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Histological renal osteodystrophy, and 25 hydroxycholecalciferol and aluminum levels in patients on continuous ambulatory peritoneal dialysis

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Renal osteodystrophy, which influences the quality of life and contributes to the morbidity of patients with endstage renal failure [1], has been reported to deteriorate in patients treated with continuous ambulatory peritoneal dialysis (CAPD) [2]. However, better control of serum calcium and phosphate in these patients [3] has provided preliminary data that show improvement in histological grading of osteitis fibrosa (OF) in our patients treated with CAPD [4].

Another form of bone disease, the osteomalacic dialysis osteodystrophy (OM), which may be associated with dialysis encephalopathy, is thought in some instances to be due to aluminum toxicity [5] from untreated or softened water used in hemodialysis in areas where the aluminum content of water supplies is high [6]. In patients undergoing CAPD any exposure to aluminum is likely to stem from the use of aluminum-containing phosphate binders (ACPB) since the process of preparation of peritoneal dialysis fluid reduces most of the trace metals.

In our unit, since the inception of the CAPD program in January 1979, 72 patients have been treated by this method in the first 2 years. In this report we present data on the improvement of histological renal osteodystrophy in CAPD patients and relate this to serum concentrations of calcium, phosphate, 25 hydroxycholecalciferol [25-(OH)CC] and immunoreactive parathormone (PTH). In addition, sequential serum aluminum concentrations are reported. These levels have been related to concentrations of aluminum in the peritoneal dialysis (PD) fluid and to the use of ACPB. One patient with aluminum toxicity prior to starting CAPD was studied to evaluate the chelating effect of disferrioxamine (DFO) on aluminum and its subsequent removal in the PD fluid.

Methods

Over the 2-year period 72 patients (43 male, 29 female; mean age, 42 years; range, 5 to 66) were treated with CAPD for a mean period of 7.8 months. Nineteen of these had previously been managed on hemodialysis (HD) or intermittent peritoneal dialysis (IPD). Their management, previously described [7], included the use of PD fluid containing 1.75 mmoles/liter calcium and 35 mmoles/liter lactate. The daily dietary intake of calcium was calculated at 600 to 700 mg while that of phosphate was 1 to 1.5 g.

Calcium, phosphate, alkaline phosphatase, 25-(OH)CC and PTH. Forty patients who had been on CAPD for 6 months or longer were studied. Serial measurements (every 3 to 6 months) were made of serum ionized and total calcium, phosphate, alkaline phosphatase, and PTH as previously described [3]. 25-(OH)CC was measured by a competitive protein binding assay, involving a preliminary extraction and purification to eliminate the interference of binding protein 25-(OH)CC that is present in serum and to remove related substances (mainly vitamin D itself) that cross react with the 25-(OH)CC binding protein. Extraction is achieved using chloroform methanol (2:1 v/v), and purification is performed by column chromatography on selicilic acid. Thirty patients of this group received oral calcium carbonate supplements 1.5 to 3.0 g daily; 11 were treated with 1 hydroxycholecalciferol (1 αOHCC).

Bone histology

Iliac bone biopsies. Transiliac bone biopsy specimens (5 to 7 mm diameters) obtained from 20 patients were examined histologically. Biopsy specimens were embedded in plastic for preparation of thin (5 μm) undecalcified sections, stained with hematoxylin and eosin, toluidine blue, and by the von Kossa and Masson-Goldner techniques. Aurine tricarboxylic acid (Aluminon) [8] was used to demonstrate aluminum at the mineralization front.

A diagnosis of osteomalacia was made when there was an excess of osteoid with abnormally wide osteoid seams comprising more than four bright lamellae when viewed between crossed polaroids and with a reduction in the proportion of surface osteoid bearing a mineralization front in toluidine blue stained sections [9]. The amounts of mineralized bone and osteoid in cancellous bone were determined using the point-counting technique. Multinucleated osteocalsts were counted in cancellous bone and expressed as the number square millimeters of the section. The severity of osteitis fibrosa was graded on a scale of 0 to 5 depending on the extent of any increased

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Table 1. Bone histology and duration of CAPD in individual patients

