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Amino acid losses during hemodialysis with infusion of amino acids and glucose

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Amino acid losses during hemodialysis with infusion of amino acids and glucose. This study evaluated the effects during hemodialysis of intravenous infusion of amino acids and glucose on plasma amino acid and glucose concentrations and amino acid losses. Eight men undergoing maintenance hemodialysis were each studied during two dialyses using glucose-free dialysate. During one hemodialysis, they were infused with 800 ml of normal saline. During the other hemodialysis, they were infused with an equal volume of water which contained 39.5 g of essential and non-essential free L-amino acids and 200 g of d-glucose. The solutions were infused throughout the dialysis procedure into the drip chamber of the venous outflow from the dialyzer. Subjects were fasted from the night before until the end of hemodialysis, and the order of administration of the two solutions was determined randomly. Plasma essential, non-essential, and total amino acids fell significantly during the infusion of normal saline and rose during the administration of amino acids and glucose. Dialysate total-free amino acid losses averaged 8.2 ± 3.1 SD g during the infusion of normal saline and 12.6 ± 3.6 g with the administration of amino acids and glucose. These findings indicate that the intravenous infusion of amino acids and glucose during hemodialysis prevents a fall in plasma amino acid and glucose concentrations and leads to only a slight increase in the losses of free amino acids into dialysate. Because most of the infused amino acids are retained, this technique may be used during hemodialysis to avoid a net outflow of amino acids, minimize disruption of amino acid and glucose pools, and provide a nutritional supplement.

Pertes en amino-acides au cours de l'hémodialyse avec perfusion d'acides aminés et de glucose. Cette étude a permis d'évaluer les effets de la perfusion intraveineuse d'acides aminés et de glucose pendant l'hémodialyse sur les concentrations plasmatiques d'acides aminés et de glucose, et les pertes d'acides aminés. Huit hommes en hémodialyse chronique ont chacun été étudiés pendant deux dialyses avec un dialysat sans glucose. Pendant une des dialyses ils étaient perfusés avec 800 ml de soluté physiologique. Pendant l'hemodialyse autre ils ont infusé avec un égal volume d'eau contenant 39,5 g de L-acides aminés libres essentiels ou non, et 200 g de d-glucose. Les solutions étaient perfusées pendant la dialyse dans la tubulure veineuse venant du dialyseur. Les malades étaient à jeûn la nuit précédante et jusqu'à la fin de la dialyse, et l'ordre d'administration des deux solutions était déterminé au hasard. Les acides aminés plasmatiques totaux, essentiels et non essentiels ont significativement diminué pendant la perfusion de soluté physiologique, et se sont élevés pendant l'administration d'acides aminés et de glucose. Dans le dialysat, les pertes totales d'acides aminés libres étaient en moyenne de 8,2 ± 3,1 g (ds) pendant la perfusion de soluté physiologique, et de 12,6 ± 3,6 g lors de l'administration d'acides aminés et de glucose. Ces résultats indiquent que la perfusion intraveineuse d'acides aminés et de glucose au cours de la dialyse empêche la chute des acides aminés et du glucose plasmatiques et n'occasionne qu'une diminution minime des pertes en acides aminés libres dans le dialysat. Puisque la plupart des acides aminés perfusés est retenue, cette technique pourrait être utilisée pendant l'hémodialyse pour éviter une fuite nette d'acides aminés, pour minimiser la dissipation des réserves d'acides aminés et de glucose et pour apporter un supplément nutritif.

Despite numerous advances in dialysis therapy, several recent studies indicate that wasting and malnutrition are still common in patients receiving hemodialysis [1–5].

In certain patients, anorexia and poor food intake may contribute to malnutrition [1, 3, 5, 6]. For this group of patients, an efficient and safe technique of parenteral nutrition might be used to supplement their usual diet. In prior studies amino acids and glucose were infused near the end of or immediately after the hemodialysis procedure [7, 8]. However, this procedure may require additional staff time and may increase the risk of fluid overload from such infusions.

On the other hand, infusion of these nutrients throughout the hemodialysis procedure could have the following advantages: *(1)* Such infusions would not increase the time of the patient's treatment in the dialysis facility; this would reduce the patient's treatment time, decrease the workload of the medical staff, and enhance the utilization of the dialysis facility. *(2)* The infused amino acids and glucose could replace the losses that occurred throughout dialysis and thereby possibly reduce the catabolic stress from hemodialysis [9–12]. *(3)* Hemodialysis can remove the water as it is infused, and, hence lower the possibility of fluid overload from such infusions.

