How much protein do parenteral amino acid mixtures provide?[1–3]

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ABSTRACT

It is commonly assumed that the weight of the amino acids in a parenteral amino acid mixture equals the amount of protein they provide. This assumption ignores the fact that the molecular weight of free amino acids is 18 mass units greater than when they are protein bound. The actual amount of protein substrate provided by commonly used free amino acid mixtures was determined by analyzing the amino acid composition of 3 commonly used parenteral amino acid solutions and the proteins that would be formed from them, and comparing the results with similar data from 3 nutritionally important proteins. After correction for hydration status, the ratio of essential amino acid mass to total mass of the amino acid mixtures was similar to albumin, myosin, and actin. However, all of the amino acid mixtures provided 17% less protein and energy than is now widely assumed. Current parenteral nutrition guidelines recommend 0.8–1.5 g mixed amino acids/kg normal weight per day, on the assumption that they are equivalent to formed proteins, but they are not equivalent. Clinicians who aim to provide 0.8–1.5 g protein/kg must administer 1.0–1.8 g mixed amino acids/kg. *Am J Clin Nutr* 2011;94:1396–8.

INTRODUCTION

It is generally assumed that the protein requirements of people who receive parenteral nutrition are the same as when they are nourished by the enteral route (1–5). Thus, the recommendation for metabolically stable, parenterally nourished people is 0.8 g mixed free amino acids/kg per day, in agreement with the dietary protein recommendation for normal adults (1, 3). A common recommendation for people with critical illness is 1.2–1.5 g protein/kg normal body weight per day, either in the form of dietary protein or as mixed free amino acids administered either parenterally or by the enteral route (5, 6).

However, the widespread assumption that the weight of a mixture of free amino acids equals the amount of protein they provide ignores the fact that a molecule of water is released when a peptide bond is formed, with the consequence that the molecular weight of a peptide-bound amino acid is 18 mass units less than its formal molecular weight. In effect, the hydration status of free amino acids dilutes the protein substrate they provide by a fraction that depends on the molecular weight of each amino acid. Once this simple biochemical fact is appreciated, it is obvious that 100 g of a mixture of free amino acids (provided either orally or by intravenous infusion) contains <100 g protein substrate. But how much less?

To determine the amount of actual protein substrate provided by nutritional amino acid mixtures, the amino acid composition of 3 commonly used parenteral amino acid products, and the proteins that would be formed from them, were analyzed and compared with similar data from 3 nutritionally important proteins: albumin, myosin, and actin.

METHODS

The amino acid compositions of 3 parenteral amino acid products [Aminosyn 15% (Hospira), Aminoven 15% (Frenius Kabi), and Clinisol 15% (Baxter)] were obtained from package inserts. The molecular weight and detailed compositions of the hypothetical protein they would form were calculated, taking into account the loss of water, acetate (for lysine acetate), or an *N*-acetyl group (for *N*-acetyltyrosine) that occurs when these amino acids are incorporated into protein. For example, the molecular weight of free leucine is 131, whereas its protein-bound molecular weight is 113; the molecular weight of lysine acetate is 206, whereas its protein-bound molecular weight is 128. The mass of one molecule of water was added to the mass of the hypothetical protein to account for partial hydration of its C- and N-terminal amino acids.

The amino acid sequences of 3 nutritionally important proteins, albumin (http://www.ncbi.nlm.nih.gov/protein/AAA98797.1), myosin (http://www.ncbi.nlm.nih.gov/protein/CAA86293), and skeletal muscle actin (http://www.ncbi.nlm.nih.gov/protein/NP_001091.1), were accessed. Detailed information on their composition was obtained by entering the data into ProtParam, a computer program available on the Expasy website (http://web.expasy.org/protparam/).

Finally, the hand-calculated analysis of the 3 amino acid mixtures was verified by entering the identification letter and

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number of molecules of each amino acid present in 200 mL of each product into ProtParam. ProtParam used this information to create a virtual protein and generate detailed information about its composition. (The minor contribution of taurine, a non-protein-bound amino acid in Aminoven, was ignored.) Except for trivial numerical differences, which were attributable to rounding errors, the conclusions of the hand and computer calculations were identical.

