Meta-analysis of Randomized Studies Evaluating Chewing Gum to Enhance Postoperative Recovery Following Colectomy

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Objective: To compare outcomes following abdominal surgery with or without the use of chewing gum in the early postoperative period.

Data Sources: MEDLINE, Embase, Ovid, and Cochrane databases.

Study Selection: Randomized controlled trials reporting 1 or more outcomes related to functional postoperative recovery. Study quality was assessed using a validated scale.

Data Extraction: Time to the first passage of flatus, time to first bowel movement, and length of postoperative stay.

Data Synthesis: Five trials (158 patients) satisfied the inclusion criteria. Time (in days) for the patient to pass flatus (weighted mean difference [WMD], −0.66; 95% confidence interval [CI], −1.11 to −0.20; \( P = .005 \)) and the time until the first bowel movement (WMD, −1.10; 95% CI, −1.79 to −0.42; \( P = .002 \)) were significantly reduced in the chewing gum group compared with controls. However, both of these results demonstrated significant heterogeneity. Postoperative length of stay was also reduced in the chewing gum group by longer than 1 day (WMD, −1.25; 95% CI, −3.27 to 0.77; \( P = .23 \)); however, this result was not statistically significant. This result was significant when studies that explicitly included patients with stomas being formed during the surgery were excluded (WMD, −2.46; 95% CI, −3.14 to −1.79; \( P < .001 \)), with no significant heterogeneity.

Conclusions: Chewing gum may enhance intestinal recovery following colectomy and reduce the length of hospital stay. Owing to the potential for substantial cost savings, larger-scale, blinded, randomized controlled trials with placebo arms are warranted.

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The aim of our study was to use meta-analytical techniques with data from randomized controlled trials to assess the effect of chewing gum postoperatively on patients who underwent colectomy. The end points assessed were return to normal bowel function and length of postoperative stay.

METHODS

DATA SOURCES AND EXTRACTION

We performed searches of MEDLINE, Embase, Ovid, and Cochrane databases to identify randomized studies comparing outcomes between patients undergoing colectomy with or without the use of chewing gum in the early postoperative period. Chewing gum and surgery were used as search terms. The “Related Articles” function in PubMed was used to broaden the search, and all abstracts, studies, and citations scanned were reviewed. References of the articles acquired were also evaluated for further relevant studies. No language restrictions were made. The last date for this search was July 18, 2006. Two reviewers (S.P. and H.S.T.) independently extracted data from each study and there was 100% agreement between them.

STUDY SELECTION

To be included in the analysis, studies had to (1) compare abdominal surgery with and without the use of chewing gum postoperatively; (2) report on at least 1 of the outcomes of interest (return to enteric function and length of postoperative stay); (3) clearly document whether or not chewing gum was used; and (4) clearly report the reasons for surgery. We excluded studies from the analysis if (1) the outcomes of interest were not clearly reported for the 2 techniques; (2) it was impossible to extract or calculate the appropriate data from the published results; or (3) there was considerable overlap between authors, centers, or patients cohorts evaluated in the published literature.

OUTCOMES OF INTEREST AND DEFINITIONS

The following outcomes were used to compare patients who did and patients who did not chew gum after colonic resection: (1) return of enteric function, as suggested by the time (in days) until flatus was first passed following surgery and the time until the first postoperative bowel movement; and (2) length of postoperative hospital stay, defined as the length of time (in days) between the day of surgery and the day of hospital discharge.

STATISTICAL ANALYSIS

The meta-analysis was performed in line with recommendations from the Cochrane Collaboration and the Quality of Reporting of Meta-analyses guidelines.14-16 The primary outcome measures were continuous variables, and we analyzed them statistically using the weighted mean difference (WMD)17 and reported them with 95% confidence intervals (CIs); this summarizes the differences between the 2 groups while accounting for sample size.

VALIDITY ASSESSMENT

To assess the quality of the randomized trials, we used the Jadad score, a validated measure of the quality of randomized controlled trials.18,19 A study with a score of 3 or more (of 5) was considered high-quality.

Heterogeneity between the studies was assessed using 3 methods. First, graphic exploration with funnel plots was used to evaluate publication bias.20,21 Second, subgroup analysis was undertaken, including studies that had quality scores of 3 or more, more than 30 patients, that only recruited open surgical cases, and that were published in or since 2005 and excluding studies that explicitly included patients with stomas. Finally, we reanalyzed the data using both random- and fixed-effects models to assess any differences in the results of the meta-analysis. Statistical assessment of heterogeneity was performed using the Cochran $\chi^2$ test for heterogeneity.22

A power calculation was carried out to assess the size of randomized controlled trials needed to demonstrate a difference of 1.25 days (at $P = .05$) between the 2 groups with 80% power. Analysis was conducted using Review Manager software, version 4.2 (The Cochrane Collaboration, Oxford, England), and Intercooled Stata, version 9.0 for Windows (Stata Corp, College Station, Texas).