Despite these considerations, some physicians are reluctant to utilize this therapy because the amino acids and glucose infused during hemodialysis might be largely removed by dialysis. These concerns led us to examine plasma amino acid and glucose concentrations and amino acid losses in eight men who were infused intravenously with 39.5 g of amino acids and 200 g of glucose throughout a hemodialysis procedure. The men were also studied while they received an equal volume of normal saline under the same conditions. The results indicate that when patients were infused with amino acids and glucose during hemodialysis, there was a modest increase in amino acid and glucose concentrations in plasma and in the losses of free amino acids in dialysate. However, the large preponderance of the infused amino acids were retained, and the fall in plasma amino acids and glucose was prevented.

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Methods

Patients. Eight clinically stable men at the Veterans Administration Medical Center, Portland, Oregon, who had been undergoing maintenance hemodialysis for 53 months (range, 22 to 141) were studied. Mean age was 55 ± 6 SD years. Neither the edema-free body weight nor the predialysis serum urea nitrogen differed on the two days of study, and the grand means of these values on both days were 79 ± 25 kg and 88 ± 22 mg/100 ml, respectively. Causes of renal failure were chronic glomerulonephritis in four patients, chronic pyelonephritis in two patients, acute cortical necrosis in one patient, and unknown in one patient.

Procedure. Each patient was studied during two 300-min hemodialyses. Patients were fasted from midnight before the study until the end of the hemodialysis treatment. During one hemodialysis, patients received an intravenous infusion of 800 ml of normal saline. During the other dialysis, patients received an infusion of 800 ml containing 39.5 g of crystalline free L-amino acids (400 ml of Aminosyn® 10%, Abbott Laboratories Hospital Products Division, North Chicago, Illinois) and 200 g of d-glucose (400 ml of 50% glucose). The latter infusate provided (g infused per dialysis): histidine, 1.20; isoleucine, 2.88; leucine, 3.76; lysine, 2.88 (infused as lysine acetate; the quantity refers to free L-lysine); methionine, 1.60: phenylalanine, 1.76; threonine, 2.08, tryptophan, 0.64; valine, 3.20; tyrosine, 0.18; alanine, 5.12; arginine, 3.92; proline, 3.44; serine, 1.68; glycine, 5.12. The amino acid composition of the infusate was confirmed by amino acid analyses. For each patient, the order of administration of the two infusates was determined randomly, and each of the solutions was given to four of the patients as their first infusion.

Infusion of each solution was begun at the exact onset of the dialysis procedure and was continued at a constant rate until the termination of the dialysis. The solutions were infused with an IVAC® (IVAC Corporation, La Jolla, California) pump into the drip chamber of the venous outflow tubing from the dialyzer. Immediately after the last blood collection, patients drank a solution containing Polycose® (Ross Laboratories, Division of Abbott Laboratories, Columbus, Ohio) and fruit juice to prevent reactive hypoglycemia.

Patients underwent dialysis with a Travenol® 1.5 M^2 hollow fiber dialyzer (five patients) or Gambro Lundia® 1.0 M^2 (one patient) or Gambro Nova® 1.5 M^2 (two patients) parallel plate dialyzers. In a given patient, the same dialyzer was used for both hemodialyses. Blood flow was set at 250 ml/min and was monitored at half-hourly intervals. Dialysate flow was monitored at 10 to 15 min intervals throughout dialysis and averaged 600 ± 50 ml/min. Ultrafiltration at −200 to −40 mm Hg was used in every patient. Mean ultrafiltration pressure did not differ with the two infusions and averaged −100 ± 50 mm Hg. Mean weight loss during hemodialysis was not different with the two infusions, 3.7 ± 2.3 kg with normal saline and 3.2 ± 1.2 kg with amino acids and glucose. The same dialysate was employed for all studies, Renalyte® (Cobe Laboratories, Denver, Colorado), and it was glucose-free. Its composition (mEq/liter) was as follows: sodium, 135; chloride, 103.5; calcium, 3.5; magnesium, 1.0; and acetate, 38.0. Dialysate potassium, (mEq/liter), was 1.0 for 3 patients, 2.0 for 4 patients, and 3.0 for 1 patient. For each patient, the same dialysate potassium concentration was used for both dialyses.

At the exact onset, midpoint (2.5 hours), and termination (5 hours) of dialysis, arterial blood was obtained from the inflow tubing prior to entry into the dialyzer for measurement of plasma free amino acids and serum (predialysis) or plasma (mid- and postdialysis) glucose, urea, potassium, and phosphorus. All dialysate outflow was collected in a small container; a dual channel pump was used to transfer the dialysate quickly, at a continuous rate, into either a one-gallon jug which was packed in dry ice or into a large vat. Thus, the dialysate in the jug, which was used for analysis of the amino acids, was frozen within a few minutes after it left the dialyzer. Total dialysate volume was determined by weighing both the small jug and the vat when they were empty and after they were filled with the dialysate.

