

Early enteral feeding versus “nil by mouth” after gastrointestinal surgery: systematic review and meta-analysis of controlled trials

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Abstract

Objective To determine whether a period of starvation (nil by mouth) after gastrointestinal surgery is beneficial in terms of specific outcomes.

Design Systematic review and meta-analysis of randomised controlled trials comparing any type of enteral feeding started within 24 hours after surgery with nil by mouth management in elective gastrointestinal surgery. Three electronic databases (PubMed, Embase, and the Cochrane controlled trials register) were searched, reference lists checked, and letters requesting details of unpublished trials and data sent to pharmaceutical companies and authors of previous trials.

Main outcome measures Anastomotic dehiscence, infection of any type, wound infection, pneumonia, intra-abdominal abscess, length of hospital stay, and mortality.

Results Eleven studies with 837 patients met the inclusion criteria. In six studies patients in the intervention group were fed directly into the small bowel and in five studies patients were fed orally. Early feeding reduced the risk of any type of infection (relative risk 0.72, 95% confidence interval 0.54 to 0.98, $P=0.036$) and the mean length of stay in hospital (number of days reduced by 0.84, 0.36 to 1.33, $P=0.001$). Risk reductions were also seen for anastomotic dehiscence (0.53, 0.26 to 1.08, $P=0.080$), wound infection, pneumonia, intra-abdominal abscess, and mortality, but these failed to reach significance ($P>0.10$). The risk of vomiting was increased among patients fed early (1.27, 1.01 to 1.61, $P=0.046$).

Conclusions There seems to be no clear advantage to keeping patients nil by mouth after elective gastrointestinal resection. Early feeding may be of benefit. An adequately powered trial is required to confirm or refute the benefits seen in small trials.

Introduction

A period of starvation (“nil by mouth”) is common practice after gastrointestinal surgery during which an intestinal anastomosis has been formed. The stomach is decompressed with a nasogastric tube and intravenous fluids are given, with oral feeding being introduced as

gastric dysmotility resolves.¹ The rationale of nil by mouth is to prevent postoperative nausea and vomiting and to protect the anastomosis, allowing it time to heal before being stressed by food. It is, however, unclear whether deferral of enteral feeding is beneficial.

Contrary to widespread opinion, evidence from clinical studies and animal experiments suggests that initiating feeding early is advantageous. Postoperative dysmotility predominantly affects the stomach and colon, with the small bowel recovering normal function 4–8 hours after laparotomy.¹ Feeding within 24 hours after laparotomy is tolerated and the feed absorbed.^{2–3} Gastrointestinal surgery is often undertaken in patients who are malnourished,^{4–6} which in severe cases is known to increase morbidity.⁷ In animals, starvation reduces the collagen content in anastomotic scar tissue^{8–9} and diminishes the quality of healing,^{9–10} whereas feeding reverses mucosal atrophy induced by starvation¹¹ and increases anastomotic collagen deposition and strength.¹² Experimental data in both animals and humans suggest that enteral nutrition is associated with an improvement in wound healing.¹³ Finally, early enteral feeding may reduce septic morbidity after abdominal trauma¹⁴ and pancreatitis.¹⁵

Several clinical trials directly comparing strategies of early feeding with nil by mouth after elective gastrointestinal surgery have been performed. These studies, however, have not been systematically reviewed. We performed a systematic review and meta-analysis of randomised trials to assess the evidence on benefit and harm of early enteral feeding.

Methods

Eligibility criteria and literature search—Clinical trials were eligible if patients had undergone elective gastrointestinal surgery and were randomly allocated to receive either enteral feeding (within 24 hours after surgery) or the traditional management of nil by mouth and intravenous fluids with introduction of enteral fluids and diet as tolerated.

Data extraction and outcomes—From each study we collected data on the site of surgery, whether an intestinal anastomosis was formed, whether the pathology was benign or malignant, the type of feed used, and the method of administration of the feed. The site of surgery was classified as pancreatic, hepatobiliary, upper gastro-

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Table 1 Characteristics of eleven trials of early enteral feeding after elective gastrointestinal surgery

