Absorption of protein in the early postoperative period in chronic conscious dogs

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Summary. Postoperative alterations in amino acid exchange across the intestinal tract and in the capacity for protein absorption were investigated in a chronic canine model. Changes in postoperative splanchnic amino acid exchange consisted of a temporary decrease of total splanchnic amino acid release, including a significant reduction in alanine production, and an increase in glutamine consumption. Contrary to results under stable metabolic conditions, branched chain amino acids were also taken up by the intestine in the early postoperative period. The changes in postoperative amino acid exchange were not, however, reflected by a corresponding alteration in protein transport capacity. The absorptive capacity for a protein hydrolysate remained stable during the early postoperative period.
Key words. Postoperative protein absorption; jejunostomy; splanchnic amino acid exchange; canine model.

Major metabolic changes, including alterations in protein metabolism, characterize the postoperative period. These catabolic reactions accompanied by prolonged periods of inadequate nutrient intake require the institution of nutritional support. Recently, not only parenteral but also enteral nutrition has been used in the immediate postoperative period[8]. The clinical efficacy of enteral nutrition evaluated both as the frequency of postoperative complications and parameters of the nutritional status is comparable to the efficacy of parenteral nutrition[13].

Comparable to parenteral nutrition, enteral feeding is associated with specific complications. During the immediate postoperative period, diarrhea is the most frequent complication of enteral nutrition resulting in decreased transit time of nutrients, reduced contact between luminal nutrients and the absorptive mucosa, decreased absorption and finally reduced efficacy of nutritional support.

Although enteral nutrition is frequently applied in clinical practice, current knowledge regarding postoperative changes in the absorptive capacity for complex nutritive substrates is limited. Systematic investigations of the related problems are therefore required to improve the efficacy by selecting the optimal substrates for enteral nutrition and provide a better understanding of the pathogenesis of complications of enteral nutrition. Especially in the early postoperative period, such measurements cannot be performed in patients. During later stages, absorption in humans has usually been evaluated by measuring substrate disappearance from small intestinal segments; such measurements are not, however, representative for the total intestinal tract owing to local specificity for absorption of luminal nutrients (e.g. glucose in the proximal small bowel, amino acids in the jejunum etc.). For these reasons a chronic canine model was used to measure portal venous appearance rather than intestinal disappearance of luminally administered substrates in the early and late postoperative periods[7].

The aim of the present study was the investigation of postoperative changes in amino acid metabolism of the gut and the measurement of protein absorption in the immediate postoperative period.

Materials and methods. Three mongrel dogs were instrumented with portal venous and carotid artery catheters, an electromagnetic flow probe around the portal vein and a catheter jejunostomy as described previously[7]. Animals were allowed food from the 4th postoperative day. Postoperative experiments were performed on days 1, 2, 3 and between 7 and 10 days after the laparotomy.

All experiments started with a 30-min control period infusing isotonic saline at 200 ml/h into the jejunum. This period was used to investigate changes of intestinal amino acid metabolism in the postoperative state. Postoperative intestinal amino acid exchange under stable metabolic conditions (= steady state) was calculated from the control period of the 7th postoperative day and from the control periods of 17 successive experiments. Animals were admitted into the steady state experiments only when serum albumin was above 30 g/l, hemoglobin above 12 g% and leucocyte count below 20000, and when the animals were consuming more than ⅔ of their daily food ration and had normal stools[1]. The control period was followed by a 180-min test period. In the experiments reported here, a protein hydrolysate containing 10.4% alpha-amino nitrogen, with an average molecular weight of 1000 (Lactry 1®, Nestle SA, Vevey) was infused intrajejunally at isoosmolar concentration at a rate of 200 ml/h.

Portal venous blood flow was continuously recorded during both control and test periods. Arterial and portal venous blood samples were drawn at 30-min intervals. Amino acid metabolism of the splanchnic tract or absorption of enterally infused amino acids was calculated according to the following equation:

$A = (C_p - C_a) \times f.$

A = absorption

C_p, C_a = portal venous and arterial substrate concentration (mg/ml)

f = portal venous flow (ml/min).

Amino acids were analyzed in protein free plasma according to Stein-Moore using an LC 5001 Biotronic automatic amino acid analyzer.

Results. The portal venous blood flow during the first three postoperative days was about 700 ml/min during the control period infusing isotonic saline. Flow increased to 900 ml/min during the infusion of the protein hydrolysate (fig. 1).