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STUDY CHARACTERISTICS

In each trial, sugarless gum was chewed 3 times a day following surgery, and the duration of chewing ranged from 5 to 45 minutes.8-10 In all 5 studies, the perioperative treatment of patients was identical between the study and control groups, other than the provision of chewing gum, but in only 2 studies were the patients explicitly stated to be allowed oral fluids before the passage of flatus.9,10 In 2 trials, patients receiving end or defunctioning stomas were clearly included,9,10 while in the others, stoma formation was not mentioned. Blinding of observers was part of the trial design in only 1 study, which was also the only study with a placebo group.9 Patients who dropped out from the treatment group were identified in 1 study10; in 2 patients owing to postoperative complications that required intensive care treatment and in another patient whose poorly fitting dentures resulted in intolerance of the gum. Analysis in this article was carried out on an intention-to-treat basis (of the data extracted from the included studies). In none of the analyzed studies were any adverse events caused by the use of chewing gum. In 1 study, 14 of 16 patients described a subjective benefit from the gum in keeping the mouth moist following surgery, while 13 of 16 were satisfied by the freedom to chew gum in the postoperative period.10

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Table 1. Study Characteristics of Randomized Controlled Trials on Gum Chewing After Colectomy

<table>
<thead>
<tr>
<th>Source</th>
<th>Type of Surgery</th>
<th>Indication for Surgery</th>
<th>Female Patients/Total Patients, No.</th>
<th>Age, Mean (SD), y</th>
<th>Jadad Quality Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asa et al,7 2002</td>
<td>Laparoscopic Colectomy</td>
<td></td>
<td>3/10</td>
<td>58.6 (9.1)</td>
<td>2</td>
</tr>
<tr>
<td>Hira et al,8 2006</td>
<td>Colectomy for colorectal cancer</td>
<td></td>
<td>5/10</td>
<td>55.6 (12.0)</td>
<td>2</td>
</tr>
<tr>
<td>Matros et al,9 2006</td>
<td>Open Colectomy</td>
<td></td>
<td>14/22</td>
<td>62.0 (14.0)</td>
<td>4</td>
</tr>
<tr>
<td>Quah et al,10 2006</td>
<td>Open Left-sided colectomy</td>
<td></td>
<td>6/19</td>
<td>67.0 (9.7)</td>
<td>3</td>
</tr>
<tr>
<td>Schuster et al,11 2006</td>
<td>Open Sigmoid colectomy</td>
<td></td>
<td>6/17</td>
<td>60.0 (6.1)</td>
<td>3</td>
</tr>
</tbody>
</table>

RESULTS FROM OVERALL META-ANALYSIS

The primary outcome measures were continuous variables and we analyzed them statistically using random-effects modeling and the WMD. Results from the overall meta-analysis are outlined in Table 1 and illustrated as a forest plot in Figure 2. Using random-effects modeling, the overall results of the meta-analysis demonstrated that both the time (in days) for the patient to pass flatus (WMD, −0.66; 95% CI, −1.11 to −0.20; P=.005) and the time until the first bowel movement (WMD, −1.10; 95% CI, −1.79 to −0.42; P=.002) were significantly reduced in the chewing gum group compared with the controls. However, both of these results demonstrated significant heterogeneity. Postoperative length of hospital stay was assessed in 4 trials7,9-11 comprising 134 patients. This was also reduced in the chewing gum group by longer than 1 day (WMD, −1.25; 95% CI, −3.27 to 0.77; P=.23); however, this result was not statistically significant. The results of the meta-analysis were similar when a fixed-effects, rather than a random-effects, model was used, and analysis by funnel plots suggested that publication bias was not a problem in the context of our study (results not shown).

