Influence of Continuous Ambulatory Peritoneal Dialysis on some Plasma and Erythrocyte Vitamins – Retrospective Study

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Abstract: This paper reports a retrospective study on the clinical and laboratory analysis of some serum and erythrocyte vitamins in our chronic renal failure patients who were treated with Continuous ambulatory peritoneal dialysis (CAPD). In the first patient and in the next 10 patients the CAPD treatment began (in years 1980–1984) at the Internal Department-Strahov of General Faculty Hospital in Prague and after 2 or 3 weeks they continued in CAPD programme at the Dialysis Centre of IV[th] Internal Clinic, Faculty Hospital in Košice. In the third group of CAPD patients (among them 8 patients were treated in Prague and 5 patients in Košice) all biochemical parameters including vitamins were determined at Nephrological laboratory of the IV[th] Internal Clinic in Košice. Besides that the aim of this paper was to show the above standard relationship and a long-term cooperation between above mentioned departments, and to contribute to Czech and Slovak reciprocity and to the history of clinical nephrology. The paper was presented on the important occasion of the 30[th] anniversary of the first continuous ambulatory peritoneal dialysis, which was performed at Internal Department-Strahov, Prague in the year 1978.

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Introduction

The opening of the first dialysis centre on January 6, 1966 was connected with peritoneal dialysis, which was performed in one patient who suffered from chronic glomerulonephritis at the Ist (later IVth) Internal Clinic of Faculty Hospital of L. Pasteur in Košice. The peritoneal catheter was inserted into the peritoneal cavity by percutoneous route. Later peritoneal dialysis was performed only in patients suffering from acute renal failure or acute poisoning, especially in patients when the haemodialysis was relatively or absolutely contraindicated, i.e. in small children [1, 2].

Continuous ambulatory peritoneal dialysis (CAPD) was a new elimination method for chronic renal failure patients which was introduced by Popovich et al. in 1978 [3]. On the basis of previous long-term cooperation with Professor Albert Válek, MD., DSc., from the IInd Internal Clinic, later Internal Department-Strahov, General Faculty Hospital, Charles University in Prague, we started with CAPD programme in chronic renal failure patients on April 25, 1980, in our clinic in Košice, too [4, 5].

The purpose of this retrospective study was to present an analysis of our three previous studies concerning the clinical and laboratory parameters of some serum and erythrocyte vitamins in CAPD patients.

Material and Methods

Twenty four CAPD patients (16 men, 8 women), mean age 42±5 years, without significant uremic syndrome were investigated. Among them were 15 patients suffering from chronic glomerulonenephritis, 6 patients suffering from chronic tubulointerstitial nephritis, 2 patients with diabetic nephropathy and 1 patient with vascular nephrosclerosis. The diet of patients was without restriction of proteins, fruit and vegetables. Malnourished CAPD patients were not included in the study. CAPD consisted of 4 daily exchanges of 2 litres of peritoneal dialysis solution (PDS) with 1.5% or 2.5% sorbitol or glucose. Peritoneal dialysis solution with sorbitol (at the beginning of CAPD treatment in former Czechoslovakia) was made at the Department of Pharmacy of Faculty Hospital of L. Pasteur in Košice. Above mentioned PDS with sorbitol was used in our first CAPD patient who was described as a single patient and in 10 CAPD patients who formed the second group of patients during 12-month study. Among them were 8 men and 2 women, mean age was 42 years. Eight of them had chronic glomerulonephritis and 2 patients had chronic tubulointerstitial nephritis. Patients were from 1 to 18 months on CAPD. Depending on residual diuresis (1500±600 ml/day) and on the degree of uremic syndrome the patients performed 2 or 4 6-hour home peritoneal dialyses during 24 hours. In these CAPD patients serum vitamin A and its protein carriers, serum vitamin C and E and erythrocyte vitamins B_1, B_2 and B_6 were determined. The 3rd group was formed by 13 CAPD patients, 7 men and 6 women, mean age 59.4±5.5 years (6 patients suffered from chronic glomerulonephritis, 4 patients from tubulointerstitial nephritis, one patient from vascular nephrosclerosis and 2 from diabetic nephropathy). These CAPD patients were treated with PDS with

