Prevention of amino acid losses during peritoneal dialysis

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Summary

The addition of amino acid supplements to peritoneal dialysis fluid has been studied in 8 patients with compromised renal function requiring peritoneal dialysis. By the addition of 10 ml of Vamin-glucose solution to each one litre of peritoneal dialysate, amino acid losses were curtailed, no significant alterations occurred in the plasma amino acid concentrations, there were no local complications and no infections were seen. This procedure is recommended as a safe, simple way of keeping a patient in positive amino acid balance during peritoneal dialysis.

Introduction

It has long been known that during peritoneal dialysis there is a considerable loss of protein, which consists mainly of albumin and IgG (Berlyne *et al.*, 1964). This protein loss in dialysate fluid during 24 hr on peritoneal dialysis is usually in the range of 20-60 g/day. Simultaneously, amino acid losses per 24 hr of peritoneal dialysis are of the order of 13g/45 litre dialysis exchange (Berlyne *et al.*, 1967).

These losses of amino acids and protein, especially albumin, must result in impaired synthesis of plasma proteins and an increase in patient morbidity due to, firstly malnutrition (Schaeffer *et al.*, 1975) and, secondly, infection (Bistrian, 1977). Hypoproteinaemia is a frequent finding after peritoneal dialysis.

It was decided to investigate whether it was possible to obviate such complications in patients by the addition of amino acids to peritoneal dialysis fluid as suggested by Gjessing, 1968.

Patients and methods

Eight patients receiving peritoneal dialysis were studied between October 1976 and July 1977. To each litre of dialysis fluid were added 10 ml of Vamin-glucose (a full amino acid profile solution, Kabivitrum). A further 9 control patients were studied between July and December 1977 who did not have amino acids added to their dialysis fluid. In 2 of the

9 patients, peritoneal dialysis effluent was analysed, whereas the other 7 patients served as controls for blood parameters only.

All patients were uraemic and required peritoneal dialysis for relief of symptoms and correction of biochemical abnormalities. Most patients were on a 30-g protein diet during peritoneal dialysis. None of the patients received intravenous feeding during the study.

Dialysate fluid was collected daily in 10-litre containers from patients receiving Vamin-glucose supplements and from 2 control patients, M.D. and J.G. Only 2 control patients were studied as the results compared very closely with previous published control data under similar conditions (Berlyne *et al.*, 1967). The dialysate fluid was then shaken vigorously before 10-ml aliquots were taken. To one ml of each aliquot were added 3 ml of loading buffer. Each litre of water-based buffer contained: 19.6 g sodium citrate; 20 ml thiodiglycol; one g phenol; 37.5 sulphosalicylic acid; norleucine as an internal standard. The sample was then analysed on an L.K.B. Biochrom 4101 Amino Acid Analyser using a sodium citrate system.

Investigations before and at the end of peritoneal dialysis included a fasting plasma amino acid profile, haemoglobin, white blood count, packed cell volume, serum electrolytes, a Technicon SMA 12/60 biochemical profile (which included serum total protein, albumin, calcium, phosphate, urea, uric acid, creatinine, bilirubin, alkaline phosphatase, lactic dehydrogenase and aspartic transaminase) and serum complement (C_3) and transferrin (modified Mancini radial immuno-diffusion technique).

The amino acids analysed were glutamic acid, proline, glycine, alanine, valine, methionine, isoleucine, leucine, tyrosine, phenylalanine, histidine and arginine. There were separation difficulties with lysine, threonine and tryptophan at the time of this study. Since the volume of dialysis fluid infused, the volume of dialysate fluid removed from the peritoneal cavity, and the concentration of amino acids in both solutions were known it was possible to calculate an amino acid balance.

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Results

Details of the patients studied and the changes in their total serum protein, albumin, complement (C₃) and transferrin during peritoneal dialysis are shown in Table 1. The serum protein comparisons between the control and amino acid supplemented peritoneal dialysis are shown in Table 2 and no

statistically significant differences were seen although the downward trend was less in the treated group for total serum protein, serum albumin and serum globulin.