Analyses. Plasma was deproteinized quickly for amino acid analysis by addition of 45 mg sulfosalicylic acid per ml plasma, and the precipitate was removed by centrifugation. Dialysate was not deproteinized. Both dialysate and the supernatant of plasma were quickly frozen at −20° C until analyzed. Amino acids were measured with a Beckman 121M Amino Acid Analyzer (Beckman Instruments, Palo Alto, California) using a lithium buffer system. This method does not measure tryptophan. Specimens were analyzed generally for amino acids within two weeks of collection. Serum and plasma glucose, urea nitrogen, and phosphorus were measured with a Technicon® SMA-12 Auto Analyzer (Tarrytown, New York). Serum and plasma potassium were measured by a Beckman Astra 8 Analyzer (Beckman Instruments, Palo Alto, California).

Statistical analyses were carried out with the paired t test, analysis of variance, and linear regression analysis [13]. Informed consent was obtained from all patients.

Results

The mean plasma amino acid levels during hemodialysis with the infusion of either normal saline or amino acids and glucose are shown in Table 1. In general, plasma concentrations of individual amino acids tended to decrease during the infusion of normal saline. The fall in individual amino acid levels was particularly significant for many non-essential amino acids. The sums of the essential amino acids, non-essential amino acids and the total amino acids in plasma[1] each fell significantly with dialysis during the normal saline infusion. Most of the decrement in plasma amino acid concentrations occurred by mid-dialysis. For example, total plasma amino acid levels fell by 26% at the mid-dialysis point ($P < 0.01$) and by 33% at the end of the dialysis (pre versus post, $P < 0.01$). During the infusion of normal saline, the magnitude of the decrease in individual plasma amino acid values during hemodialysis (predialysis minus postdialysis concentrations, mmoles/liter) was correlated with the initial (predialysis) plasma values ($y = 0.41\chi - 11.3$, $r = 0.74$, $N = 205$, $P < 0.001$). A similar relation was also observed when the fall in the individual plasma amino acids by mid-dialysis (predialysis minus mid-dialysis concentrations) was compared to the initial values ($y = 0.30\chi - 5.9$, $r = 0.69$, $N = 204$, $P < 0.001$).

During the infusion of amino acids and glucose, there was an increase in the plasma concentration of many amino acids

[1]For calculation of the sums of the essential, non-essential, and total amino acids, see the legend to Table 1.

Table 1. Pre-, mid-, and postdialysis plasma amino acids during infusion with normal saline (8 studies) or amino acids and glucose (8 studies), μmoles/liter

