Ornithine α-ketoglutarate metabolism after enteral administration in burn patients: bolus compared with continuous infusion1,2

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ABSTRACT Ornithine α-ketoglutarate (OKG) has been successfully used as an enteral supplement in the treatment of catabolic states, including burn injury. However, specific questions remain unanswered concerning burn patients, including OKG metabolism and metabolite production, appropriate mode of administration, and dose. We thus performed a kinetic study and followed plasma ornithine and OKG metabolite concentrations on day 7 postburn in 42 (35 men, 7 women) consecutive burn patients aged 33 ± 2y with a mean (± SEM) total burn surface area (TBSA) of 31 ± 1%. Patients were randomly assigned to receive OKG as a single bolus (10 g; n = 13) or in the form of a continuous gastric infusion (10, 20, or 30 g/d over 21 h; n = 13) or an isonitrogenous control (n = 16). Plasma pharmacokinetics of ornithine followed a one-compartment model with first-order input ([r] = 0.993, P < 0.005). OKG was extensively metabolized in these patients (absorption constant = 0.028 min⁻¹, elimination half-life = 89 min), with the production of glutamine, arginine, and proline; proline was quantitatively the main metabolite [in OKG bolus, area under the curve (AUC)ₗₜₐₜₐₜₜ, proline, 41.4 ± 5.6 mmol·min/L; glutamine, 20.4 ± 5.7 mmol·min/L; and arginine, 7.3 ± 1.9 mmol·min/L]. Proline production was dose-dependent and quantitatively similar between modes of OKG administration. Glutamine and arginine production were not dose-dependent and were higher in the bolus group than in the infusion group. Overall, the bolus mode of OKG administration appeared to be associated with higher metabolite production compared with continuous infusion in burn patients, especially for glutamine and arginine. Am J Clin Nutr 1997;65:512–8.

KEY WORDS Ornithine α-ketoglutarate, burn injury, metabolites, kinetics, enteral administration

INTRODUCTION

Burn injury is associated with a durable hypermetabolic state (1) with increased protein turnover (2). Increased muscle protein breakdown and energy expenditure are responsible for the dramatic body wasting observed in patients with severe burns. Nutritional support plays a key role in the treatment of burn patients (3–5); however, conventional diets are unable to provide some specific amino acids, which become essential in these patients because of their catabolic state, especially during the hypercatabolic “flow” phase (days 2–14). Recent clinical trials have reported benefits from the use of specific nutritional therapies in burn patients, including arginine (6), branch-chain amino acid (7), and ornithine α-ketoglutarate (OKG) (8–13) supplementation. In several controlled prospective studies, OKG at the single dose of 10 (9–11) or 20 g/d in two 10-g boluses (8, 13) reduced protein hypercatabolism (9), improved nutritional status (9, 11, 13), and accelerated wound healing (13). In burned rats, a high dose of OKG (5 g·kg⁻¹·d⁻¹) decreased muscle protein breakdown induced by burn injury and restored the free glutamine pool (14).

The possibility that OKG might stimulate insulin and/or growth hormone production, as observed in trauma patients (15), is doubtful in burn patients (10). Alternatively, some OKG metabolites that regulate protein turnover, such as glutamine, arginine, and proline, become depleted 1 wk after injury (16). Data obtained in healthy subjects (17) or in experimental models (12) suggest that the production of these metabolites depends on the mode of enteral administration and/or the dose administered. Data extrapolated from healthy subjects (17), however, should be interpreted cautiously because quantitative requirements are higher and qualitative utilization of nutrients is modified in burn patients (1, 4).

We thus performed a prospective kinetic study in a large group of severely burned patients to address the specific issues of OKG metabolism and metabolite production as a function of the mode of enteral administration and the dose. Pharmacokinetic parameters of ornithine and appearance of metabolites were studied 7 d postburn, the peak time of hypermetabolic response in burn patients (16, 18). Patients were randomly assigned to receive enterally the molecule in the form of a bolus (10 g) or as a continuous gastric infusion (10, 20, or 30 g/d over 21 h). These doses and modes of enteral administration are those used in clinical practice (12), 10 g being the upper limit of OKG given in bolus, above which diarrhea appears (17). Results obtained in the present study should help to standardize the use of OKG as an enteral supplement in the nutritional management of burn patients.

