Intravenous Essential Amino Acid Therapy

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Dear Sir,

In a recent issue, Akpolat et al. [1], practicing at the Hacettepe University in Ankara, Turkey, reported on a case of hyperammonemic encephalopathy in a renal patient receiving intravenous essential amino acids (EAA; NephroAmine®). Although there are no doubts surrounding the clinical observations and corresponding laboratory findings, this is a serious case of misuse of intravenous EAA. Whether infused with or without energy (the report does not state whether the EAA was infused along with dextrose, electrolytes or other important nutrients required for protein synthesis from amino acids), the infusion of 1,000 cm³ of NephroAmine in 8 h represents a dose 2 times the highest recommended dose for the average 70-kg man. In this case, the 20-year-old woman more than likely weighed less than 70 kg making the overdose even larger.

It should be pointed out that inappropriate use and overdosing can, as the result of a natural metabolic sequelae, lead to hyperammonemia, and as in the case reported by Akpolat et al. encephalopathy. Discontinuing the overload of intravenous EAA would be expected to reduce serum ammonia and the corresponding encephalopathy as reported by Akpolat et al. Three references are cited by Akpolat et al. [2-4] in which hyperammonemia occurred. All three are case reports of a single patient for a grand total of 3 patients. In all three instances, similar overdosing of intravenous EAA occurred. Overdosing more than likely was the cause of the hyperammonemia. Rapp et al. [2] administered 6.22 g of essential amino acid nitrogen to a 59-year-old woman who more than likely weighed less than 70 kg. This is at least 2 times the recommended dose of 1.6-3.2 g of EAA nitrogen. In this case, the dose was reduced to 2.1 g of nitrogen per day and in 24 h serum ammonia decreased from 192 to 70 µmol/L. The patient was awake and responsive.

Grazer et al. [3] administered 42 g of protein (assumed to be amino acids in this case) per day to a 47-year-old woman weighing 40 kg for 11 days before becoming symptomatic with hyperammonemia. The recommended dose of EAA is 0.2-0.4 g/kg/day. In this case, approximately 3 times the recommended dose was used.

Lamiell et al. [4] administered a mixture of 1,000 ml of EAA and 750 ml of 70% dextrose to a 77-kg, 70-year-old male patient. Hyperammonemia (and hypophosphatemia) was encountered in a crossover regimen, strongly implicating EAA as the culprit. EAAs were more than likely the cause of the hyperammonemia but only because the dose was again at least twice the typical dose. The authors recognized and acknowledged the overdose and infer that the lack of L-arginine in some EAA-based total parenteral nutrition (TPN) leads to hyperammonemia. Arginine is required for detoxifying ammonia via the Krebs urea cycle but is a dispensable amino acid which can be de novo synthesized by man. The preformed

ammonia in EAA solutions such as NephrAmine is very low (average 400 µg/dl) while the amount of ammonia absorbed from the gastrointestinal tract of patients who receive nothing per os is minimal. Hence, endogenous arginine is adequate for controlling serum ammonia and keeping encephalopathy at bay when EAA TPN is performed using the recommended dose of approximately 0.4 g of EAA/kg body weight. Adequate amounts of energy to meet basal requirements in order to minimize the catabolism of EAA to ammonia, as well as electrolytes, vitamins and trace elements should be withheld or supplemented based on serum chemistries.

One must remember that proteins contain approximately 16% nitrogen, i.e., 16 g of total nitrogen is equivalent to 100 g protein $[(100 \div 16) \times \text{g of total nitrogen} = \text{g of protein equivalents}]$.

One must also remember that proteins are made up of approximately 30% EAA. The EAAs make up, therefore, only 30% of the 16 g of nitrogen found in proteins, or 4.8 g of EAA nitrogen/100 g of protein $[(100 \div 4.8) \times \text{g of total nitrogen} = \text{g of protein equivalents for EAA}]$. As Lamiell et al. [4] point out, 'EAA in renal failure is different from that of mixed amino acids and should be dosed using all of the accumulated knowledge of amino acid metabolism, protein synthesis and renal disease. Since the FDA approval of NephrAmine and its market introduction in 1978, over three million units have been sold. Assuming that patients received on average two units per day for 14 days, over 107,000 patients have been treated with this product. All four reports, including the most recent report appearing in your journal, amount to a grand total of 4 patients, all receiving high doses of EAA.

When used appropriately, intravenous EAA therapy is efficacious for maintaining nitrogen equilibrium or minimizing protein catabolism, reducing the rate of urea formation and minimizing deterioration of serum potassium, magnesium and phosphorous balance.

References

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