	Predialysis,		Mid-dialysis, *2.5 hr*		Postdialysis, *5 hr*	
	Normal saline	Amino acids and glucose	Normal saline	Amino acids and glucose	Normal saline	Amino acids and glucose
Essential						
Histidine	85 ± 12[e,g]	84 ± 10	67 ± 8	89 ± 8[c]	63 ± 9	86 ± 15[c]
Isoleucine	58 ± 14	50 ± 14[e,g]	51 ± 16	113 ± 21[c]	53 ± 15	121 ± 39[c]
Leucine	99 ± 26	88 ± 20[e,g]	99 ± 30	148 ± 25[b]	105 ± 29	157 ± 54[c]
Lysine	214 ± 54[e,g]	189 ± 28	153 ± 29	227 ± 32[c]	138 ± 20	219 ± 31[c]
Methionine	33 ± 5[g]	32 ± 5[e,g]	24 ± 5	56 ± 8[c]	19 ± 3	62 ± 14[c]
Phenylalanine	57 ± 7[f]	54 ± 11[e,g]	47 ± 6	80 ± 15[c,h]	46 ± 7	93 ± 15[c]
Threonine	114 ± 103	147 ± 96	78 ± 63	189 ± 86[c]	83 ± 51	160 ± 134[b]
Valine	175 ± 41	169 ± 41[e,g]	136 ± 59	269 ± 46[c]	140 ± 43	289 ± 59[c]
Total essential[i]	835 ± 104[d,f]	813 ± 104[e,g]	655 ± 133	1171 ± 149[c]	647 ± 115	1187 ± 187[c]
Semi-essential						
Cystine	183 ± 77[e,g]	189 ± 65[e,g]	104 ± 27	88 ± 26	68 ± 19	51 ± 18
Tyrosine	42 ± 9[e,g]	37 ± 7[a,e,g]	30 ± 4	16 ± 4[c]	27 ± 3	13 ± 3[c]
Non-essential						
Alanine	278 ± 72[e,g]	264 ± 65[e,g]	160 ± 49	368 ± 75[c]	129 ± 32	405 ± 96[c]
Arginine	138 ± 20[g]	104 ± 47[e,g]	95 ± 16	175 ± 36[c]	78 ± 30	179 ± 34[c]
Asparagine	90 ± 29[e,g]	54 ± 28[c]	60 ± 14	41 ± 15[a]	61 ± 24	36 ± 11[b]
Aspartic acid	72 ± 30[e,g]	66 ± 13[e,g]	41 ± 11	36 ± 6	26 ± 7	29 ± 11
Glutamic acid	99 ± 36	85 ± 40	93 ± 38	83 ± 35	85 ± 43	95 ± 60
Glutamine	468 ± 68[f]	470 ± 122[d,g]	412 ± 58	394 ± 97	393 ± 83	348 ± 131
Glycine	359 ± 227	338 ± 135[e,g]	273 ± 133	561 ± 207[c]	237 ± 59	644 ± 178[c]
Ornithine	65 ± 13[e,g]	68 ± 25[g]	44 ± 7	61 ± 21	42 ± 9	56 ± 23[c]
Proline	270 ± 138[f]	291 ± 93	211 ± 60	364 ± 101[c]	180 ± 53	344 ± 165[c]
Serine	43 ± 40	61 ± 52	35 ± 28	89 ± 49[c]	35 ± 24	70 ± 60[b]
Total non-essential[j]	1882 ± 362[e,g]	1801 ± 362[e,g]	1424 ± 251	2172 ± 505[c]	1266 ± 239	2206 ± 306[c]
Citrulline	109 ± 25[e,g]	101 ± 28[a,e,g]	70 ± 13	67 ± 15[h]	60 ± 10	58 ± 15
Taurine	80 ± 38[e,g]	68 ± 28[b,e,g]	56 ± 24[i]	51 ± 24	44 ± 35	45 ± 22
1-methylhistidine	46 ± 32	51 ± 48[f]	31 ± 22	38 ± 38	25 ± 15	28 ± 30
3-methylhistidine	44 ± 25[e,g]	45 ± 20[e,g]	25 ± 42	27 ± 11	23 ± 11	20 ± 9
Total amino acids[j]	3131 ± 547[e,g]	3009 ± 365[d,f]	2339 ± 276	3565 ± 564[c]	2112 ± 313	3560 ± 412[c]

[a,b,c] Differs from values obtained at the same time during infusion of normal saline; $P < 0.05$, $P < 0.01$, $P < 0.001$, respectively.
[d,e] Difference between predialysis and mid-dialysis values obtained during the same infusion; $P < 0.05$, $P < 0.01$, respectively.
[f,g] Difference between predialysis and postdialysis values obtained during the same infusion; $P < 0.05$, $P < 0.01$, respectively.
[h,i] Difference between mid-dialysis and postdialysis values obtained during the same infusion; $P < 0.05$, $P < 0.01$, respectively.
[j] Total essential amino acids were calculated as the sum of histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, and valine; total non-essential amino acids were calculated as the sum of alanine, arginine, asparagine, aspartic acid, glutamic acid, glutamine, glycine, ornithine, proline, and serine; total amino acids were also calculated as the sum of total essential and non-essential amino acids, cystine, tyrosine, citrulline, and taurine.
[k] Mean ± SD.

(Table 1). The change in plasma amino acid levels was related to the composition of the infusate; the plasma values of every amino acid which was infused tended to increase, except for tyrosine, which was given in very low quantities, and for histidine. In contrast, those amino acids which were not infused tended to decrease in plasma. The sums of the essential, non-essential, and total plasma amino acids[i] each rose significantly during infusion of amino acids and glucose. Most of the rise in plasma amino acids occurred by mid-dialysis; the increase in total plasma amino acids was 19% by this time, $P < 0.01$, while by the end of dialysis the rise in plasma total amino acids was 20% (pre versus post, $P < 0.01$).

The plasma amino acid levels during treatment with normal saline versus amino acids and glucose showed few differences at the onset of dialysis therapy (Table 1). However, plasma concentrations of individual amino acids at mid-dialysis and the end of dialysis were usually greater during the amino acid and glucose infusion. Similarly, the sum of essential, non-essential and total amino acids were each greater at mid-dialysis and at the end of dialysis with the infusion of amino acids and glucose as compared to normal saline (Table 1). In general, those plasma amino acids which were not increased at mid-dialysis and postdialysis with the former infusion were not present in the infusate.

The free amino acids lost in the dialysate during hemodialysis are shown in Table 2. During the infusion of amino acids and glucose, there were significantly greater losses of most individual amino acids and of the sums of essential, non-essential, and total amino acids. However, the total quantity of amino acids removed with the two infusions was not markedly different, 8.2 ± 3.1 g (range, 3.8 to 11.4 g) during the infusion of normal saline and 12.6 ± 3.6 g (range, 5.9 to 15.4 g) during the administration of amino acids and glucose.