glucose, C.A.P.D. Clear flex L3 system (Bieffe Medital S.p.a.) was used. The CAPD treatment lasted from 2 to 19 months. The residual diuresis was 1300±450 ml/day. We investigated in the third group of patients' plasma, peritoneal dialysate, peritoneal clearance and transfer of urea, creatinine, ascorbic and oxalic acid using 1.5% glucose in PDS and three days later using 2.5% glucose in PDS. The first CAPD patient and patients of the second group were supplemented during the whole study by vitamin B_1: 2 mg/day, vitamin B_2: 2 mg/day, vitamin B_6: 6 mg/day and vitamin C: 200 mg/day. Three CAPD patients were treated with erythropoietin and supplemented by 20 mg Pyridoxine/day in the 3rd group of patients [6]. The other patients of the 3rd group were supplemented by Pyridoxine 5 mg/day. Serum vitamins A and E were determined by means of fluorometric methods [7], serum prealbumin and retinol-binding protein were determined by means of radial immunodiffusion methods [8]. Erythrocyte vitamins B_1, B_2 and B_6 were determined by means of indirect methods, i.e. by assessing catalytic activity of erythrocyte transketolase, glutathione reductase and aspartate aminotransferase. The effect of coenzymes [thiamine pyrophosphate (TPP), flavine adenine dinucleotide (FAD) and pyridoxal-5-phosphate (PLP)] on the relevant catalytic activity of erythrocyte enzymes was in indirect relationship with the concentration of erythrocyte vitamin B_1, B_2 and B_6, and was expressed in per cents [9]. Vitamin C in serum and in peritoneal dialysate was determined by means of photometric method [10]. The plasma and peritoneal dialysate oxalic acid levels were determined by enzymatic method using oxalate oxidase which is free from vitamin C interference [11].

The statistical analysis of obtained results was performed using paired or unpaired t-test at the Institution of Medical Informatic, Medical Faculty of P. J. Šafárik University in Košice.

Results

On April 25, 1980 Tenckhoff peritoneal catheter was implanted into the peritoneal cavity to our 41-year-old patient with chronic glomerulonephritis in chronic renal failure at the IInd Surgical Clinic of General Faculty Hospital of Charles University in Prague. The patient performed four daily peritoneal dialyses not only at home but also during 14-day holidays in the High Tatras. The patient was an editor in Czechoslovak television in Košice and he did not interrupt his work during CAPD treatment. Two sterile peritonitis (leukocyte count was 2.2 and 2.5×10^9/l and aerobic and anaerobic cultivation of peritoneal dialysate were sterile) occurred in the patient during 18 months of CAPD treatment. No other complication was observed. From clinical point of view during 12-month of CAPD study the patient was not hyperhydrated and was without oedema, mean blood pressure was 21±1.5/11.7±2.0 kPa, and diuresis was 1750±200 ml/day. From laboratory point of view the mean value of serum urea was 18.5±2.5 mmol/l, serum creatinine was 743±52 μmol/l, serum potassium was 5.2±0.5 mmol/l, serum sodium was 142.0±1.5 mmol/l, blood haemoglobin was 105.3±5 g/l and haematocrit was

0.32±0.02. Serum and erythrocyte vitamins are depicted in Table 1 [5]. CAPD treatment lasted 18 months and than the patient was transferred on haemodialysis treatment.

In the group of CAPD patients, who formed the second part of the study, serum vitamin A, retinol-binding protein and vitamin E levels were significantly increased ($p<0.01$) during the 12-month study, serum prealbumin was above the upper margin of the control group ($p<0.05$) (Figure 1). Our control group consisted of 30 healthy blood donors. Erythrocyte vitamin B_1 expressed as the effect of TPP on catalytic activity of erythrocyte transketolase was in the normal range (10.5±2.5%) ($p>0.05$) during the whole study (normal range: 0–25%). Erythrocyte vitamin B_2 expressed as the effect of FAD on catalytic activity of erythrocyte glutathione reductase was in the normal range (8.3±1.7%) ($p>0.05$) during the 12-month study (normal range: 0–23%). Erythrocyte vitamin B_6 expressed as the effect of PLP on catalytic activity of erythrocyte aspartate aminotransferase was in the normal range (13.1±2.0%) ($p>0.05$) during the whole study (normal range: 0–20%) (Figure 2). Serum vitamin C was significantly increased in CAPD patients in comparison with control group ($p<0.01$). At the onset mean value of vitamin C was the highest, in the 3rd month it decreased, but was still higher than the range of control group ($p<0.01$) (Figure 3) [12, 13].

