Aluminium absorption in chronic renal failure

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RESUMEN

Absorción de aluminio en la insuficiencia renal crónica.
Se utilizaron dos tipos de «tests» de larga y corta duración para valorar la absorción de hidróxido de aluminio en pacientes en diálisis. Si bien el primero fue parcialmente útil para identificar a un grupo de pacientes con osteomalacia inducida por aluminio que parecían «hiperabsorber» este elemento, el segundo dio resultados contradictorios y no demostró variaciones en la absorción de aluminio.

SUMMARY

Aluminium absorption in chronic renal failure.
Short and long-term tests were designed to evaluate aluminium gastrointestinal absorption. Although the former seemed to be able to identify patients with aluminium-related osteomalacia who hyperabsorbed aluminium the latter gave contradictory results and failed to prove any increase in aluminium absorption.

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Introduction

Effective treatment of tap water used for dialysis by de-ionisation or reverse osmosis should prevent accumulation of aluminium (Al) from this route in patients with chronic renal failure provided the dialysate Al levels are regularly monitored. Some patients who have never been dialysed have developed signs and symptoms identical to the dialysis encephalopathy syndrome [1] while others may develop only Al bone disease. These complications are considered to be as a result of absorption of Al from phosphate binding agents. Many patients with chronic renal failure regularly take aluminium hydroxide [$Al(OH)_3$] without developing overt signs of Al toxicity suggesting that some may absorb Al more actively than others. Balance studies in general are notoriously difficult to perform and this is particularly the case in dialysis patients. However in one study of 8 uraemic pre-dialysis patients absorption of Al was greatest in the 2 whose iliac bone Al content increased after oral Al therapy [2].

Unfortunately there is no suitable radio-isotope that can be used to measure Al absorption. Thus studies have been restricted to observation of changes in serum Al using atomic absorption spectrophotometry. In a previous pilot study we have shown that Al absorption may be increased in patients with histologically-proven Al-related osteomalacia [3]. In the present study we describe our experience using two indirect tests of Al absorption in patients being treated with haemodialysis and CAPD. "Long" aluminium absorption study.

Patients and methods

Eleven patients (5 male and 6 female, age range 26 to 64 years) who had been treated with CAPD and $Al(OH)_3$ for a minimum of 2 years were studied using the Al absorption protocol which we have described previously [3]. This involved stopping oral Al therapy for 2 weeks followed by 2 $Al(OH)_3$ capsules 3 times daily [2.8 g $Al(OH)_3$) for 2 weeks. Serum Al, calcium, phosphate, alkaline phosphatase, PTH and ferritin levels were measured at the beginning of the study and at the end of the first and second weeks of therapy. Serum Al levels were measured by electrothermal atomic absorption spectrophotometry and PTH levels by a double antibody radio-immunoassay using an antiserum able to recognise both ends of the PTH molecule.

Patients were allocated to two groups on the basis of serum Al levels during the 2 years of Al therapy. Those with results which did not exceed 1.5 µmol/l were regarded as "stable" while those whose levels intermittently rose above 2 µmol/l were grouped as "labile" (range of highest recorded serum Al 2.7 to 6.4 µmol/l). CAPD fluid levels of Al were always less than 0.1 µmol/l.

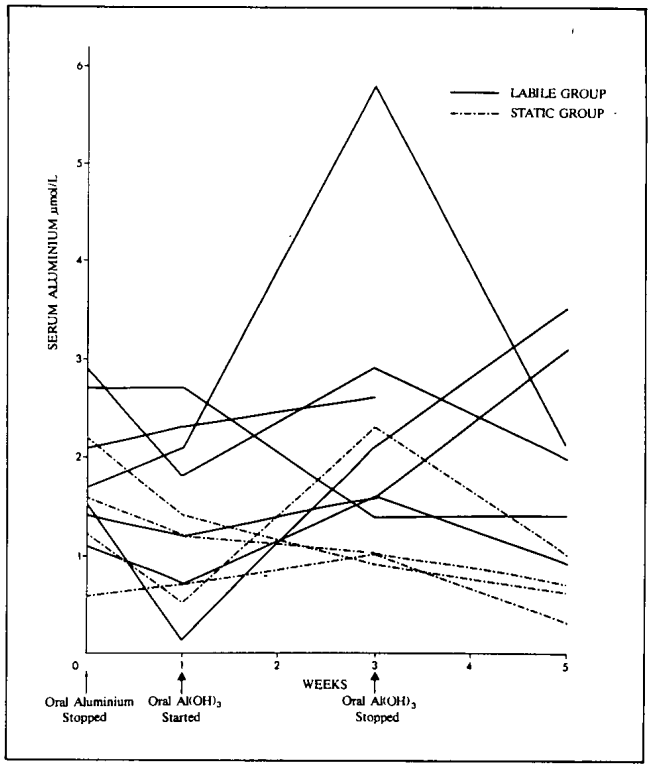

Fig. 1.—Serum aluminium levels during "long" absorption test in 11 patients on CAPD.