RESULTS

Several similarities among and differences between the 3 amino acid mixtures and albumin, myosin, and actin are shown in **Table 1**. The obvious and important difference is that the amino acid solutions provide 17% less protein substrate than does the sum of their constituent amino acids. Thus, a 15% amino acid mixture, which contains 15 g amino acids per 100 mL, actually provides only 12.5 g protein substrate per 100 mL.

When precisely calculated by using modern molecular data, N mass/total mass (g/g) for albumin (0.166), myosin (0.172), and actin (0.165) corresponded well to the measured values of 0.160–0.165 that have long been used to interconvert N and high-quality protein mass (7, 8). By contrast, after correction for hydration, N mass/total mass of all 3 amino acid mixtures was considerably higher than normal (*see* Table 1). Moreover, the number of amino acids per gram of hydration-corrected amino acid mixture was greater, and the average molecular weight considerably less, than that found in albumin, myosin, and actin.

This higher density of amino acids and N in the hydration-corrected amino acid mixtures does not, however, imply that they provide a product that is somehow richer in protein value. As shown in Table 1, the density of essential amino acids in all 3 mixtures is similar to that in albumin, myosin, and actin. The higher amino acid and N density of the amino acid mixtures is simply an artifact arising from their higher proportion of low-molecular-weight nonessential amino acids and their higher proportion of the N-rich nonessential amino acid arginine.

DISCUSSION

It is currently taken for granted that the dose of amino acids in a parenteral amino acid mixture is equivalent to the amount of dietary protein one would provide if a patient could be fed by mouth. Clinical reviews of this topic commonly use the terms *amino acids* and *protein* interchangeably (3, 9). Concisely put, 100 g mixed amino acids are assumed to equal 100 g high-quality dietary protein. However, the protein substrate provided by mixed amino acids is diluted by the equivalent of a molecule of water that is present in each free amino acid, but absent when it is protein bound. Parenteral amino acid mixtures actually provide 17% less "protein" than is now widely assumed.

Although the issue has been debated (10), there is no doubt that infused amino acids provide metabolic energy equal to their rate of administration, because patients are seldom in significant positive N balance and therefore oxidize amino acids at a rate equal to or greater than their rate of administration. The present analysis indicates that the Atwater factor of 4 kcal/g, which was derived for protein, is 3.3 for parenteral amino acid products.

A similar conclusion applies to elemental enteral formulas. For example, product information for Vivonex Plus (Nestlé) indicates that it provides 45 g protein per 1000 mL formula. This product actually provides ~37 g of protein substrate per 1000 mL.

Has this longstanding conceptual error led to the underprovision of amino acids to parenterally fed patients? It is impossible to know. Reliable information regarding either minimum or optimum parenteral amino acid provision is lacking (9). The protein requirements of parenterally fed people are not likely to be less than normal, however. Until studies indicating otherwise are published, any providers of parenteral nutrition who want to adhere to the principles that underlie current guidelines, which

TABLE 1
AA composition of parenteral AA mixtures and proteins[1]

Variable	Aminosyn 15% (100 mL)	Aminoven 15% (100 mL)	Clinisol 15% (100 mL)	Albumin	Myosin	Actin
Total molecular weight (mass units)						
Product	15,077	15,296	14,960			
Protein[2]	12,479	12,346	12,462	69,367	222,870	42,051
Number of AAs in 15 g						
Product	117	131	121			
Protein[2]	141	162	145	132	131	135
Average molecular weight						
Product	129	118	124			
Protein[2]	107	94	103	114	115	112
N mass/total mass (g/g)[3]						
Product	0.147	0.167	0.154			
Protein[2]	0.178	0.206	0.185	0.166	0.172	0.165
Essential N/protein (g/g)[4]	0.069	0.066	0.079	0.072	0.071	0.069
Percentage of EAAs (mol/mol)[5]	42.2	31.9	42.6	43.5	43.3	43.9
Percentage of arginine (mol/mol)	7.7	8.8	7.0	4.4	5.2	4.8

[1] AA, amino acid; EAAs, essential amino acids; N, nitrogen.
[2] Refers to the protein that would be formed from the AAs in 100 mL of the mixture.
[3] N mass/total mass of the AAs in the product or protein.
[4] N mass of the 9 EAAs/total protein mass.
[5] Percentage of all AAs that are essential.

recommend 0.8–1.5 g protein/kg normal weight per day, ought to infuse 1.0–1.8 g free amino acids/kg per day. In short, 100 g parenteral amino acid mixture is equivalent to 83 g high-quality dietary protein.

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