Table 2 shows the values of the mean peritoneal clearances and peritoneal transfers of urea, creatinine, ascorbic and oxalic acid in 13 CAPD patients using PDS with 1.5% (A) and 2.5% (B) glucose. The mean value of plasma ascorbic acid was above the upper margin of normal range (29–85 μmol/l) but the values of plasma oxalic acid were significantly increased in all patients ($p<0.01$) in comparison with normal range (3.8±1.7 μmol/l). All investigated parameters

Table 1 – Serum or erythrocyte vitamins in J. S. patient during 12 months continuous ambulatory peritoneal dialysis

Biochemical parameter	0 month	3rd month	6th month	9th month	12th month
1. Serum vitamin A (μmol/l)	5.77	6.55	8.19	7.80	10.50
2. Serum β-carotene (μmol/l)	2.03	1.65	1.80	1.50	1.35
3. Serum prealbumin (g/l)	0.375	0.364	0.40	0.32	0.45
4. Serum retinol-binding protein (g/l)	0.132	0.130	0.166	0.199	0.218
5. Erythrocyte vitamin B_1 Effect of TPP (%)	5.0	22.5	–	10.2	8.0
6. Erythrocyte vitamin B_2 Effect of FAD (%)	9.6	3.6	–	0.7	5.7
7. Erythrocyte vitamin B_6 Effect of PLP (%)	20.9	30.0	–	17.0	13.9
8. Serum vitamin C (μmol/l)	70.9	31.8	344.0	204.5	53.9
9. Serum vitamin E (μmol/l)	37.3	32.9	44.5	45.9	55.5

TPP – thamine pyrophosphate; FAD – flavin adenine dinucleotide; PLP – pyridoxal-5-phosphate

