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Enteral and parenteral nutrition: evidence-based approach

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Nutrition support for patients in hospital has become an essential form of therapy. Total parenteral nutrition (TPN) was the preferred way of giving nutrition to hospital patients for many years but enteral nutrition (EN) is now the preferred route. EN is believed to promote gut function and prevent translocation of intestinal bacteria, thus reducing the incidence of sepsis in critically ill patients. In consequence, the use of TPN has been discouraged as a dangerous form of therapy. Critical review of the data suggests that in the human subject TPN does not cause mucosal atrophy or increase translocation of bacteria through the small intestine. However, overfeeding, which is easy with TPN, can explain the results of studies which have shown that TPN increases sepsis. Furthermore, the risks of TPN-induced complications have been exaggerated. When there is risk of malnutrition and EN is not tolerated, or there is gut failure, TPN is an equally effective and safe alternative.

Total parenteral nutrition: Enteral nutrition

The role of malnutrition as a risk factor for increased morbidity was recognized about 40 years ago in hospitalized patients. Malnutrition in hospital patients was treated by the use of total parenteral nutrition (TPN). It was widely accepted that if some nutrition is good, more must be better and the term 'hyperalimentation' was coined and practised. However, this enthusiasm gave way to reality that TPN not only did not reduce morbidity, but also increased complications under certain circumstances.

It was hypothesised that TPN by not feeding the intestinal tract caused atrophy of the intestine, increased bacterial translocation and promoted sepsis in critically-sick patients resulting in multi-system organ failure. Feeding nutrients through the intestinal tract prevented this sepsis and resulted in less morbidity and mortality than TPN. In the present review it is proposed to critically examine the relative merits of enteral nutrition (EN) and TPN.

Parenteral nutrition *v.* standard care

Gut failure

In patients with extensive intestinal resection, unless TPN is given severe malnutrition was documented, leading to increased morbidity and mortality. TPN at home prolongs life and reduces complications (Jeejeebhoy *et al*. 1973; Howard & Hassan, 1998; Messing *et al*. 1999).

Critical illness

Heyland *et al*. (1998) performed a meta-analysis of twenty-six randomised controlled trials involving 2211 patients in which TPN was compared with standard care. They found that in patients undergoing surgery and in those with burns or pancreatitis and in the intensive care unit TPN did not reduce mortality and overall morbidity. However, TPN significantly reduced morbidity in patients who were malnourished (risk ratio 0·52 (95 % CI 0·3, 0·91)).

In order to show that TPN reduces complications it has to be studied in those patients where there are increased complications. Naber *et al*. (1997) have shown that the presence of malnutrition increases the risk of morbidity in hospital patients. Thus, it is not surprising that TPN was of benefit only in malnourished patients.

Peri-operative total parenteral nutrition

Twomey and colleagues (Klein *et al*. 1997), by data pooling in patients receiving pre-operative TPN, showed that there was a 10 % risk reduction of complications, but post-operative TPN increased complications by 10 %. In patients undergoing hepatectomy, pre-operative TPN reduced the incidence of overall complications, sepsis and diuretic use (Fan *et al*. 1994). In contrast, in the Veterans' Association trial (VA TPN Cooperative Study, 1991) the use of

Abbreviations: EN, enteral nutrition; TPN, total parenteral nutrition.

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Table 1. Total parenteral nutrition (TPN) and intestinal atrophy in human subjects

Reference	Outcome
Guedon *et al*. (1986)	No atrophy after 21 d of NPO
Rossi *et al*. (1993)	Atrophy after 9 months of NPO
Pironi *et al*. (1994)	Atrophy after 2–3 months of TPN
Sedman *et al*. (1995)	No atrophy with TPN *v.* enteral for ≥10 d
Groos *et al*. (1996)	Atrophy after 7–12 weeks of TPN

NPO, nil per os (nothing fed by mouth).

pre-operative TPN giving 4180 kJ (1000 kcal) above requirements increased the risk of sepsis, especially in those patients who were not malnourished at entry. Clearly, it is bad to feed excess energy to well-nourished individuals. Bozzetti *et al*. (2000) had found that TPN reduced non-infectious complications and did not increase sepsis.