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SUBJECTS AND METHODS

Patients

Fifty-four consecutive patients admitted to the burn intensive care unit of the St-Antoine Hospital for severe thermal burn injury who had a total burn surface area (TBSA) of 20–50% were scheduled to be included in a large clinical trial performed to evaluate the nutritional efficacy of enterally administered OKG (19). Exclusion criteria were as follows: age < 15 y or > 60 y, admission later than 48 h after burn injury, hepatic failure (prothrombin time < 50%, alanine aminotransferase or alkaline phosphatase activities more than three times the normal range), kidney failure, and no enteral nutritional support required. The procedures followed were in accord with the Helsinki Declaration of 1975 as revised in 1983.

Kinetics were determined on day 7 postburn, the peak time of the hypermetabolic response (16, 18). Patients with septicaemia or intolerant to enteral nutrition at the time the kinetics were performed were excluded; thus, 42 patients participated in the study. Their demographic data and routine biological blood indexes on the day of the kinetic studies are presented in Tables 1 and 2, respectively. No significant differences were noted between the three groups, except for TBSA, which was significantly lower in the OKG infusion group than in the control group (Table 1). This small difference in the TBSA, however, likely had negligible effects with regard to the metabolic disturbances in these patients; therefore, our burn patients were considered to be homogeneous groups of severely burned but curable patients (8–11). In addition, the unit burn standards (UBS = %TBSA + 3 × percentage of full thickness burn) were not significantly different between groups (Table 1).

Nutrition

After their admission to the intensive care unit, all patients received the same gastric continuous enteral nutrition infusion, which consisted of a polymeric commercialized diet (Dripsol 81; Promedica Diététique, Paris) via a nasal tube. Individual nutritional requirements were evaluated on the basis of body weight by using the Harris-Benedict formula. Daily energy intake was progressively increased from 2.1 MJ/d (day 1 or 2 postinjury) to an average of 12.5 MJ/d and nitrogen intake from 4 to 24 g/d by day 7 postburn. Before the kinetics were determined, patients received enteral nutrition for 5 (n = 10) or 6 (n = 32) d; no significant differences were observed between the groups. Energy and nitrogen intakes on the day the kinetics were determined are given in Table 3.

Patients were randomly assigned to receive a supplement to the enteral nutrition solution, consisting of ornithine α-ketoglutarate (OKG) (Cetorin; Laboratoires Logea, Issy-Les-Moulineaux, France) (n = 26) on the day kinetics were determined or an isonitrogenous amount of a soy protein mixture containing the same amount of nitrogen per gram as OKG (Protif-1; Jacquemaire, Paris) (n = 16). The amino acid composition per 100 g of control supplement was as follows: 4.0 g isoleucine, 6.5 g leucine, 5.1 g lysine, 1.0 g methionine, 1.0 g cysteine, 4.2 g phenylalanine, 3.2 g tyrosine, 4.1 g threonine, 0.7 g tryptophan, 3.8 g valine, 5.9 g arginine, 2.1 g histidine, 3.4 g alanine, 9.9 g aspartic acid, 15.6 g glutamic acid, 3.3 g glycine, 6.0 g proline, and 4.1 g serine.

Patients received OKG as a single bolus before the start of enteral nutrition (n = 13) or as a continuous gastric infusion with daily enteral nutrition (n = 13); an isonitrogenous control (n = 16) was administered by continuous gastric infusion. Because the upper limit of OKG delivered as a single bolus (10 g) is the onset of diarrhea (17), we performed a dose-response study (10, 20, and 30 g/d) in the continuous-infusion groups only. For bolus administration, 10 g OKG was dissolved in 200 mL water and flushed in the enteral tube at 0900. Daily enteral nutrition administered by continuous gastric infusion was immediately started for 21 h. For the continuous infusion, OKG (10 g, n = 4; 20 g, n = 6; or 30 g, n = 3) or the isonitrogenous control (10 g, n = 6; 20 g, n = 5; or 30 g, n = 5) were mixed with the daily enteral nutrition solution, which was infused starting at 0900 and lasting 21 h. On the day the kinetics were determined, enteral nutrition was delivered in a volume of 3 L.

