THE CONTROL OF METABOLIC BONE DISEASE BY MAINTENANCE HAEMODIALYSIS


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Introduction

Maintenance haemodialysis was started at Fulham Hospital in March 1964. A dialysis fluid calcium concentration of 5 mg% was employed from March 1964 until May 1966. During this period, our first three patients developed slight radiological evidence of bone disease with subperiosteal erosions of the phalanges and one of these patients showed a progressive rise in the plasma alkaline phosphatase level reaching a maximum of 18 King-Armstrong units %. In addition, towards the end of this period, Pendras and Erickson (1966) reported that the incidence of bone disease was greatest in those patients who had been dialysed the longest. Experiments were therefore carried out in 1966 to determine the most suitable dialysis fluid calcium concentration for patients on intermittent dialysis. As a result of these experiments, a dialysis fluid calcium concentration of 6.0 ± 0.2 mg% has been employed since May 1966. Using this dialysis fluid calcium concentration and with twice weekly dialysis for 14 hours at a time with the Kill dialyser (Cuprophan PT 150), two of our first three patients mentioned above have shown complete healing of the radiological bone changes and the third patient has shown improvement; in addition, the raised plasma alkaline phosphatase level in this patient has returned to normal.

Total plasma calcium was estimated using Trinder's (1960) colorimetric microdetermination technique. The standardisation of this method was checked frequently with parallel determinations by flame photometry. Plasma phosphate was determined by a Technicon Auto-Analyzer method. Plasma alkaline phosphatase was determined by the method of Kind and King (1954). Plasma ultrafiltrable calcium was determined by a modification of the method of Toribara et al. (1957). Dialysis fluid calcium concentrations were determined by flame photometry (Eppendorf).

THE OPTIMUM DIALYSIS FLUID CALCIUM CONCENTRATION

To establish the most suitable dialysis fluid calcium concentration, an individual single pass system was used to study calcium balance during the dialysis of one patient. The dialysis fluid was prepared as an individual batch and after a single passage through the dialyser was collected in a large receiving tank. A dialysis flow rate of 500 ml/min. was employed with dialysis fluid at 37°C and dialysis during the experiments was continued for 12 hours. An aliquot of the dialysis fluid was taken for estimation of the initial calcium concentration in the dialysis fluid. When the dialysis was completed, the dialysate in the receiving tank was mixed and an aliquot taken for estimation of the final dialysis fluid calcium concentration. Pre- and post-dialysis arterial blood samples were taken for plasma calcium estimation. A total of 13 experiments were carried out, with initial dialysis fluid calcium concentrations varying from 2.95 mg% to 8.05 mg%. The results of these experiments are shown in Figure 1. In this figure, the calcium transfer in mg per 12 hour dialysis is plotted against the initial
concentration of calcium in the dialysis fluid. When the initial dialysis fluid calcium concentration is less than about 5.5 mg%, calcium is usually removed from the patient during dialysis. Using an initial dialysis fluid calcium concentration of approximately 6.0 mg%, there is no transfer of calcium or a small positive transfer of calcium into the patient during dialysis. With initial dialysis fluid calcium concentrations of > 6.0 mg%, a positive transfer of calcium into the patient occurs.

**PLASMA CALCIUM LEVELS**

The level of plasma calcium is also important in determining whether calcium is lost or gained by the patient during dialysis. In Figure 2 are shown the mean plasma calcium and phosphate levels for all the patients before starting dialysis and during the first 2 years of dialysis treatment. The plasma calcium measured in 30 patients before starting intermittent dialysis had a mean value of 8.3 mg% (range 6.1–10.4 mg%). After a period of two months’ intermittent dialysis, the mean value in 29 patients was 9.65 mg% (range 9.2–12.2 mg%). After six months’ intermittent dialysis, the mean plasma calcium concentration in 28 patients was 9.9 mg%. At one year, the mean plasma calcium for 16 patients was 9.5 mg%; and at 18 months, the mean plasma calcium in 10 patients was 9.3 mg%. Thus, during the first year of intermittent dialysis there is a tendency for plasma calcium levels to rise. Some patients develop hypercalcaemia when the risk of losing calcium during dialysis is greatest.

