Early enteral nutrition after surgical treatment of gut perforations: A prospective randomised study

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ABSTRACT

Background: Withholding enteral feeds after an elective gastrointestinal surgery is based on the hypothesis that this period of "nil by mouth" provides rest to the gut and promotes healing.

Aims: To assess whether early postoperative naso-gastric tube feeding in the form of a balanced diet formula is safe in and beneficial to patients who have undergone surgical intervention for perforation of the gut.

Setting: A surgical unit of a Medical College Hospital.

Design and Subjects: Prospective randomised open control study.

Methods and Material: Patients undergoing surgical intervention for peritonitis following perforation of the gut were randomised to the study group receiving feedings of a balanced diet formula through a naso-gastric tube from the second postoperative day, or the control group in which patients were managed with the conventional regimen of intravenous fluid administration. The groups were compared for incidence and duration of complications, biochemical measurements and other characteristics like weight loss/gain.

Statistical Analysis: Chi square test and 'T' test.

Results: One hundred patients were enrolled in each group. 88% subjects in the study group achieved positive nitrogen balance on the eighth postoperative day as compared to none in the conventionally managed group. The relative risks (95% confidence interval) of morbidity from wound infection, wound dehiscence, pneumonia, leakage of anastomoses and septicaemia were 0.66 (0.407-1.091), 0.44 (0.141-1.396), 0.70 (0.431-1.135), 0.54 (0.224-1.293) and 0.66 (0.374-1.503) respectively. Average loss of weight between the first and tenth day was 3.10 kg in the study group as compared to 5.10 kg in the conventionally managed group ('P' value $<$ 0.001, 95% Confidence Interval - 2.46-1.54).

Conclusion: Early enteral nutrition is safe and is associated with beneficial effects such as lower weight loss, early achievement of positive nitrogen balance as compared to the conventional regimen of feeding in operated cases of gut perforation.

KEY WORDS: Enteral nutrition, gut perforation, naso-gastric tube

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After elective gastrointestinal surgery, the trend has been to keep the patient 'nil by mouth' and decompress the stomach by a naso-gastric tube. There is a general consensus that gastric and colonic atony following laparotomy lasts 24-48 hours and that the small bowel, in fact, recovers function within four to six hours.[1] Over the last few years, great emphasis has been laid on early enteral feeding by a naso-jejunal tube or via jejunostomy distal to the site of anastomosis.[2,3,4] Very few clinical trials[5-9] have evaluated the efficacy and safety of early enteral nutrition in patients who have undergone laparotomy for generalised peritonitis following perforation of the gut. Hence, we undertook a trial to assess the safety, feasibility and benefits of enteral feeding by a naso-gastric tube 48 hours after emergency gastrointestinal surgery.

Material and Methods

This prospective randomised study was carried out in a surgical unit in a medical college hospital between May 2000 and February 2003. The study proposal was studied and approved by the department review committee. Patients with enteric perforations underwent emergency surgery after undergoing relevant investigations. Intravenous fluids, and anti-microbial agents were routinely administered prior to surgery and naso-gastric tube aspiration was routinely performed. Following surgery, those patients who had not undergone ileostomy were included in the study after obtaining informed consent. The subjects were randomised to receive enteral formula within 48 hours (Group A) or to receive intravenous alimentation for up to 7 days (Group B) using random tables. The treating surgeons did not in any way record the observations. Figure 1 provides a diagrammatic representation of the study plan.

Postoperatively, besides parenteral fluids, a broad-spectrum antibiotic combination of a cephalosporin, metronidazole, and an aminoglycoside was given to subjects in both the groups for five days. The antibiotics were changed or continued for a longer duration, if dictated by circumstances. Continuous aspiration through a naso-gastric tube was provided for 48 hours.