	No of patients		Type of feed	Route of feeding	Pathology (%)		Site of surgery (%)		
	Active	Control			Malignant	Benign	Upper	Lower	Hepatobiliary
Sagar et al, 1979 ¹⁸	16	16	Standard	NJ	NR	NR	0	100	0
Schroeder et al, 1991 ¹³	15	15	Elemental	NJ	NR	NR	27	73	0
Binderow et al, 1994 ¹⁹	32	32	Oral	Oral	NR	NR	0	100	0
Reissman et al, 1995 ²⁰	80	81	Oral	Oral	NR	NR	0	100	0
Carr et al, 1996 ²¹	14	14	Standard	NJ	NR	NR	NR	NR	NR
Beier-Holgersen et al, 1996 ²²	30	30	Standard	ND	65	35	13	87	0
Ortiz et al, 1996 ²³	95	95	Oral	Oral	87	23	0	100	0
Heslin et al, 1997 ²⁴	97	98	Immune enhancing	J	93	7	51	0	49
Hartsell et al, 1997 ²⁵	29	29	Standard	Oral	64	28	0	100	0
Watters et al, 1997 ²⁶	15	16	Standard	J	93	7	96	0	4
Stewart et al, 1998 ²⁷	40	40	Oral	Oral	NR	NR	0	100	0

NJ=nasojejunal tube, ND=nasoduodenal tube, J=jejunostomy, NR=not reported.

intestinal (proximal to the jejunum), or lower gastrointestinal (distal to the duodenum). Outcomes potentially related to feeding included anastomotic dehiscence, infection of any type, wound infection, pneumonia, intra-abdominal abscess, vomiting, mortality, and length of hospital stay. The unplanned reinsertion of a nasogastric tube was recorded.

Analysis—We combined results from individual studies on the relative risk scale using fixed effects meta-analysis.¹⁶ Data on length of hospital stay were pooled with non-standardised mean differences. We used a χ^2 test to test for homogeneity of relative risks. We used funnel plots to determine the presence of publication bias and related biases and performed a statistical test of funnel plot asymmetry.¹⁷

Results

Characteristics of trials, patients, and interventions

We identified 13 randomised controlled trials, all of which were published in English.^{13 18–29} We excluded two of these trials because no information on relevant outcomes was given.^{28 29} We obtained additional unpublished data for six of the studies.^{19–27}

Patients had a wide variety of gastrointestinal conditions. Table 1 gives details of the 11 trials that we included.

Methodological quality of trials

Reporting on concealment of allocation of treatment and blinding was poor. In three trials allocation was

concealed with sealed envelopes,^{21 22 24} and one trial used an open table with random numbers,¹⁸ but in the remaining studies the exact method of randomisation was unclear. In the study by Heslin et al the outcomes were assessed by “a physician not associated with the surgical team.”²⁴ In all other studies outcome assessment was probably open, although this was explicitly stated in only one report.²⁶

Outcomes

The effects of early feeding on anastomotic dehiscence, infections, vomiting, and mortality are detailed in table 2 and summarised in the figure. Seven trials showed that early feeding led to a reduction in risk of anastomotic dehiscence with a combined relative risk of 0.53 (95% confidence interval 0.26 to 1.08, P=0.080) and no evidence of heterogeneity between studies ($\chi^2=2.10$, P=0.96). Results were similar when 31 patients in whom no anastomosis had been formed were excluded from the denominator of five trials (combined relative risk 0.54, 0.26 to 1.09).^{18 20 22 23 25} There was little evidence that results differed between the two studies in which the anastomosis was known to be proximal to the site of feeding^{24 26} and the six trials in which it was distal (P=0.42).^{15 19 20 23 25 27}

The risk of any type of infection was obtained in all but two trials (table 2).^{19 26} The combined relative risk was 0.72 (0.53 to 0.98), indicating a significant (P=0.036) reduction in the risk of infection, with little evidence of heterogeneity between trials ($\chi^2=10.7$,

Table 2 Relative risk (95% CI) of anastomotic dehiscence, infection, and death in eleven randomised trials of early enteral nutrition