In general, those amino acids lost in the dialysate in greater quantities during the infusion of amino acids and glucose as compared to normal saline were present in the former infusate. Conversely, amino acids which were not increased in dialysate with the amino acid and glucose solution were usually not present in the infusate. The finding that the amino acid losses into dialysate were greatest for the amino acids which were infused can be explained by the higher plasma concentration for those amino acids (Table 1). Indeed, there was a direct correla-

Table 2. Free amino acids lost in dialysate[a]

	Normal saline ($N = 8$)	Amino acids and glucose ($N = 8$)	Significantly different
	mg/TV Dialysate		
Essential			
Histidine	225 ± 128	330 ± 114	$P < 0.025$
Isoleucine	149 ± 70	346 ± 117	$P < 0.01$
Leucine	284 ± 156	466 ± 146	$P < 0.05$
Lysine	462 ± 224	735 ± 259	$P < 0.01$
Methionine	173 ± 241	203 ± 92	
Phenylalanine	174 ± 90	292 ± 109	
Threonine	333 ± 172	643 ± 209	$P < 0.05$
Valine	434 ± 205	782 ± 316	$P < 0.025$
Total essential	2306 ± 917	3792 ± 1201	$P < 0.025$
Semi-essential			
Cystine	621 ± 352	576 ± 244	
Tyrosine	109 ± 79	78 ± 33	
Non-essential			
Alanine	357 ± 160	800 ± 301	$P < 0.005$
Arginine	411 ± 147	816 ± 155	$P < 0.001$
Asparagine	234 ± 110	201 ± 133	
Aspartic acid	95 ± 67	96 ± 69	
Glutamic acid	269 ± 247	273 ± 256	
Glutamine	1513 ± 561	1737 ± 365	
Glycine	708 ± 292	1754 ± 596	$P < 0.005$
Ornithine	155 ± 87	221 ± 104	$P < 0.05$
Proline	484 ± 226	1047 ± 332	$P < 0.005$
Serine	166 ± 113	294 ± 86	$P < 0.01$
Total non-essential	4576 ± 1491	7643 ± 1976	$P < 0.005$
Citrulline	246 ± 143	263 ± 118	
Taurine	279 ± 300	125 ± 55	
1-Methylhistidine	131 (range 0 to 248)	328 (range 0 to 659)	
3-Methylhistidine	94 (range 0 to 228)	130 (range 0 to 290)	
Total amino acids[b]	8151 ± 3050	12586 ± 3564	$P < 0.01$

[a] Mean ± SD.
[b] Total amino acids were calculated as the sum of the total essential and non-essential amino acids, cystine, tyrosine, citrulline, and taurine.

tion between the plasma concentrations of individual amino acids during dialysis and the quantity of free amino acids in dialysate. This relationship was observed for each of the two infusions whether the independent variable was taken as the plasma amino acids at predialysis (amino acids and glucose $r = 0.72$, $N = 205$; normal saline $r = 0.52$, $N = 204$), at mid-dialysis, (amino acids and glucose $r = 0.77$, $N = 206$; normal saline $r = 0.65$, $N = 203$), at the termination of dialysis (amino acids and glucose $r = 0.81$, $N = 205$; normal saline $r = 0.67$, $N = 201$), or as the average of the initial, mid-dialysis, and final concentrations (Fig. 1, a and b).

The changes in serum or plasma glucose, urea, potassium, and phosphorus are shown in Table 3. During the infusion of normal saline, plasma glucose fell in seven of eight patients (P = NS). In contrast, during the administration of amino acids and glucose, plasma glucose rose in all subjects ($P < 0.001$). The mean plasma glucose concentrations were significantly greater with the latter infusion as compared to normal saline both at mid-dialysis ($P < 0.01$) and the end of dialysis ($P < 0.01$). In four patients, postdialysis plasma glucose fell below 70 mg/100 ml (range, 59 to 63 mg/100 ml) when they received normal saline. In contrast, during the infusion of amino acids and glucose, postdialysis plasma glucose concentrations were neither low nor very elevated (Table 3).

Serum and plasma urea nitrogen, potassium, and phosphorus levels each decreased significantly during both dialyses in every subject. In a comparison between normal saline versus amino acids and glucose, there was no difference in plasma urea nitrogen, potassium, or phosphorus concentrations at any of the three times of blood sampling. Similarly, the changes in urea nitrogen, potassium, and phosphorus between predialysis and mid-dialysis, predialysis and postdialysis, or mid-dialysis and postdialysis were each no different during the two infusions. Plasma potassium sometimes fell to abnormally low values during both infusions. Postdialysis plasma potassium levels were less than 3.0 mEq/liter in three of eight patients receiving normal saline and in two of eight patients given amino acids and glucose. One patient receiving each infusion had a postdialysis plasma phosphorus level less than 2.0 mg/100 ml.