In the subjects belonging to Group A , the naso-gastric tube was used for both feeding and aspiration. Hundred grams of a balanced diet formula (containing proteins, fats, carbohydrates, vitamins, minerals and fibre) dissolved in 500 ml of gram dry weight (GDW) 5 % (600 Calories) was given slowly at the rate of 50 ml/hour by an intravenous drip set connected to a naso-gastric tube. The rate of feeding was slowed down or the feeding was stopped, if patient developed intolerable distension, uneasiness, vomiting, hiccough or abdominal pain. The feeds were administered to an awake patient who was propped up at 30^0. The patient received another 300-400 calories in the form of intravenous dextrose. The conventionally managed patients received calories only in the form of dextrose-containing fluids intravenously, which amounted to 600 calories on an average.

From the fifth postoperative day, in addition to enteral feeds, patients belonging to Group A were kept on intravenous patency line. Between the eighth and tenth day the naso-gastric tube was removed and complete oral feeds in the form of semi-solid diet were commenced. Subjects in Group B were assessed for the feasibility of oral intake on the fifth postoperative day and those found suitable were given sips of an appetising liquid. Those tolerating the sips graduated to 500-ml liquids and then semi-solids over the next two days. Those who did not tolerate oral feed stayed on intravenous fluids till they could take feeds orally.

Patients were closely monitored and feeding was slowed or stopped if complications related to tube feeding occurred. The patients were watched closely for signs of a leak from the repaired perforation of the gut.

Postoperatively, the patients were subjected to certain investigations at regular intervals:
Determination of weight on the first, seventh and tenth postoperative days and/or at the time of discharge;
Biochemical and haematological investigations that were done included: estimation of haemoglobin concentration, levels of albumin and creatinine in the serum, blood urea levels and urinary urea levels on the third and eighth postoperative days;
Nitrogen balance was calculated by estimating nitrogen input and output from urinary urea by the following formula:
Nitrogen Balance = (Protein intake/6.25)-(UUN + 4), where:
6.25 grams of protein has 1gram of nitrogen, UUN is urinary urea nitrogen, or grams of nitrogen excreted in the urine over a 24-hour period. "Insensible losses" via the skin and GI tract accounted for 4 grams of nitrogen lost each day.

Nitrogen input was calculated by dividing the protein intake (9.7g in one 50g sachet) by 6.25. Calorie intake was also calculated.
Since the minimum nitrogen loss by this formula is four grams per day, we did not calculate the nitrogen balance in the control group as the maximum nitrogen intake in them was 2.4 grams.

Septicaemia was defined as systemic inflammatory response syndrome (SIRS) with documented infection. In addition, standard values were used for its diagnosis, i.e. axillary temperature > 38^0C/ <36^0C; Heart Rate >90/ min; Respiratory Rate >20/ min; W.B.C count in excess of 12000 cells/mm^3 or <4000 cells/mm^3 or with over 10% immature cells. Vomiting was defined as documented regurgitation of feed/ bile and gastric secretions of over 100 ml. Diarrhoea was defined as more than 3 motions per day and/or stool volume in excess of 500 ml/day. Distension was defined as an increase in the abdominal girth by more than 2.5 cm, when there was no sign of a leak.

Differences between the values of serum albumin, nitrogen balance and weight gain/ loss were considered as markers of nutritional status. These were expressed as percentage of patients showing an increase/ decrease in value. Mean weight loss between the first and seventh day and the seventh and tenth day was calculated. The stay of each patient in the hospital was noted and the nutritional state at the time of discharge recorded. The mean duration of hospital and