Patient no.	Biopsy 1			Biopsy 2			Biopsy 3		
	CAPD *Months*	OFG *0 to 5*	OM +/−	CAPD *Months*	OFG *0 to 5*	OM +/−	CAPD *Months*	OFG *0 to 5*	OM +/−
1	0	0	−	12	0	−			
2	0	2.5	−	14	1	−	24	2	−
3	2	0	−	12	1	−	24	1.5	−
4	0	2	−	12	0	−	24	0	−
5[a]	0	+	−	14	0	+	22	0	+
6[b]	0	1	(H)	12	0	−	24	0	−
7	4	3.5	−	10	3	−			
8	0	4	−	2	3	−	6	2.5	−
9[c]	−10	0	−	12	0	−			
10	0	0	−	12	0	−			
11	0	1	−	14	0	−			
12	0	2.5	−	4	1.5	−			
13	0	0	−	9	0	−			
14	0	3	−	12	2	−			
15	0	2	−	12	1	−			
16	−16	1.5	−	12	0	−			
17	0	0	−	12	0	−			
18	0	0	−	13	0	−			
19	−8	2.5	+	12	1.5	(H)			
20	0	3	−	7	0	−			

Abbreviations: OFG, osteitis fibrosa grade; OM, osteomalacia; (H) healed.

[a] Biopsy 1 relates to a knee bone sample obtained at the repair of ruptured quadriceps tendon. Iliac bone biopsies during the previous 5 years showed severe OF temporarily improved by 1 OHD_3 therapy. Total parathyroidectomy was performed after 6 months of CAPD.

[b] Biopsy 1 showed largely healed (H) OM as a result of 1 OHD_3 therapy. A biopsy specimen taken 5 months earlier showed OFG 1 and OM (see text).

[c] Subtotal parathyroidectomy (3.5 glands weighed 4,635 mg) 14 months before CAPD.

resorption, osteoblastic activity, marrow fibrosis, and woven bone formation [10].

Patients with bone histology. An initial biopsy specimen was obtained at the commencement of CAPD or within 1 month in 15 of the 20 patients (listed as 0 in Table 1). In two more patients the initial biopsy specimen was taken after 2 and 4 months of CAPD, respectively, and in three at 8, 10, and 16 months prior to starting CAPD.

At least one additional bone sample was obtained in each of the 20 patients. One patient died and the second sample was obtained at necropsy after 4 months of CAPD; in another the second biopsy was carried out at the time of parathyroidectomy after 6 months CAPD and in a third at the time of renal transplantation after 7 months CAPD. In the remaining 17 patients further biopsy specimens were obtained after 10 to 14 months CAPD and in 5 of the 20 a third biopsy was available after 22 to 24 months CAPD (Tables 1 and 2).

Aluminum levels in serum and PD fluid. The concentration of serum aluminum was measured at the start of CAPD and then at three to six monthly intervals in 27 patients; 10 patients were followed for 19 to 24 months. Nine of these 27 patients had been exposed previously to aluminum either in the form of ACPB or as a result of hemodialysis using softened water only. ACPB were deemed unnecessary for the control of serum phosphate during CAPD in all but six patients in whom the use of Alucaps (3 to 6 capsules daily) was begun 9 to 18 months after starting CAPD.

Forty-six normal subjects acted as controls and, in addition, 73 chronic renal failure patients not on dialysis and who had not been exposed to aluminum also had serum aluminum levels measured. Aluminum content of PD fluid (Travenol®) was estimated in ten randomly selected PD bags, together with effluent samples from the patient study treated with DFO.

Aluminum levels were measured by the flameless atomic absorption spectrophotometer. Blood samples for these estimations were collected through plastic cannula, and after immediate separation the serum was stored at −40°C.

Case report

A 52-year-old female, with medullary cystic fibrosis, reached endstage renal failure in 1974 and was transplanted. An iliac crest biopsy specimen showed moderately severe OF (grade 2.5) but no OM. However, transplant nephrectomy had to be performed for severe rejection and in 1975 she commenced hemodialysis, using softened but otherwise untreated water in an area with a very high aluminum water content. By 1976 the OF improved by OM had developed, and the bone biopsy specimen gave a positive staining reaction to aluminum. By 1977 she had very high serum aluminum levels (180 μg/liter) fracturing osteodystrophy; worse osteomalacia was revealed on the bone biopsy specimen which again showed a positive stain for aluminum (dialysis osteodystrophy).

