that parenteral Gln primarily serves for maintenance of the intestinal mucosa and secondarily to preserve muscle Gln pool and to improve overall N-economy during stress.

Peptides for parenteral nutrition: which ones?—whither the future

Peptides are new candidates for parenteral nutrition. Their potential use is based on the assumption that 'tailored' amino-acid solutions will increase the benefits of intravenous nutrition during episodes of catabolism and for specific patient groups. Specific diseases accompanied by certain amino-acid deficiencies, antagonisms or imbalances in various organ tissues might selectively require one or more 'favourite peptides' which are appropriate for use just in that given condition to support the attenuated tissue.

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Influence of Alpha-Ketoglutarate Infusion on Glutamate and Glutamine Metabolism

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Net breakdown of body protein and increased urinary nitrogen loss is common with major surgery, accidental injury and septicemia. One major metabolic sign of this protein-catabolic situation is a reduced concentration of free glutamine in skeletal muscle which correlates with a decreased protein synthesis.

In this study we investigated the influence of an infusion of alpha-ketoglutarate (A-KG) on the glutamine metabolism of (1) intensive care units patients and on (2) organ balances of anaesthetized dogs. We compared (3) the effect of an equimolar infusion of A-KG, glutamine and alanylglutamine, respectively on peripheral glutamine balances.

1. The present study was done to investigate the influence of alpha-ketoglutarate infusions to ICU patients on glutamine (GLN) and glutamate (GLU) metabolism and on blood chemistry.

We infused a 10% solution of sodium-AKG for 48 h (6 g on 1st day, 12 g on 2nd day) as a supplement to TPN (2 g AS, 35 kcal/kg bw/day) to 5 patients (2 with necrotising pancreatitis, 2 with Akijama, 1 with mamma CA).

Plasma A-KG was analysed enzymatically, plasma GLN and GLU by means of HPLC (OPA), blood chemistry was analysed with routine methods before, 24 and 48 h after the start of A-KG infusions.

The infusion of A-KG (i) evoked no visible side effects and did not alter routine-blood chemistry, (ii) increased the arterial A-KG levels and the A-KG uptake across the leg, and (iii) had no significant effect on arterial levels or A-V differences of GLN of GLU.

2. We investigated the effect of 1 h infusion of 10 μmol/kg body weight/min of glutamine, alanylglutamine (ALA-GLN) or alpha-ketoglutarate (A-KG) respectively, on the amino-acid exchange across the hindquarter in post-operative anaesthetized dogs. This study was performed because glutamine, contrary to

(μmol/l) $\bar{x} \pm s$	Before	After 48 hours
AKG	16.06 ± 1.72	75.2 ± 19.8***
ΔA-Fv	+5.7 ± 3.3	+13.9 ± 4.5*
GLN	431.8 ± 114	469.4 ± 142
ΔA-Fv	−42.8 ± 25.5	−28.2 ± 17.6
GLU	56.7 ± 22	54.2 ± 13.2
ΔA-Fv	+17.75 ± 22.7	+14.5 ± 8.8
Sodium (mmol/l)	139.4 ± 3.2	140.4 ± 6.4

+ = uptake; − = release

ALA-GLN or A-KG, is not stable in aqueous solution and can therefore hardly be used as an infusion substrate for parenteral nutrition.

The arterial levels of glutamine increased during the infusion of glutamine (from 448 ± 48 to 1453 ± 130 μmol/l) and of ALA-GLN (from 407 ± 51 to 1165 ± 123 μmol/l) but remained constant during the infusion of A-KG (basal period 454 ± 29, infusion period 391 ± 24 μmol/l). The arterial levels of ALA-GLN and A-KG were higher than the venous concentrations, indicating that an uptake of these two substances across the hindquarter had taken place (A-C: $+29 \pm 1$ μmol/l during ALA-GLN infusion, A-C: $+3 \pm 2$ μmol/l A-KG basal period, A-C $+44 \pm 5$ μmol/l during A-KG infusion). Neither ALA-GLN nor A-KG significantly influenced the blood flow. The arteriovenous difference of glutamine diminished during the infusion of glutamine (from -174 ± 25 to $+52 \pm 32$ μmol/l, $p < 0.01$) and of ALA-GLN (from -80 ± 14 to -3.3 ± 22 μmol/l, $p < 0.05$), but remained unchanged during A-KG infusion (-100 ± 9 in the basal period and -118 ± 14 μmol/l during infusion).

We conclude that the dipeptide ALA-GLN, unlike A-KG, is able to substitute glutamine as an infusion substrate for measuring plasma glutamine levels across hindquarter in a catabolic dog model.

3. Five beagle dogs (10–16 kg) were fasted overnight and on the morning of the study all dogs were subjected to general endotracheal anaesthesia. Each animal was subjected to a laparotomy through a midline abdominal incision for placement of silastic catheters in the distal aorta, portal vein, hepatic vein, renal vein and jugular vein. We compared the A-KG and amino-acid balances of a control period (NaCl infusion) with A-KG infusions at a rate of 10 (infusion period 1) and 20 (infusion period 2) μmol/min/kg, respectively.

Basal whole blood arterial levels of A-KG (between 5 and 10 μmol/l) increased up to 400 μmol/l during infusion period 1 and up to levels of 1500 during infusion period 2. The infusion of A-KG had no influence on plasma glutamate or glutamine levels. Positive arteriovenous concentrations of A-KG across hindquarter, liver, kidney and gut indicated an A-KG utilization of all investigated organs (skeletal muscle, liver, gut, kidney) in a dose dependent manner. The A-KG infusions had no influence on glutamine or glutamate exchange across skeletal muscle, liver and gut. However, the A-KG infusions decreased the glutamine uptake and increased the glutamate release from the kidney.

We conclude that the infusion of even unphysiologically high amounts of A-KG did not increase plasma GLN levels nor reduce the protein catabolism of skeletal muscle. However A-KG is taken up by various organs and may serve as a source of energy.