Discussion

Our study indicates that when patients who were fasted overnight underwent hemodialysis using glucose-free dialysate and standard dialyzers there was a loss of about 8 g of free amino acids into dialysate and both plasma amino acid and glucose concentrations fell. These findings are similar to those of earlier studies [14–18] in which patients were often fasting and losses of free amino acids were generally reported to be 6 to 8 g per dialysis [14, 15]. When patients eat during hemodialysis, amino acid losses rise slightly [14]. Young and Parsons reported somewhat smaller losses during hemodialysis, equivalent to

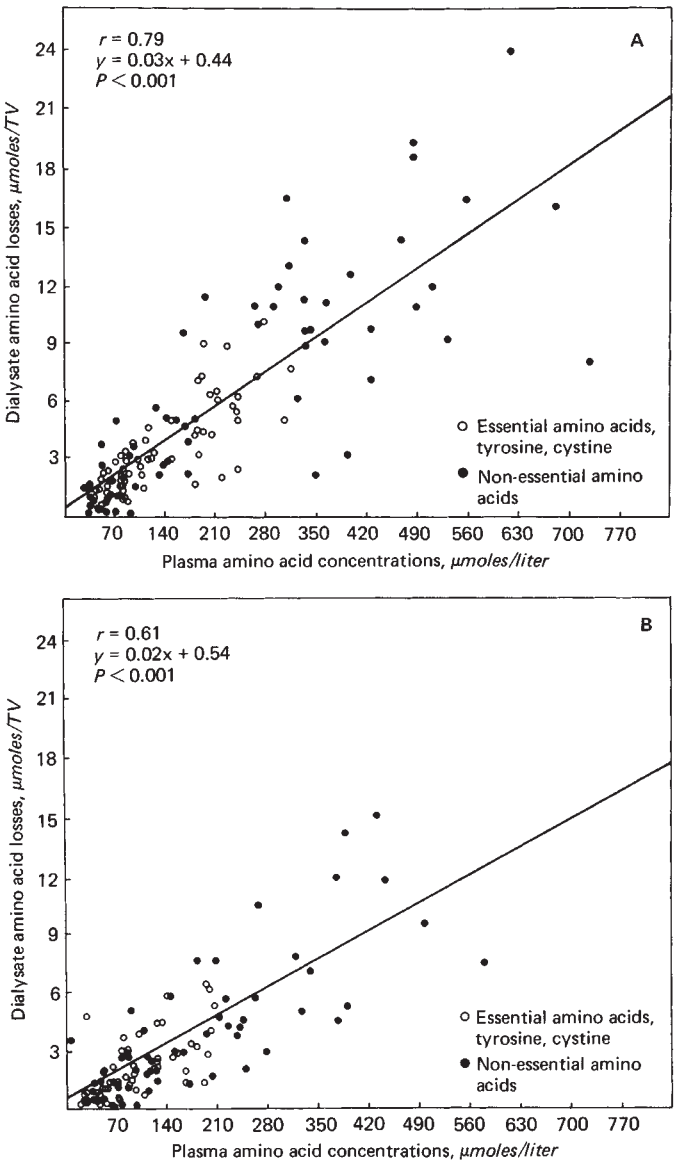

Fig. 1. A *Amino acids and glucose solution.* The figure depicts a direct correlation between the average individual plasma-free amino acids (mean of pre-, mid-, and postdialysis concentrations of each amino acid) and the loss of the free amino acids during hemodialysis. Each data point represents a value for one amino acid in a single study from one patient. **B** *Normal saline solution.* Direct correlation between the average individual plasma free amino acids (mean of pre-, mid-, and postdialysis concentrations of each amino acid) and the loss of the free amino acids during hemodialysis is shown. Each data point represents a value for one amino acid in a single study from one patient.

about 1.0 to 8.0 g of protein [16]. However, they used a recirculating dialysate delivery system, which may have reduced amino acid losses modestly, and their amino acid losses were estimated from alpha amino nitrogen. In previous studies, hemodialysis usually was carried out for longer periods of time with less efficient dialyzers. Considering these differences, the similarity in amino acid losses in the present study and in these previous investigations is worth noting.

In the current study, when patients received an infusion containing 39.5 g of amino acids and 200 g of d-glucose, the free amino acid losses into dialysate were only slightly greater, 12.6 ± 3.6 g, and the fall in plasma amino acids and glucose was prevented. Thus, 68% of the infused amino acids were retained. This can be seen in Table 4 where the intake and removal of amino acids during the hemodialysis treatments are shown. These considerations may underestimate the degree of retention because only 15 amino acids were infused and 23 amino acids were measured in dialysate (Table 2). If the comparison between intake and loss of amino acids is restricted to the amino acids infused (excluding tryptophan which was not measured in plasma or dialysate), it is apparent that (30.6 g ÷ 38.8 g) × 100 or 79% of the infused amino acids were retained.

