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TRACE ELEMENT ABNORMALITIES IN CONTINUOUS AMBULATORY PERITONEAL DIALYSIS

A Leung, I Henderson, D Halls, G Fell, A C Kennedy

Royal Infirmary, Glasgow, United Kingdom

Summary

Trace element profiles were studied for 25 continuous ambulatory peritoneal dialysis (CAPD) patients. There was a significant rise in serum concentrations of aluminium and chromium. The source of chromium accumulation is from CAPD dialysate while oral ingestion of aluminium hydroxide seems to be the major cause of increase in serum aluminium. A significant fall in serum zinc, plasma selenium and whole blood lead and cadmium was observed.

Introduction

Continuous ambulatory peritoneal dialysis (CAPD) is an increasingly popular form of renal replacement therapy in chronic renal failure patients. Abnormalities in trace metal metabolism may occur in CAPD patients due to various factors such as contamination of dialysate, loss through the peritoneal membrane, decreased protein-binding, dietary deficiency and ingestion of phosphate binders. We have studied the trace element profiles in 25 CAPD patients and have compared the results with those of chronic renal failure patients not yet on dialysis and normal healthy controls.

Methods

Blood samples were taken in 25 CAPD patients through a plastic cannula and placed in nitric acid washed polystyrene tubes. Serum or plasma were separated from red cells within two hours of collection.

Aluminium and chromium mass transfer during CAPD were studied in 10 patients using two timed four hourly exchanges. Drainage volumes were measured and blood and dialysate samples collected before and after the CAPD exchange for aluminium and chromium assay. Net aluminium and chromium balance was calculated by the following equation: Mass transfer = (Inflow volume x dialysate concentration) - (Drainage volume x drainage concentration).

Trace metal concentration in blood and dialysate were determined by atomic absorption spectrometry with electrothermal atomization. Student's 't' test was used for statistical analysis.

Results

A significant increase in serum aluminium and chromium occurred in CAPD patients (Table I).

TABLE I. Trace element profiles in CAPD patients

Trace metal		Normals mean±SD	n=25 CAPD	n=25 CRF
Aluminium*	μmol/L	0.4±0.2	1.3±0.8[c]	1.0±1.0[a]
Chromium*	nmol/L	4±3	99±49[c]	12±5[c]
Selenium**	μmol/L	1.5±0.3	1.0±0.4[c]	1.0±0.3[c]
Zinc*	μmol/L	14.5±1.8	12.7±2.6[c]	11.5±3.2[c]
Copper*	μmol/L	15.0±3.1	16.9±3.6[a]	17.9±4.2[b]
Lead***	μmol/L	0.58±0.27	0.43±0.27	0.36±0.13[c]
Cadmium***	nmol/L	13±2	9±6[b]	8±7[b]

*=serum; **=plasma; ***=whole blood trace element concentrations
a=p<0.05; b=p<0.01; c=p<0.001

A significant reduction in serum zinc, plasma selenium and whole blood lead and cadmium in CAPD was observed (Table I).

A net negative aluminium balance during a four hour CAPD exchange could be achieved in patients with serum aluminium >1μmol/L (Table II).

TABLE II. Aluminium mass transfer during a four hour CAPD exchange

Patient	Serum aluminium conc. μmol/L	Dialysate aluminium conc. μmol/L	Inflow volume litre	Drainage aluminium conc. μmol/L	Drainage volume litre	Net aluminium balance μmol/L
1	1.8	0.8	1.98	2.7	2.09	−4
2	1.4	0.1	1.48	0.2	1.48	−0.1
3	1.1	0.8	0.98	0.8	0.98	0
4	0.9	0.1	1.48	0.1	1.58	0
5	1.0	0.1	1.98	0.1	2.28	0
6	0.7	1.6	1.48	0.7	1.71	1.2
7	0.7	0.8	1.98	0.3	2.13	0.9
8	0.5	0.7	1.48	0.1	1.21	0.9
9	1.0	0.6	0.98	0.1	1.08	0.5
10	0.1	1.7	1.48	0.4	1.6	1.9

Mean CAPD dialysate aluminium concentration = 0.7±0.5μmol/L
Conversion from SI to traditional unit 1μmol/L = 2.7μg/100ml

A net positive chromium balance during a four hour CAPD exchange was observed in all 10 patients studied and the mean CAPD dialysate chromium concentration was 34±24μmol/L, i.e. nearly 10 times higher than normal serum (Table III).

TABLE III. Chromium mass transfer during a four hour CAPD exchange

Patient	Serum chromium conc. nmol/L	Dialysate chromium conc. nmol/L	Inflow volume litre	Drainage chromium conc. nmol/L	Drainage volume litre	Net chromium balance nmol/L
1	94	63	1.98	52	2.09	16
2	51	10	1.48	10	1.48	0
3	116	13	0.98	10	0.98	3
4	33	42	1.48	22	1.58	27
5	62	21	1.98	13	2.28	12
6	50	17	1.48	15	1.71	0
7	63	58	1.98	30	2.13	51
8	63	20	1.48	24	1.21	1
9	58	77	0.98	44	1.08	30
10	55	17	1.48	13	1.6	4

Mean CAPD dialysate chromium concentration = 34±24nmol/L
Conversion from SI to traditional unit 100nmol/L = 5.2μg/L

Discussion

Except for aluminium there have been only a few studies on trace metal abnormalities in CAPD patients [1,2]. The potential causes of altered trace metal metabolism in CAPD include: failure of renal excretion; reduced dietary intake and gastrointestinal absorption, altered protein binding; ingestion of phosphate binders; contamination of dialysate and loss across the peritoneal membrane. Peritoneal mass transfer studies are tedious and difficult and have been reported only once in the literature [2].