	Anastomotic dehiscence	Infections					Vomiting	Death
		Any infection	Wound infection	Pneumonia	Intra-abdominal abscess			
Sagar et al ¹⁸	0.33 (0.01 to 7.58)	0.71 (0.29 to 1.75)	0.60 (0.17 to 2.07)	NR	1.00 (0.16 to 6.20)	NR	NR	
Schroeder et al ¹³	NR	3.00 (0.13 to 68.6)	NR	3.00 (0.13 to 68.6)	NR	NR	NR	
Binderow et al ¹⁹	NR	NR	NR	NR	NR	1.75 (0.85 to 3.56)	NR	
Reissman et al ²⁰	0.34 (0.01 to 8.16)	1.27 (0.35 to 4.54)	2.02 (0.19 to 21.9)	0.34 (0.01 to 8.16)	1.01 (0.06 to 15.9)	1.56 (0.78 to 3.13)	NR	
Carr et al ²¹	NR	0.14 (0.01 to 2.53)	NR	NR	NR	NR	0.33 (0.01 to 7.54)	
Beier-Holgersen et al ²²	0.50 (0.10 to 2.53)	0.14 (0.04 to 0.57)	0.10 (0.01 to 0.73)	0.5 (0.05 to 5.22)	0.20 (0.01 to 4.00)	0.88 (0.55 to 1.42)	0.50 (0.01 to 2.53)	
Ortiz et al ²³	0.50 (0.09 to 2.67)	0.80 (0.33 to 1.94)	0.83 (0.26 to 2.64)	1.00 (0.14 to 6.95)	1.00 (0.06 to 15.8)	NR	NR	
Heslin et al ²⁴	0.76 (0.17 to 3.30)	0.95 (0.62 to 1.44)	1.64 (0.71 to 3.78)	0.43 (0.12 to 1.63)	2.02 (0.19 to 21.9)	1.38 (0.86 to 2.21)	0.67 (0.12 to 3.94)	
Hartsell et al ²⁵	0.33 (0.01 to 7.86)	3.00 (0.13 to 70.7)	NR	3.00 (0.13 to 70.7)	NR	1.40 (0.75 to 2.62)	0.33 (0.01 to 7.86)	
Watters et al ²⁶	0.27 (0.03 to 2.12)	NR	NR	NR	NR	NR	NR	
Stewart et al ²⁷	3.00 (0.16 to 71.5)	0.56 (0.20 to 1.51)	0.11 (0.01 to 2.00)	1.00 (0.06 to 15.4)	NR	1.00 (0.55 to 1.82)	0.33 (0.01 to 7.95)	
Combined relative risk	0.53 (0.26 to 1.08)	0.72 (0.53 to 0.98)	0.71 (0.44 to 1.17)	0.73 (0.33 to 1.59)	0.87 (0.31 to 2.42)	1.27 (1.01 to 1.61)	0.48 (0.18 to 1.29)	
P value from test for heterogeneity	0.96	0.22	0.074	0.85	0.84	0.52	0.99	

NR=not reported or no events occurred.

$P=0.22$). Similar reductions were observed for wound infection and pneumonia (figure). There was an increase in the risk of vomiting among patients fed early (1.27, 1.01 to 1.61, $P=0.045$).

Mortality was reported in all but two studies,^{19 26} but deaths occurred in only five (table 2). There were four deaths in the early feeding groups compared with 10 deaths in control groups (relative risk 0.48, 0.18 to 1.29, $P=0.15$). Length of hospital stay was reported in all 11 studies. The mean length of stay ranged from 6.2 days to 14.0 days in early feeding groups and from 6.8 days to 19.0 days in control groups. Combined results showed a significant reduction by 0.84 day (0.36 to 1.33 days, $P=0.001$), with some evidence of heterogeneity between studies ($\chi^2=16.2$, $P=0.094$).

Funnel plots

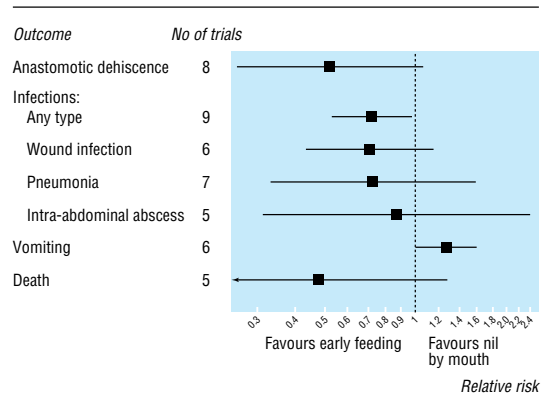
We examined funnel plots for all nine outcomes (the seven shown in table 2 plus length of stay and replacement of nasogastric tubes). There was no clear evidence of asymmetry in any of these plots ($P>0.10$ by regression test¹⁷), except for mortality ($P=0.068$).

