

## ALUMINIUM CONTAINING ORAL PHOSPHORUS BINDERS AND THE ALUMINIUM CONTENT OF BONE

H Raidt, M Vishedyck, H Kellinghaus, D Steinhausen, U Graefe  
*University of Münster, Münster, FRG*

### Summary

The impact of oral  $\text{Al}(\text{OH})_3$  on the aluminium content of bone was investigated in 54 patients on chronic haemodialysis. No correlation but a higher mean bone aluminium was found in 19 patients using water softeners for dialysate preparation. Thirty-five patients with additional reverse osmosis demonstrated a close correlation between bone aluminium and ingested aluminium. We conclude that orally administered  $\text{Al}(\text{OH})_3$  is an important source of aluminium overload in dialysis patients.

### Introduction

It has been documented that aluminium contamination of water used for the preparation of dialysate might lead to accumulation of this trace element in the brain of dialysis patients causing dialysis encephalopathy. It has become clear that other organs such as bone and the haemopoietic system might also suffer from aluminium intoxication. The risk of aluminium overload in these patients would be significantly lower if reverse osmosis water pretreatment was used for the production of dialysate. However there is evidence that intestinal absorption of aluminium after ingestion of aluminium containing oral phosphorus binders might occur [1-5].  $\text{Al}(\text{OH})_3$  containing drugs are frequently prescribed for patients with chronic renal failure. The impact of this absorption is still controversial. In the present study we investigated the possible influence of orally ingested  $\text{Al}(\text{OH})_3$  on the aluminium content of bone in patients on haemodialysis.

### Patients and methods

Fifty-four patients (43 male, 11 female) aged from 22 to 66 years (mean age  $41.4 \pm 12.8$  years) with a mean total time on dialysis of  $68.2 \pm 44.9$  months underwent bone biopsies for different clinical reasons. In 19 patients (group I)

dialysate was prepared with water treated by softeners alone which do not extract aluminium. Thirty-five patients (group II) have used a combination of water softeners and reverse osmosis for water pretreatment since the initiation of their treatment for chronic intermittent haemodialysis. Patients are dialysed three times weekly for three to five hours with a 1.6m<sup>2</sup> hollow fibre dialyser. Anterior iliac crest bone biopsies were performed with a Bordier-Meunier needle. For each sample one piece was used for histological examination and another for quantitative measurement of aluminium content. The latter was done by electrothermal atomic absorption spectrometry after nitric acid destruction of the bone sample. The aluminium content is expressed as  $\mu\text{g/g}$  wet weight. The total amount of ingested  $\text{Al}(\text{OH})_3$  as oral phosphorus binders was calculated for each patient since the initiation of chronic dialysis, and reported as absolute dosage as well as in  $\text{g/kg}$  body weight. Linear regression coefficients between the total ingested  $\text{Al}(\text{OH})_3$  and bone aluminium content were calculated and tested for their significant differences from zero and from each other for all patients and either subgroup.

## Results

The mean aluminium content of the bone is somewhat higher for those 19 patients using only water softeners (group I:  $\bar{X} = 56 \pm 38 \mu\text{g}$ ) as compared to the

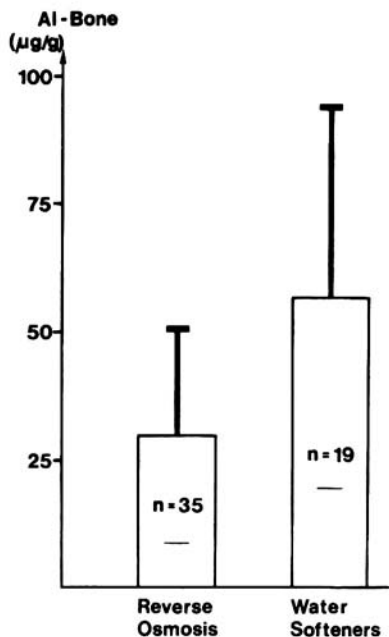


Figure 1. Mean aluminium content of the bone for patients using water softeners and those using reverse osmosis (difference not significant)