### Table 1

Demographic data of burn patients at the time of admission to the intensive care unit

<table>
<thead>
<tr>
<th>Feature</th>
<th>Control (n = 14 M, 2 F)</th>
<th>OKG bolus (n = 11 M, 2 F)</th>
<th>OKG infusion (n = 10 M, 3 F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>36 ± 5</td>
<td>36 ± 5</td>
<td>36 ± 3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73 ± 3</td>
<td>66 ± 4</td>
<td>74 ± 5</td>
</tr>
<tr>
<td>TBSA (%)</td>
<td>35 ± 2</td>
<td>32 ± 3</td>
<td>25 ± 2&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>UBS</td>
<td>75 ± 9</td>
<td>64 ± 9</td>
<td>57 ± 7</td>
</tr>
</tbody>
</table>
<sup>1</sup> ± SEM. OKG, ornithine α-ketoglutarate: TBSA, total burn surface area; UBS, unit burn standard = %TBSA + 3 × percentage of full thickness burn.
<sup>2</sup> Significantly different from control, P < 0.05 (ANOVA and Dunnett’s procedure).

### Table 2

Routine biological blood indexes of burn patients on the day kinetics were determined (day 7 postinjury)<sup>1</sup>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control (n = 16)</th>
<th>OKG bolus (n = 13)</th>
<th>OKG infusion (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine aminotransferase</td>
<td>683 ± 133</td>
<td>850 ± 83</td>
<td>667 ± 117</td>
</tr>
<tr>
<td>Bilirubin (µmol/L)</td>
<td>20 ± 4</td>
<td>21 ± 3</td>
<td>13 ± 2</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>96 ± 6</td>
<td>86 ± 7</td>
<td>98 ± 11</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>7.2 ± 0.6</td>
<td>6.5 ± 0.6</td>
<td>6.3 ± 1.1</td>
</tr>
<tr>
<td>Prothrombin time (%)</td>
<td>83 ± 4</td>
<td>85 ± 4</td>
<td>86 ± 4</td>
</tr>
</tbody>
</table>
<sup>1</sup> ± SEM. OKG, ornithine α-ketoglutarate. There were no significant differences between groups by ANOVA and Dunnett’s procedure.

### Table 3

Daily energy and nitrogen intakes on the day plasma kinetics were determined<sup>1</sup>

<table>
<thead>
<tr>
<th>Feature</th>
<th>Control (n = 16)</th>
<th>OKG bolus (n = 13)</th>
<th>OKG infusion (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy intake (MJ/d)</td>
<td>11.8 ± 1</td>
<td>12.3 ± 1</td>
<td>13.1 ± 1</td>
</tr>
<tr>
<td>Nitrogen intake (g/d)</td>
<td>22.9 ± 1.1</td>
<td>23.7 ± 1.4</td>
<td>24.7 ± 0.7</td>
</tr>
</tbody>
</table>
<sup>1</sup> ± SEM. OKG, ornithine α-ketoglutarate. There were no significant differences between groups by ANOVA and Dunnett’s procedure.
Analysis

Sampling

On the day of the kinetic studies, enteral nutrition was stopped at 0600. After a washout period of 3 h, venous blood samples were drawn at 0900 (time 0) through a catheter into a tube containing heparin as an anticoagulant. Venous blood samples were drawn at the following time points: 30, 60, 90, 120, 180, 300, and 420 min after nutrition began. The 7-h kinetic period was selected on the basis of plasma pharmacokinetic data obtained previously after administration of a single 10-g OKG bolus in healthy subjects in the postabsorptive state (20) or fed a standardized regimen (21). In these two studies, the plasma concentrations of both ornithine (20, 21) and OKG metabolites (20) returned to basal values 300 min after administration of the OKG bolus. We also took into consideration technical limitations associated with a longer period of kinetic study in our burn unit.

Blood samples were centrifuged at 1500 × g for 10 min at 4 °C within minutes after sampling. For amino acid analysis, plasma was immediately deproteinized with sulfosalicylic acid (50 g/L), centrifuged at 4 °C for 15 min, and stored at -20 °C. Amino acid analysis was usually performed on the following day, with a maximum delay of 1 wk to ensure glutamine stability.

Biochemical analysis and pharmacologic calculations

Plasma creatinine, glucose, alanine aminotransferase, bilirubin, and urea were routinely measured with an Astra 8 analyzer (Beckman, Palo Alto, CA). Plasma amino acids were measured by ion-exchange chromatography using the ninhydrin reaction for detection on a Beckman 6300. To simplify the representation of plasma amino acid concentrations during kinetic studies, results were normalized with basal concentrations (time-0 values).