Results

The changes in serum Al levels before and after Al(OH) therapy are shown in figure 1. Serum Al levels rose in 5 of the patients in the "labile" group and in 3 of the 5 patients in the "stable" group. No correlation was found between the change in serum Al and parathyroid hormone, ferritin, calcium and alkaline phosphatase levels or with the change in calcium levels during the study (table I).

"Short" aluminium absorption study.

Patients and methods

To avoid possible problems with non-compliance and to attempt to make the test more practicable a "short" Al absorption study was carried out. This involved giving fasting patients 6 grams of $Al(OH)_3$ made into a palatable form as a cream based jelly low in calcium and phosphate. Blood samples were taken hourly for 6 hours. Six patients from our pilot study [3] were re-examined. Changes in serum Al are shown in figure 2. Although one patient had a sharp rise at one

Table I. Serum PTH, Ferritin, calcium, Alk. Phosphatase before oral $Al(OH)_3$ and changes in serum aluminium and calcium levels during therapy

Patient No.	Δ Al µmol/l	PTH ng/l	Ferritin ng/l	Calcium mmol/l	Δ Calcium mmol/l	Alk. Phos. IU
1 (L)	3.7	> 5000	420	2.47	.06	164
2 (L)	1.1	710	3100	2.43	−.04	85
3 (S)	1.8	450	53	2.61	−.34	140
4 (L)	0.9	1200	980	2.83	−.09	66
5 (S)	0.3	4600	153	2.6	−.06	180
6 (L)	0.4	340	16	2.68	.01	101
7 (L)	1.0	1100	2000	2.45	.01	107
8 (L)	0.3	< 250	400	2.63	−.01	134
9 (L)	1.3	970	1044	2.29	.04	56
10 (S)	−.2	1100	193	2.13	.04	48
11 (S)	−.5	< 250	35	2.42	−.11	125

(L): Labile patients.
(S): Static patients.

Table II. Changes in aluminium absorption and PTH levels before and after parathyroid surgery

Patient No.	Pre Δ Al µmol/l	Post Δ Al µmol/l	Pre PTH ng/l	Post PTH ng/l
1	0.1	0.4	650	650
2	0.0	0.4	1700	1500
3	0.0	0.0	> 5000	340
4	0.2	2.6	> 5000	620
5	0.8	1.5	1200	< 250
6	0.8	0.0	1300	< 250
7	0.8	1.5	2300	500
8	0.0	0.2	3900	< 250
9	1.4	0.9	200	< 100
10	1.1	0.7	890	< 100

hour the highest levels in the rest were at 5 and 6 hours. No correlation was found between the changes in Al in the two studies.

This absorption test was also carried out on 10 renal patients one day before and three days after parathyroid surgery to assess the influence of circulating parathyroid hormone. Patients received 2 µg of 1 alpha-hydroxy vitamin D_3 for 4 days pre-operatively increasing to 4-6 µg in the immediate period after the operation to prevent post operative hypocalcaemia. The changes in serum Al levels before and after parathyroid surgery and the corresponding parathyroid hormone levels are shown in table II. The 2 patients whose parathyroid hormone levels did not fall had had unsuccessful attempts to remove auto-transplanted parathyroid tissue.