It is not likely that much of the amino acids infused were lost in the urine since the mean urine output in the current patients was only 14 ml/day. Moreover, although fractional excretion of amino acids increases in advanced renal failure [19], the absolute clearance is low and therefore could not account for substantial urinary losses even in hemodialysis patients who are not oliguric. Finally, the plasma amino acid levels during the study were not markedly higher during the infusion of amino acids and glucose as compared with normal saline and did not exceed typical postprandial values [20]. Thus, it is very unlikely that urinary amino acid excretion would increase substantially in hemodialysis patients during such amino acid infusions.

Because amino acids were lost even when there was no amino acid infusion (Table 2), one may more realistically assess the effect of the amino acid infusion on total amino acid gain by comparing the quantity of amino acids infused with the amino acid solution to the increment in amino acids removed by dialysis. Thus, an additional 4.4 g of amino acids were removed when the amino acids and glucose were infused (Table 4). Calculated in this way, 35.1 g or 90%, (35.1 g ÷ 38.8 g) × 100, of the infused amino acids were retained. The slight increment in amino acid losses during the amino acid and glucose infusion reflects the relatively modest increase in the plasma amino acids. Indeed, with both infusions, there was a direct correlation between the average plasma concentrations of individual amino acids during each dialysis and the quantity of amino acids lost into dialysate (Fig. 1, a and b), an observation previously reported from this laboratory [14]. The dialysance of amino acids will, of course, also affect the losses, although for the amino acids evaluated in this study, the dialysance does not vary greatly [18].

It has been suggested that dialysis may be a catabolic event, possibly because of the losses of amino acids and glucose [9–12]. In fact, the present study indicates that during hemodialysis in fasting patients, not only is there a negative amino acid and glucose balance, but there may be disruption in amino acid pools. For example, it can be calculated that during infusion of normal saline, 8.2 g or 54.3 mmoles of amino acids were removed, and plasma amino acid levels fell by 1.0 ± 0.6 mmoles/liter. If one assumes that intravascular and extracellular amino acid concentrations are identical, it can be estimated that there was a fall in extracellular amino acids (including intravascular) equal to 15.9 mmoles (calculated as 79 kg mean body weight of the eight patients × 0.20 liters extracellular fluid/kg body weight × mmoles decrease in amino acids/liter

Table 3. Pre-, mid-, and postdialysis glucose, urea nitrogen, potassium, and phosphorus concentrations during infusion of normal saline or amino acids and glucose[a]

	Predialysis, *0 hr*		Mid-dialysis, *2.5 hr*		Postdialysis, *5 hr*	
	Normal saline	Amino acids and glucose	Normal saline	Amino acids and glucose	Normal saline	Amino acids and glucose
Glucose, *mg/100 ml*	83 ± 11	89 ± 11	73 ± 11	157 ± 36	70 ± 13 (59–92)	136 ± 26 (93–179)
Urea nitrogen, *mg/100 ml*	92 ± 35	92 ± 28	51 ± 19	52 ± 21	33 ± 13 (58–16)	38 ± 15 (69–19)
Potassium, *mEq/liter*	5.20 ± 0.63	5.3 ± 0.9	3.3 ± 0.8	3.5 ± 0.5	3.3 ± 0.4 (2.9–4.0)	3.1 ± 0.5 (2.5–3.9)
Phosphorus, *mg/100 ml*	4.6 ± 1.4	4.6 ± 1.3	2.9 ± 0.7	2.4 ± 0.7	2.7 ± 0.5 (1.7–3.3)	2.8 ± 0.6 (1.8–3.5)

[a] Values in parentheses reflect the range of values.

Table 4. Amino acid balance during hemodialysis with infusion of amino acids and glucose as compared with infusion of normal saline

	Total quantity of free amino acids		
Solution infused	Infused	Lost into dialysate *g/dialysis*	Retained during hemodialysis *g/dialysis*
(A) Normal saline	0	8.2	−8.2
(B) 39.5 g Amino acids and 200 g glucose	39.5	12.6	26.9
(C) Difference in net uptake between *(A)* and *(B)*	—	—	35.1

extracellular fluid). The rest of the amino acids lost during hemodialysis with normal saline infusion, about 38.9 mmoles, must be derived from intracellular sites. For some amino acids, such as isoleucine, leucine and valine, and quantity removed may reflect a substantial proportion of the intracellular pool [21, 22]. Thus, during hemodialysis with normal saline infusion, it is possible that, in addition to the fall in extracellular amino acids, there may be either a major disruption in intracellular free amino acid pools, a net breakdown of protein and peptides which replaced the intracellular amino acid losses, or a combination of these two phenomena.