Theory of the benefits of enteral nutrition

Prevents mucosal atrophy

This concept was developed from animal studies which showed that giving TPN resulted in significant intestinal villus atrophy within a few days (Miura *et al*. 1992). However, human studies have not shown any intestinal atrophy with complete bowel rest and TPN even after 1 month of withdrawing food by mouth (Table 1).

Prevents bacterial translocation

Rigorous studies were performed in human subjects, in which bacterial translocation from the intestine was identified by culturing the same organism in the blood as well as in the intestine and the mesenteric lymph nodes. These studies showed that translocation occurs, especially with intestinal obstruction, but its incidence is no different between patients receiving TPN or EN (Sedman *et al*. 1994). Even the majority of patients suffering from trauma did not have septicaemia from organisms found in the gut and only two patients of 132 had translocation (Moore *et al*. 1992).

Nutrients and sepsis

Progressive starvation will ultimately lead to death and malnutrition is associated with an increased risk of complications. Furthermore, it is not as well recognized that in the presence of sepsis an increased intake of energy (carbohydrates or fats) increases the risk of complications (Zaloga & Roberts, 1994). The risk of complications with increased energy intake is especially associated with the development of hyperglycaemia (Golden *et al*. 1999) and hyperglycaemia is prone to occur in patients with sepsis who are insulin resistant. In septic guinea-pigs, increased intake of energy caused an increase in mortality (Yamazaki *et al*. 1986). In tumour necrosis factor-infused animals simply feeding sufficient energy to promote normal growth caused increased complications (Matsui *et al*. 1993).

The trials comparing EN and TPN should be examined with a view to determining whether they were comparable in terms of energy intake. Excess energy intake with EN or TPN influences the risk of sepsis.

Enteral nutrition *v.* total parental nutrition: outcome analysis

Pancreatitis

McLave *et al*. (1997) randomized thirty-two patients to receive either TPN or EN and did not observe any difference in rates of infection or morbidity. Windsor *et al*. (1998) randomized thirty-four patients with acute pancreatitis to either TPN or EN and did not observe any difference in incidence of sepsis, length of hospital stay, computed tomography score or organ failure. Kalfarentzos *et al*. (1997) randomized thirty-eight patients to either EN or TPN and showed that patients receiving TPN had a higher incidence of sepsis but did not increase the stay in the intensive care unit or the hospital. In this study, also, TPN did not increase the need for antibiotics or ventilator support.

Inflammatory bowel disease

A randomized controlled trial comparing TPN with EN or TPN given together with an oral diet in Crohn's disease did not show any increased complications due to TPN, and the rate or remission between the two modalities of Crohn's disease was the same (Greenberg *et al*. 1998). In acute colitis it was shown that patients receiving TPN had an increased rate of sepsis; however, the rate of colectomy or remission of disease activity were not different between the two groups (Gonzalez-Huix *et al*. 1993).

Trauma

Moore *et al*. (1989) randomized twenty-nine patients to EN and thirty patients to TPN. There was significantly increased incidence of sepsis in patients receiving TPN ($P = 0{\cdot}03$). However, patients on TPN received significantly more energy ($P = 0{\cdot}01$), higher levels of insulin and had numerically higher levels of plasma glucose. They were overfed as compared with EN patients. Kudsk *et al*. (1992) randomized ninety-eight patients to either EN or TPN; again the patients on TPN received significantly more energy ($P = 0{\cdot}02$). The patients randomized to TPN who had high injury severity score or high adominal trauma index scores had increased sepsis. Despite the increased sepsis they did not receive more antibiotics nor did they remain longer in hospital.

Sepsis

Cerra *et al*. (1988) randomized sixty-six patients who were septic and hypermetabolic to EN or TPN and found that there was no difference in the incidence of multi-system organ failure or death between the two groups.

Procedure-related complications

The general belief is that procedure-related complications are greater in patients receiving TPN because of catheter

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related problems. In contrast to belief, the facts are that in seven of nine randomized trials of EN *v*. TPN where procedure-related complications were reported, the incidence was higher during EN (Lipman, 1998).