During the control period the total release of amino acids from the gut decreased from 2.464 µmol/kg × min during stable metabolic conditions to values close to 0 during the first postoperative day (fig. 2 and 4). The release of alanine (ALA) from the intestinal tract was found to be decreased to 0.8 µmol/kg × min compared with a value of 1.2 µmol/kg × min during steady state conditions. On the first postoperative day, the extraction of glutamine (GLN) by the gut increased from 1.3 µmol/kg × min during steady state to 2 µmol/kg × min (figs 2 and 4). A number of other amino acids were also taken up by the intestinal tract in the immediate postoperative period, in contrast to a corresponding release during stable metabolic conditions (leucine, valine, isoleucine, serine, threonine). Two days later, on the third postoperative day, the pattern of postabsorptive amino acid metabolism of the intestinal tract had returned to normal, comparable with a steady state pattern (fig. 3). The total amino acid release, the uptake of GLN and the release of alanine (ALA) are comparable with values measured during steady state, which is defined as the period following recovery of the dog (fig. 4).

Postoperative jejunal infusion of a protein hydrolysate resulted in differences in portal venous appearance of different groups of amino acids. The appearance of neutral amino acids (glycine, alanine, serine and threonine) increased from

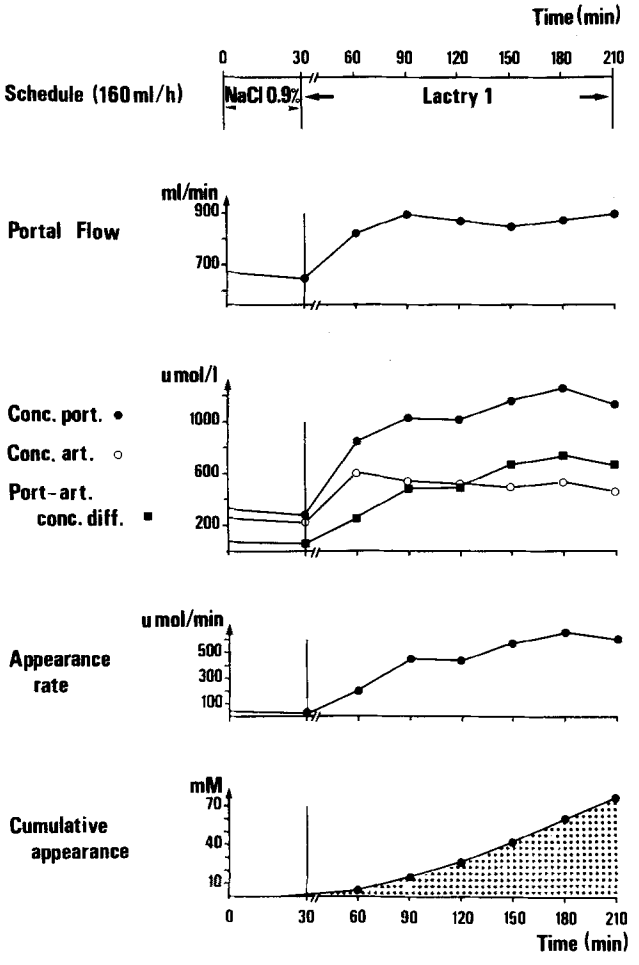

Figure 1. Absorption of alanine (ALA) during intrajejunal infusion the protein hydrolysate indicated. Infusion substrate: 1 g whey protein/kg b.wt/h. containing 57.3 mM ALA (Lactry 1, Nestlé SA, Verey). Portal venous flow was measured continuously plasma amino acids were measured at 30-min intervals in portal venous and arterial blood. Arteriovenous concentration differences and appearance rates were calculated according to the formula indicated above (cp. methods).

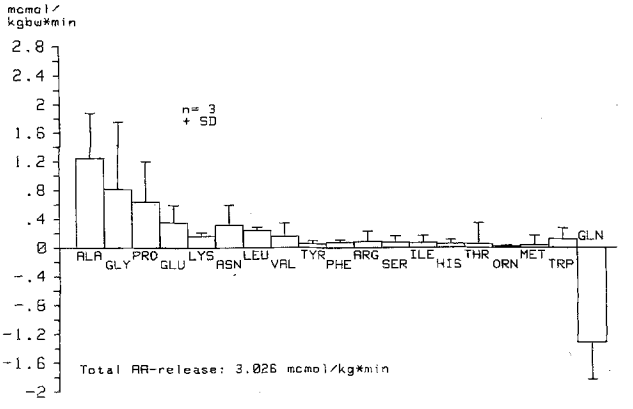

Figure 3. Amino acid exchange across the intestinal tract during 30-min intrajejunal infusion of 0.9% NaCl (= postabsorptive state) on the 3rd postoperative day.