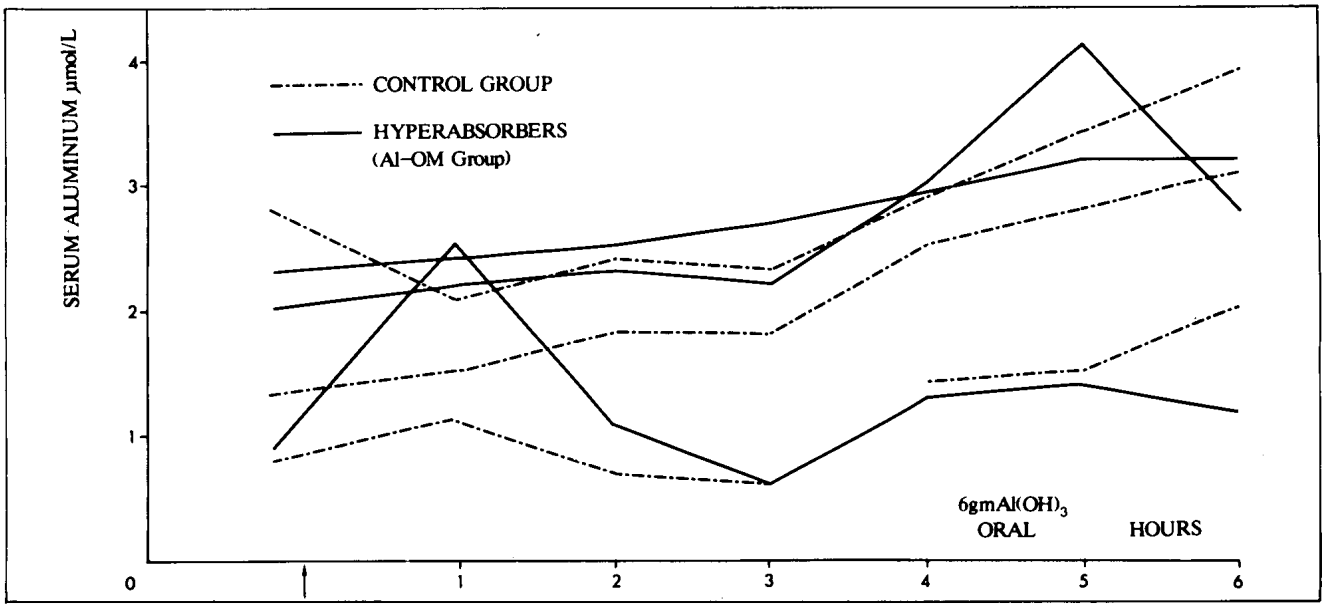

Fig. 2.—Serum aluminium levels during "short" absorption test in patients previously studied using "long" absorption test.

Discussion

There is abundant evidence that Al containing phosphate binders may cause osteomalacia in some patients with chronic renal failure who have never been dialysed. There is also growing awareness that these phosphate binders may cause osteomalacia in some dialysis patients who have not been exposed to high dialysate Al levels. Clinical and laboratory findings suggest that these patients hyperabsorb Al and that they have a higher than normal risk of developing Al toxicity. Although our pilot study suggested that such patients might be identified by a long term Al absorption test the results of the present studies are not so encouraging.

Our attempt to make the test more practicable by giving a single 6 g dose of $Al(OH)_3$ failed to identify patients with Al-related OM who were considered to be hyperabsorbers. This may be due to the rapid dispersal of absorbed Al into tissues which in the long term study may have become partly saturated leading to a gradual rise in serum Al during the study. Another possibility, and this is a general criticism of this type of study, is that the blood samples may have become contaminated with Al despite adequate precautions being taken. The effect of such contamination on the results obtained will be much greater when serum Al levels are low, as in the present study, than when they are high.

We also attempted to overcome the potential influence of variations in dialysate Al concentrations on serum levels of Al during the "long" absorption test by studying CAPD patients. Unfortunately we did not have bone biopsy proof of Al toxicity and our attempt to identify hyperabsorbers on the basis of high serum Al levels measured over a 2 year period coupled with the results of the absorption test has been unsuccessful. This may, of course, simply highlight the unreliability of serum Al levels as indicators of Al absorption or toxicity. Bone biopsies will now be taken from these patients to establish whether this long term study is likely to have any clinical application.

The "long" absorption study has the obvious disadvantages that it takes 4 weeks to perform and that it requires patient compliance with regular consumption of $Al(OH)_3$. These factors are likely to limit the practical use of this test even if it can be used to identify hyperabsorbers. The "short" absorption test has the advantages that compliance can be assured, it only takes a few hours to complete and it can be repeated if necessary with little difficulty.

Patients at risk of developing Al-related osteomalacia can only be identified by bone biopsy once the complication has occurred. Desferrioxamine infusion may also be able to identify patients but again only once the Al has been deposited. As removal of Al from bone is a slow process which if desferrioxamine is used is also expensive and potentially hazardous it would be more sensible to attempt to identify hyperabsorbers of Al before osteomalacia occurs. The results of both these tests are equivocal to date and clearly further studies are necessary to correlate the results with the histological appearances of bone.

References

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