

THE INFLUENCE OF ALUMINIUM ON PARATHYROID HORMONE LEVELS IN HAEMODIALYSIS PATIENTS

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Summary

In order to investigate the relationship between parathyroid hormone (PTH) and aluminium we studied 86 haemodialysis patients whom we separated into three groups according to their serum PTH values. Group I: PTH < 600 ng/L; Group II: PTH 600–900 ng/L; Group III: PTH > 900 ng/L. A significant difference was found between Groups I and III in the serum aluminium (Group I: 4.85 μ mol/L; Group III: 2.84 μ mol/L, $p < 0.003$) and serum calcium (Group I: 2.43 mmol/L; Group III: 2.32 mmol/L, $p < 0.0125$). The association of higher serum aluminium and calcium with lower PTH concentrations suggests that aluminium can suppress PTH release through an elevation of the serum calcium.

Introduction

Convincing evidence exists that aluminium can cause dialysis encephalopathy and also the osteomalacia seen in some dialysis patients but the factors influencing and regulating aluminium metabolism are less clear.

Recent reports [1,2] suggest that in animals exogenous PTH can increase aluminium absorption from the gut and consequently aluminium deposition in bone and brain. On the other hand, in the human [3] aluminium seems to modify endogenous PTH release by a direct or indirect mechanism. On clinical and pathological grounds there is increasing evidence that long-term aluminium exposure can lead to osteomalacia associated with normal or low PTH values. In addition, some of these patients develop hypercalcaemia even in the absence of calcium supplements or Vitamin D therapy. The aim of this study was to further investigate the relationship between aluminium, calcium and PTH in a group of patients on long-term haemodialysis.

Patients and methods

We studied 86 patients who had been treated by haemodialysis for longer than six months (range 6–110 months, mean 39.1 months) (Table I). The dialysis

TABLE I. Details of the patients subdivided into three groups based on the serum PTH levels

	Group I	Group II	Group III
Serum PTH (ng/L) (Mean \pm SEM)	600 (324 \pm 26.3)	600–900 (764 \pm 28.3)	900 (2765 \pm 209)
Number of patients	29	10	47
Age (years) (range)	42 (19–60)	43 (32–55)	38 (17–62)
Mean number of months on haemodialysis (range)	38 (6–110)	41.1 (10–105)	38.1 (6–89)

schedule ranged from 12 to 18 hours per week. Reverse osmosis water treatment was used in the presence of high tap water aluminium. The dialysate calcium was between 1.25 and 1.55 mmol/L being constant for each patient. We measured serum calcium and phosphorus monthly by the SMAC auto-analyser and we excluded those patients who showed transient hypercalcaemia related to Vitamin D therapy during the period of the study. Serum samples for calcium and PTH measurement were taken together, the method used for the latter being a double antibody radioimmunoassay in which the normal range is between the limit of detection (150–600 ng/L). Serum and water aluminium were measured by electrothermal atomic absorption spectrometry [4].

Aluminium hydroxide (Al(OH)₃) was used as a phosphorus binder and calcium supplements were not administered. Other drugs which could influence aluminium, calcium or PTH metabolism are listed in Table II.

The patients were separated into three groups according to their serum PTH concentrations:

Group I	Serum PTH below 600 ng/L (29 patients, normal PTH group)
Group II	Serum PTH 600–900 ng/L (10 patients, borderline PTH group)
Group III	Serum PTH above 900 ng/L (47 patients, high PTH group)

Statistical analyses were performed by Student's *t* test.

TABLE II. Details of drug therapy which would influence aluminium, calcium and PTH metabolism

Group	Serum PTH (ng/L)	Al(OH) ₃ intake (grams)		Patients on 1 α /1.25 Vitamin D3	Patients on beta blockers	Patients on Cimetidine
		One month dose	Total dose since start of haemodialysis			
I	<600	118	3564	18 of 29 (62%)	9 of 29 (31%)	4 of 29 (14%)
II	600-900	112	3644	4 of 10 (40%)	2 of 10 (20%)	1 of 10 (10%)
III	>900	101	3403	30 of 47 (63%)	13 of 47 (28%)	4 of 47 (9%)

Results

No significant differences were detected among groups I, II and III regarding age and time on haemodialysis (Table I). A statistically significant difference was found between groups I and III in the serum aluminium ($p < 0.003$) and serum calcium ($p < 0.0125$) concentrations (Table III). These differences could not be explained by the effect of drugs which are known to influence calcium, aluminium or PTH metabolism (Table II).

TABLE III. Serum phosphorus, calcium and aluminium in the groups of patients with low, intermediate and high serum PTH levels

Group	Serum PTH (ng/L)	Serum phosphorus (mmol/L) (\pm SEM)	Serum calcium (mmol/L) (\pm SEM)	Serum aluminium (μ mol/L) (\pm SEM)
I	<600	1.66 \pm 0.11	2.43 \pm 0.04*	4.85 \pm 0.68**
II	600-900	1.79 \pm 0.18	2.40 \pm 0.04*	3.48 \pm 0.55**
III	>900	1.64 \pm 0.08	2.32 \pm 0.03*	2.84 \pm 0.22**

* $p < 0.0125$

** $p < 0.003$

Discussion

Knowledge of PTH and aluminium metabolism has increased in recent years. In experimental animals, PTH is thought to play a role in the absorption of aluminium from the gastrointestinal tract and its deposition in brain and bone

[1,2]. There are some reports from studies in man which support this idea and suggest that parathyroidectomy may lower the serum aluminium. It has also been claimed that as a consequence dialysis dementia might benefit from this operation [5]. On the other hand there is a widespread clinical impression that patients with aluminium toxicity have a tendency to hypercalcaemia and suppression of the parathyroid glands. These two facts can be linked by the following explanation: PTH will enhance aluminium absorption and thus its deposition in bone leading to slowly progressive osteomalacia [6–8]. As aluminium deposition in bone increases there is a corresponding decrease in the normal bone mineralisation process and thus a decrease in the incorporation of calcium in bone [9]. Consequently the serum calcium will rise leading to parathyroid suppression with a fall in the serum PTH. The low bone turnover and the blocking of the mineralisation front by aluminium predisposes the patient to hypercalcaemia which may be precipitated by calcium supplements or Vitamin D metabolites [10]. As an alternative to this indirect pathway, the high serum aluminium could also have a direct toxic effect on parathyroid tissue thus preventing or suppressing PTH release [11].

In this study significantly higher serum aluminium and calcium values were present in the group of patients with lower serum PTH compared with those with higher PTH concentrations. This finding suggests that aluminium can suppress PTH release through an elevation of the serum calcium. However, a direct action of aluminium on the parathyroid glands cannot be excluded. Further studies are required to explain fully the relationship between serum aluminium and parathyroid hormone.

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