Her treatment was subsequently changed to hemodialysis on deionized water and over the ensuing 2 years she started developing soft tissue calcification, probably related to high phosphate levels and hyperparathyroidism (PTH 2 U/liter, normal 0 to 1.5; bone biopsy OF grade 2). Subtotal parathyroidectomy (3.5 glands weighing 904 mg) was undertaken in April 1980, by which time she was on CAPD and had developed

Table 2. Quantitative bone histological data in CAPD patients

Patient no.	CAPD[b] *Months*	Percent measured area occupied by: Total bone	Mineralized bone	Osteoid	Percent mineralization	Maximum number osteoid lamellae	Osteomalacia +/−	Number osteoclasts per mm²	Osteitis fibrosa *Grade (0 to 5)*
2	1[c]	26.1	24.3	1.80	93.1	3	−	2.59	2.5
3	24	17.0	15.8	1.24	92.7	2	−	0.86	1.5
4	0	19.6	17.0	2.60	86.7	3	−	1.26	2
	12	14.1	13.1	0.99	93.0	2	−	0	0
	24	23.1	21.9	1.15	95.0	3	−	0.56	0
5	14	17.1	10.9	6.21	63.7	7	+	0.03	0
	22[c]	28.4	20.2	8.15	71.3	7	+	0	0
6	−5	22.9	18.9	4.06	82.3	6	+	0.24	1
	0[c]	33.6	31.4	2.24	93.3	2	(H)	0.78	1
	12	23.5	22.2	1.31	94.4	2	−	0.25	0
	24	25.8	24.3	1.47	94.3	2	−	0.17	0
7	4	49.5	45.6	3.83	92.3	3	−	15.62	3.5
	10	27.2	25.8	1.43	94.7	2	−	3.73	3
8	0	29.6	27.6	2.06	93.0	1	−	6.34	4
	2	34.4	32.1	2.31	93.3	2	−	2.92	3
	6	18.4	17.3	1.08	94.1	2	−	2.02	2.5
9[a]	−10	24.3	23.4	0.86	96.4	2	−	0	0
10	0	17.0	16.7	0.27	98.4	2	−	0.30	0
	12	18.3	17.8	0.55	97.0	2	−	0	0
11	0	16.7	16.0	0.68	95.9	2	−	0.97	1
	14	15.2	13.2	2.00	86.8	2	−	0.03	0
12	−1	20.6	18.7	1.88	90.9	4	−	1.83	2.5
	4	14.0	12.6	1.39	90.1	3	−	0.68	1.5
13	9	19.2	18.5	0.73	96.2	3	−	0.18	0
14	0	24.1	21.8	2.26	90.6	2	−	3.10	2.5
	12[c]	21.9	20.2	1.64	92.5	2	−	1.30	1.5
15	0	28.9	26.3	2.57	91.1	3	−	2.48	2
	12	21.4	20.0	1.44	93.3	3	−	0.26	1
16	−16	19.5	18.4	1.07	94.5	2	−	0.89	1.5
	12	15.4	14.7	0.65	95.8	2	−	0.08	0
17	1	10.8	10.6	0.17	98.4	2	−	0.41	0
18	0	19.5	19.4	0.09	99.5	2	−	0.05	0
19	−8	43.2	28.4	14.79	65.8	8	+	1.94	2.5
	12[c]	24.4	23.3	1.15	95.3	2	(H)	0.37	1.5
20	0	36.1	30.6	5.54	84.7	4	−	5.03	3
	7[c]	19.2	18.6	0.56	97.1	2	−	0.39	0
Normal mean ± SD		22.7 ± 3.1	22.6 ± 3.0	0.13 ± 0.10	99.5 ± 0.4	1 to 4	−	0.08 ± 0.06	−

[a] Patient no. 9 underwent parathyroidectomy 14 months pre-CAPD.
[b] Less than 1 month from start of CAPD indicated as 0.
[c] Improvement was evident while the patient took 1 α OHD_3.

speech disturbances an impaired memory and intellect, classical signs of early dialysis dementia.

In view of the report of Ackrill et al relating the successful use of DFO on an aluminum toxic hemodialysis patient [11], DFO in 2 g (then 4 g) was given weekly as an intravenous infusion while CAPD was continued. Serum aluminum levels and aluminum content of all PD effluents were measured over the week between injections. After 2 months on this treatment she reverted to hemodialysis because of peritonitis and DFO treatment was continued on hemodialysis for a further 2 months.

When giving 2 g DFO i.v. to this patient, the serum aluminum level rose within 24 hr which coincided with increased aluminum in PD fluid (Table 3). This effect of DFO was a maximal 24 to 48 hr after its injection. Overall the use of 4 g DFO once a week removed about 4 mg of aluminum which over the 2 months of treatment resulted in the removal of about 30 mg while a similar quantity would have been lost on hemodialysis. Over this period, however, there was no change in the neurological deficit. There were no side effects from the use of DFO.

