Risk/benefit in prophylaxis and treatment of secondary hyperparathyroidism. A comparison of two low calcium peritoneal dialysis fluids

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Abstract
Objective. A comparison of (i) levels of plasma ionized calcium (Ca), phosphate (P) and iPTH, (ii) risk of hypercalcaemia and (iii) need for Al-containing P binders, in patients on CAPD treated with calcium carbonate as the main P binder and twice weekly oral doses of alfacalcidol for control of secondary hyperparathyroidism during a 1 year follow-up after switching from a dialysis fluid with a Ca concentration of 1.75 mmol/l to 1.25 mmol/l (n = 39) or 1.35 mmol/l (n = 37).

Results. In both groups, a significant initial increase of iPTH was seen. However, iPTH was again suppressed to baseline levels after 2–6 weeks of treatment. No statistically significant difference was observed between the two groups. In both groups median PTH levels were kept below 2.5 times the upper normal limit for non-uraemic patients; median P concentrations below 1.80 mmol/l and median iCa levels within 1.25–1.30 mmol/l. The incidence of hypercalcaemia was low and did not differ between the two groups (1.04 vs 1.20 cases of plasma iCa>1.45 mmol/l per 100 treatment weeks). The proportion of patients requiring treatment with Al-containing P binders was unchanged from the start to the end of the study period, but significantly greater in the group dialysed with a Ca concentration of 1.25 mmol/l (an average of 21% as compared to 10% in the other group).

Conclusion. When changing from high Ca dialysate (1.75 mmol/l) to dialysate with a Ca concentration of 1.25 or 1.35 mmol/l, close attention to PTH control has to be paid during the initial months of treatment. Adequate control of plasma levels of iCa, P and PTH could be achieved with both lower Ca dialysates without either hypercalcemia or use of Al-containing P binders in the majority of patients. The small number of patients treated with Al-containing P binders, however, would probably benefit from dialysate fluids with even lower Ca concentrations.

Key words: dialysate calcium; plasma calcium; plasma phosphate; plasma iPTH; aluminium

Introduction
There is a current tendency to lower the calcium concentration of the dialysis fluid in order to increase tolerance to therapy with calcium containing phosphate binders and vitamin D metabolites. When this approach is chosen, it is essential to ensure the adequacy of calcium and vitamin D supplementation and the compliance of the patient to treatment. Presently, the ideal dialysate calcium concentration for the majority of patients on CAPD is not known. The objective of the present study was to compare the effect on plasma iPTH during a 1 year follow-up after switching from a dialysis fluid with a calcium concentration of 1.75 mmol/l to 1.25 mmol/l or 1.35 mmol/l in unselected patients on CAPD. Further, another purpose was to compare the incidence of intercurrent hypercalcaemia and the proportion of patients requiring treatment with aluminium containing phosphate binders in the two low calcium dialysate groups.

Methods

Treatment schedule
Prior to entry into the study all patients were using dialysis fluids with a calcium concentration of 1.75 mmol/l. Without randomization patients were switched to low calcium dialysate with a calcium concentration of 1.25 mmol/l (dCa 1.25) or 1.35 mmol/l (dCa 1.35).

CaCO₃ was administered routinely to all patients to maintain plasma phosphate less than 1.70 mmol/l. When phosphate was <1.70 mmol/l and ionized calcium <1.30 mmol/l, 1α(OH)vitamin D₃ (LEO Pharmaceuticals, Denmark) was administered orally two times weekly. Aluminium amino-
acetate was only used temporarily in cases of combined hypercalcaemia and hyperphosphatemia.

Statistics

The Wilcoxon's matched pairs test was used for comparisons within groups and the Mann–Whitney U-test for comparisons between groups.

Results

Subjects

Two subjects in the dCa 1.25 and eight subjects in the dCa 1.35 study were withdrawn before 3 months of study and excluded. Ten subjects in the dCa 1.25 and 11 in the dCa 1.35 study were followed for more than 3 months, but withdrawn before 12 months of study. Reasons for withdrawals were change to haemodialysis/IPD, kidney transplantation or severe intercurrent illness. Thus, 39 patients in the dCa 1.25 and 37 patients in the dCa 1.35 study were included and followed for an average of 10 months (range 3–12 months).

Plasma ionized calcium

Apart from a small initial decrease of ionized calcium in both studies (P<0.01 in the dCa 1.25 study; P<0.05 in the dCa 1.35 study) after change to low calcium dialysate, plasma ionized calcium remained stable during 1 year of treatment. Median ionized calcium concentrations at start and end of both studies were within 1.25–1.30 mmol/l.

Incidence of hypercalcaemia

The incidence of severe hypercalcaemia was low and did not differ between the two groups (Table 1).

Plasma phosphate

Median plasma phosphate was maintained less than 1.80 mmol/l in both studies with CaCO₃ as the main phosphate binder.

Treatment with aluminium containing phosphate binders

The proportion of patients requiring treatment with aluminium aminoacetate was significantly greater in the dCa 1.25 study (an average of 21%), compared with the dCa 1.35 study (an average of 10%). The proportion of patients receiving this treatment remained unchanged from start to end of the study period.

Plasma iPTH

In both studies, a significant initial increase of iPTH was seen (P=0.002 in the dCa 1.25 study; P=0.01 in the dCa 1.35 study) (Figure 1). PTH was again suppressed to initial values after 2–6 weeks of treatment. No significant difference was observed between the two studies. The initial increase of iPTH observed in both studies seemed to be related to the initial decrease of ionized calcium. In both studies median PTH was maintained within the recommended intervals for uraemic patients, which according to Quarles et al. [1] probably are 1.5–2.5 times the upper normal limit for non-uraemic patients.
Conclusion

When changing from high calcium (1.75 mmol/l) dialysate to dialysate with a calcium concentration of 1.25 or 1.35 mmol/l in unselected CAPD patients, close attention to PTH control has to be paid during the first months of treatment. PTH did not differ significantly between the two study groups. Adequate control of PTH and phosphate could be achieved with both low calcium dialysis fluids in unselected patients treated with CaCO\(_3\) as the main phosphate binder and 1-α(OH) vitamin D\(^3\) for control of secondary hyperparathyroidism without either hypercalcaemia or use of aluminium-containing salts in the majority of patients. The small number of patients treated with aluminium containing phosphate binders for longer periods, however, would probably benefit from dialysis fluids with even lower calcium concentrations.

References