A comparison of the decrement in plasma glucose with the expected glucose losses during dialysis [10] also suggests that most of the glucose removed during hemodialysis with normal saline infusion was replaced by degradation of amino acids or glycogen. Because, in our study, the infusion of amino acids and glucose resulted in net accretion and a rise in many plasma amino acids and glucose, it is probable that depletion of intracellular as well as extracellular amino acids and glucose was avoided and enhanced gluconeogenesis, glycogenolysis, and lipolysis might have been prevented.

It is possible that ingestion of a nutritious meal during or immediately before hemodialysis might accomplish the same results as infusion of amino acids and glucose. However, Grodstein and his associates recently demonstrated that gastric emptying is impaired, even during uneventful hemodialysis in relatively healthy patients [23]. Thus, it is not clear to what extent food intake can replace the losses of amino acids and glucose during hemodialysis. It may be that even relatively healthy patients who are not able to eat well during hemodialysis and have uneventful dialysis treatments might benefit from such intravenous supplements of amino acids and glucose. This would need to be demonstrated in prospective studies.

For the wasted or malnourished patient who eats poorly, has gastrointestinal malfunction, or catabolic stress due to intercurrent illness, the infusion of amino acids and glucose offers an opportunity to supplement dietary protein and energy intake as well as to replace the dialyzed amino acids. For example, if a 70 kg man ingested an inadequate diet providing him an average only of 55 g/day of protein, his weekly net protein and amino acid intake would be: (55 g protein/day · 7 days) or 385 g per 7 days. With the infusion of amino acids and glucose, his protein and amino acid intake would be: (55 g protein/day · 7 days) + (39.5 g amino acids/dialysis) (3 dialysis/7 days) − (4.4 g increment in amino acid losses/dialysis) (3 dialysis/7 days) = 490.3 g/week or 1.0 g/kg/day. It is recognized that the effects of daily fluctuation in the protein and amino acid intake of such a patient would need to be investigated. However, in our experience, the food intake of malnourished hemodialysis patients is often lowest on dialysis days when these supplements would be given; these amino acid and glucose infusions may actually decrease daily variations in nutrient intake. Such patients might also benefit from the administration of vitamins and minerals during hemodialysis. Moreover, because several amino acids which were not included in the infusate were also removed during hemodialysis (Table 2), it might be of value to infuse a greater variety of amino acids with this procedure.

Some investigators have recommended that amino acids or keto-acids should be infused during the last 60 to 90 min of hemodialysis or immediately after dialysis has ended [7]. This form of therapy may have some disadvantages in comparison to the infusion of these nutrients throughout the dialysis procedure. First, the administration of amino acids or glucose at the end of hemodialysis would allow some degree of amino acid and glucose depletion to occur before the infusion is started (Table 1), particularly if the patient did not eat or absorb food during dialysis. Also, it is possible that rapid infusion of these nutrients could be associated with undesirably high blood levels or less efficient metabolic utilization of these nutrients and possibly greater dialysis losses.

On the other hand, infusion of amino acids and glucose throughout dialysis into the venous blood line leaving the dialyzer has a number of potential advantages. First, the dialysis patient may receive nutritional supplements several times each week without increasing the time for treatment or for occupancy of a bed or chair in the dialysis facility. Second, there is no need to insert the needle or catheter into a vein with

a high blood flow; when patients are not on dialysis this is usually necessary so that the hypertonic solutions will not cause thrombophlebitis. Third, such infusions should prevent depletion of amino acid and glucose pools throughout the dialysis procedure. Fourth, the water received from the infusion can be removed during the dialysis, and the hazards of positive water balance from such infusions can be reduced. Finally, as this study demonstrates, most of the infused amino acids are retained and the plasma amino acid and glucose concentrations generally do not rise above postprandial levels [20].

It is possible that these nutrients could be administered to patients by adding the compounds to the dialysate [24]. This is feasible for glucose; however, as long as rather large volumes of dialysate are used for hemodialysis, the cost of adding sufficient amino acids to dialysate will probably exceed the expense of intravenous administration.

When these supplemental amino acid and glucose infusions are used, it is important to administer a carbohydrate source, such as bread or a high carbohydrate drink, during the last 20 to 30 min of infusion. Otherwise, reactive hypoglycemia may occur. Previous observations (unpublished) suggest that reactive hypoglycemia can occur if such a carbohydrate source is not administered; on the other hand, we have never observed hypoglycemia when such supplements were given.

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