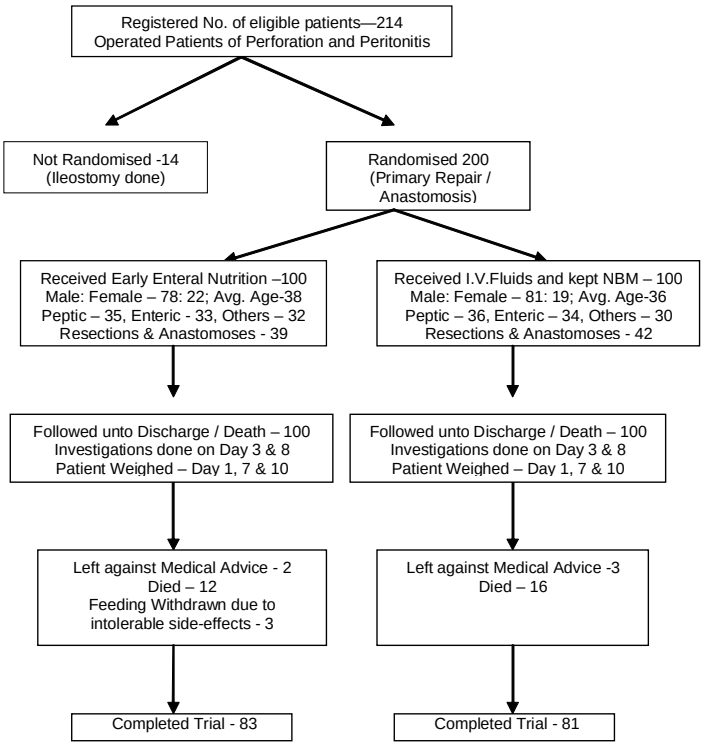

Figure 1: Schematic representation of the study plan.

Table 1: Plan of feeding in the two groups

	Group A [Early enteral feeding Group]					Group B [Conventional Treatment Group]
Post op day	Total calorieInput	Calories by enteral route	Grams of balanced diet formula/ml of 5% GDW	Calories by parenteral route	Rate of feeding ml/hour	Calories received /day
0	600	-	-	600	-	600
1	600	-	-	600	-	600
2	1000	600	100/500	400	50	600
3	1500	1200	200/1000	300	100	600
4	2100	1800	300/1500	200	150	600
5	2500	2400	400/2000	100	200	600 + Oral Sips (150 Calories)
6	3100	3000	500/2500	100	200 Calories)	600 +500 ml Liquids (400
7	3100	3000	500/2500	100	200	600 + Semi-solid Diet (600 Calories; 10g Proteins)
8	3600	3600	600/3000	-	250	Semi-solid/normal diet (1400 calories; 15g proteins approximately)

I.C.U stay, and mean weight loss were compared by 'T' test.

The results were analysed using Relative Risk (of developing a complication), Odds Ratio, χ^2 test (test of significance depicted by '*P*' value) and 'T' test (for testing the significance of the difference between two means). Chi-square (χ^2) test was used to compare the incidences of complications in the two groups. The total duration for which a complication lasted in each group was also noted in terms of 'man-days', which were then compared. This gave an assessment of how quickly the complications were controlled once they had occurred.

Results

Two hundred patients (100 in each group) were enrolled in the study. The indications for emergency surgery included perforation of the gut due to conditions such as peptic ulcer, enteric fever, trauma and malignancies. Most of the perforations [192/200] included in the series were more than 48 hours old. All patients had severe peritonitis and septicaemia. Eighty three subjects in the study group (Group A) and 81 subjects from the conventional treatment group (Group B) completed the trial. In Group A two subjects left the hospital against medical advice. There were 12 deaths in this group and three had to be withdrawn from the study for the occurrence of intolerable side-effects (two cases of intractable diarrhoea and one case of intractable vomiting). In Group B, there were 16 deaths and three left the hospital against medical advice. No patient had any intolerable side-effects. Group A demonstrated a lower risk of complications such as leak, wound dehiscence, wound infection, septicaemia, pneumonia and death (Table 2). However, these differences were not statistically significant. The relative risk and odds ratios for major complications were lower for Group A. However, these differences were not statistically significant. The risk of minor complications such as vomiting, diarrhoea and abdominal distension was more in Group A, although the difference was not statistically significant. When the episodes of minor complications in the two groups were compared, the relative risks and odds ratios were in favour of the conventionally managed cases but the difference was not statistically significant.

