidence of heterogeneity for the three main outcomes. Pooled estimates showed a reduction in time to flatus by 14 h (95% CI: −20 to −8 h, $p = 0.001$), time to bowel movement by 23 h (95% CI: −32 to −15 h, $p < 0.001$) and a reduction in length of hospital stay by 1.1 days (95% CI: −1.9 to −0.2 days, $p = 0.016$).

Conclusions: Chewing sugarless gum following elective intestinal resection is associated with improved outcomes. Insufficient data were available to demonstrate a reduced rate of clinical complications or reduced cost. An adequately powered, methodologically rigorous trial of gum chewing is required to confirm if there are any benefits and if these result in differences in clinical outcomes such as infection.

1. Introduction

Ileus may delay patient recovery following abdominal surgery.[1] The extent of ileus following abdominal surgery is influenced by the degree of surgical trauma and bowel manipulation.[2] The effect of surgical trauma on ileus is mediated through a stress response that results in a state of high sympathetic activity; a known extrinsic inhibitor of intestinal motility.[3] In addition inflammatory mediators such as nitric oxide, vasoactive intestinal peptide, substance P and calcitonin gene-related peptide are released as part of the stress response and these also appear to contribute to postoperative ileus.[2,4,5]

The influence of peri-operative interventions on the duration of ileus has been extensively studied.[6–8] Anaesthetic drugs such as atropine, enflurane and halothane tend to inhibit bowel motility and have the greatest effect on the colon.[9] Opiates in particular, have a marked effect, with one study demonstrating a dose–response relationship between the amount of morphine given and the time to return of bowel function.[10] Conversely local anaesthetic containing epidurals reduces the length of ileus compared to systemic opiate therapy.[11]

There is some evidence that other therapies such as early postoperative mobilisation, early feeding, use of nasogastric tubes or prokinetics reduce postoperative ileus.[12–16]

Chewing gum is a type of sham feeding that promotes intestinal motility, via cephalic-vagal stimulation. In normal volunteers chewing gum is as effective as food in stimulating cephalic-phase gastric secretion and has therefore been used as a modified form of

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sham feeding to investigate physiological responses such as gastric secretion.[17,18] Several randomized controlled trials have investigated the effects of gum chewed after abdominal surgery. We have performed a systematic review and meta-analysis of these studies to assess the evidence for benefit and harm from chewing gum following elective intestinal surgery.

2. Methods

2.1. Eligible studies

Eligible studies were clinical trials where patients had undergone elective intestinal surgery and were randomly allocated to receive either chewing gum or not in addition to standard postoperative care.

2.2. Search strategy and trial identification

We performed computerised searches of PubMed, Embase and the Cochrane Controlled Trials Register (issue 2, 2006) using the search terms, "gum-chewing", "chewing-gum", "post-operative"/"postoperative ileus", "paralytic ileus", "bowel"/"colonic"/"rectal" "resection"/"surgery", "sham-feeding". In addition Google searches were done using similar search terms. Reference lists from eligible trials were identified in an attempt to locate any further publications. Authors were contacted to request for additional data or information on trial methodology, which had not been reported. We wrote to chewing gum companies (Wrigleys®, Kanebo Foods) to see if they were aware of any other unpublished trials or data. The titles of the articles located by the searches were scanned by EJN and where apparently relevant the abstract was read by EJN and SJL, and if the article still appeared relevant a copy of the full manuscript was obtained. Full manuscripts were reviewed by EJN and SJL and a final decision made about inclusion by EJN, SJL, ST and KBH.

