Renal osteodystrophy, vitamin D and aluminium in CAPD patients

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RESUMEN

Se estudia la evolución de osteodistrofia en 74 pacientes urémicos sometidos a DPCA durante más de 6 meses. El Ca del dializado fue de 1,75 mmol/l. Ingesta de Ca de 600-700 mg. y 1-1,5 g. diarios de fosfato. 46 recibieron carbonato cálcico (1-3 g. día), 29 quelantes del fosfato y 33 1-α-OH-colecalciferol. La concentración media de Ca sérico iónico y total estuvo en límites normales a lo largo de toda la observación (1,16-1,23 mmol/l.). Los niveles medios de fosfato plasmático fueron altos (1,5-1,8 mmol.), con tendencia a normalizarse a partir del sexto mes. Los niveles plasmáticos de 25-OH colecalciferol bajaron significativamente a partir de los 9 meses de tratamiento. Así, 23 pacientes presentaron niveles bajos de este parámetro (inferiores a 10 mmol/l.). La concentración media de 25-OH en drenado peritoneal fue de 2 nmol/l.

Se practicó biopsia ósea en 29 pacientes al año de tratamiento y en 9 a los dos años. Se observó mejoría de la osteítis fibrosa en 20 casos al primer año y 3 al segundo, y empeoramiento en uno y dos casos respectivamente; 27 no presentaban datos de osteomalacia al primer año, un paciente mejoró y el otro la desarrolló. Ninguno de los 9 biopsiados al segundo año había desarrollado esta entidad. Se observaron niveles significativamente elevados de aluminio plasmático (30 ± 3 Hg/l.) mantenidos a lo largo de toda la observación.

Las tinciones para aluminio en las biopsias fueron negativas, excepto en un caso con dicho hallazgo positivo previamente en HD.

Palabras clave: Osteodistrofia en DPCA, PTH en DPCA, 25-OH-colecalciferol en DPCA.

SUMMARY

Seventy-four patients on CAPD for 6 months or longer were managed using a PD fluid containing 1.75 mmol/l. calcium. Dietary intake of calcium was 600-700 mg. daily while that of phosphate was 1.0-1.5 g.; 46 were on calcium carbonate, 29 on phosphate binders and 33 on 1-α-OH-colecalciferol.

Serum ionized and total calcium concentrations were within the normal range. Serum phosphate levels ranged between 1.5-1.8 mmol/l. PTH levels were normal in all but 10 patients, six of whom previously on HD, with severe osteitis fibrosa (OF), required parathyroidectomy. 25-OH colecalciferol (25-OHCC) levels showed decline to subnormal with 9 or more months on CAPD. PD effluent showed significant 25-OHCC activity with mean levels of 2.0 nmol/l. Bone histology showed improvement in OF grading in 20 over 29 patients at 1 year. Seven patients starting at grade O did not develop OF. One patient showed deterioration and 1 was ammeliorated. Only one patient developed osteomalacia (OM) after 1 year of treatment.

Serum aluminium level were higher than normal (30 ± 30 Hg/l.) at start and did not change afterwards when measured in 27 patients.

Key words: Osteodystrophy in CAPD, PTH in CAPD, 25-OH-colecalciferol in CAPD.

INTRODUCTION

Renal osteodystrophy, which influences the quality of life and contributes to the morbidity of patients with end stage renal failure [1], has been reported to progress in patients treated by CAPD in some series [2,3] or improve [4,5]. However, better control of serum calcium and phosphate in these patients [6] has provided preliminary data that show improvement in histological grading of osteitis fibrosa (OF) in patients treated by CAPD [4].

This paper relates to the improvement in histological renal osteodystrophy in CAPD patients related to serum concentrations of calcium, phosphate, 25 hydroxycholecalciferol (25 OHCC), parathormone (PTH) and aluminium in the renal unit at Newcastle-upon-Tyne.

PATIENTS

Seventy-four patients (mean age 46) who had been on CAPD for 6 months or longer were studied. Their management described before [4] included the use of PD fluid containing 1.75 mmol/l. calcium, 35 mmol/l. lactate. Daily dietary intake of calcium was 600-700 mg. while that of phosphate was 1.0-1.5 g. 46 were on calcium carbonate (1-3 g. daily), 29 on aluminium-containing phosphate binders (ACPB), 33 on 1-α-hydroxycholecalciferol (1-α-OHCC). These patients had serum ionised and total calcium, phosphate, 25 OHCC, PTH and aluminium levels measured. In 29 patients paired bone biopsies at the start of CAPD and approximately 12 months later were studied for changes in OF and osteomalacia (OM) [7]. Nine of these were further studied at two years of CAPD.

