

Randomised trial of safety and efficacy of immediate postoperative enteral feeding in patients undergoing gastrointestinal resection

Cornelia S Carr, K D Eddie Ling, Paul Boulos, Mervyn Singer

See editorial

Abstract

Objectives—To assess whether immediate postoperative enteral feeding in patients who have undergone gastrointestinal resection is safe and effective.

Design—Randomised trial of immediate postoperative enteral feeding through a nasojejunum tube *v* conventional postoperative intravenous fluids until the reintroduction of normal diet.

Setting—Teaching hospitals in London.

Subjects—30 patients under the care of the participating consultant surgeon who were undergoing elective laparotomies with a view to gastrointestinal resection for quiescent, chronic gastrointestinal disease. Two patients did not proceed to resection.

Main outcome measures—Nutritional state, nutritional intake and nitrogen balance, gut mucosal permeability measured by lactulose-mannitol differential sugar absorption test, complications, and outcome.

Results—Successful immediate enteral feeding was established in all 14 patients, with a mean (SD) daily intake of 6.78 (1.57) MJ (1622 (375) kcal before reintroduction of oral diet compared with 1.58 (0.14) MJ (377 (34) kcal) for those on intravenous fluids ($P < 0.0001$). Urinary nitrogen balance on the first postoperative day was negative in those on intravenous fluids but positive in all 14 enterally fed patients (mean (SD) -13.2 (11.6) g *v* 5.3 (2.7) g; $P < 0.005$). There was no difference by day 5. There was no change in gut mucosal permeability in the enterally fed group but a significant increase from the test ratios seen before the operation in those on intravenous fluids (0.11 (0.06) *v* 0.15 (0.12); $P < 0.005$). There were also fewer postoperative complications in the enterally fed group ($P < 0.005$).

Conclusions—Immediate postoperative enteral feeding in patients undergoing intestinal resection seems to be safe, prevents an increase in gut mucosal permeability, and produces a positive nitrogen balance.

Introduction

Malnutrition predisposes to postoperative complications: increased incidence of infection¹ and prolonged hospital stay.² Malnourished patients undergoing major surgery have improved outcome with total parenteral nutrition,³ but this has complications related to site of venous access, metabolic disturbances,⁴ and prolonged postoperative ileus.⁵

Conventional treatment after bowel resection entails starvation with administration of intravenous fluids until passage of flatus. Postoperative gastric stasis causes nausea and vomiting thus inhibiting oral intake, but it has been shown that small bowel function continues.⁶ Early enteral feeding improves the outcome in patients with trauma⁷ and burns,^{9,10} though few studies have examined its use after bowel resection. Schroeder *et al* found improved wound

healing in an enterally fed group after bowel resection but calculated that dietary requirements were not fulfilled until the introduction of normal diet.¹¹

We undertook a pilot study in patients undergoing bowel resection by comparing conventional management with immediate enteral feeding in which protein calorie requirements were met within 8 to 12 hours postoperatively. Assessment was made of safety, nutritional state, clinical outcome, and effects on gut mucosal permeability.

Subjects and methods

Patients undergoing intestinal resection were considered. Exclusion criteria were emergencies and allergy or intolerance to the constituents of the feed. Fully informed consent was obtained and approval obtained from the hospital ethics committee.

Record was made of the type of surgery, postoperative drugs (opiates and antiemetics), ventilation or renal replacement, time to flatus and full feeding, daily nutritional intake, complications, sepsis score,¹² and clinical outcome.

Nutritional state was assessed preoperatively, on day 1 postoperatively, and at five day intervals until discharge. Mid-arm muscle circumference, triceps skinfold thickness, handgrip dynamometry,¹³ body weight, serum albumin concentration, and 24 hour urinary nitrogen balance were measured.

A differential sugar absorption test¹⁴ (5 g lactulose, 2 g mannitol, and 22.3 g glucose in 100 ml of water) was given preoperatively and on day 5 postoperatively. A urine sample was taken 12 to 24 hours later and immediately frozen. Analysis was performed by using gas liquid chromatography.