2.3. Data extraction and outcomes

We extracted the following data from each study; patient's age and sex, diagnosis, site of bowel resected, blood loss, duration of operation, stoma formation, postoperative fluid regime, analgesia, prokinetics (e.g. erythromycin, metoclopramide, cisapride), feeding and mobilisation regimes, use of nasogastric tubes, and duration of follow-up. We extracted outcomes on the following trial outcomes: time from the end of surgery to the passage of flatus and stool, clinical complications (such as myocardial infarction, ICU admission, wound infection, pneumonia, ileus, urinary tract infection, atrial fibrillation, death), length of postoperative hospital stay and tolerance of gum chewing. Data were extracted independently by two authors (EJN, SJL), checked for consistency and disagreements were resolved by consensus (EJN, SJL, KBH, ST).

2.4. Trial quality

Several aspects of trial design have been shown to be associated with biased estimates of treatment effects,[19,20] these include generation of the allocation sequence, concealment of allocation and masking of outcome assessors and participants to treatment allocation during the trial. Two of us (EJN, SJL) independently assessed the methodological quality of the included trials. We considered generation of allocation sequence and concealment of allocation to be adequate if the resulting sequences were random and if participants and enrolling investigators could not predict the assignment. In addition we also recorded the method of randomization generation, criteria for inclusion and exclusion. Any differences were resolved by discussions between the two of us and where necessary a third assessor (ST).

2.5. Statistical methods

We combined results from individual studies on a continuous scale using random effects meta-analysis.[21] Trial endpoints (time to flatus, time to bowel movement and length of postoperative hospital stay) were continuously distributed data, so were pooled and analysed using weighted mean differences. We used I^2 tests to assess the presence of heterogeneity. The presence of publication bias and related biases was examined with funnel plots and by a statistical test of funnel plot asymmetry.[22] Results are presented as means and 95% confidence intervals (CI). All analyses were performed using Stata, version 7.0 (Stata Corporation, College Station, Texas).

3. Results

3.1. Studies located

Electronic searches firstly identified 1925 publications (chewing gum). Combining the search terms "chewing gum"/"gum-chewing" and "postoperative" revealed 16 potentially relevant publications. Seven of these were randomized controlled trials fulfilling the inclusion criteria outlined above.[23–29] The other papers were comments on one of the included trials or trials involving patients undergoing tonsillectomy or maxillofacial surgery. Hand search of the references from the seven trials revealed no further trials. Google searches identified two further trials that were published only as abstracts.[30,31] No trials were excluded because of the methodological flaws or lack of relevant information. We therefore identified nine randomized controlled trials.[23–31] Additional unpublished data were obtained for three of the trials.[24,25,30]

3.2. Trial characteristics

A total of 437 participants undergoing elective intestinal resections were enrolled in the trials (Table 1). In seven of the trials a range of colonic or rectal procedures were undertaken.[23–27,30,31] In three trials laparoscopic resections were performed.[23,30,31] In one trial the type of gastrointestinal surgery done on children was not explicit.[28] In the study by Kouba et al.[29] patients underwent a radical cystectomy for cancer with ureteric diversion and formation of an ileal conduit. In all the trials patients in the intervention group received sugarless gum from the morning of the first postoperative day (Table 2). No differences between control or intervention groups were seen with regard to patient's baseline characteristics (mean ages 61.4 for gum chewing group and 61.9 years in the control group) or operative and postoperative management (Tables 1 and 2). No differences were seen by allocation with duration of surgery and operative blood loss (Table 1). Data on factors that are known to influence postoperative ileus such as number of previous abdominal operations, fluid management, diet, prokinetics and analgesia use were poorly recorded (Tables 1 and 2). Only Schuster et al.[27] recorded the anaesthetic used (propofol, opiate and inhalation agent) and stated that prokinetics were not used. Prokinetics were used routinely in the trial by Kouba et al.[29]

3.3. Quality of trials

The quality of trial design was generally suboptimal. Sample size calculations were stated as being done in three trials.[25,26,30] Patients were randomly allocated to receive the intervention

Table 1
Surgical history, surgery duration and analgesia.