Table 3 shows the amino acid balance results. The patients who had 10 ml of Vamin-glucose added to their dialysis fluid were all in strongly positive

TABLE 1. Clinical features, duration of dialysis, serum total protein, serum albumin, serum C₃ and serum transferrin

Patient	Sex	Diagnosis	No. of days on dialysis	Serum total protein (NR 61–79 g/l)		Serum albumin (NR 37–46 g/l)		Serum C ₃ (NR 0.5–0.9 g/l)		Serum transferrin (NR 2.0–3.2 g/l)	
				*	†	*	†	*	†	*	†
H.F.	M	Analgesic nephropathy	4	66	57	40	35	0.45	0.42	1.6	1.7
J.R.	M	Glomerulonephritis	4	57	52	29	27	0.08	0.10	2.2	1.9
R.H.	M	Bilateral vesico-ureteric reflux, HT, chronic pyelonephritis	7	62	55	30	28	0.80	0.88	1.2	1.4
L.D.	F	Congenital abnormalities of post-renal tract, ileal loop, HT	6	64	51	35	26	0.52	0.42	2.9	1.1
L.W.	F	Pyelonephritis, renal calculi, HT	7	68	69	31	31	0.74	0.70	2.3	2.3
C.P.	M	Prostatectomy, haemorrhage, acute renal failure	6	55	60	31	32	0.74	0.57	1.6	1.9
D.J.	M	HT	5	68	60	40	33	0.57	0.56	1.7	2.0
M.B.	F	Glomerulonephritis	7	60	47	40	29	0.51	0.50	2.7	1.8

HT, hypertension; PD, peritoneal dialysis; NR, normal range; *, before PD; †, after PD.

TABLE 2. Changes in serum concentrations (all in g/l) before and after peritoneal dialysis

	Total serum protein mean (± s.d.)	Serum albumin mean (± s.d.)	Serum globulin mean (± s.d.)	Serum transferrin mean (± s.d.)	Serum C ₃ mean (± s.d.)
Dialysis fluid* with supplement <i>n</i> =8	-6.1 (6.3)	-4.0 (4.4)	-2.1 (2.3)	-0.3 (0.78)	-0.04 (0.07)
Control group* <i>n</i> =9	-8.3 (5.3)	-6.0 (2.0)	-2.3 (3.9)	-0.2 (0.3)	-0.04 (0.16)

* There was no statistically significant difference between these 2 sets of results.

TABLE 3. Amino acid balance of patients (in mmol)

	Treated Group (<i>n</i> =8)		Controls	
	Amino acid loss calculated per 100 litres of dialysate collected		Amino acid loss calculated per 100 litres of dialysate collected	
	Mean	(± s.d.)	M.D.	J.G.
Vamin glucose in:				
Glutamic acid	+12.92	(5.99)	0.28	1.44
Proline	+20.52	(6.99)	8.12	40.85
Glycine	+0.80	(1.64)	3.83	5.83
Alanine	+1.71	(3.82)	3.87	9.57
Valine	+11.02	(6.09)	2.39	2.52
Methionine	+4.35	(1.80)	0*	3.70
Isoleucine	+9.45	(2.72)	1.98	1.20
Leucine	+12.55	(4.20)	1.54	2.11
Tyrosine	+0.14	(0.54)	0.54	1.23
Phenylalanine	+9.55	(4.27)	0.92	2.36
Histidine	+1.23	(4.76)	1.24	2.05
Arginine	+7.10	(1.38)	0.51	1.48
Cystine			2.18	1.44

* Not measurable.

balance for glutamic acid, proline, valine, methionine, isoleucine, leucine, phenylalanine and arginine. These were the amino acids which in the supplemented dialysis fluid were relatively more concentrated in comparison to plasma values. The balances for these amino acids were positive in all the patients even when they were having excess fluid taken off by the use of hypertonic dialysis solution. Conversely, glycine and alanine, which are in the same concentration, and tyrosine in lower concentration in the supplemented dialysis fluid than in normal plasma, resulted occasionally in a negative balance for these amino acids. The individual plasma amino acid concentrations before and after peritoneal dialysis in control and treated groups did not show any significant changes. These results suggest that amino acid fluxes are dependent upon simple diffusion gradients and that absorption of amino acids from the peritoneal dialysate is by simple diffusion.