Pharmacokinetic analyses of concentration versus time profiles of ornithine were performed with the PCNONLIN program (version 4.1; Statistical Consultants Inc, Lexington, KY). Areas under the curve (AUC) of change in amino acid plasma concentrations were calculated by the trapezoidal method (22). The AUC over the 7-h kinetic period (AUC0-7h) reflects amino acid appearance in the plasma during the kinetic study. The AUC over infinity (AUC0-∞) is a calculated index that represents the total amount of amino acids in plasma after OKG administration. This index is particularly useful when the kinetic observation period is shorter than the infusion period and/or the period of metabolite production. In the bolus group, the AUC0-∞ of different metabolites was calculated from the 7-h kinetic data after log transformation of plasma values by using a one-compartment model and linear regression of the last three plasma concentrations. In the continuous-infusion groups, the AUC0-∞ of metabolites was calculated by using the steady state concentration.

Statistical analysis

Results were expressed as means ± SEMs. Statistical analysis was performed by using repeated-measures analysis of variance (ANOVA) and Dunnett’s procedure, except for curve fitting (ornithine kinetic) and correlations between AUC0-7h of different metabolites and AUC0-7h of ornithine (ANOVA). For all statistical tests, the significance level was set at \( P < 0.05 \).

RESULTS

Ornithine plasma pharmacokinetics

Control group

No significant changes in ornithine plasma concentrations were noted during the 7-h kinetic period (Figure 1). The AUC0-7h of ornithine was significantly different from 0 (Figure 2); there was no significant effect of the dose infused on ornithine appearance (Figure 2).

OKG bolus group

Plasma ornithine increased briskly to reach an apparent maximum at 60 min; concentrations at 420 min were still significantly higher than basal values (Figure 1). OKG delivered as a bolus was associated with an AUC0-7h of plasma ornithine (Figure 2) that was significantly higher than that of the control group: 67 ± 14 compared with 4 ± 1 mmol · min⁻¹ · L⁻¹ (\( P < 0.05 \)). Plasma ornithine profiles were fitted to a one-compartment model with first-order input (r = 0.993, \( P < 0.005 \)) and calculated pharmacokinetic indexes for ornithine are presented in Table 4.

OKG continuous infusion group

When OKG was infused over 21 h, plasma ornithine increased slowly after the beginning of nutrition to reach an apparent plateau at 300 min (Figure 1). The concentration at the steady state was proportional to the dose of OKG infused (data not shown). The AUC0-7h of ornithine (25 ± 14 mmol · min⁻¹ · L⁻¹) was higher than that of the control group and was proportional to the dose of OKG infused (Figure 2). Calculated pharmacokinetic parameters for ornithine in the different infusion groups (10, 20, and 30 g/d) are presented in Table 4.

FIGURE 1. Mean (± SEM) plasma ornithine concentrations after enteral administration of ornithine α-ketoglutarate (OKG). Plasma ornithine was monitored for 7 h after enteral nutrition began and results were normalized with those at time 0. *Significantly different from time-0 concentration, \( P < 0.05 \) (repeated-measures ANOVA).
Metabolite production

Glutamine

In the control group, no significant changes in plasma glutamine concentrations were observed during the 7-h kinetic period (Figure 3); the AUC_{0-7h} of glutamine was not significantly different from 0 (−1.9 ± 6.5 mmol·min·L) and there was no significant effect of the dose infused on glutamine production (data not shown).

After the OKG bolus was administered, plasma glutamine increased significantly at 30 min to reach an apparent maximum at 180 min and remained significantly higher than the prenutrition value at 420 min. The AUC_{0-7h} of glutamine was significantly higher than that of the control group (20.4 ± 5.7 compared with −1.9 ± 6.5 mmol·min·L). The AUC_{0-7h} (67 mmol·min·L) and glutamine elimination half-life (11 h) for a 10-g OKG bolus were calculated by linear regression on the last three plasma concentrations (r = −0.9998).

There were no significant changes in plasma glutamine concentrations when OKG was infused over 21 h. The AUC_{0-7h} of plasma glutamine (10.0 ± 3.5 mmol·min·L) was not significantly higher than that of the control group. Glutamine production was not dose-dependent: no correlation was found between the AUC_{0-7h} of glutamine and that of plasma ornithine (r = 0.331, P = 0.270). The AUC_{0-5} (pooled dose: 58 mmol·min·L) was calculated from the steady state concentration (mean: = 257 μmol/L) and glutamine elimination half-life (11 h).

