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A randomized trial of intravenous glutamine supplementation in trauma ICU patients: response to the comments by Ozcelik et al.

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Dear Editor

We appreciate the comments by Ozcelik et al. [1] on our paper on intravenous glutamine supplementation in trauma ICU patients [2]. We agree with Ozcelik on the complex interdependence effects of pharmacutrients in critically ill patients. But because arginine and glutamine are amino acids that have a complicated metabolism we consider it hazardous to extrapolate the concept of “extra dose of glutamine–high levels of arginine–increase in the mortality”. It is well known that the uptake of glutamine by the gut is followed by conversion of part of this glutamine to the amino acid citrulline. In fact, about 80–90 % of the citrulline is derived from the gut glutamine to citrulline conversion, but the total production of citrulline is only 2 % of the whole body’s consumption of glutamine. The majority of the citrulline is converted to arginine in the kidney, but only about 15 % of the apparent arginine is via this route. Plasma arginine levels can be affected under special conditions in which the disposal capacity of arginine is enhanced, and it was reported that the reduction in plasma arginine level in sepsis was caused by a

reduced citrulline to arginine conversion coupled with a decreased citrulline production [3].

In relation to a higher mortality being associated with a high dose of glutamine, we suppose that Ozcelik and colleagues are referring to the REDOX study [4]. In the REDOX we found a lot of potentially confusing factors (extremely high doses, normal basal levels of glutamine, combination of routes of administration, renal failure...). We agree with Wernerman [5] that at present we do not know whether the patients who died did so with high glutamine concentrations. In our results we describe that the risk for a given patient may be increased if a low glutamine concentration is present at admission and we do not reach normal levels after supplementation (substitute a deficiency).

In relation to the plasma arginine levels (normal range 75–175 $\mu\text{mol/L}$) we must remark that during the study the values, rather than being higher, were in the low or normal range. At admission the mean value was 60 $\mu\text{mol/L}$ (72.5 % of the patients were under normal values) although at the end of the study the mean value was 81 $\mu\text{mol/L}$ (25.5 % of the patients were under normal values). We must highlight the non-significant differences between the plasmatic arginine levels at the end of the study: in the patients with normal plasma levels of glutamine, arginine levels were 108 $\mu\text{mol/L}$, while in the remaining patients they were 96 $\mu\text{mol/L}$.

Finally, Ozcelik et al. state that our group said that low plasma glutamine levels were associated with mortality. This is a misunderstanding. In the “Results” section we literally wrote the following: “Nevertheless, low glutamine levels at day 6 were associated with increased numbers of infected patients (58.8 vs 80.9 %; $p = 0.032$), longer ICU length of stay (9 vs 20 days; $p < 0.01$), and longer hospital length of stay (24 vs 41 days; $p = 0.01$). There were no statistically

significant differences regarding mortality.”

Conflicts of interest Abelardo Garcia-de-Lorenzo declared having received honoraria for speaking from Baxter, Fresenius, and B. Braun. Jon Pérez-Bárcena, Antonio Buño, and Juan A. Llompарт-Pou declared no conflict of interest.

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