Results

Calcium, phosphate, and alkaline phosphatase. Serum ionized and total calcium concentrations were within the normal range while mean serum phosphate levels ranged between 1.5 to 1.8 mmoles/liter without the use of phosphate binders (Fig. 1). Mean total alkaline phosphatase levels were within the normal range and individual levels did not correlate with the histological grading of OF.

Immunoreactive parathyroid hormone (PTH). PTH levels fell within the normal range in all but ten patients, six of whom were previously on hemodialysis with severe OF requiring parathy-

Table 3. Aluminum levels in serum and PD fluid in relation to use of desferrioxamine in the aluminum toxic patient

Serum aluminum level at start of CAPD	*69 μg/liter*
Serum level 24 h after 2 g DFO i.v.	*420 μg/liter*
Mean aluminum in PH fluid/exchange in first 24 to 48 hr after desferrioxamine	*400 μg*
Mean aluminum in PH fluid/exchange after 4 days	*150 μg*
Amount aluminum removed in 1 week	*4 mg*

roidectomy (Fig. 2). Levels in these patients fell subsequently.

25 Hydroxycholecalciferol [25-(OH)CC]. These showed a significant decline to subnormal levels with 12 or more months of CAPD. Twenty-three patients after 9 months had levels of less than 10 nmoles/liter (normal range, 10 to 70). In 11 patients 1 αOHCC was given as vitamin D replacement therapy. Peritoneal dialysate effluent showed significant 25-(OH)CC activity with a mean level of 2.0 nmoles/liter (0 to 4.3; 11 samples) with protein loss of 0.4 to 1.8 g/liter in the fluid.

Bone histology

Quantitative histology was possible in at least one bone biopsy specimen from 19 of the 20 patients (Table 2). Some other biopsy specimens were slightly traumatized and unsuitable for quantification.

Initial biopsy. Thirteen patients had some degree of osteitis fibrosa as revealed in the initial bone biopsy. Four had osteosclerosis (total bone >32.3% that is, normal mean ± 3 SD). Three of these patients (numbered 7, 19, and 20; Table 2) had severe osteitis fibrosa, and woven bone contributed to the osteosclerosis. In the other patient (no. 6) there was mild osteitis fibrosa and osteomalacia noted in a biopsy specimen taken 5 months previously that had largely healed after treatment with 1 αOHCC.

Although many patients showed an excess of surface osteoid of both lamellar and woven texture, this was generally attributable to the osteitis fibrosa; only one patient (no. 19) had osteomalacia accompanying osteitis fibrosa at the outset of CAPD.

Subsequent biopsies. (1) Up to 10 months of CAPD. In five patients a biopsy specimen was obtained after 4 to 10 months of CAPD. One (no. 13) patient still had no osteitis fibrosa at 9 months, and in two patients severe osteitis fibrosa had improved considerably (no. 8) or resolved (no. 20) after 1 αOHCC therapy at 6 and 7 months of CAPD, respectively. In the remaining two patients with initial osteosclerosis this resolved as the osteitis fibrosa improved (nos. 7 and 20). *(2) 12 to 14 months of CAPD.* Biopsy specimens were available in 15 patients. Of the six patients initially without osteitis fibrosa only one had developed osteitis fibrosa (mild, grade 1.5) at 12 months (no. 3). In the other nine patients osteitis fibrosa improved or resolved. In patient no. 19 treated with 1 αOHD_3 this was accompanied by healing of the osteomalacia. Osteomalacia developed for the first time in one patient after 14 months