RESULTS

Serum ionised and total calcium concentrations were within the normal range (ionised calcium: mean levels 1.16-1.23; normal range 1.15-1.30 mmol/l.) while mean serum phosphate levels ranged between 1.5-1.8 mmol/l. (fig. 1). PTH levels fell within the normal range in all but 10 patients, six of whom previously on haemodialysis with severe OF required parathyroidectomy; levels in these six patients fell subsequently (fig. 2). 25 OHCC levels showed a significant decline to subnormal levels with 9 or more months of CAPD. 23 patients after nine months had levels of less than 10 mmol/l. (normal range 10-70). In 11 patients 1-α-OHCC was given as vitamin D replacement. PD effluent showed significant 25 OHCC activity with mean levels of 2.0 nmol/l.

TABLE I

HISTOLOGICAL BONE DISEASE IN CAPD PATIENTS - PAIRED BIOPSIES

	At 1 year (n = 29)	At 2 years (n = 9)
Osteitis fibrosa:		
No development (grade 0 at start)	7 (0)	4 (0)
Improved	20 (14)	3 (3)
Unchanged (grade 1)	1	0
Worse (0 to 1)	1	2
Osteomalacia:		
No development	27	9
Improved	1	0
Developed	1	0

(Figures in brackets indicate number of patients in 1-α-OHCC.)

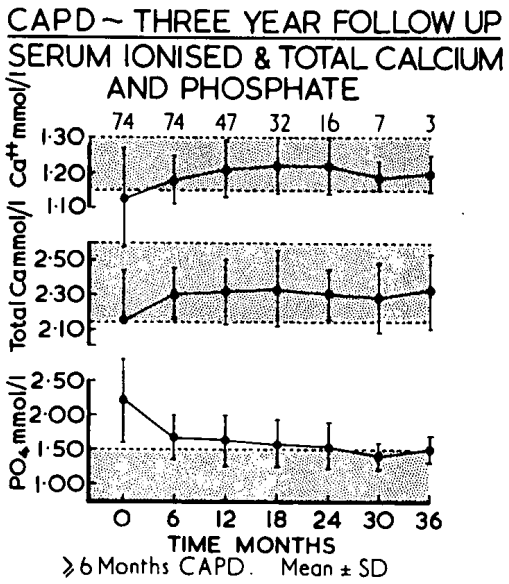

Fig. 1.—*Mean ± ISD levels of serum ionised calcium, total calcium and serum phosphate in CAPD patients (≥ 6 months on CAPD). See text for details of $CaCO_3$, Aluminium and Vitamin D therapy. The shaded areas denote normal ranges.*

Bone histology

Details of histological grading for OF and OM are shown in Table I. Overall 20 patients showed improvement in OF grading (14 were on 1 OHCC) at 1 year; only one patient showed slight deterioration (grade 0 to grade 1 on a scale of 0-5 with increasing severity) while 7 starting at grade 0 did not develop OF. At two years of CAPD, twp became slightly worse (grade 1 to 2, 2 to 2.5) while 3 improved; 4 remained at grade 0.

One patient developed OM after 1 year. She had a parathyroidectomy and her bone stained positive for aluminium and had been on haemodialysis prior to CAPD. None other showed any OM development.

Aluminium levels

The concentration of serum aluminium was measured at the start of CAPD and then at 3-6 monthly intervals in 27 patients, with 10 being followed for 19-24 months. The mean levels at start (30 ± 30 µg/l.) did not dif-

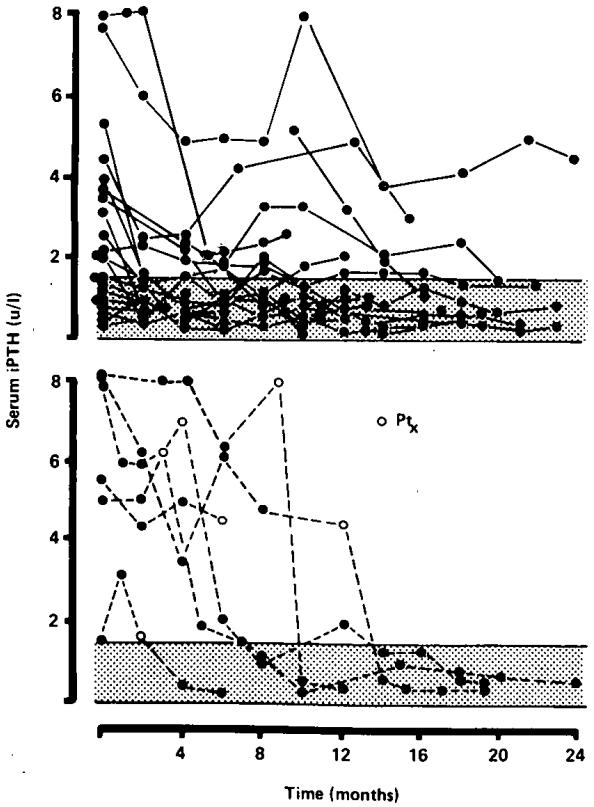

Fig. 2.—*Sequential PTH levels in CAPD patients (top figure) and in 6 patients requiring parathyroidectomy (PTx - 0) (Lower figure). Normal iPTH levels shown by the shaded area. The 6 patients requiring PTx had severe hyperparathyroidism prior to starting CAPD.*