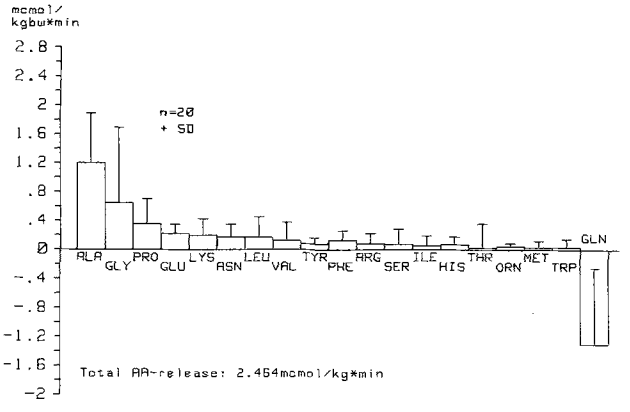

Figure 4. Amino acid exchange of the intestinal tract during stable metabolic conditions based on the control periods of 20 successive experiments.

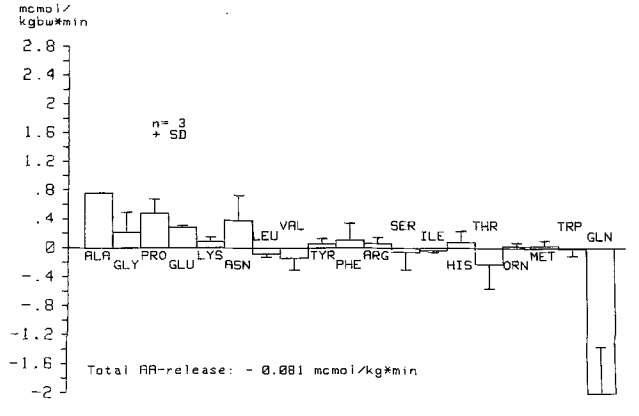

Figure 2. Amino acid exchange across the intestinal tract during 30-min intrajejunal infusion of 0.9% NaCl (= postabsorptive state) on the 1st postoperative day. Positive values indicate intestinal amino acid release into the portal vein, negative values intestinal consumption of the corresponding amino acid.

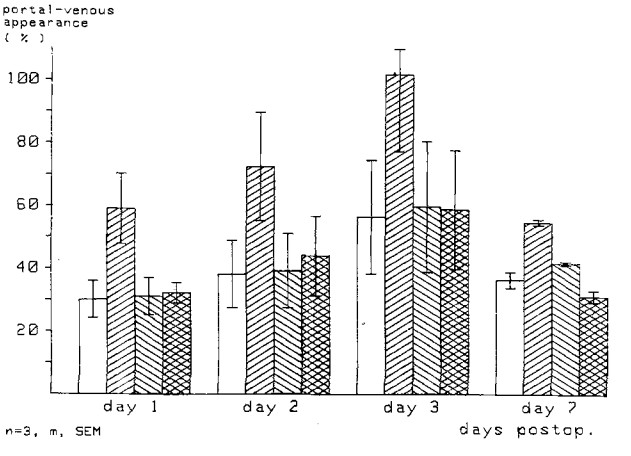

Figure 5. Portal venous appearance of neutral amino acids during jejunal infusion of a protein hydrolysate in the early postoperative period. Absorption is expressed as the percentage of the amino acid load infused. Successive bars for each day correspond to the amino glycine (GLY), alanine (ALA), serine (SER) and threonine (THR).

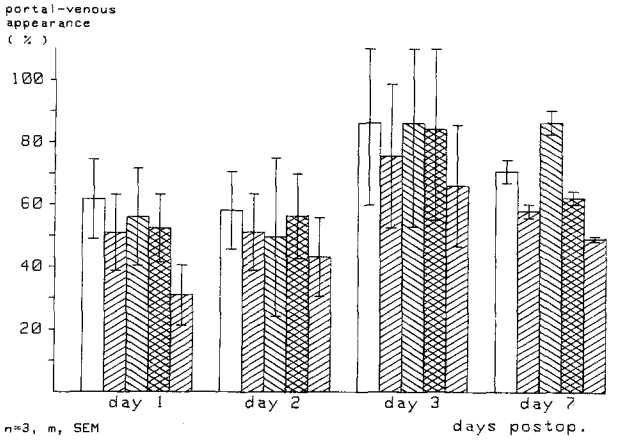

Figure 6. Portal venous appearance of cyclic amino acids during jejunal infusion of a protein hydrolysate in the early postoperative period. Absorption is expressed as the percentage of the amino acid load infused. Successive bars for each day correspond to the amino acids phenylalanine (PHE), tyrosine (TYR), proline (PRO), histidine (HIS) and tryptophane (TRP).