Arginine

In the control group, there were no significant changes in plasma arginine concentrations during the 7-h kinetic period (Figure 4); the AUC_{0-7h} of arginine was not significantly different from 0 (1.2 ± 1.3 mmol·min·L). There was no effect of the dose infused on arginine production (data not shown).

After the OKG bolus, plasma arginine increased rapidly to reach an apparent maximum at 90 min and returned to basal values at 420 min. The AUC_{0-7h} of plasma arginine was significantly higher than that of the control group (7.3 ± 1.9 compared with 1.2 ± 1.3 mmol·min·L). The AUC_{0-5} (40 mmol·min·L) and arginine elimination half-life (23 h and 30 min) for a 10-g OKG bolus were calculated by linear regression on the last three points (r = −0.9999).

In the infusion group, there was no significant change in plasma arginine concentration over the 7-h study period. The AUC_{0-7h} of plasma arginine (3.5 ± 1.0 mmol·min·L) was not significantly different from that of the control group. Arginine production was not dose-dependent: no correlation was found between the AUC_{0-7h} of arginine and the AUC_{0-7h} of

| TABLE 4 |
| Calculated pharmacokinetic parameters for ornithine after enteral administration of ornithine α-ketoglutarate (OKG) |

<table>
<thead>
<tr>
<th>OKG bolus (10 g/d)</th>
<th>10 g/d</th>
<th>20 g/d</th>
<th>30 g/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tmax (min)</td>
<td>64</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Cmax (μmol/L)</td>
<td>303</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total AUC_{x} (mmol·min/L)</td>
<td>64.1</td>
<td>62.5</td>
<td>125.0</td>
</tr>
<tr>
<td>T90% Css (min)</td>
<td>—</td>
<td>300</td>
<td>300</td>
</tr>
<tr>
<td>Css (μmol/L)</td>
<td>48</td>
<td>96</td>
<td>144</td>
</tr>
</tbody>
</table>

1 The absorption constant was 0.028 min⁻¹ and the elimination half-life was 89 min. AUC, area under the curve; Css, concentration at the steady state; T90%, Css, time to reach 90% of the steady state concentration; Tmax, time for which the concentration was maximum; Cmax, maximum concentration.
plasma ornithine ($r = 0.328, P = 0.270$). The AUC_{0-7h} (pooled dose) was calculated from the steady state concentration (mean: 8.7 μmol/L) and the arginine elimination half-life (23 h and 30 min).

**Proline**

In the control group, plasma proline concentrations increased significantly during the kinetic study, resulting in a significant AUC_{0-7h} of plasma proline of 13.2 ± 4.0 mmol·min /L (Figure 5). No dose effect was observed for proline production (data not shown).

After administration of the OKG bolus, plasma proline increased progressively to reach an apparent maximum at 300 min. The AUC_{0-7h} of plasma proline was significantly higher than that of the control group (41.4 ± 5.6 compared with 13.3 ± 4.0 mmol·min /L). The AUC_{0-7h} and elimination half-life of proline could not be calculated, the 240-min time point being out of the terminal regression phase (data not shown).

In the infusion group, the proline profile was similar to that observed in the bolus group. The AUC_{0-7h} of plasma proline (23.2 ± 3.8 mmol·min /L) was not significantly higher than that of the control group. Proline production was dose-dependent: a significant positive correlation was found between the AUC_{0-7h} of proline and the AUC_{0-7h} of plasma ornithine ($r = 0.660, P = 0.014$). The AUC_{0-7h} could not be calculated from the steady state concentration because the steady state was not reached by 420 min.

**DISCUSSION**

In this study we report for the first time that enterally administered OKG is rapidly and efficiently metabolized in severely burned patients. Importantly, our results suggest that the mode of enteral administration of OKG may be decisive for the generation of key metabolites, such as glutamine and arginine in burn patients.

The pharmacokinetic analysis of enterally delivered OKG was assessed previously in healthy subjects in the fasted and fed states (20, 21). After administration of 10 g OKG in the form of a single bolus in fasted subjects, plasma ornithine peaked at 60 min, whereas the increase in α-ketoglutarate was very small (20). Maximum plasma ornithine concentrations occur more slowly in subjects fed a standardized regimen (eg, at 90 min) (21). In our study, the 10-g bolus of OKG was rapidly absorbed (maximum peak of ornithinemia at 64 min) and was almost totally metabolized within 420 min, as observed in healthy subjects (20, 21). For the first time we also showed that ornithine pharmacokinetics follow a one-compartment model with first-order input and output.