After we had obtained informed consent the patients were randomly allocated (by closed envelope) to receive feeding or to be managed conventionally. Fed patients had a double lumen nasojejunum tube (Medicina, Manchester) passed perioperatively, with the surgeon verifying the position. The conventionally treated patients received intravenous fluids with nil by mouth until passage of flatus.

Feeding was started on returning from the operating theatre by using standard isocaloric feed (Fresubin, Fresenius, Cheshire). Energy and water requirements were calculated from the weight of the patient, and a mixture of Fresubin and water provided the full basic fluid requirements (35 ml/kg body weight/day). Initially feeding was at 25 ml an hour and was increased by 25 ml four hourly until the target volume was reached, at which point intravenous fluids were stopped. Distension or pain would lead to cessation of the feed. Oral fluids started on passage of flatus and increased to normal diet over 48 hours. Intravenous fluids and enteral feeding were stopped with the introduction of diet.

Data are presented as means (SD) and were analysed by Student's two tailed *t* test. A *P* value less than 0.05

Departments of
Cardiothoracic Surgery and
Surgery, University
College London Medical
School, Middlesex
Hospital, London
WIN 8AA

Cornelia S Carr, registrar in
cardiothoracic surgery
Paul Boulos, consultant
colorectal surgeon

Department of Medicine,
University College London
Medical School,
Whittington Hospital,
London N19 5NF
K D Eddie Ling, research
scientist

Bloomsbury Institute of
Intensive Care Medicine,
Department of Medicine,
University College London
Medical School, Rayne
Institute Building, London
WC1E 6JJ
Mervyn Singer, senior
lecturer in intensive care

Correspondence to:
Dr Singer.

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was considered significant. Where there were significant differences between the two treatment groups the 95% confidence interval for that difference is shown.

Results

Thirty patients were randomised. Two patients did not proceed to resection, and their data were not included. Fourteen patients were randomised to enteral feeding. Their mean (SD) age was 60.1 (7.5) years; five were women; and the mean body mass index (weight (kg)/(height (m)²) was 24.14 (4.31). They were all successfully fed with no tube blockages or cessation of feed. The corresponding figures for the 14 patients randomised to conventional feeding were 51.1 (8.2) years; six women; and 22.05 (3.87) for body mass index.

Table 1 summarises all the results. The mean intake of energy (6.78 (1.57) v 1.58 (0.14) MJ/day (1622 (375) v 377 (34) kcal/day); 95% confidence interval for difference -6.11 to -4.30 (-1462 to -1028); P<0.001) and protein (60.6 (3.8) v 0.8 (0.1) g/day; -68.1 to -51.5; P<0.001) was significantly higher in the enterally fed patients. The nitrogen balance was significantly higher in the enterally fed patients on only the first postoperative day (5.3 (0.7) v -13.2 (3.1) g; -25 to -11.6 g; P<0.005). The lactulose:mannitol absorption ratio was numerically higher in the enterally fed patients (0.15 (0.12) v 0.11 (0.06) preoperatively, but this difference did not reach significance. Also the apparently lower preoperative v postoperative lactulose:mannitol in the enterally fed patients was not significantly different. Enteral feeding (0.1 (0.03)), however, resulted in a significant attenuation in gut permeability when compared with conventional feeding (0.5 (0.26); 0.1 to 0.6; P<0.05).

Table 1—Clinical characteristics of patients undergoing gastrointestinal resection according to method of postoperative nutrition. Figures are means (SD) unless otherwise stated