Discussion

This meta-analysis yielded three principal findings. Firstly, there does not seem to be a clear advantage in keeping patients nil by mouth after elective gastrointestinal resection. Secondly, in these patients early feeding may be beneficial. Thirdly, we believe these results indicate the necessity for an adequately powered clinical trial to assess early enteral feeding in patients undergoing elective gastrointestinal surgery.

Complications after operation

Anastomotic dehiscence is a major complication of gastrointestinal surgery with considerable morbidity and mortality.³⁰ The combined estimate of the effects of early feeding failed to reach conventional levels of significance but eight out of nine studies that reported anastomotic dehiscence indicated benefit. A significant relative reduction in the risk of infection of any type was observed for patients receiving early enteral nutrition, with the greatest reduction seen in the frequency of wound infections. In most of the trials assessed infections were not clearly defined. In absolute terms results were heterogeneous, with the number of



Risk of anastomotic dehiscence, infections, vomiting, and death after elective gastrointestinal surgery: results from meta-analyses of randomised trials comparing early enteral feeding with regimen of nil by mouth

What is already known on this topic

Enteral feeding within 24 hours after gastrointestinal surgery is tolerated

Theoretically, early enteral feeding improves tissue healing and reduces septic complications after gastrointestinal surgery

What this study adds

There is no benefit in keeping patients "nil by mouth" after gastrointestinal surgery

Septic complications and length of hospital stay were reduced in those patients who received early enteral feeding

In patients who received early enteral feeding there were no significant reductions in incidence of anastomotic dehiscence, wound infection, pneumonia, intra-abdominal abscess, and mortality

patients who would need to be treated to prevent one infection of any type ranging from three²² to 58.²⁴

The length of hospital stay after surgery was reduced in eight of the eleven studies. Overall the reduction corresponds to about one day, which is economically important. Reduction in complication rates may explain this observation, as might a faster return of gastrointestinal function. Early postoperative feeding after non-gastrointestinal surgery has also been shown to reduce length of stay in hospital.^{31 32}

Quality of trials and heterogeneity

The 11 randomised trials identified were clinically heterogeneous and most of them were small and of doubtful methodological quality. It is noteworthy that the effect of early nutrition seemed to be homogeneous across a set of trials that were clearly heterogeneous in clinical terms. Our ability to detect heterogeneity between trials, however, was limited by the small number of trials and by the often inadequate reporting.

Conclusion

There is little evidence from these trials that keeping patients nil by mouth is beneficial after elective gastrointestinal resection. Although the data are clearly insufficient to conclude that early feeding is of proved benefit, we believe that there is a good case for an adequately powered clinical trial to assess early enteral feeding in such patients.

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Efficacy of progesterone and progestogens in management of premenstrual syndrome: systematic review

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Abstract

Objective To evaluate the efficacy of progesterone and progestogens in the management of premenstrual syndrome.

Design Systematic review of published randomised, placebo controlled trials.

Studies reviewed 10 trials of progesterone therapy (531 women) and four trials of progestogen therapy (378 women).

Main outcome measures Proportion of women whose symptoms showed improvement with progesterone preparations (suppositories and oral micronised). Proportion of women whose symptoms showed improvement with progestogens. Secondary analysis of efficacy of progesterone and progestogens in managing physical and behavioural symptoms.

Results Overall standardised mean difference for all trials that assessed efficacy of progesterone (by both routes of administration) was -0.028 (95% confidence interval -0.017 to -0.040). The odds ratio was 1.05 (1.03 to 1.08) in favour of progesterone, indicating no clinically important difference between progesterone and placebo. For progestogens the overall standardised mean was -0.036 (-0.059 to -0.014), which corresponds to an odds ratio of 1.07

(1.03 to 1.11) showing a statistically, but not clinically, significant improvement for women taking progestogens.

Conclusion The evidence from these meta-analyses does not support the use of progesterone or progestogens in the management of premenstrual syndrome.

Introduction

Premenstrual syndrome is defined as the recurrence of psychological and physical symptoms in the luteal phase, which remit in the follicular phase of the menstrual cycle. It is estimated that up to 1.5 million women in the United Kingdom experience such severe symptoms that their quality of life and interpersonal relationships are greatly affected. Over 35% of these women will seek medical treatment.¹

The rationale for the use of progesterone and progestogens in the management of premenstrual syndrome is based on the unsubstantiated premise that progesterone deficiency is the cause.² There is no consistent evidence that low concentrations of progesterone are found in women with the premenstrual syndrome.^{3,4} However, as premenstrual syndrome