With regard to metabolite production, our study is the first to report that enteral administration of OKG increases glutamine plasma concentrations in burn patients (+20% at maximum concentration (Cmax) in the bolus, +10% at steady state concentration in the infusion), as observed previously in healthy subjects (17) and trauma patients (15). In an experimental model of burn injury (14), OKG restored the muscle pool of free glutamine. An increase in arginine and proline plasma concentrations was noted previously in healthy (20) and burn (8) subjects receiving the molecule as a bolus. As observed previously (20), proline was quantitatively the main OKG metabolite. Compared with healthy subjects (20), metabolite production after a single 10-g OKG bolus was delayed in burn subjects. This was especially true for proline, with an apparent maximum at 300 min (compared with 60 min in healthy subjects), and proline plasma concentrations returned to basal.
values at 240 min in healthy subjects (20). Our ornithine kinetic data strongly suggest that delayed plasma clearance of ornithine was not involved in this phenomenon. Metabolite production after OKG administration is the result of a specific interaction between ornithine and α-ketoglutarate because neither ornithine hydrochloride (20), calcium α-ketoglutarate (20), nor ornithine α-ketoisocaproate (23) generated a significant amount of glutamine when administered enterally or orally. Ornithine and α-ketoglutarate can be interconverted via glutamate semialdehyde to form glutamine and proline (24). These reactions are in equilibrium and are fully reversible. Most likely, this specific interaction is located in the intestine and the liver (25, 26).

The most intriguing finding of this study was that the production of glutamine and arginine was influenced by the mode of OKG delivery. When OKG was infused in burn patients their production was not dose-dependent over a range of 10–30 g OKG/d and was lower than after a 10-g bolus. According to our data, production of glutamine and arginine after administration of three 10-g boluses/d would be more than three times higher than if these 30 g were infused. By contrast, proline production was not influenced by the mode of OKG delivery and was clearly dose-dependent in the infusion group. The plasma proline profile should be monitored for at least an additional period of 7 h to allow calculation of proline production over infinity.

The differences in glutamine and arginine production between modes of delivery might be explained by a displacement of the glutamate semialdehyde equilibrium (24). It could be hypothesized that when OKG was infused, ornithine was mostly transformed in proline, whereas α-ketoglutarate was mostly utilized for the very active gluconeogenesis (1) before it could be glutaminated. By contrast, after administration as a bolus, a significant amount of α-ketoglutarate probably escaped the Krebs cycle to form glutamine, whereas an excess of ornithine shifted toward the production of arginine and glutamine. Note that the Cmax of ornithine after administration of 10 g OKG was 300 μmol/L for the bolus, compared with 50 μmol/L for the infusion over 21 h.

The importance of glutamine, arginine, and proline in various catabolic states, including burn injury, is supported by numerous experimental and clinical studies. Glutamine is a major energy source for rapidly dividing cells, a precursor for purines and pyrimidines, a gluconeogenic substrate, and a nitrogen carrier (27). In addition, experimental studies suggest that glutamine may have a direct role in the control of muscle protein turnover (28). Arginine has immunostimulant properties (29) and burn injury is associated with depressed humoral and cellular immunity (30). In the same way, OKG has been reported to improve immunity in burned rats (31). In burn patients, an arginine-supplemented diet reduced the rate of wound infection, overall morbidity, and shortened the hospital stay compared with other standard formulations (6). In experimental models of trauma, arginine limits nitrogen losses and accelerates wound healing (32). Proline is the precursor of hydroxyproline (33), a major component of collagen, and stimulates protein synthesis. In two prospective double-blind studies, OKG at the dose of 20 g/d (in two separate boluses) accelerated reepithelization of donor sites and spontaneous healing in burn patients (12).

In this prospective study, we established that after enteral administration of OKG in burn patients, OKG was well absorbed and metabolized and led to the production of glutamine, arginine, and proline. The bolus mode, however, appeared to generate higher concentrations of glutamine and arginine than did the continuous infusion. The clinical efficacy of different modes of enteral administration of OKG and its dose-dependence are currently under investigation.

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REFERENCES