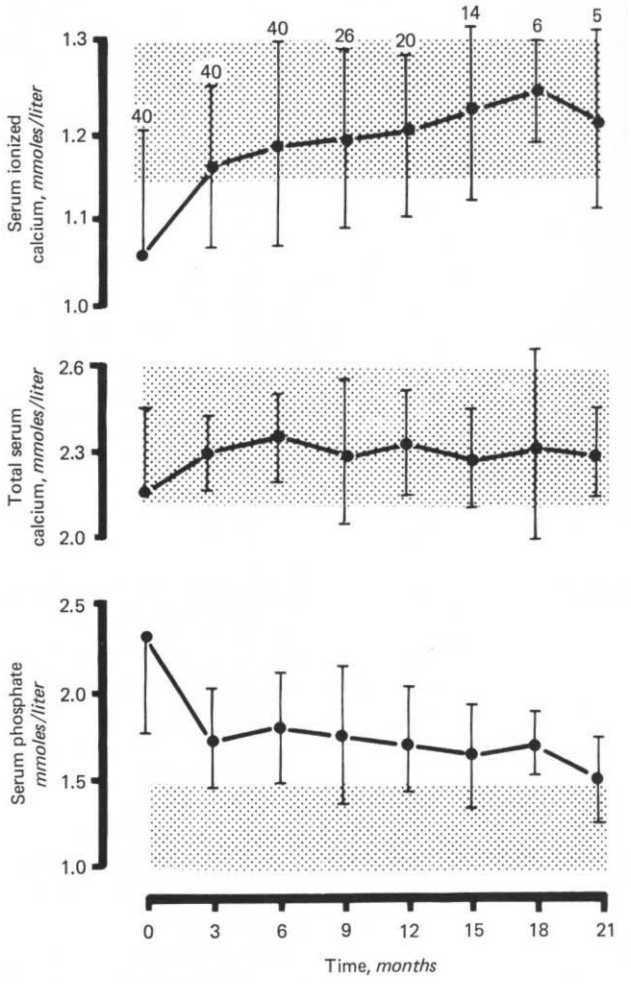

Fig. 1. *Mean (±1 SD) serum ionized and total calcium levels and serum phosphate concentrations in patients on CAPD in excess of 6 months.* The *shaded area* represents the normal range. The number of patients studied at each point in time are indicated above the SD *bars*. Thirty patients were on $CaCo_3$ supplements and 11 on 1 αOHCC. None of these patients were on ACPB.

of CAPD (no. 5). She had had a total parathyroidectomy after 6 months of CAPD (4 glands, total weight 979 mg) and the bone stain for aluminum was positive. She had been exposed previously to aluminum while on hemodialysis; the possibility of aluminum-induced osteomalacia cannot be excluded. *(3) 22 to 24 months of CAPD.* Of the five patients studied, two (nos. 2 and 3) showed some mild deterioration in osteitis fibrosa compared with the previous biopsies at 14 and 12 months, respectively. In three patients (nos. 4, 5, and 6) there was no recurrence of the previously improved osteitis fibrosa. Osteomalacia persisted at 22 months CAPD in patient no. 5, and the bone aluminum stain remained positive.

Use of 1 αOHCC. Of the 20 patients, only five were treated with 1 αOHCC (nos. 5, 6, 14, 19, and 20; Table 2).

Aluminum levels. Sequential serum aluminum levels over 0 to 24 months of CAPD treatment are shown in Figure 3. The mean values at various time periods on CAPD did not differ from the mean level at the start of CAPD (Table 4). However, these were significantly higher than the normal controls (mean ± 2 SD; 7 ±

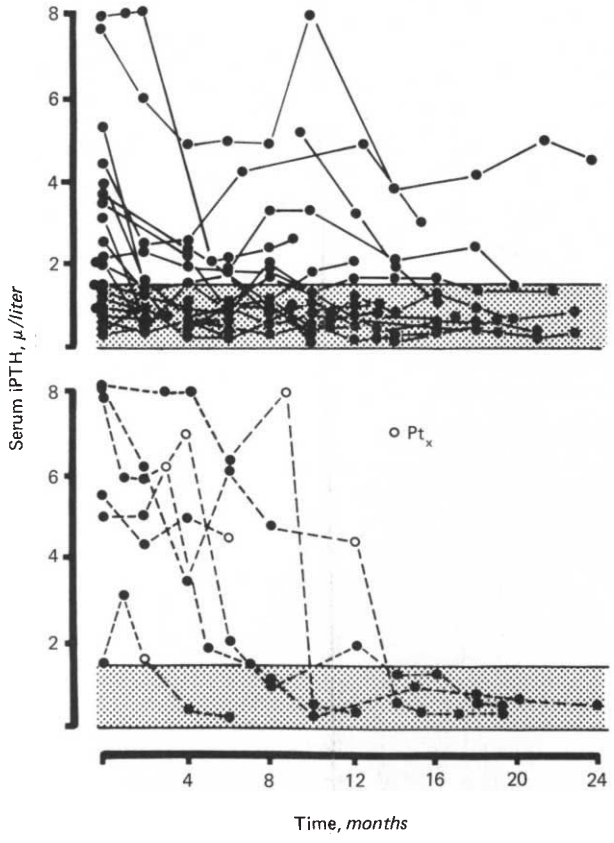

Fig. 2. *Serial PTH levels in CAPD patients, six of whom with severe OF previously on hemodialysis requiring parathyroidectomy* (○ bottom figure) *2 to 12 months after starting CAPD.*

