

## CLINICAL @LERT

# Total parenteral nutrition with glutamine dipeptide shortened hospital stays and improved immune status and nitrogen economy after major abdominal surgery

Morlion B<sup>†</sup>, Stehle P, Wachtler P, et al. Total parenteral nutrition with glutamine dipeptide after major abdominal surgery. A randomized, double-blind, controlled study. *Ann Surg* 1998 Feb;227:302–8.

## Question

Is total parenteral nutrition with glutamine dipeptide after major abdominal surgery effective for improving patients' nitrogen economy and immune status and for shortening the length of hospital stay?

## Design

6 day randomised, double blind, controlled trial.

## Setting

Hospital in Germany.

## Patients

28 patients (mean age 68 y, 57% women) who were 42 to 86 years of age and were admitted for elective resection of carcinoma of the colon or rectum. Exclusion criteria were evident metabolic diseases, or chronic renal or liver diseases.

## Intervention

All patients received 5 days of continuous total parenteral nutrition containing nitrogen (TPN), 0.24 g/kg/day (isonitrogenous) and 122 kJ/kg/day (isoenergetic). TPN was supplemented by either amino acids, 1.2 g/kg day, plus the glutamine dipeptide l-alanyl-L-glutamine (Ala-Gln), 0.3 g/kg/day (n=15), or amino acids, 1.5 g/kg/day (n=13). TPN was given through a central venous catheter.

## Main outcome measures

Length of stay in hospital, nitrogen balance on days 2–5

after the operation, and immune status (lymphocyte count) on days 1, 3, and 6 after the operation.

## Main results

Patients in the Ala-Gln group had a shorter hospital stay than did those in the control group (15.5 v 21.7 days, p<0.05). Nitrogen balance was better for patients who received Ala-Gln than for those in the control group (mean daily nitrogen balance -2.31 v -5.73, p<0.001; cumulative nitrogen balance at 5 days -7.44 v -23.04, p<0.01). Patients in the Ala-Gln group had better lymphocyte recovery than did those in the control group on days 3 (1.82 v 1.16 lymphocytes/nL, p<0.05) and 6 (2.41 v 1.52 lymphocytes/nL, p<0.01). No side effects were reported.

## Conclusion

Total parenteral nutrition with the glutamine dipeptide l-alanyl-L-glutamine led to a shorter hospital stay and better nitrogen economy and lymphocyte recovery in patients who had major abdominal surgery.

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## Commentary

Few have done more than Furst, Stehle and colleagues<sup>1</sup> to develop the concept of the conditional essentiality of glutamine in metabolic stress and to develop a means by which this amino acid can be practically added, as an alanine dipeptide, to parenteral feeds from which it has hitherto been lacking. The double blind randomised trial by Morlion *et al* assesses the clinical efficacy of such supplementation. It was conducted in 28 patients, well nourished as judged by weight for height, undergoing elective surgery for colorectal cancer. They were randomised to receive isonitrogenous (0.24 g nitrogen/kg/day) isoenergetic (29 kcal/kg/day) total parenteral nutrition over five days postoperatively such that one group received within its total nitrogen allocation 0.3 g/kg/day L-alanyl-L-glutamine, or about 20 g of the dipeptide—equivalent to 13.5 g glutamine. Mean (SEM) length of hospital stay in the controls was 21.7 (2.8) days and in the intervention group 15.5 (0.72) days (p<0.05).

Length of hospital stay is a clinical endpoint which, as a surrogate for both clinical and economic efficiency, could be argued to be second only to mortality in

importance. Early hospital mortality can confound results but in this trial there was no mortality. Stay in hospital may be skewed and require analysis using non-parametric statistics. In this study results of length of stay are expressed as mean (SEM) suggesting that a *t* test was used. The length of hospital stay was determined by the “attending surgeon”, and the control length of stay was very similar to the unit's previous experience, if long by some standards. The homogeneity of the patient group strengthened the power of the study but raises questions of extrapolation to other clinical situations.

Though a number of studies have indicated benefit from early routine postoperative enteral<sup>2</sup> or oral feeding,<sup>3,4</sup> recent controlled trials<sup>5,6</sup> using unsupplemented feeds make routine postoperative parenteral nutrition difficult to justify in well-nourished patients. None the less this trial provides evidence of a benefit of an alanine-glutamine dipeptide supplemented feed over standard parenteral feeding. It should not imply that such an approach is optimal in this clinical context; use of early enteral or sip feeding might have been as effective or better. It is inter-

esting to speculate whether this strengthens the idea that enteral feeding is superior to parenteral feeding through its trophic effect on the gut. Glutamine enhanced parenteral feeding may, by preserving intestinal mucosal integrity, have an effect more comparable with enteral feeding than standard parenteral feeds.

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