The duration in which the major complications were controlled was significantly lower in the patients receiving early enteral nutrition. This was reflected in the fewer number of 'man-days' lost (Table 2). The number of 'man-days' lost was higher in the subjects belonging to Group A compared with those belonging to Group B (Table 3).

Table 4 shows the difference between the study group (Group A) and the conventional group (Group B) in terms of biochemical, haematological and other clinical parameters. It was worth noting that a significantly higher proportion of cases received calories above a threshold value in Group A. The mean duration of stay, in general and in the ICU, was lower in the study group. However, these differences were not significant statistically.

Discussion

Similar to some other studies,[10,11] our study has demonstrated

Table 2: Relative risk of major and minor complications

Complication	Study group	Control group	*P value* (DF –1)	95% CI	Odds Ratio	Relative risk (95% CI)
Abdominal distension	20	18	0.823	-9.08-13.08	1.28	1.11 (0.626-1.971)
Vomiting	13	7	0.157	-2.44-14.44	1.98	1.86 (0.773-4.454)
Diarrhoea	16	11	0.303	-4.62-14.62	1.54	1.45 (0.710-2.976)
Pneumonia	21	30	0.145	-3.26-21.26	0.62	0.70 (0.431-1.135)
Wound infection	27	31	0.103	-8.8-16.8	0.58	0.66 (0.407-1.091)
Wound dehiscence	4	9	0.152	-1.92-11.92	0.42	0.44 (0.141-1.396)
Leak	7	13	0.157	-2.44-14.44	0.50	0.54 (0.224-1.293)
Septicaemia	20	30	0.103	-2.16-22.16	0.58	0.66 (0.407-1.091)
Death	12	16	0.417	-5.78-13.78	0.71	0.75 (0.374-1.503)

Table 3: Duration of complications in terms of man-days lost

Complication	Man days lost group A	Man days lost group B	*'P' value,* D.F.– 1, (95% CI)	Relative Risk (95% CI)
Wound infection	130	180	0.003 (-17.52–82.48)	0.73 (0.592–0.899)
Septicaemia	127	191	<0.001 (-31.22–96.78)	0.67 (0.545–0.826)
Pneumonia	118	166	0.003 (-16.70–79.30)	0.72 (0.576–0.895)
Duration of ICU Stay	159	210	0.005 (-16.2–85.8)	0.76 (0.634–0.922)

Table 4: Clinical and biochemical parameters in the two groups

Parameter	Group A	Group B	*'P'* Value (95% CI)
Mean duration of stay (days)	10.59	10.70	0.865 (-1.17–1.39)
Mean duration of ICU Stay	1.59	2.10	0.908 (-8.29–9.31)
Calories received			
Post Op Day-4 (% cases receiving over 1500 Calories	65%	0%	< 0.001
Post Op Day-8 (% cases receiving over 2500 Calories)	84%	0%	< 0.001
Mean weight loss between			
Day 1 and 7 (kg)	2.60	3.70	
Day 7 and 10 (kg)	0.50	1.40	
Total weight loss between Day 1 and 10 (kg)	3.10	5.10	<0.0001 (-1.54–2.46)
Positive nitrogen balance by the 8th post-operative day	88%	None	<0.001
Serum albumin Level	Avg. rise 0.10gm%	Avg. fall 0.20gm%	<0.001

that there is no evidence to suggest that bowel rest and a period of starvation are beneficial for the healing of wounds and anastomotic integrity. Indeed, the evidence is that luminal nutrition may enhance wound healing and increase anastomotic strength, particularly in malnourished patients.

Most studies [6,9,12] showed that the duration of septicaemia was significantly reduced along with a reduction in the duration of hospital stay. In our study, the average duration of stay in the study cases was 10.59 days (as compared to 10.70 in conventionally managed group). Although this difference was not significant statistically, patients in the study group were in much better general condition and had lost lesser weight than the patients who received conventional management, signifying the importance of alimentation.