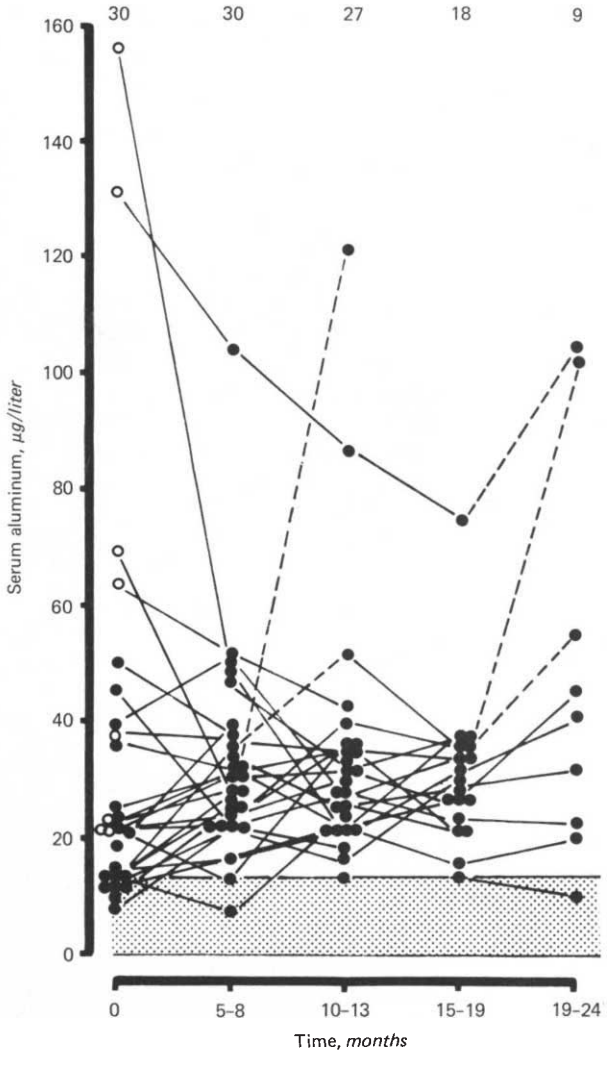

Fig. 3. *Sequential serum aluminum levels over 0 to 24 months on CAPD patients.* Six patients received ACPB after CAPD and their levels are indicated by (-----) after exposure to aluminum. Nine patients (○) had aluminum exposure prior to CAPD. *Solid circles* at time zero relate to patients not previously exposed to aluminum.

6 μg/liter) or the chronic renal failure group not exposed to aluminum (17 ± 16 μg/liter). However, if the values of these nine patients with previous aluminum exposure prior to CAPD are excluded from analysis, there was a steady increase in the mean values in the remaining patients, although this was not statistically significant (Table 4).

In most patients without further aluminum exposure in the form of ACPB, the serum aluminum levels generally steadied at between 30 and 40 μg/liter, having fallen in those with high levels (from previous aluminum exposure) and risen in those with low levels at the start (Fig. 4). Subsequent use of ACPB in six patients resulted in a marked increase in serum aluminum levels. Aluminum levels in the PD fluid were 18.25 ± 8.66 μg/liter and did not vary within or between batches.

Discussion

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

One patient who began CAPD had OM which healed completely at 1 year (patient no. 19, Table 2). Her biopsy specimens were negative when stained for aluminum. Another patient (no. 5) who developed OM after parathyroidectomy was on phenytoin with 25-(OH)CC levels in the low normal range, but the cause for OM in her is more likely to be aluminum exposure on HD prior to starting CAPD. The bone histology substantiates this because the bone stain for aluminum was positive. The etiology of her OM in this case is complex, as is the role of parathyroidectomy in its causation, but it is conceivable that in the absence of parathormone the toxic effects of aluminum may become more manifest.

The improvement in histological OF is in contrast with the radiological deterioration reported by Calderaro et al [2]. It is interesting to speculate why this progression has not been seen in our patients. The use of PD fluid calcium concentration of 1.75 mmoles/liter in our patients may be crucial in promoting a positive calcium balance [12] as the lower PD calcium level of 1.50 mmoles/liter may have led to a negative balance [2]. Also in our series, most patients had low serum ionized calcium levels

Table 4. Mean (± 1 SD) serum aluminum levels in CAPD patients[a]

Time *months*	Total group	Aluminum exposure prior to CAPD	Group without aluminum exposure
0	30.18 ± 29.89 (27)	59.11 ± 49.50 (9)	21.8 ± 12.36 (18)
5 to 8	31.14 ± 20.17 (27)	43.34 ± 28.65 (9)	26.78 ± 9.1 (18)
10 to 13	30.69 ± 14.7 (26)	40.0 ± 20.9 (8)	27.52 ± 10.5 (18)
15 to 19	30.7 ± 13.6 (18)	34.0 ± 19.3 (6)	28.85 ± 7.46 (12)

[a] The numbers in parentheses refer to the number of patients.