SUBGROUP ANALYSIS

Subgroup analysis was performed to assess the robustness of our findings and to explore heterogeneity between studies. There were 3 high-quality studies with a Jadad score of 3 or greater9-11. These studies comprised 115 patients and were also the studies that included more than 30 randomized patients. This subgroup of studies resulted in a significantly shorter time to pass flatus (WMD, −0.29; 95% CI, −0.44 to −0.15; P<.001) but had no heterogeneity. The other 2 outcomes were the same for this subgroup as for the overall analysis. Studies evaluating open surgery only and studies published in or since 2005 demonstrated similar results as the overall meta-analysis. However, when studies that explicitly included patients with stomas being formed during the surgery (for which they were being admitted) were excluded, all 3 outcomes were significantly reduced. Time until the first bowel movement (WMD, −1.76; 95% CI, −2.81 to −0.71; P=.001) and postoperative length of stay (WMD, −2.46; 95% CI, −3.14 to −1.79; P<.001) also demonstrated no heterogeneity in this subgroup. Subgroup analysis was not performed on the number of times gum was chewed, as all studies required patients to chew gum 3 times a day. The duration of gum chewing was also not used as a subgroup for analysis because, of the 5 studies included, 2 did not state the duration, 1 stated chewing for at least 5 minutes, 1 stated chewing for 45 minutes, and 1 stated chewing for 30 minutes.

COMMENT

With increasing pressure on limited health care resources and continually needing to improve the quality of patients’ perioperative experience, interventions with the potential to limit the discomfort of postoperative ileus and reduce the length of postoperative stay are welcomed. We have reviewed the current evidence from randomized controlled trials comparing outcomes between patients undergoing colonic resection with or without the use of chewing gum in the early postoperative period and have shown that benefits are offered in resolving ileus. Although the results of this meta-analysis suggest a benefit in length of stay for the chewing gum group, this outcome only achieved statistical significance on subgroup analysis. To show a statistically significant difference of 1.25 days (at P=.05) between the 2 groups with 80% power, a traditional randomized controlled trial would require 80 patients in each arm.

Postoperative ileus is regarded as an inevitable response to the trauma of abdominal surgery and is a major contributing factor to postoperative pain and discomfort associated with abdominal distension, nausea, vomiting, and cramping pain.24 In the United States, the problem has been estimated to account for up to $1 bil-
Table 2. Meta-analysis Results of Gum Chewing After Colectomy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. of Patients</th>
<th>No. of Studies</th>
<th>WMD (95% CI) a</th>
<th>P Value</th>
<th>Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall results</td>
<td>158</td>
<td>5</td>
<td>−0.66 (−1.11 to −0.20)</td>
<td>.005</td>
<td>20.12 &lt; .001</td>
</tr>
<tr>
<td>Time to first passing flatus</td>
<td>158</td>
<td>5</td>
<td>−1.10 (−1.79 to −0.42)</td>
<td>.002</td>
<td>19.16 &lt; .001</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td>134</td>
<td>4</td>
<td>−1.25 (−3.27 to 0.77)</td>
<td>.23</td>
<td>50.60 &lt; .001</td>
</tr>
<tr>
<td>Jaded quality score ≥ 3 (and studies with &gt; 30 patients)</td>
<td>115</td>
<td>3</td>
<td>−0.29 (−0.44 to −0.15)</td>
<td>&lt; .001</td>
<td>0.01 &gt; .99</td>
</tr>
<tr>
<td>Time to first passing flatus</td>
<td>115</td>
<td>3</td>
<td>−0.68 (−1.25 to −0.11)</td>
<td>.02</td>
<td>7.85 .02</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td>115</td>
<td>3</td>
<td>−1.29 (−3.50 to 0.92)</td>
<td>.25</td>
<td>50.45 &lt; .001</td>
</tr>
<tr>
<td>Studies of open surgery (and studies from 2005 and on)</td>
<td>139</td>
<td>4</td>
<td>−0.56 (−1.05 to −0.08)</td>
<td>.02</td>
<td>15.68 .001</td>
</tr>
<tr>
<td>Time to first passing flatus</td>
<td>139</td>
<td>4</td>
<td>−0.85 (−1.47 to −0.23)</td>
<td>.07</td>
<td>12.03 .007</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td>115</td>
<td>3</td>
<td>−1.29 (−3.50 to 0.92)</td>
<td>.25</td>
<td>50.45 &lt; .001</td>
</tr>
<tr>
<td>Excluding studies that explicitly included patients with stomas</td>
<td>77</td>
<td>3</td>
<td>−0.94 (−1.66 to 0.22)</td>
<td>.01</td>
<td>9.88 .007</td>
</tr>
<tr>
<td>Time to first passing flatus</td>
<td>77</td>
<td>3</td>
<td>−1.76 (−2.81 to −0.71)</td>
<td>.001</td>
<td>4.73 .09</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td>53</td>
<td>2</td>
<td>−2.46 (−3.14 to −1.79)</td>
<td>&lt; .001</td>
<td>0.44 .51</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; WMD, weighted mean difference.

a A WMD of less than 0 favors the chewing gum group.