Detail	Enteral feeding (n=14)	Conventional feeding (n=14)
Investigation data		
Energy/day:		
MJ	6.8 (1.57)*	1.58 (0.14)
kcal	1622 (375)*	377 (34)
Protein/day (g)	60.6 (14.4)	0.8 (0.2)
Nitrogen balance:		
Preoperative	1.5 (1.9)	1.7 (2.2)
Postoperative:		
Day 1	5.3 (2.7)*	-13.2 (11.6)
Day 5	1.2 (1.2)	1.0 (0.8)
Lactulose:mannitol ratio:		
Preoperative	0.15 (0.12)	0.11 (0.06)
Postoperative	0.1 (0.03)	0.5 (0.26)*
Clinical outcome		
No of patients with:		
Nausea/vomiting	1	7
Distension	2	4
Diarrhoea	0	1
Bleeding duodenal ulcer	0	1
Infection (wound, urinary)†	0	3
Length of stay (days)	9.8 (6.6)	9.3 (2.8)
Days to oral intake	6	6
Days to passage of flatus	6	6
Days to defaecation	4	5
Nutritional data at day 5 after operation		
Loss in mid-arm circumference (cm)	0.3 (0.1)	0.4 (0.1)
Loss in skinfold thickness (cm)	0.07 (0.02)	0.005 (0.01)
Drop in handgrip strength (kg)	6.7 (3.2)	9.6 (2.1)
Weight loss (kg)	0.5 (0.2)	1.8 (0.3)
Drop in serum albumin (g/l)	11.6 (2.5)	11.5 (2.3)

*P<0.005.

†One patient in conventional treatment group died with sepsis score ≥20.

Key messages

- Immediate enteral feeding after gastrointestinal resection is possible
- It is safe, with patients experiencing fewer complications
- There seems to be an improvement in nutritional state
- Patients may have an improved outcome

There appeared to be fewer complications among the enterally fed group, but overall clinical outcomes did not differ significantly. Also the nutritional data were similar between the two groups.

Discussion

In this study feeding was started two to three hours after surgery and continued until normal diet was possible. Full feeding was achieved quickly and was well tolerated with no excessive distension. No patients progressed to postoperative total parenteral nutrition. The functional integrity of the bowel mucosa was assessed by a differential sugar absorption test. Mannitol is absorbed transcellularly and lactulose paracellularly (40 to 100-fold lower absorption than mannitol). Both sugars are excreted unchanged in the urine. Increased intestinal permeability allows greater amounts of lactulose to be absorbed thus raising the urinary lactulose:mannitol ratio. This occurs in critically ill patients,¹⁴ patients with multiple trauma,¹⁵ and patients undergoing major vascular procedures.¹⁶ Our finding that immediate enteral feeding after bowel resection seems to prevent the rise in intestinal permeability suggests a protective role, whether by providing a physical barrier or via direct metabolic and nutritive effects on the intestinal mucosa remains unknown. The observed higher protein and energy intake in the enterally fed patients may have contributed to the improved gut mucosal integrity.

Total parenteral nutrition costs about £60 a day compared with enteral feeding at £12 a day and intravenous fluids at £3 a day. Postoperative enteral feeding may reduce the need for total parenteral nutrition and reduce expenditure and complications.

We conclude that immediate enteral feeding is safe and well tolerated by patients undergoing bowel resection. In addition to the considerable improvement in total calorie and protein intake there is a significant attenuation in gut mucosal permeability.

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Cohort study of predictive value of urinary albumin excretion for atherosclerotic vascular disease in patients with insulin dependent diabetes

Torsten Deckert, Hiroki Yokoyama, Elisabeth Mathiesen, Birgitte Rønn, Tonny Jensen, Bo Feldt-Rasmussen, Knut Borch-Johnsen, Jan Skov Jensen

Abstract

Objective—To examine whether slightly elevated urinary albumin excretion precedes development of atherosclerotic vascular disease in patients with insulin dependent diabetes independently of conventional atherogenic risk factors and of diabetic nephropathy.

Design—Cohort study with 11 year follow up.

Setting—Diabetes centre in Denmark.

Subjects—259 patients aged 19-51 with insulin dependent diabetes of 6-34 years' duration and without atherosclerotic vascular disease or diabetic nephropathy at baseline.

Main outcome measures—Baseline variables: urinary albumin excretion, blood pressure, smoking habits, and serum concentrations of total cholesterol, high density lipoprotein cholesterol, sialic acid, and von Willebrand factor. End point: atherosclerotic vascular disease assessed by death certificates, mailed questionnaires, and hospital records.