Reference	Surgery	Mean age		Number randomised		Previous operations		Mean duration of surgery (min)		Laparoscopic: open		Epidural:patient controlled analgaesia	
		Active	Control	Active	Control	Active	Control	Active	Control	Active	Control	Active	Control
Asao (2002)	Colonic resection for cancer	59	61	10	9	NR	NR	166	154	10:0	9:0	Removed on morning of second POD:NR	
Schuster (2006)	Sigmoid resections for cancer and diverticulitis	60	63	17	17	3	2	108	115	0:17	0:17	7:10	89
Quah (2006)	Left-sided colorectal cancer	67	68	19	19	5	8	155	150	0:19	0:19	Removed on morning of second POD:NR	
Matros (2006)	Colonic resection for benign and malignant disease	62	58	22	21	13	15	158	174	0:22	0:21	19:NR	20:NR
Hirayama (2006)	Colonic resection for cancer	56	61	10	14	NR	NR	251	193	0:10	0:14	10:NR	14:NR
Kouba (2007)	Radical cystectomy with ileal conduit formation	65	67	51	51	NR	NR	NR	NR	0:51	0:51	0:51	0:51
McCormick (2006)	Colonic resection for benign and malignant disease	NR	NR	62	40	NR	NR	NR	NR	35:18	16:19	NR	NR
Watson (2008)	Colonic resection for benign and malignant disease	71	69	28	29	NR	NR	NR	NR	18:10	16:13	15:5	18:7
Zhang (2008)	Gastrointestinal surgery	9	7	9	9	NR	NR	115	31	NR	NR	Neither	Neither

NR = not recorded, POD = postoperative day.

(gum chewing) or not (control group) in all trials except that by Kouba et al.,[29] where consecutive patients were recruited into two cohorts (no gum chewing then gum chewing). Randomization occurred before surgery in one study,[30] after surgery in one study,[23] on the first postoperative morning in another,[25] in the other studies the timing of randomization was not explicit. Matros et al.[25] stratified randomization on the basis of the type of operation and Watson et al.[30] by laparoscopic or open approach. Allocation sequence generation was described in four trials, three used computer generated randomization[25,26,30] and one used a sequential randomized card pull.[27] Allocation concealment was not recorded in five trials,[23–25,28,31] and the remaining trials used sealed envelopes. Assessors were blinded in three trials,[25,26,30] analysis was as intention to treat where stated[23–28,31] and

Table 2
Intervention, dietary and fluid management and clinical complications.

Reference	Gum chewing frequency/duration	NG tube:oral fluid:onset of diet	Onset of mobilisation	Clinical complications	
				Active	Control
Asao (2002)	Tid, until oral intake begins	Removed on morning of first POD:NR:morning after first flatus	NR	None	1 Ileus
Schuster (2006)	Tid, for 1 h, until discharge from hospital	Nil:NR:NR	First POD	1 AF	1 AF, 1 ileus
Quah (2006)	Tid, for >5 min, until intake of solid diet	Not routinely used: NR (oral 30–60 ml/day): after first stool	When possible	2 Wound infection, 2 haemorrhage, 1 death	1 Pneumonia, 1 UTI, 2 haemorrhage, 1 AF, 1 re-admission
Matros (2006)	Tid, for 45 min	Removed on morning of first POD:NR (up to 30 ml/h until flatus):after first flatus	Early	1 Wound infection, 1 abdominal abscess, 1 ileus, 1 ITU admission	3 Wound infection, 2 pneumonia, 1 abdominal abscess, 1 dehiscence, 2 ileus, 1 MI
Hirayama (2006)	Tid, for 30 min	NR:NR:NR	NR	2 Wound infection, 1 pneumonia, 1 urological	4 Wound infection, 1 urological, 2 nausea
Kouba (2007)	Every 2–4 h	Removed on morning of first POD:started POD 2:POD 4	NR	3 Ileus, 1 diarrhoea, 1 GI bleed	4 Ileus, 1 diarrhoea
McCormick (2006)	Qid, for 15 min	NR:NR:NR	NR	NR	NR
Watson (2008)	Tid, for 30 min	Not routinely used: as tolerated:as tolerated	Early	1 Anastamotic leak, 1 cardiac, 1 wound infections	1 Splenic injury, 1 surgical emphysema, 3 wound infections, 1 death
Zhang (2008)	Tid	NR:NR:after first flatus	NR	None	None