Histidine, which was not measured in all patients, gave varying results and in D.J., in particular, there was an apparent negative histidine balance. However, further evaluation of the technique has revealed that 3-methylhistidine (3-MH), a non recyclable metabolite of muscle tissue (Long *et al.*, 1975), and histidine appeared in the same peak. This problem has been noted previously (Condon and Asatoor, 1971). Probably any apparently high histidine peak in the present method must contain 3-MH which indicates a catabolism of the patient.

Discussion

The results for the amino acids other than histidine suggest that the method of absorption is by simple diffusion across the peritoneal membrane. The more concentrated the amino acid in the dialysis fluid in relation to the plasma concentration the more positive the balance for that amino acid. If this mechanism is the same for lysine, threonine and tryptophan which they did not measure, and there is no reason for believing otherwise, the authors would anticipate that the balance for these amino acids using Vamin-glucose would also be positive.

There was no statistically significant difference in the plasma amino acid profiles at the beginning and end of peritoneal dialysis or between those patients receiving supplemented dialysis solution and those who did not. Therefore, it may be concluded that measurement of actual amino acid losses is the optimal way of assessing amino acid nitrogen losses, that additions of Vamin-glucose do not cause aberrations of the amino acid profile so as to cause toxicological effects and that the plasma amino acid concentrations, since they represent less than 1% of the total amino acid pool, are a poor marker of amino acid metabolism (Bergstrom *et al.*, 1972).

During haemodialysis amino acid losses of 2–3 g/hr occur (Schaeffer *et al.*, 1975). However, Young and Parsons (1966) noted that although there are significant falls in plasma amino acid concentrations immediately after haemodialysis, these return to pre-dialysis values within 6 hr of completing dialysis. The post-dialysis fasting amino acid profiles in the present study were estimated on the day following completion of peritoneal dialysis because re-equilibration between intracellular and extracellular amino acid concentrations could be anticipated by that time.

It can be seen from the 2 control patients (Table 3) that there were marked losses of proline, glutamic acid, cystine, glycine, alanine, leucine, isoleucine, phenylalanine, tyrosine, histidine and arginine. These findings are in accordance with those of Berlyne *et al.* (1967). However, low concentrations of methionine were found in the dialysate fluid of the present patients whereas Berlyne *et al.* (1967) found high concentrations of dialysate methionine as their patients were on dietary methionine supplements.

Since the half-life of albumin is about 16 days it is not surprising that there were no statistically significant changes in serum albumin between the patients who had Vamin-glucose-supplemented dialysis fluid and the patients who did not.

Table 2 demonstrates the problems of using complement (C_3) and transferrin as markers of nutritional adequacy (Hill *et al.*, 1977; Silk, 1978). Patient J.R. had an immune complex-mediated glomerulonephritis which is associated with low concentrations of complement C_3 . Patient M.B. had a small haemorrhage into the peritoneal cavity at the start of peritoneal dialysis and this was associated with a very large fall in serum transferrin. Since many factors affect serum transferrin and complement C_3 concentrations in renal disease it might be anticipated that no significant difference would be found between the Vamin-glucose supplemented and the control group.

Currently there is not a good discriminator of rapid change in nutritional status or immune competence to use in such patients and it would be necessary to follow-up these patients for several weeks after peritoneal dialysis and then re-assess their nutritional status. The authors' approach prevents amino acid losses from the amino acid pool which implies that albumin and immunoglobulins will be re-synthesized more rapidly than if the amino acid pool is depleted.

During this work and subsequent observations with Vamin glucose-supplemented dialyses the authors have not noted local or systemic adverse reactions to the amino acid solution. Since the regimen of adding Vamin-glucose to dialysis fluid

was started they have not had any cases of infection in the peritoneal cavity.

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