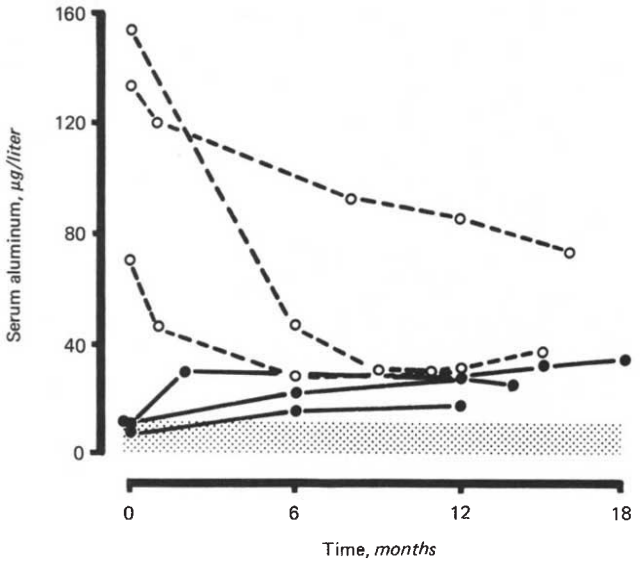

Fig. 4. *Serial serum aluminum levels in six patients, three of whom with elevated levels and three with normal levels at the start of CAPD.* Symbols: O-----O, previous exposure to aluminum; ●——●, no exposure to aluminum.

when they began CAPD and were treated with oral supplements of calcium carbonate which also acts as a mild phosphate binder and may help to counteract the mild acidosis. Phosphate binding agents have not been used unless the serum phosphate is persistently greater than 1.8 mmoles/liter.

Six patients with severe renal osteodystrophy (OF grades, 3 to 4) on HD who were transferred to CAPD showed no symptomatic biochemical or radiological improvement after 2 to 12 months of CAPD (Fig. 3). They underwent parathyroidectomy. In these patients the severe hyperparathyroidism may be due to autonomous or "tertiary" stage as four of the six patients were hypercalcemic without vitamin D or calcium carbonate supplements.

Our results show that with time serum concentrations of 25-(OH)CC decline appreciably and that 60% of the patients on CAPD for longer than 9 months had subnormal levels. The losses of protein-bound 25-(OH)CC in the PD effluent may account for the diminishing levels, a mechanism not too dissimilar from that occurring in the nephrotic syndrome [13]. It may be necessary to replace these losses. However, due to vitamin D resistance, required blood levels may well be higher in renal failure than in healthy subjects [14] and higher still in CAPD patients due to losses in the PD effluent. Calderaro et al administered 50,000 U of vitamin D weekly to their CAPD patients and reported normal levels of 25-(OH)CC.

Serum aluminum levels were higher in chronic renal failure patients not exposed to aluminum compared to normal subjects; however, levels in CAPD patients were elevated above these two groups and rose steadily in those starting with normal serum aluminum levels. This is in contrast to the preliminary findings of Wolf et al [15] who reported normal values in four CAPD patients. They were unable to detect aluminum in their PD fluid. We were able to demonstrate aluminum contamination of the fluid; it is debatable whether or not this is likely to be the source of aluminum in patients not taking ACPB. However, since those patients with initially elevated levels showed a decline in time to values of 30 to 40 μg/liter, a level also attained by those not previously exposed to aluminum and starting with normal serum aluminum levels, it is likely that the aluminum was from the PD fluid. In hemodialysis patients it has been shown that aluminum transfer is dependent on the free diffusible plasma aluminum concentration, which is usually 20% of the total plasma value [16]. If a similar principle could apply to peritoneal dialysis, then aluminum would be transferred to the patient from the PD fluid even when serum levels were higher than those in the PD fluid, the acceptable aluminum concentration in the PD fluid would then be one equal to or lower than the mean value of free diffusible plasma aluminum found in normal controls. Clearly, more work needs to be done on the kinetics of aluminum transfer in peritoneal dialysis before a "safe" value for PD fluid is advocated. However, recently acute aluminum intoxication in CAPD patients has been reported related to high PD fluid aluminum levels. These investigators advocate a "safe" level of about 15 μg/liter; values in excess of these have been associated with rising serum aluminum levels in their patients [17]. Their experience is similar to ours: The serum aluminum rose further in patients exposed to ACPB.