Aluminium

Aluminium accumulation occurs in CAPD patients and in severe cases can lead to systemic toxicity especially fracturing osteomalacia. In a separate study, we have shown that ingestion of oral aluminium hydroxide is the main cause for the increase in serum aluminium in CAPD patients [3]. The mean CAPD dialysate aluminium concentration is relatively low (0.7±0.5μmol/L) and a negative aluminium mass transfer during CAPD exchange can be achieved in patients with high serum concentrations. However, it remains prudent to monitor serum aluminium in all CAPD patients even though they are not taking aluminium-containing phosphate binders since severe aluminium toxicity secondary to gross contamination of CAPD dialysate by aluminium have been reported [4].

Chromium

A nearly 10-fold rise in serum chromium was found in CAPD patients compared to CRF patients and normal controls. Cornelis et al first reported hyperchromiumaemia in one CAPD patient using a different assay technique, neutron activation analysis [5]. This has been subsequently confirmed on more extensive studies on five patients by the Belgian group [2] and 13 patients by our group [6].

Our results are in close agreement with the Belgian workers and strongly suggest that a significant amount of chromium is absorbed to the systemic circulation from contaminated CAPD dialysate. Thomson et al, measuring whole blood chromium, have also reported a rise in chromium concentration in CAPD patients in comparison to CRF patients and normal controls [1]. The clinical significance of this gross disturbance in serum chromium needs to be urgently investigated. Our results of chromium transfer study also suggest serum chromium is bound to large plasma molecules and despite lower dialysate chromium concentration in all patients compared with serum values, a positive transfer into the systemic circulation still occurred.

Selenium

Our observation of low plasma selenium concentrations in CAPD patients concurs with previous observations [2]. Selenium is an essential trace element and its deficiency has been associated with myopathy and increased risk of cancer. Reduction in dietary intake and decreased gastrointestinal absorption are likely causes since the same reduction in selenium is also seen in the CRF group. Wallaeys et al have found that the selenium concentration in CAPD dialysate is extremely low and triples after use [2]. Whether this contributes to the overall selenium status is not certain.

Zinc

Zinc is an important component of many metalloenzymes and an essential trace element for normal metabolism in man. Zinc deficiency may cause weakness, anorexia, hypogeusia and hypogonadism [7]. A significant lower plasma zinc concentration was found in our CAPD patients. This agrees with previous studies [2] and similar findings in haemodialysis patients have been reported [8]. We have not been able to document any clinical sympatomatology related to zinc deficiency in our CAPD patients. Zinc is bound to albumin and loss into the peritoneum is possible. The status of zinc in uraemic and dialysis patients is complex and remains controversial. There is some evidence suggesting a translocation of zinc between different tissues in uraemia and interaction with other trace metals [9]. Previous studies on red cell zinc concentration have not been able to clarify the situation and Wallaeys et al have reported elevated values in CAPD patients while Thomson et al have found the reverse [1,2].

Copper

Copper is required for lysyl oxidase activity which is necessary for cross-linking of collagen including bone matrix [9]. Copper deficiency may also be associated with megaloblastic and sideroblastic anaemia and leucopenia [1]. Normal serum copper concentrations in CAPD patients have been reported previously but the result in red cell copper status have been conflicting [1,2]. We have found a small but significant increase in serum copper in our CAPD patients. Acute intoxication due to copper contamination during haemodialysis has been reported previously but the chronic effect of elevated serum copper concentration is more difficult to determine [9]. Serum copper is largely bound to carrier proteins, the level of which may change in different disease states and any interpretation of serum copper concentration must take this into account. The status of body copper stores in uraemia and dialysis needs to be evaluated more fully.

Cadmium and lead

Thomson et al have reported a reduction in whole blood cadmium in patients with CRF and on intermittent peritoneal dialysis but not in CAPD [1]. Little is known about whole blood lead concentration in CAPD but a normal red cell lead concentration has been reported [1]. Various factors such as anaemia, cigarette smoking and occupational exposure may affect cadmium and lead status other than uraemia and dialysis. Our present results suggest a reduction in whole blood cadmium and no significant change in lead in CAPD patients but a larger scale study will be necessary to evaluate the full effect of CAPD on cadmium and lead status.

In conclusion, significant disturbances in blood concentration of trace elements were observed in CAPD patients. These include the accumulation of potentially toxic elements aluminium and chromium and lowering of serum or plasma concentration of the essential trace elements zinc and selenium. Further investigation, especially tissue trace metal content and total body burden are very desirable in this new form of renal replacement therapy.

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