Conclusion

TPN is the form of nutritional support most suited to patients with gut failure in whom it is life-saving and beneficial when there is malnutrition. Unfortunately, overfeeding easily occurs with TPN and increases the risk of sepsis. There is little evidence that intestinal atrophy and increased bacterial translocation occur in human subjects on TPN. TPN is associated with less procedure-related complications than EN. In short, where indicated because of the inability to give EN, TPN is beneficial in the treatment of malnutrition but is not a cure for all illnesses. These conclusions have received support from a recent 562 patient trial of EN *v.* TPN which concluded that TPN did not increase sepsis, EN delivered less than the target nutritional intake and the procedure-related complications were greater with EN (Woodcock *et al.* 2000).

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References

Bozzetti F, Gavazzi C, Miceli R, Rossi N, Mariani L, Cozzaglio L, Bonfanti G & Piacenza S (2000) Perioperative total parenteral nutrition in malnourished, gastrointestinal cancer patients: a randomized, clinical trial. *Journal of Parenteral and Enteral Nutrition* **24**, 7–14.

Cerra FB, McPherson JP, Konstantinides FN, Konstantinides NN & Teasley KM (1988) Enteral nutrition does not prevent multiple organ failure syndrome (MOSF) after sepsis. *Surgery* **104**, 727–733.

Fan ST, Lo CM, Lai EC, Chu KM, Liu CL & Wong J (1994) Perioperative nutritional support in patients undergoing hepatectomy for hepatocellular carcinoma. *New England Journal of Medicine* **331**, 1547–1552.

Golden SH, Linda Kao WH, Peart-Vigilance C & Brancati FL (1990) Perioperative glycemic control and the risk of infectious complications in a cohort of adults with diabetes. *Diabetes Care* **22**, 1408–1414.

Gonzalez-Huix F, Fernandez-Banares F, Esteve-Comas M, Abad-Lacruz A, Cabre E, Acero D, Figa M, Guilera M, Humbert P, de Leon R & Gassul MA (1993) Enteral versus parenteral nutrition as adjunct therapy in acute ulcerative colitis. *American Journal of Gastroenterology* **88**, 227–232.

Greenberg GR, Fleming CR, Jeejeebhoy KN, Rosenberg IH, Sales D & Tremaine WJ (1998) Controlled trial of bowel rest and nutritional support in the management of Crohn's disease. *Gut* **29**, 1309–1315.

Groos S, Hunefeld G & Luciano L (1996) Parenteral versus enteral nutrition: morphological changes in human adult intestinal mucosa. *Journal of Submicroscopic Cytology and Pathology* **28**, 61–74.

Guedon C, Schmitz J, Lerebours E, Metayer J, Audran E, Hemet J & Colin R (1986) Decreased brush border hydrolase activities without gross morphologic changes in human intestinal mucosa after prolonged total parenteral nutrition of adults. *Gastroenterology* **90**, 373–378.

Heyland DK, MacDonald S, Keefe L & Drover JW (1998) Total parenteral nutrition in the critically ill patient. A meta-analysis. *Journal of the American Medical Association* **280**, 2013–2019.

Howard L & Hassan N (1998) Home parenteral nutrition. 25 years later. *Gastroenterology Clinics of North America* **27**, 481–512.

Jeejeebhoy KN, Zohrab WJ, Langer B, Phillips MJ, Kuksis A & Anderson GH (1973) Total parenteral nutrition at home for 23 months without complication and with good rehabilitation. A study of technical and metabolic features. *Gastroenterology* **65**, 811–820.

Kalfarentzos F, Kehagias J, Mead N, Kokkinis K & Gogos CA (1997) Enteral nutrition is superior to parenteral nutrition in severe acute pancreatitis: results of a randomized trial. *British Journal of Surgery* **84**, 1665–1669.

Klein S, Kinney J, Jeejeebhoy KN, Alpers D, Hellerstein M, Murray M & Twomey P (1997) Nutritional support in clinical practice: review of published data and recommendations for future research directions. National Institutes of Health, American Society for Parenteral and Enteral Nutrition, and American Society for Clinical Nutrition. *American Journal of Clinical Nutrition* **66**, 683–706.

Kudsk KA, Croce MA, Fabian TC, Minard G, Tolley EA, Poret A, Kuhl MR & Brown RO (1992) Enteral versus parenteral feeding. *Annals of Surgery* **215**, 503–513.