Several crucial questions arise. Firstly, is the steady state serum aluminum level of about 30 μg/liter of any significance over a period of years? At present there is no evidence that this level maintained for a number of years leads to aluminum toxicity. Certainly over the 2 years none of the CAPD patients developed OM of the type previously found in our hemodialysis population. What may be more important to establish is whether or not the aluminum burden increases with time and what aluminum load is reflected by a serum aluminum level of 30 to 40 μg/liter. This currently is difficult since the serum level

reflects only recent aluminum exposure; thus, even at these levels there is a small, long-term potential risk of aluminum toxicity especially if ACPB, which led in this study to a rise in aluminum levels, are necessary to control serum phosphate levels. It would then be important to obtain dialysis fluid with as low an aluminum content as is possible and look for a nonaluminum containing phosphate binding agent.

Desferrioxamine is normally a good iron chelator and has been used for this purpose in several conditions of iron loading including hemodialysis [18]. It is also able to chelate aluminum in tissues [11]. On CAPD the aluminum losses are small. Nonetheless, patients showing toxic effects attributable to aluminum may benefit from treatment by CAPD, which does reduce high serum aluminum levels, and, in addition, leads to easier control of serum phosphate.

To minimize the aluminum problem and to manage the low levels of 25-(OH)CC, our current practice is to administer calcium carbonate supplements to normalize serum ionized calcium concentrations. 1 αOHCC is prescribed if either 25-(OH)CC levels are low and/or if there is histological or clinical evidence of OF or OM. The serum phosphate concentration is maintained below 1.8 mmoles/liter (normal range, 0.8 to 1.5) by calcium carbonate and dietary phosphate restriction. If this is unsuccessful, then phosphate binding agents are introduced and serum aluminum concentrations are monitored.

There is the risk that, with time, the persistently positive calcium balance achieved by using 1.75 mmoles/liter calcium concentration in the PD fluid [12], may lead to metastatic calcification, especially if this is combined with 1 αOHCC, calcium supplements, and possible high serum phosphate levels. The dorsalis pedis calcification in the long-term CAPD patients in this study may be a reflection of this and demands careful monitoring of serum ionized calcium and phosphate concentrations. There is a need for constant review of the PD fluid calcium concentration as a lower concentration may be necessary in long-term patients once calcium depletion is corrected.

In conclusion, CAPD appears to achieve good control of renal osteodystrophy. However, 25-(OH)CC levels are low and patients may need cautious amounts of vitamin D replacement therapy. Serum aluminum levels are elevated in those patients not exposed to ACPB and this may be related to the PD fluid aluminum content. The levels rise further when ACPB are introduced, though this has not, to date, resulted in toxicity. Nonetheless, it would seem advisable to minimize aluminum contamination of PD fluid.

Summary. Eleven of the 20 paired bone biopsy specimens showed significant improvement is osteitis fibrosa (OF) 4 to 14 months after CAPD (five on 1 αOHCC), and in five patients at 2 years there was no significant deterioration. Six patients without OF at the beginning remained unchanged at 12 months while one patient developed osteomalacia (OM) after parathyroidectomy. These patients, managed on calcium carbonate supplements and in most cases no aluminum-containing phosphate binders (ACPB), maintained normal serum ionized and total calcium levels while mean serum phosphate levels ranged between 1.5 and 1.8 mmoles/liter on a dialysate calcium of 1.75 mmoles/liter. There was a decline in the parathormone level in all but ten patients, six of whom with previous severe OF on hemodialysis required parathyroidectomy. 25-(OH)CC levels declined to subnormal levels related to losses in the PD fluid in the majority of patients. Mean serum aluminum levels were higher than normal health controls; these may have been related to aluminum in the PD fluid. Levels rose further when ACPB was introduced. One patient with aluminum toxicity from prior exposure was treated with desferrioxamine given parenterally with the removal of the chelated aluminum in the PD fluid. CAPD appeared to achieve good control of renal osteodystrophy, but 25-(OH)CC levels were low and cautious amounts of vitamin D replacement therapy may be necessary. Serum aluminum levels were elevated and these may be related to the PD fluid aluminum content.

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