Of more importance with regard to calcium transfer during dialysis, however, are the ionised and ultrafiltrable calcium levels in the plasma. In Figure 3 the total plasma calcium levels in these patients are plotted against the ultrafiltrable calcium levels. These estimations were carried out on a pre-dialysis arterial blood sample. The results of 25 normal control subjects fall within the area delimited by the irregular polygon. It can be seen that several of the patients had higher levels of both total and ultrafiltrable calcium in the plasma than the normal subjects. However, using a dialysis fluid calcium concentration of 6 ± 0.2 mg%, it can be seen that for the majority of the patients there should be little or no removal of calcium during dialysis. The 4 exceptions were all patients who had been dialysed for less than one year.
Fig. 2. Mean (± I.S.D.) values of plasma calcium and phosphate in all patients. All estimations carried out on samples taken at the end of the longer of the two interdialysis periods.

PLASMA PHOSPHATE LEVELS

The mean plasma phosphate in 25 patients before starting intermittent dialysis was 9.26 mg% (range 3.2–19.0 mg%). The plasma phosphate levels fell rapidly at first and after two months’ intermittent dialysis the mean value was 5.68 mg%. Following this, there was a

Fig. 3. Relation between total plasma calcium and ultrafiltrable calcium in dialysis patients. Total Ca: total plasma calcium; U/F[Ca]: ultrafiltrable calcium. The results of 25 estimations in control normal subjects fell within the area of the irregular polygon.
continued gradual fall in plasma phosphate so that after 2 years' intermittent dialysis, the mean plasma phosphate was 4.13 mg%. 

Two patients were given aluminium hydroxide gel during the first few months of intermittent dialysis and five other patients were given aluminium hydroxide gel during the first few weeks of intermittent dialysis in order to keep the calcium-phosphorus product below 75 and in this way to prevent the development of metastatic calcification. A few patients developed low plasma phosphate levels after two years' intermittent dialysis. We consider that this might be an important factor in the development of bone disease if the calcium × phosphorus product were allowed to fall below 25. These patients have therefore been given calcium phosphate.

CLINICAL ASPECTS

Before starting maintenance haemodialysis

Five patients had radiological evidence of bone disease before starting intermittent dialysis. All five patients had subperiosteal erosions of the phalanges and three also had osteosclerosis of the lumbar spine. Four of the five patients also had a raised plasma alkaline phosphatase concentration. Only one of the five patients had symptomatic bone disease, and this patient had pseudoclubbing due to resorption of the tips of the terminal phalanges and marked vascular calcification.

Slit lamp microscopy of the anterior eye revealed limbal calcification in 14 of 29 patients prior to starting intermittent dialysis and conjunctival calcification in 8 of 29 patients prior to starting intermittent dialysis.

During maintenance haemodialysis

In our experience, metastatic calcification has never developed or got worse after starting

![Terminal phalanx of right middle finger of patient with most severe bone disease. Dates of X-rays (from left to right) were 21.1.66, 28.11.66, 7.2.67, 10.11.67. The second X-ray was taken at the time of starting dialysis. Pseudoclubbing of the fingers was noted at this time. After two months' dialysis, the finger tips were tender and the metastatic calcification had disappeared. After dialysis for one year there was a return towards normal in the mineralisation and architecture of the terminal phalanx.](image-url)
intermittent dialysis. Our follow-up of these patients has included 4-monthly slit lamp microscopy of the anterior eye, 6-monthly skeletal surveys and monthly checks of plasma calcium, phosphate and alkaline phosphatase. In addition, acute calcium gout has not occurred in any patient.

With the exception of our first 3 patients who were all dialysed for at least one year against a dialysis fluid calcium concentration of 5 mg%, radiological bone disease has not developed after starting intermittent dialysis. No patient has developed symptoms of bone disease, e.g. bone pain or painful feet while on intermittent dialysis.

On the contrary, all 5 patients with radiological evidence of bone disease before starting intermittent dialysis have shown improvement and in 2, the subperiosteal erosions have healed completely. Four of the 5 patients have been treated by dialysis alone. The remaining patient, the most severe case, with symptomatic and radiological bone disease before starting intermittent dialysis was given vitamin D for 2 months together with calcium carbonate and calcium phosphate supplements. Figure 4 shows the same terminal phalanx in this patient at various times before and during intermittent dialysis treatment and clearly demonstrates the removal of metastatic calcification and later reformation of the tip of the phalanx.

The cortical thickness of long bones has also been assessed measuring the right 2nd metacarpal by the method of Morgan et al. (1967). There has been no decrease in cortical thickness in any patient and in particular, no evidence of progressive demineralisation in those patients dialysed for more than two years. In addition, in two patients with radiological bone disease, the cortical thickness has increased.

REFERENCES