NR = not recorded, POD = postoperative day, ITU = intensive care unit, AF = atrial fibrillation, MI = myocardial infarction, UTI = urinary tract infection.

outcome measures were only described in sufficient detail in one trial.[30] Matros et al.[25] included a third "placebo" group, who wore an acupressure bracelet in a sham location on the dorsum of the wrist.

3.4. Outcomes

The time taken until patients reported passing flatus following their operations was reported in all nine studies (Fig. 1). The mean duration of delay ranged from 47 ± 37 h to 69 ± 7 h in the chewing gum group and from 63 ± 35 h to 90 ± 18 h in the control group. Combined results (random effects model) showed a reduction by 14 h (95% CI: −20, −8 h, $p < 0.001$), with some evidence of between-study heterogeneity ($\chi^2 = 19$, $p = 0.015$ and $I^2 = 58\%$).

The time taken until patients reported passing a stool following their operations was reported in eight studies (Fig. 1). The mean duration of delay ranged from 63 ± 5 h to 86 ± 30 h in the chewing gum group and from 87 ± 33 h to 139 ± 53 h in the control group. Combined results (random effects model) showed a reduction by 23 h (95% CI: −32, −15 h, $p < 0.001$), with some evidence of between-study heterogeneity ($\chi^2 = 15$, $p = 0.034$ and $I^2 = 54\%$).

The postoperative length of hospital stay was reported in seven studies[23,25–27,29–31] (Fig. 1). The mean duration of stay ranged from 4.0 ± 0.4 days to 13.5 ± 3.0 days in the chewing gum group and from 5.1 ± 1.1 days to 14.5 ± 6.1 days in the control group. Combined results (random effects model) showed a reduction by 1.1 days (95% CI: −1.9, −0.2 days, $p = 0.016$), with evidence of substantial between-study heterogeneity ($\chi^2 = 27$, $p < 0.001$ and $I^2 = 78\%$). Meta-analysis of the length of postoperative hospital stay is heavily influenced by the relatively small standard deviations and larger sample sizes of the trial by Kouba et al.[29] The studies by Asao et al.[23] and Quah et al.[26] have relatively longer hospital stays than other studies. Whilst a beneficial direction of effect for chewing gum is seen across all the studies, the confidence intervals pooled estimates are wide when using random effects models due to the substantial heterogeneity. The confidence interval is narrower, although the point estimate similar, if a fixed effect model is used, with most of the weight going to the trial by Kouba et al.[29] which has relatively small standard deviations and a relatively large sample size.

In general, the Kouba et al.[29] study dominates the results of analyses. The studies by Asao and Hirayama[23,24] show a more