Results—Thirty patients developed atherosclerotic vascular disease during follow up of 2457 person years. Elevated urinary albumin excretion was significantly predictive of atherosclerotic vascular disease (hazard ratio 1.06 (95% confidence interval 1.02 to 1.18) per 5 mg increase in 24 hour urinary albumin excretion, $P=0.002$). Predictive effect was independent of age; sex; blood pressure; smoking; serum concentrations of total cholesterol, high density lipoprotein cholesterol, sialic acid, and von Willebrand factor; level of haemoglobin A_{1c}; insulin dose; duration of diabetes; and diabetic nephropathy (hazard ratio 1.04 (1.01 to 1.08) per 5 mg increase in 24 hour urinary albumin excretion, $P=0.03$).

Conclusion—Slightly elevated urinary albumin excretion independently predicted atherosclerotic vascular disease in patients with insulin dependent diabetes.

Introduction

Macrovascular complications—that is, atherosclerotic vascular diseases—are the commonest causes of early death in patients with insulin dependent diabetes mellitus.¹ In particular, patients with clinical diabetic nephropathy have an extremely high morbidity from macrovascular disease.^{2,3} However, even patients who remain free from diabetic nephropathy have a mortality from macrovascular diseases that is four times higher than that of the general population.³ Preliminary studies have suggested that this excess mortality in people with insulin dependent diabetes might particularly occur among those with slightly elevated urinary albumin

excretion,^{4,5} as is seen in patients with non-insulin dependent diabetes and non-diabetic people.⁶⁻¹² It is, however, not known whether clinical vascular disease in these patients develops before the start of diabetic nephropathy (that is, during the course of slightly elevated urinary albumin excretion) or whether elevated urinary albumin excretion precedes atherosclerotic vascular disease independently of the conventional atherogenic risk factors that are often increased in these patients.¹³⁻¹⁸ The aim of this study was to clarify these points.

Subjects and methods

PATIENTS

Between 1983 and 1986 we recruited a cohort of 288 patients with insulin dependent diabetes mellitus,^{15 19-24} making up about 40% of all the patients with similar age and duration of diabetes attending the outpatient clinic of the Steno Diabetes Center. Patients were excluded if they had atherosclerotic vascular disease (subjective symptoms or changes on a 12 lead resting or exercise electrocardiogram compatible with ischaemic heart disease) or clinical nephropathy (urinary albumin excretion > 300 mg/24 h), if they took any drugs apart from insulin, and if they were not white. By the autumn of 1994 nine patients had died and five had emigrated, leaving 274 for follow up evaluation of their vascular status by means of a mailed questionnaire. After two mailings 250 of the patients had responded, and we obtained the hospital records and death certificates of the patients who had died. Thus, the overall ascertainment was 259/288 (90%).

The participants gave their informed consent. The study was in accordance with the Declaration of Helsinki and approved by the regional ethics committee.

BASELINE MEASUREMENTS

Patients' blood pressure was measured with a standard sphygmomanometer and an appropriately sized cuff after they had rested lying down for 10 minutes. The average of two measurements was recorded. Hypertension was defined as systolic blood pressure ≥ 160 mm Hg or diastolic blood pressure ≥ 95 mm Hg (World Health Organisation criteria). Body mass index was calculated as weight (kg)/(height (m)²). Urinary albumin excretion was measured with a radial immunodiffusion technique²⁵ (intra-assay coefficient of variation, 5%; intra-individual coefficient of variation, 47-50%²⁶). The value recorded was an average of two or three 24 hour sterile urine samples that gave negative results on urine analysis. Microalbuminuria was defined as a urinary albumin excretion of 30-300 mg/24 h in two sterile urine collections.

Steno Diabetes Center,
Niels Steensensvej 2,
DK-2820 Gentofte,
Denmark

Torsten Deckert, *consultant*
Hiroki Yokoyama, *research fellow*

Elisabeth Mathiesen,
research fellow

Birgitte Rønn, *research fellow*
Tonny Jensen, *research fellow*

Bo Feldt-Rasmussen,
research fellow
Knut Borch-Johnsen,
research fellow

Jan Skov Jensen, *research fellow*

Correspondence to:
Dr Skov Jensen.

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