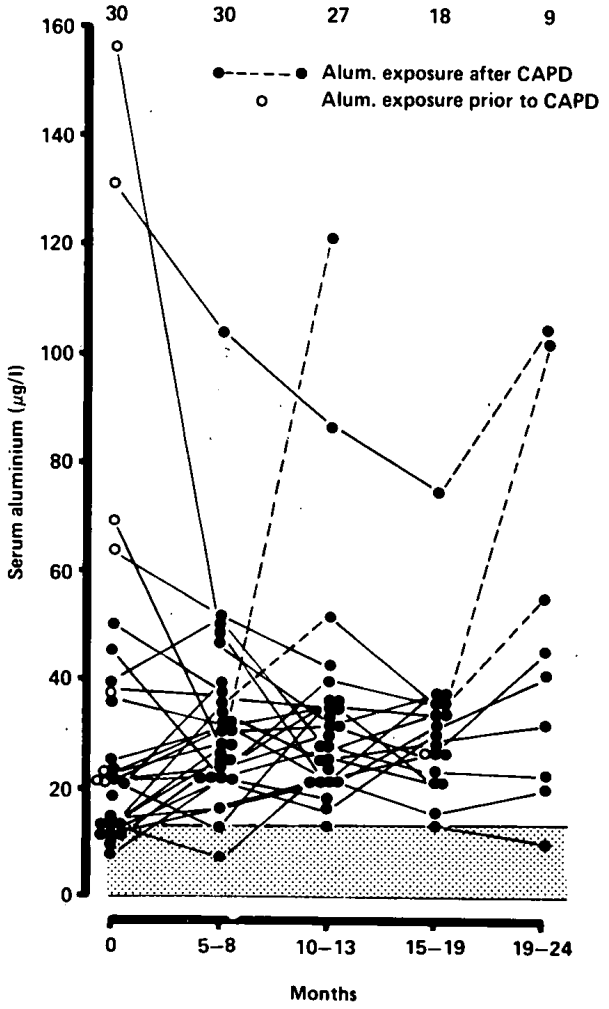

Fig. 3.—*Sequential serum aluminium levels in CAPD patients. The shaded area shows the normal range. Serum aluminium rose after administration of aluminium hydroxide (——*) but fell in those with high levels from previous aluminium exposure (o).*

fer from those at various time intervals but were significantly higher than normal controls (mean ± 2SD 7 ± 7 µg/l.) or chronic renal failure patients not exposed to ACPB (17 ± 16 µg/l.). In most patients, the aluminium levels steadied at around 30 µg/l., having fallen in those with high levels (from previous exposure) and risen in those with low levels at the start (fig. 3). Aluminium levels in the PD fluid prior to use was 18.25 ± ± 8 µg/l.

DISCUSSION

Over the short period of the study, the majority of patients showed either definite improvement or no deterioration in the histological grading of OF. The deterioration in 2 patients at 2 years was mild. These results are encouraging and suggest easier management of renal osteodystrophy on CAPD, with drugs such as 1-α-OHCC and avoidance of possible toxic effects of substances such as aluminium.

The improvement in histological OF is in contrast with the radiological deterioration of other groups [2,3], but in agreement with the experience of CHAN et al. [5]. The use of PD calcium of 1.5 mmol/l. may be too low (as used in the Toronto group) as opposed to the 1.75 in the Newcastle series, who in addition prescribe calcium carbonate supplements as most patients had low ionised calcium levels at start of CAPD. The calcium carbonate also acts as a mild phosphate binder and may help to counteract the mild acidosis. ACPB was used when serum phosphate exceeded 1.8 mmol/l. and this was necessary in 39 % of these patients.

Serum concentrations of 25 OHCC decline appreciably with time and 60 % of patients on CAPD for longer than 9 months had subnormal levels. The losses of protein bound 25 OHCC in the PD effluent probably accounts for the diminishing levels, a mechanism not too dissimilar from that occurring in the nephrotic syndrome [8]. Cautious Vit. D replacement may be necessary but care should be taken to avoid hypercalcaemia.

Serum aluminium levels were elevated, as were those in the PD fluid. Whether these high serum levels in CAPD were due to the PD fluid aluminium contamination is debatable. None of the patients with these levels showed any signs of toxicity nor any aluminium staining on bone biopsies. Nonetheless caution must be exercised with aluminium especially since ACPB led to higher serum values. More work needs to be done on the

kinetics of aluminium transfer before a «safe» value for PD fluid is advocated. However, recently acute aluminium intoxication in CAPD patients has been reported related to very high PD fluid aluminium levels [9]; these workers advocate a «safe» level of about 15 µg/l., values in excess of which have been associated with rising serum aluminium levels in their patients.

CAPD appears to achieve good control of histological renal osteodystrophy. However 25 OHCC levels are low and cautious vitamin D replacement therapy may be necessary. Serum aluminium levels are elevated and may be related to the PD fluid contamination. Calcium carbonate supplements are necessary early on in CAPD but phosphate control is easier than on haemodialysis.

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