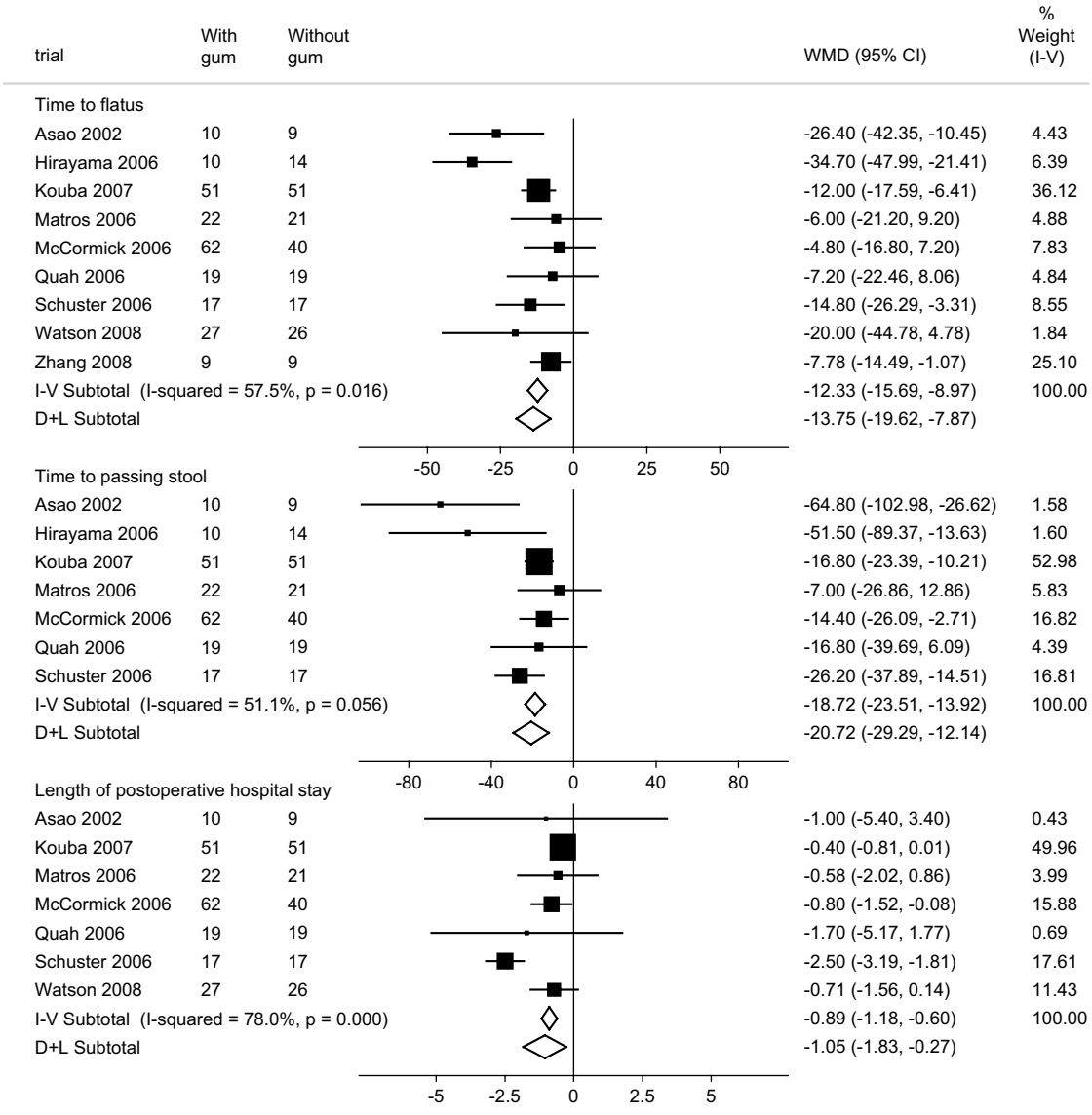

Fig. 1. Outcomes (time to first flatus, passing of stool and length of hospital stay).

beneficial effect than most other studies for time to passing flatus and stool and receive some weight in random effects analyses, therefore contributing to observed heterogeneity.

Where reported complication rates were uncommon, there was no evidence of a difference between treatment and control groups (Table 2). Reporting of complications in one trial[25] was ambiguous, with terms such as "urological" and "respiratory" used rather than specific diagnoses. Overall infectious complications of any type were reduced in patients who chewed gum (OR 0.53, 95% CI: 0.21, 1.34) (Table 2).

3.5. Funnel plots

Funnel plots were examined for three of the endpoints, time to flatus, time to passing stool postoperation and length of postoperative hospital stay. There was no evidence of asymmetry in any of the plots, although the total number of studies and patients is small, which makes interpretation difficult. The results of Egger's regression test did not provide any evidence of publication bias, but again, the power to detect potentially important effects is low with so few studies.