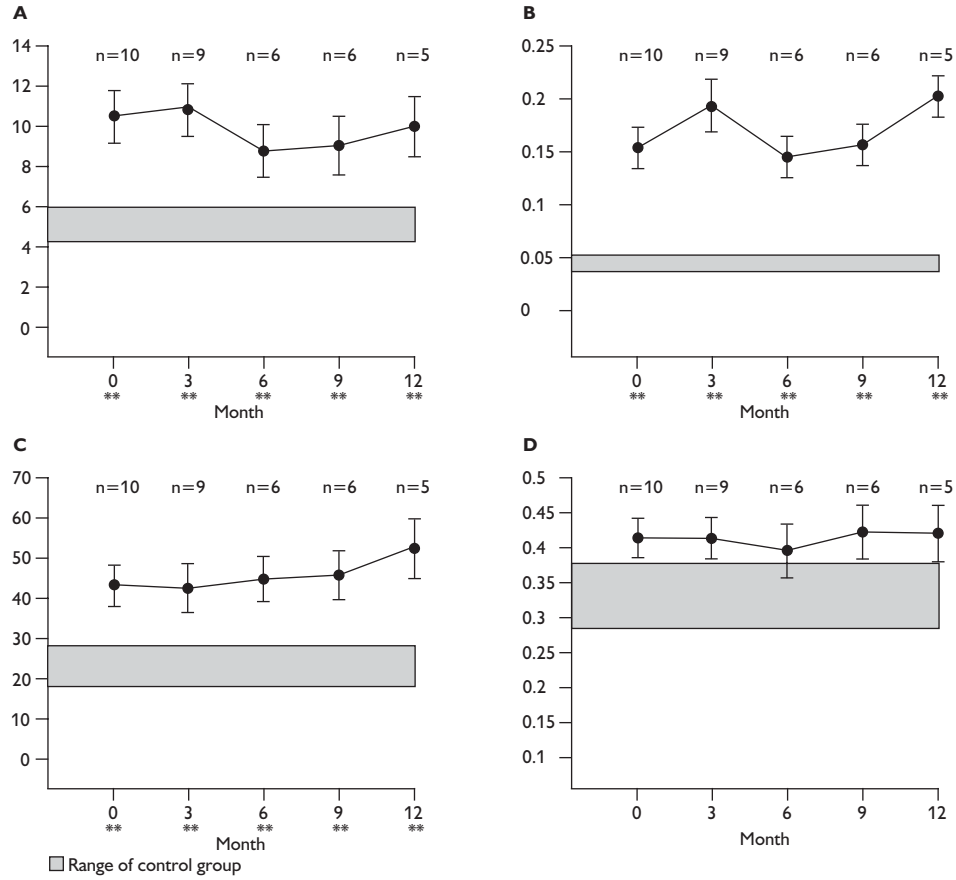

Figure 1 – (A) Serum vitamin A (μmol/l), (B) retinol-binding protein (g/l), (C) prealbumin (g/l) and (D) vitamin E (μmol/l) during 12 months of continuous ambulatory peritoneal dialysis.

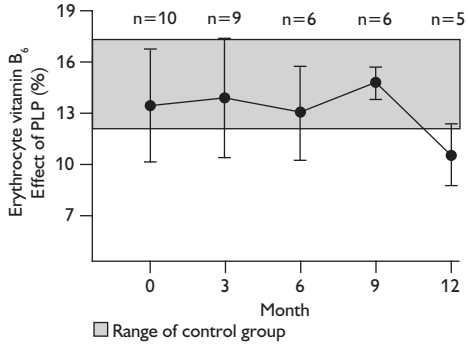

Figure 2 – Erythrocyte vitamin B_6 as the effect of pyridoxal-5-phoshate during 12 months of continuous ambulatory peritoneal dialysis.

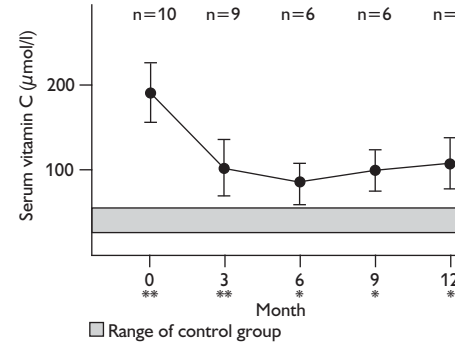

Figure 3 – Serum vitamin C during 12 months of continuous ambulatory peritoneal dialysis.

were found in peritoneal dialysate. Mean peritoneal clearances of urea, creatinine and ascorbic acid were nearly the same values; the lowest was in oxalic acid (79% of urea peritoneal clearance using PDS with 1.5% glucose and 63.8% using PDS with 2.5% glucose). Peritoneal transfer, i.e. the loss of some substance into dialysate within 6 hours, was the highest for urea; the lowest transfer was for oxalic acid. The mean peritoneal clearances except of oxalic acid and peritoneal transfers of all investigated parameters were significantly higher using PDS with 2.5% glucose ($p<0.01$). Direct relationships between plasma oxalic acid and serum creatinine ($r=0.7414$, $p<0.01$), and between plasma oxalic and ascorbic acid ($r=0.6197$, $p<0.05$) were found. Besides we found direct relationships between peritoneal transfer of oxalic and ascorbic acid using PDS with 1.5% glucose ($r=0.4925$, $p<0.05$) and with 2.5% glucose ($r=0.5760$, $p<0.05$) [14].

Discussion

The diuresis did not diminish and pericardial murmur disappeared during the long-term treatment in the first CAPD patient. The values of haemoglobin and haematocrit non significantly increased in spite of the fact that the patient was not treated by erythropoietin or blood transfusion. Aseptic peritonitis was connected

Table 2 – Peritoneal clearance and peritoneal transfer of urea, creatinine, vitamin C and oxalic acid in CAPD patients using peritoneal dialysis solution (PDS) with 1.5% glucose (N=13), (A) and 2.5% glucose (N=13), (B)