Figure 2. Forest plot of results of overall meta-analysis. CI indicates confidence interval; WMD, weighted mean difference.
table, such as colectomies, will be associated with high levels of postoperative ileus. Additional problems in the postoperative patient include the need for analgesia; the amount of morphine used has previously been shown to strongly correlate with the time to the return of small intestinal motility. The potential benefits of thoracic epidural anesthesia in reducing ileus have been assessed and include a reduction in the need for parenteral morphine as well as achieving blockade of the thoracolumbar sympathetic outflow, which inhibits gastrointestinal motility while leaving the craniosacral parasympathetic innervation (stimulatory to gut function) intact. Randomized trials have shown significant reductions in the length of postoperative ileus in patients treated with thoracic epidural anesthesia compared with morphine in the form of patient-controlled anesthesia. Pharmacological adjuncts that have been evaluated in relation to improving postoperative intestinal function in randomized controlled trials include cisapride (which showed significant benefits but has subsequently been withdrawn owing to an adverse effect profile), erythromycin (no significant benefit), and peripherally acting µ-opioid receptor antagonists (shown to offer significant benefits in resolving ileus and reducing length of hospital stay).

The variety of potential targets for interventions to reduce ileus and the length of hospital stay has led several authors to promote the use of multimodal rehabilitation strategies, which may include the use of drugs, epidural anesthesia, and early feeding. Although early feeding has been shown to reduce the length of stay for patients when used alone or as part of a multimodal program, a failure to tolerate such strategies in up to 20% of patients has been reported. The potential for failure of early feeding underlies studies to investigate gum chewing as a form of “sham feeding,” which is thought to be effective by direct cephalic-vagal stimulation, the triggering of gastrointestinal hormone release, and increasing the production of both saliva and pancreatic secretions.

Advantages of our study include the identification of evidence concerning the effectiveness of postoperative gum chewing from 5 randomized trials, all reporting outcomes on patients undergoing colonic resection, with consistency in reported end points between them. We have shown that despite variation in findings from individual studies, overall the published evidence supports the hypothesis that gum chewing reduces the duration of postoperative ileus, as represented by the time to passage of flatus and first bowel movement. Although there was a mean reduction in length of stay of longer than 1 day in the chewing gum group, this did not reach statistical significance, and thus we cannot rule out the possibility that the observed reduction was due to chance. This may represent insufficient power to detect a significant difference for this outcome. A power calculation suggested that 80 patients in each arm would be required to show a significant difference of 1.25 days, which is greater than the combined populations of all studies on this subject. Quah et al powered their study to detect a 2-day difference in time to return of flatus or bowel movements on the basis that a shorter time would unlikely be clinically significant. We would challenge this view on economic terms at least. A reduced length of stay, of even 1 day, for an intervention with extremely low cost and no reported adverse effects would represent substantial savings for the National Health Service when applied to the entire United Kingdom population.

Disadvantages of our meta-analysis are reflected mainly in the heterogeneity between studies. Despite assessing outcomes only in patients undergoing colonic surgery, there are differences in methodologies that might explain the heterogeneity. The inclusion of patients with defunctioning or end stomas may have affected the length of stay outcomes as well as the assessment of times until the passage of flatus and bowel motions. Studies have highlighted that stoma formation tends to negate the benefits of strategies to reduce the length of hospital stay. This is underlined by the fact that when the studies that included some patients who definitely underwent stoma formation were excluded, a statistically significant reduction in length of stay was shown, and heterogeneity for all outcomes was either absent or reduced. In addition, despite looking for evidence of the effects of chewing gum on recovery from abdominal surgery, it is important to note that all included studies reported on outcomes following colorectal surgery, making the results more representative of the outcomes following colorectal procedures.

In conclusion, we feel that the current evidence suggests that gum chewing following abdominal surgery offers significant benefits in reducing the time to resolution of ileus; however, the studies are insufficiently powered to identify a significant benefit in length of stay. The potential benefits to individual patients, in health economics terms, are such that a well-designed, large-scale, blinded, randomized, controlled trial with a placebo arm is warranted to answer the question of whether gum chewing can significantly reduce the length of stay after abdominal surgery or whether it merely represents a placebo effect.

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Author Contributions: Drs Purkayastha and Tilney contributed equally to the production of this manuscript and should be considered joint first authors. Dr Tekkis had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Purkayastha, Tilney, and Darzi. Acquisition of data: Purkayastha and Tilney. Analysis and interpretation of data: Purkayastha, Tilney, and Tekkis. Drafting of the manuscript: Purkayastha, Tilney, and Darzi. Critical revision of the manuscript for important intellectual content: Purkayastha, Tilney, and Tekkis. Statistical analysis: Purkayastha, Tilney, and Tekkis. Study supervision: Darzi and Tekkis.

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