4. Discussion

We found consistent evidence of benefit for patients from chewing gum following intestinal surgery. Outcomes such as time to first flatus and bowel movement were reduced and post-operative stay was reduced by approximately one day. Although the evidence is based on small trials, such a potentially simple and cheap intervention could have important health and economic benefits. The findings are unlikely to be due to chance but the estimate of effect size is imprecise.

Funnel plots for the three endpoints, time to first flatus, passing of stool and the length of postoperative stay showed no evidence of asymmetry. However, the ability to uncover publication bias is limited when meta-analyses are based exclusively on small trials. Our ability to detect source of heterogeneity between trials was limited. Methods of randomization and blinding of outcome assessment were often not described in adequate detail. Reporting on factors that could have modified the recovery of the patients such as the type of anaesthesia, experience of the surgeon, postoperative pain control, the use of antibiotics and the success of the operation were incomplete and may explain some of the observed heterogeneity.

The study by Kouba et al.[29] had a large impact on our results because of its size and the narrow confidence intervals of the outcomes. Arguably the patients participating in this study underwent a very different type of surgery, associated with longer operative times and increased complications. However, recovery times are often influenced by ileus resolution and the reported lengths of hospital stay were similar to the other studies. Dropping this study from our analysis does increase the benefit seen from chewing gum with regard to length of hospital stay but has little impact on time to flatus and the passing of stool. Our analysis has benefitted by the inclusion of data (279 patients) from four studies not previously included in published reviews. By more than doubling the number of patients without any loss of effect makes the reported benefits of gum chewing more robust.

Chewing alone has been shown to stimulate intestinal motility, gastric, pancreatic and duodenal secretions through direct cephalic-vagal stimulation and release of neuropeptides.[32] The effect of chewing on the length of hospital stay is similar to that observed with early introduction of feeds.[33] It is not clear from these studies whether there is also a reduction in risk of vomiting, infections, anastamotic dehiscence and death. However, the risk of infection was reduced in the intervention group, an effect similar to that seen with early enteral feeding.[33]

Postoperative paralytic ileus is a common complication of surgery, with unfavourable consequences for patients and health-care systems. Food may be poorly tolerated after operations and only taken in small amounts. Chewing gum is a method of "sham" feeding which helps to stimulate bowel motility and avoids the unwanted side effects of feeding a recovering bowel such as vomiting.[33] Early enteral feeding after gastrointestinal surgery is associated with improved clinical outcomes,[33] so if ileus resolves more promptly then feeding can be tolerated sooner. "Enhanced Recovery Programmes" for patients undergoing colorectal surgery, including greater use of laparoscopic procedures, epidural analgesia, early feeding and early mobilisation, are associated with reduced length of postoperative hospital stay.[34,35] Interestingly we did not see a reduced length of hospital stay in the two studies where data from patients undergoing laparoscopic surgery[23,30] were extractable when compared to patients receiving open surgery. Our findings may be applicable to other types of surgery such as upper gastrointestinal or vascular, where early enteral nutrition may be more difficult to achieve. In this study chewing gum appears to reduce postoperative ileus at the average cost of $0.60 per patient (4 c per stick of gum), and may be a highly cost effective method of reducing the length of hospital stay by a mean of approximately two days.

The evidence available suggests substantial benefit from a simple intervention. The endpoints i.e. time to flatus and passing of stool are imprecise markers of ileus resolution. We believe that there is a good case for an adequately powered rigorous clinical trial to assess chewing gum as an adjunct to early feeding in patients undergoing elective gastrointestinal surgery. Such a trial should examine potential mechanisms by which chewing gum may work, such as enabling 'earlier' and greater nutritional intake. Such a trial should include clinical complications such as risk of infection as primary endpoints.

Conflict of interest
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