Keele et al[13] found that supplementing "normal" oral diet in hospital wards with as little as 300 calories and 12 g of protein per day resulted in a reduction of postoperative complications in patients undergoing gastrointestinal surgery. In our enteral feeding group, more than 65% patients were getting over 1500 calories on post-operative day (POD)-5 while 84% patients were getting over 2500 calories by POD-8, while no conventionally managed patient reached a daily intake of 1500 calories. In the study group 90% of the calories were being given enterally. Their mean daily intake was 2600 calories on POD-8 as compared to 877 calories for those on intravenous fluids. Singh et al[5] achieved a positive nitrogen balance by the third and Hoover et al[4] by the fourth postoperative day. In our study, on the eighth postoperative day, 88% patients in the study group were in positive nitrogen balance as compared to 0% in the conventionally managed group. This apparent delay in achieving a positive nitrogen balance can be attributed to the fact that our study cases were fed almost a day later than the corresponding patients in the studies referred to above.

In our study, weight loss between the first and seventh day was 2.6 kg in the study group as compared to 3.7 kg for the conventionally managed group and between the seventh and tenth day it was 0.5 kg for the study group and 1.40 kg for the conventionally managed group. The total weight loss between the first and tenth day was 3.1 kg vs. 5.1 kg, for the study and control groups respectively. Between the seventh and tenth day, in the study group, some patients (20%) in fact, recorded a gain in weight during the latter part of their stay (33% maintained a status quo). Hoover et al[4] showed that patients who were given early enteral feeds did not demonstrate any weight loss. Since all their cases were undergoing elective upper gastrointestinal surgery, they were not in a state of septicaemia or increased catabolism preoperatively. These cases could, therefore, be fed immediately by a jejunostomy tube. But jejunostomy feeding may result in certain complications,[7] which are avoided by our technique.

In our study, the incidence of distension and diarrhoea correlated well with the work of Heslin et al.[7] This was different from Carr et al[3] who in fact demonstrated less distension and diarrhoea in their enterally fed group. Carr et al[3] demonstrated that the incidence of nausea and vomiting was much higher in the enterally fed patients as compared to the control group. In contrast, the incidence of nausea and vomiting was only marginally increased in the enterally fed patients in the study carried out by Heslin et al.[7] The difference in the route of feeding, naso-jejunal versus feeding jejunostomy could be the reason for this difference.

The analyses of the results indicate that even after generalised peritonitis the gastrointestinal tract recovers its tone and function within 48 hours. The gut perforation after repair remains secure, and is not put to any risk of leakage by enteral nutrition started at 48 hours after surgery. The already proven advantages of early enteral nutrition[7,8] after elective gastrointestinal surgery are clearly seen in patients with peritonitis as well. The study cases clearly did better as far as parameters such as weight, nitrogen balance and serum albumin were concerned. Unfortunately, in this study we have not been

able to calculate the savings in terms of manpower and cost. The long-term results in the form of intestinal obstructions and incisional hernias are also not available. We would have liked to have a third group of patients getting parenteral hyperalimentation but the expenditure to run such a trial would have been enormous and thus the most commonly used regimen was compared with a novel, inexpensive and seemingly beneficial regimen. A study comparing enteral and parenteral feeds supplying the same amounts of nutrition would shed more light on the exact benefits of the enteral route, if any, over the parenteral route. There was no way of knowing how much of the weight loss was due to oedema fluid and how much was the lean body mass lost. In the study group, some patients who would have had a negative nitrogen balance and low calorie intake were lost (died, were discharged or left against medical advice). This might have improved the results of the study group.

Though the incidence of major complications was reduced, the differences were not significant, the reduction in 'Man–Days' of major complications was substantial. This implies that the complications in enterally fed patients were controlled much more quickly than in conventionally managed patients. This suggests that the incidence of complications cannot be the parameter for the usefulness of enteral feeding in cases of emergency surgery for perforations of the gut, because the complications are inherent in the condition, e.g. wound infection or septicaemia in a case of faecal peritonitis. We thus, very strongly recommend early enteral nutrition in operated cases of gut perforations.

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