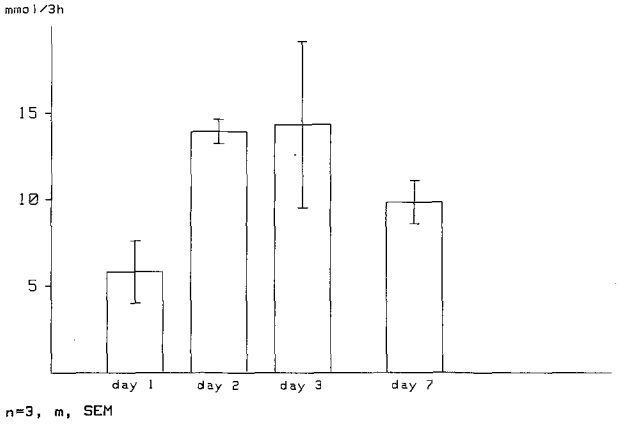

Figure 7. Portal venous appearance of glutamine (GLN) during jejunal infusion of a protein hydrolysate in the early postoperative period. Absorption is expressed in mmoles GLN recovered in the portal vein.

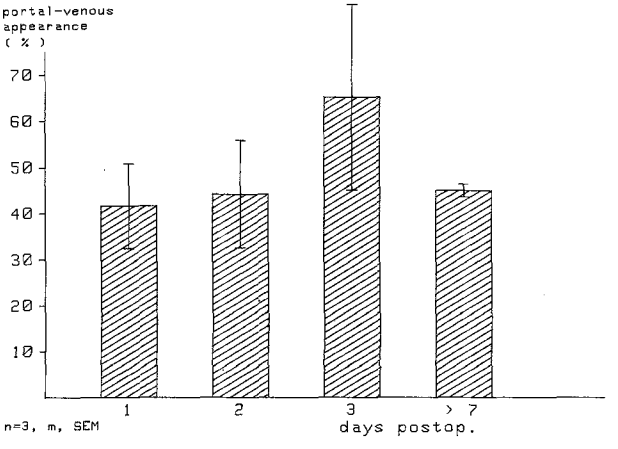

Figure 8. Total portal venous appearance of amino acids calculated on the basis of 17 amino acids during intrajejunal infusion of a protein hydrolysate in the early postoperative period. Absorption is expressed as the percentage of the amino acid load infused.

about 40% of the infused quantity on the first postoperative day to about 60% on the third postoperative day. However, the portal venous appearance during steady state conditions was comparable to absorption on the first postoperative day (fig. 5). This was found for the majority of amino acids investigated as well as for a total amino acid absorption calculated on the basis of 17 amino acids (fig. 8). With respect to the cyclic amino acids (phenylalanine, tyrosine, proline, histidine, tryptophane) a different pattern was observed: these amino acids showed an increase in appearance from day 1 to day 3 after the operation. Contrary to the findings with other amino acids, the absorption of these cyclic amino acids, calculated as a percentage, was higher during steady state than on the first postoperative day (fig. 6). The same pattern as for cyclic amino acids was found for glutamine (fig. 7).

Discussion. Absorption of enteral nutrients cannot be measured in patients in the immediate postoperative period. Also, luminal disappearance rates measured over short intestinal segments in healthy humans can be neither extrapolated to the absorptive capacity of the total intestinal tract nor regarded as representative for the immediate postoperative period. Therefore, a previously described canine model mimicking clinical nutrition with respect to nutrient application via jejunostomy in the early postoperative period was used to evaluate both the amino acid exchange over the intestinal tract and the absorptive capacity of the total gut in the early postoperative period.

Portal venous appearance of jejunally infused substrates was used as the measure of absorption. Calculation of uptake from the gut by this method depends not only on precise amino acid analyses in both portal venous and arterial plasma but also on valid portal venous flow measurements. The electromagnetic flow measuring technique is a sensitive method enabling continuous portal venous blood flow measurements in chronic conscious dogs. During the early postoperative period portal venous blood flow averaged 700 ml/min, values comparable to those communicated in the literature using dye dilution techniques [14]. The increase of portal venous flow following nutrient application is well documented both in man and in various animal species [9]. In our experiments, this response was also seen in the immediate postoperative period.

Amino acid exchange over the intestinal tract is the basis of absorption studies in that it provides information about the amino acid metabolism by the gut in the postabsorptive state. At the same time such measurements validate the sensitivity of the methods used, because the postabsorptive amino acid metabolism of the canine gut has previously been investigated [14]. The data obtained were in agreement with earlier results [3-5, 14], but in addition, our method enabled simultaneous monitoring of an unlimited number of substrate balances over the intestinal tract. Thus, complete amino acid profiles of intestinal uptake and release during the postabsorptive period were ducumented.

