

Gut mucosal nutritional support – enteral nutrition as primary therapy after multiple system trauma

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Abstract

Over the past 10 years, several clinical and experimental studies report the potential benefit of enteral nutrition as primary therapy after multiple system trauma. In this study, 98 patients sustaining blunt and penetrating trauma were randomised to receive either enteral or parenteral feeding for 15 days. There were significantly fewer infectious complications in patients randomised to receive enteral feeding with particular benefit shown in the most severely injured patients. Serum protein concentrations correlated with the clinical outcome with an increase in constitutive protein and decrease in acute phase protein concentrations occurring in the enteral group through a decrease in septic complications and possible direct hepatic 'reprioritisation'. Enteral feeding serves as a primary therapy affecting the outcome of critically ill patients.

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In 1980, Alexander *et al*¹ found a lower septic morbidity and higher survival rate in burned children randomised to receive a protein enriched rather than a standard protein enteral diet and proposed that either the quality or quantity of enteral protein was important in outcome after burn injury. Within two years, Kudsk and Sheldon noted a significantly lower death rate when malnourished² or well nourished uninjured rats³ were randomised to receive enteral administration of standard total parenteral nutrition solution compared with animals given the same solution intravenously. Subsequently, intense laboratory investigations record deterioration of gastrointestinal barriers with intravenous feeding, which are maintained when nutrients are delivered enterally. Subsequent clinical studies in select populations of patients sustaining burns,⁴ closed head injury,⁵⁻⁷ and blunt and penetrating trauma substantiates the efficacy of enteral nutrition.^{8,9}

Many clinicians remain sceptical of the importance of enteral nutrient administration and, without convincing data showing clear clinical benefits, avoid intubation of the post-pyloric gastrointestinal tract in critically ill patients. Unfortunately, in the few randomised, prospective studies to date, the most severely injured patients have been excluded from study.^{8,9} To compare the efficacy of early

enteral with early parenteral feeding on the outcome of severely injured trauma patients during the first 15 days of their stay in hospital, unselected trauma patients admitted to a very active urban trauma centre who were at risk of developing septic complications were randomised to the two methods of feeding.¹⁰ Outcome measurements included septic morbidity, nutrient delivery, and postinjury complication rates.

Methods

Ninety eight patients 18 years of age or greater who sustained injuries with an abdominal trauma index (ATI) ≥ 15 had jejunostomy tube placement after management of intra-abdominal injuries. Within eight hours, the nutrition support service at our institution randomised these patients to receive either enteral or parenteral feeding using a computer generated randomisation table. Increasing severity of injury did not exclude patients from randomisation and study. Injury severity scores (ISS) were calculated soon after admission. Patients were not excluded because of excessive blood loss (>25 units in 24 hours), reoperation in 72 hours, or an ATI >40. The study design and consent was approved by the institutional review board of the University of Tennessee, Memphis. Enteral or parenteral nutrition was started in all patients within 24 hours except eight patients in whom continued haemorrhage dictated early abdominal closure and reoperation within 72 hours. In these patients, jejunostomies were placed at the time of the second surgery and patients were randomised to either enteral or parenteral feeding at that time.

The enteral formula chosen was the low bid enteral product at our institution at the start of this study (Vital HN, Ross Laboratories, Columbus, Ohio), and there was no corporate sponsorship. The total parenteral nutrition group received a parenteral formula with similar concentrations of protein (Travasol, Clintec Nutrition, Deerfield, IL), carbohydrate, and fat. Nutrition advanced toward a goal rate of 1.5-2.0 g/kg/d of protein/amino acids and 30-35 kcal/kg/d of non-protein calories. Urine collections were obtained from the first 25 patients admitted to the trauma intensive care unit on days 1, 4, 7, and 10 and venous blood was obtained for protein analysis on the same days in the first 68 patients entered into the clinical studies.