	Biochemical parameter	Plasma	Peritoneal dialysate	Peritoneal clearance (ml/min)		Peritoneal transfer
A	1. Urea	17.1 ± 4.0 (mmol/l)	16.0± 3.4 (mmol/l)	4.8 ± 0.6		29.5 ± 6.8 (mmol/6h)
	2. Creatinine	713.7 ± 181.0 (μmol/l)	649.9 ± 163.3 (μmol/l)	4.6 ± 0.6	a	1203.0 ±330.9 (μmol/6h)
	3. Vitamin C	95.3 ± 27.2 (μmol/l)	87.0 ± 27.6 (μmol/l)	4.7 ± 1.2		163.1 ± 57.0 (μmol/6h)
	4. Oxalic acid	30.9 ± 10.9 (μmol/l)	22.5± 5.8 (μmol/l)	3.8 ± 0.6		40.9 ± 11.9 (μmol/6h)
B	1. Urea	18.0 ± 5.2 (mmol/l)	708.8 ± 196.1 (mmol/l)	5.8 ± 0.6**		38.1 ± 3.4** (mmol/6h)
	2. Creatinine	799.9 ± 210.2 (μmol/l)	17.3 ± 4.8 (μmol/l)	5.4 ± 0.6**	a	1550.8±443.2** (μmol/6h)
	3. Vitamin C	102.7± 25.3 (μmol/l)	92.4 ± 25.9 (μmol/l)	5.5 ± 1.2**		202.6± 62.3** (μmol/6h)
	4. Oxalic acid	39.0 ±11.9 (μmol/l)	23.6± 11.9 (μmol/l)	3.7 ± 0.6		51.6± 10.4** (μmol/6h)

Amount of peritoneal dialysate (1.5% PDS): 1852.7 ± 158.0 ml/6h
Amount of peritoneal dialysate (2.5% PDS): 2188.1 ± 202.3 ml/6h
[a]$p<0.01$ versus peritoneal clearance of urea, ** $p<0.01$ versus values 1.5% PDS

with transient increase of dialysate leucocytes above the value of 0.5×10^9/l, but with sterile cultivation [5].

From the results obtained in a long-term 12-month CAPD study the following data can be read. Serum vitamin A and its protein carrier retinol–binding protein were constantly increased during a period of one year in spite of the fact that they had relatively great peritoneal transfer and loss into the dialysate [12, 13]. Erythrocyte vitamins B_1, B_2 and B_6 which were determined by means of indirect methods were in normal ranges. In the first years of CAPD treatment we administered to patients large dose of vitamin C 200 mg/day. The value of serum vitamin C in our patients during 12 months of CAPD was still significantly above the range of control group, in spite of a great peritoneal transfer and loss of this vitamin into the dialysate (149 ± 25 μmol/6 h) [15]. In the present time the supplementation by vitamin C in CAPD patients is not necessary because they have a diet without restriction of proteins and vegetable and fruit [16]. Serum vitamin E was increased during the whole study like vitamin A and was not influenced by that treatment. In the present time it is known that increased oxidative stress and consequent increased oxidability of low-density lipoproteins has been proposed as an explanation for accelerated cardiovascular complication in chronic renal failure patients undergoing dialysis. From that reason we administered in the last years 400 mg/day of vitamin E to our CAPD patients. Vitamin E is one of the effective and suitable antioxidant drug in chronic renal failure patients [17].

In the 3rd part of CAPD study we found the significant increase of plasma oxalic acid in all patients. Peritoneal clearance and peritoneal transfer of oxalic acid in that group of patients was lower in comparison to urea using both concentration of glucose in PDS. Peritoneal transfer of oxalic acid significantly increased using 2.5% glucose in PDS as a result of higher ultrafiltration. No influence on its peritoneal clearance was found. Probably the reason of that finding was that concentration of dialysate oxalic acid was nearly the same value using both PDS, and plasma oxalic acid was significantly higher using 2.5% PDS in comparison to 1.5% PDS. CAPD is an elimination method by means of which high plasma concentrations of oxalic acid in uremic patients cannot be significantly influenced. Oxalic acid is one of the well known uremic toxin, which leads to fibrosis of many parenchymal organs and to the progression of atherosclerosis [18]. From this point of view it is not necessary to supplement CAPD patients by vitamin C which is the precursor of oxalic acid.

Conclusion

On the basis of obtained results in our patients with chronic renal failure during CAPD we did not recommend to supplement orally vitamins A, B_1, B_2 and vitamin C because the diet of these patients was without restriction of proteins, vegetable and fruit. Adequate daily dose of vitamin B_6 was 6 mg which led to the erythrocyte vitamin B_6 level to normal range. In the patients who were treated by erythropoietin during CAPD, the daily supplementation dose of vitamin B_6

was 20 mg. According to contemporary knowledge the CAPD patients would be supplemented by 400 mg/day of vitamin E [17].

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