Out of these profiles, some particular data appear worthy of discussion. Glutamine is an important energy source for the gut. This has been shown by studies in both animals and man [6, 15]. About 25% of the glutamine extracted by the intestine is converted to alanine and released to the portal vein. Some glutamine nitrogen also appears as ammonia, citrulline and proline [17]. In agreement with preceding reports [14], uptake of glutamine by the intestinal tract was found to be increased in the early postoperative period. This increase in glutamine extraction by the intestinal tract seems to be a reaction specific for the postoperative period, because merely fasting dogs for 96 h leads to minimal changes only in glutamine uptake [12].

We speculate that the extracted glutamine is mainly used as a source of metabolic energy, because the output of amino

acids by the intestinal tract (e.g. alanine, proline) is reduced in the early postoperative period.

Branched chain amino acids (BCAA) are an important respiratory fuel of muscle tissue especially during starvation. They also play a role in the regulation of protein turnover [2]. During stable metabolic conditions, BCAA were released by the intestine in the postabsorptive state. In contrast, BCAA were taken up by the intestinal tract during the early postoperative period. We speculate that the intestine might use BCAA as a respiratory fuel in the postoperative period.

Alanine as an important gluconeogenic amino acid is known to be released from the gut to the portal vein [3, 4]. In the postoperative period, a decrease of intestinal alanine output was observed confirming corresponding reports of others [14]. SOUBA and co-workers suggest a decreased conversion of glutamine to alanine as the underlying mechanism of reduced splanchnic alanine output in the postoperative period [14].

Studies of amino acid metabolism in humans both during stable metabolic conditions and intraoperatively from portal venous and brachial artery blood samples document comparable changes [6, 11]. These reports on amino acid metabolism correspond to results obtained with the animal model used.

However, these data were evaluated in this investigation as the basis for the monitoring of protein absorption in the early postoperative period. Would alterations of the postoperative amino acid metabolism be associated with a corresponding change of the absorptive capacity? Intrajejunal infusion of a protein hydrolysate resulted in portal venous recovery rates between 40% and 60%. The high rate of infusion (1 g/kg × h), exceeding the range of clinical use (1–2 g/kg × d), is a potential cause for this low rate of absorption.

For most amino acids, absorption from the protein hydrolysate investigated on the first postoperative day did not differ from that during the later period of steady state conditions. Therefore, in spite of significant postoperative changes in the amino acid metabolism of the postabsorptive state no relevant change in the overall amino acid transport capacity from a defined hydrolysate was observed in the early postoperative period.

For some amino acids (PHE, TYR, PRO HIS, TRP, GLN) a decreased rate of absorption was observed on the first postoperative day. However, the magnitude of these changes was small (about 10%). Therefore, they do not appear to have significance with respect to clinical practice.

For most amino acids but also for the total amino acid load a transitional increase of portal venous appearance from the intrajejunally infused protein hydrolysate was observed in the early postoperative period. Correspondingly, after a 10-day period of dietary restriction an increased absorption of amino acids from both a protein hydrolysate and a free amino acid mixture has been reported for the rat [10]. A decrease in absorptive capacity due to decreased enzyme content of the gut only after a more extended period of starvation was observed [10]. We speculate that a short period of starvation had stimulated the transport capacity of the small intestine. The metabolic alterations of the intestinal tract in the postoperative period, with an increase in intestinal glutamine consumption and a concurrent decrease in portal venous appearance of glutamine from protein, confirm the importance of glutamine as a respiratory fuel of the gut. We speculate, therefore, that an increased glutamine content of enteral nutrient formulas might improve tolerance to enteral feeding and increase its efficacy by providing the preferred splanchnic fuel of the postoperative period.

In summary, measurement of portal venous appearance is appropriate for quantitative investigation of the absorption of complex nutrients even in the early postoperative period. In contrast, methods evaluating absorption from short intestinal segments only (e.g. perfusion techniques, thiry vella loop) cannot accurately reflect protein absorption, because such models do not take account of the regional transport specificities of the intestinal tract. Alterations in splanchnic amino acid metabolism have been demonstrated in the postoperative period, whereas the transport capacity for a defined protein hydrolysate remained unchanged.

We are aware of the limitations of the findings so far: the results are based on three dogs and evaluation of one protein component. Further conclusions clearly require controlled experiments comparing different protein components including a non-nitrogen calorie source. The experiments presented here do, however, provide evidence that the intestinal transport capacity for the type of protein investigated (hydrolysate rich oligopeptides) is not reduced in the early postoperative period.

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