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Patient characteristics

	Enteral (n=51)	Parental (n=45)
Age (Mean (SEM) (y)	30.4 (1.7)	30.6 (1.4)
ATI	29.1 (1.8)	29.1 (1.4)
ISS	25.1 (1.7)	25.1 (1.9)
Length of stay in hospital (days)	20.5 (2.8)	19.6 (2.8)
Blunt injury (%)	16.0 (31.4)	10.0 (22.2)
Penetrating injury (%)	35.0 (68.6)	35.0 (77.8)
Total blood requirements (units)	8.9 (1.5)	9.6 (2.1)
Ventilator days	2.8 (0.7)	3.2 (1.0)

ATI=abdominal trauma index; ISS=injury severity score.

Pneumonia, intra-abdominal abscess, empyema, line sepsis, necrotising fasciitis, or wound infections with dehiscence during the first 15 days were considered septic complications. Urinary tract and minor wound infections were not considered septic complications in this study. Diarrhoea was defined as unformed, watery stool occurring three or more times/24 hour period.

Both enteral and parenteral nutrition were continued in patients until they could tolerate an oral diet. Two patients failed enteral nutrition because they could not tolerate at least 50% of nutrient goals by one week. These two patients were switched to total parenteral nutrition, but their complications were included in the enteral analysis. No enrolled patients were dropped from the study except for two deaths within four days as a result of progressive multiple organ dysfunction syndrome.

Results

Ninety six of 98 patients completed the study. There were no significant differences in age, ATI, ISS, length of stay in hospital, mechanism of injury, blood requirements, or ventilator days between the two patient groups (Table).

There were also no significant differences in nitrogen balance between the enteral nutrition and total parenteral nutrition groups on any day although the enteral nutrition patients received significantly less nutrition than the total parenteral nutrition group mean (SEM) (15.7 (4.2) *v* total parenteral nutrition 19.1 (3.3) non-protein calories/kg/d ($p<0.05$)). The maximum rate of nutrition given (29.0 (1.5) *v* total parenteral nutrition – 31.7 (1.2) non-protein calories/kg/d) was similar between the groups.

There were significantly fewer cases of pneumonia (6/51 *v* total parenteral nutrition 14/45, $p<0.02$), intra-abdominal abscesses (1/51 *v* total parenteral nutrition 6/45, $p<0.04$), and line sepsis (1/51 *v* total parenteral nutrition 6/45, $p<0.05$) in the enterally fed patients. Four of the five cases of empyema occurred in the total parenteral nutrition fed group. Dehiscence and fasciitis rates were comparable. Of the six patients in the total parenteral nutrition group with line sepsis, five had a simultaneous pneumonia, intra-abdominal abscess, or empyema, or all three. Enteral feeding was associated with significantly fewer infections/patient (0.25 (0.06) *v* total parenteral nutrition 0.71 (0.14, $p<0.03$) and significantly fewer infections/infected patients

(1.08 (0.08) *v* total parenteral nutrition 1.6 (0.8), $p<0.04$). Of the 12 enterally fed patients who developed an infection, nine developed a single focus of infection. Of the 20 patients in the total parenteral nutrition group who developed an infection, 14 had two or more infections develop.

Enteral nutrition had minimal benefit in the patients who were the least severely injured with no significant differences in infection rates in patients with an ISS ≤ 20 or an ATI ≤ 24 . In the patients with ATI ≥ 24 , however, total parenteral nutrition was associated with a sevenfold increase in the risk of infection. In those patients with a high ISS (>20), infection developed in 13 of 25 (52%) of the total parenteral nutrition group *v* only five of 34 (14.7%) of the enteral nutrition group ($p<0.002$), so that total parenteral nutrition feeding was associated with an increase of septic complications by a factor of 6.3. Total parenteral nutrition was associated with a significantly higher incidence of infection after pancreatic ($p<0.02$) and liver ($p<0.02$) injuries and barely missed statistical significance for stomach ($p<0.08$) and splenic ($p<0.07$) injuries.

Of patients with an ATI ≥ 40 (n=14: seven enteral nutrition, seven total parenteral nutrition), requiring more than 25 units of blood during the first 24 hours (n=4; three enteral nutrition, one total parenteral nutrition), or requiring reoperation within the first 72 hours (n=8; six enteral nutrition, two total parenteral nutrition), enteral feeding seemed to be associated with a lower incidence of pneumonia, intra-abdominal abscess, or empyema or all three while almost reaching statistical significance ($p=0.07$). In this severely injured population, total parenteral nutrition was associated with significantly more infections/patient (0.4 (0.2) *v* total parenteral nutrition 1.2 (0.3), $p=0.03$) and significantly more infections/infected patients (1.0 (0) *v* total parenteral nutrition 1.6 (3.0) $p<0.01$).