Lipman TO (1998) Grains or veins: Is enteral nutrition really better than parenteral nutrition? A look at the evidence. *Journal of Parenteral and Enteral Nutrition* **22**, 167–182.

McLave SA, Greene LM, Snider HL, Makk LJ, Cheadle WG, Owens NA, Dukes LG & Goldsmith LJ (1997) Comparison of the safety of early enteral vs parenteral nutrition in mild acute pancreatitis. *Journal of Parenteral and Enteral Nutrition* **21**, 14–20.

Matsui J, Cameron RG, Kurian R, Kuo GC & Jeejeebhoy KN (1993) Nutritional, hepatic, and metabolic effects of cachectin/tumor necrosis factor in rats receiving total parenteral nutrition. *Gastroenterology* **104**, 235–243.

Messing B, Crenn P, Beau P, Boutron-Ruault MC, Rambaud JC & Matuchansky C (1999) Long-term survival and parenteral nutrition dependence in adult patients with the short bowel syndrome. *Gastroenterology* **117**, 1043–1050.

Miura S, Tanaka S, Yoshioka M, Serizawa H, Tashiro H, Shiozaki H, Imaeda H & Tsuchiya M (1992) Changes in intestinal absorption of nutrients and brush border glycoproteins after total parenteral nutrition in rats. *Gut* **33**, 484–489.

Moore FA, Moore EE, Jones TN, McCroskey BL & Peterson VM (1989) TEN versus TPN following major abdominal trauma-reduced septic morbidity. *Journal of Trauma* **29**, 916–923.

Moore FA, Moore EE, Poggetti RS & Read RA (1992) Postinjury shock and early bacteremia. A lethal combination. *Archives of Surgery* **127**, 893–897.

Naber THJ, Schermer T, de Bree A, Nusteling K, Eggink L, Kruimel JW, Bakkeren J, van Heereveld H & Katan MB (1997) Prevalence of malnutrition in nonsurgical hospitalized patients and its association with disease complications. *American Journal of Clinical Nutrition* **66**, 1232–1239.

Pironi L, Paganelli GM, Miglioli M, Biasco G, Santucci R, Ruggeri E, Di Febo G & Barbara L (1994) Morphologic and cytoproliferative patterns of duodenal mucosa in two patients after long-term total parenteral nutrition: changes with oral refeeding and relation to intestinal resection. *Journal of Parenteral and Enteral Nutrition* **18**, 351–354.

Rossi TM, Lee PC, Young C & Tjota A (1993) Small intestinal mucosa changes, including epithelial cell proliferative activity, of children receiving total parenteral nutrition (TPN). *Digestive Diseases and Sciences* **38**, 1608–1613.

Sedman PC, MacFie J, Palmer MD, Mitchell CJ & Sagar PM (1995) Preoperative total parenteral nutrition is not associated with mucosal atrophy or bacterial translocation in humans. *British Journal of Surgery* **82**, 1663–1667.

Sedman PC, Macfie J, Sagar P, Mitchell CJ, May J, Mancey-Jones B & Johnstone D (1994) The prevalence of gut translocation in humans. *Gastroenterology* **107**, 643–649.

VA TPN Cooperative study (1991) Perioperative total parenteral nutrition in surgical patients. *New England Journal of Medicine* **325**, 525–532.

Windsor AC, Kanwar S, Li AG, Barnes E, Guthrie JA, Spark JI, Welsh F, Guillou PJ & Reynolds JV (1998) Compared with parenteral nutrition, enteral feeding attenuates the acute phase response and improves disease severity in acute pancreatitis. *Gut* **42**, 431–435.

Woodcock NP, Zeigler D, Palmer MD, Buckley P, Mitchell CJ & Macfie J (2000) Enteral versus parenteral nutrition: a pragmatic study. *Nutrition* **17**, 1–12.

Yamazaki K, Maiz A, Moldawer LL, Bistrian BR & Blackburn GL (1986) Complications associated with overfeeding of infected animals. *Journal of Surgical Research* **40**, 152–158.

Zaloga GP & Roberts P (1994) Permissive underfeeding. *New Horizons* **2**, 257–263.

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