There were several complications related to enteral feeding that could not be ignored. One patient developed a bowel obstruction secondary to technical error at the jejunostomy tube site placement. Total parenteral nutrition was associated with a significantly lower rate of diarrhoea than patients fed enterally (total parenteral nutrition 7/45 and enteral nutrition 11/51, $p<0.01$).

Changes in serum protein concentrations were consistent with the reduction in septic morbidity in the enterally fed population. While there were no significant differences in serum albumin, α_1 -acid glycoprotein, or fibronectin, transferrin improved significantly on days 7 and 10 in the enterally fed group, and these values were significantly higher than total parenteral nutrition fed patients on days 7 and 10. Pre-albumin values remained significantly below baseline on days 4 and 7 in the total parenteral nutrition group. In the enteral group, however, pre-albumin values gradually increased after an initial depression on day 5 and on day 7 was significantly higher than in the total parenteral nutrition group. C reactive

protein, a marker of the acute inflammatory response, increased significantly from baseline on days 4, 7, and 10 in the total parenteral nutrition group but gradually dropped with enteral feeding becoming significantly lower in the enteral population on days 7 and 10.

Discussion

Acute injury increases metabolic requirements, stimulates hepatic acute phase protein synthesis, accelerates lean tissue mobilisation, and produces significant nitrogen and weight loss. Septic complications prolong hypermetabolism and increase nitrogen loss while accelerating the development of malnutrition and potentially increasing the incidence of infection and death. While administration of nutrients has been used to reduce nitrogen loss by the body, only recently has it been clear that the route of nutrient administration influences subsequent septic complications.

Alexander *et al*¹ first reduced septic morbidity and increased survival by feeding a high protein diet to paediatric burn patients. Subsequently, Moore *et al*^{8,9} reduced the development of intra-abdominal abscesses and pneumonia after injury by giving early enteral nutrition after blunt and penetrating trauma. Border *et al*¹¹ confirmed a lower septic rate in intensive care unit patients who received most of their nutrition by the gastrointestinal tract. These findings also extended to patients sustaining severe closed head injuries. Rapp⁵ and Young⁶ noted some beneficial effects with early total parenteral nutrition; septic complications, such as pneumonia, developed in a high percentage of patients. Graham *et al*⁷ found that the incidence of bacterial infections and the number of days in the intensive care unit could be significantly lowered with the administration of early enteral feeding.

This study in unselected trauma patients at risk of developing septic complications confirms that nutrients given by enteral methods reduces septic morbidity significantly better than parenteral nutrition. The most dramatic effects occur in the most severely injured trauma patients with high ATIs or high ISSs. The acute phase protein response seemed to mirror the changes in septic morbidity with a return of the transport proteins to normal and a decrease in acute phase proteins more rapidly with enteral feeding. Sganga *et al*¹² concluded that the development of sepsis was associated with a decrease in the transport proteins,

albumin and transferrin and increased concentrations of the acute phase proteins such as α_1 -glycoprotein and C reactive protein. In at study the investigators failed to control for the route and amount of nutrient given. Moore *et al*¹³ noted a hepatic 'reprioritisation' and blunting of the acute phase response in enterally fed patients but, because of insufficient numbers, did not unravel the interaction between septic complications and hepatic effects of enteral nutrition. This study illustrates the increase in constitutive proteins and decrease in acute phase protein occurring through a decrease in septic complications and possible direct hepatic effects. A reduction in septic complications seems to be the most important factor.

While the mechanisms for reduced septic morbidity and changed hepatic protein concentrations remain unknown, the principles are obvious. Physicians should obtain enteral access whenever possible and deliver nutrients as tolerated into the gastrointestinal tract of critically ill patients. Numerous clinical studies to date provide convincing evidence that enteral feeding serves as a primary therapy affecting the outcome of critically ill patients.

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