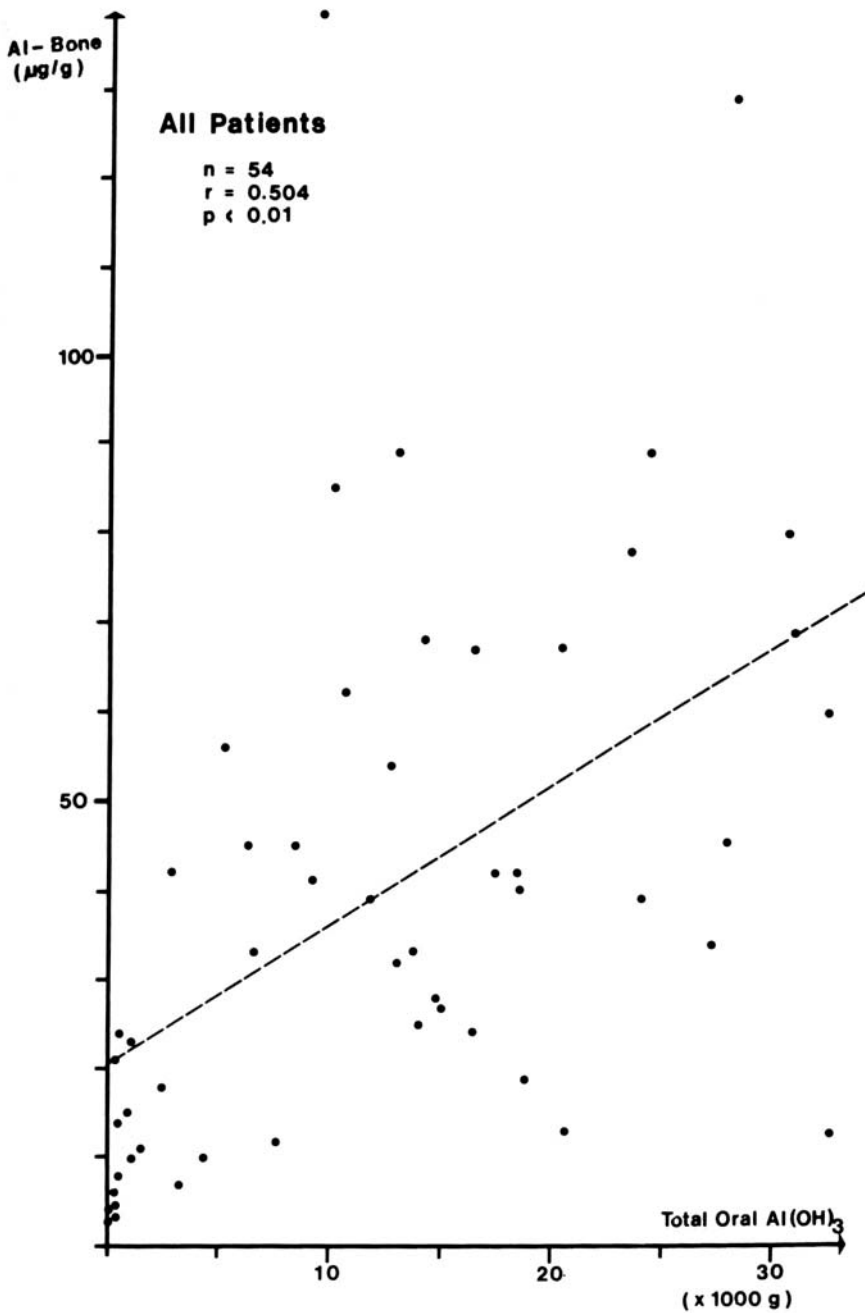


Figure 2. Correlation between bone aluminium and total ingested Al(OH)<sub>3</sub> for all patients

### Reverse Osmosis

n = 35  
r = 0.803  
p < 0.001

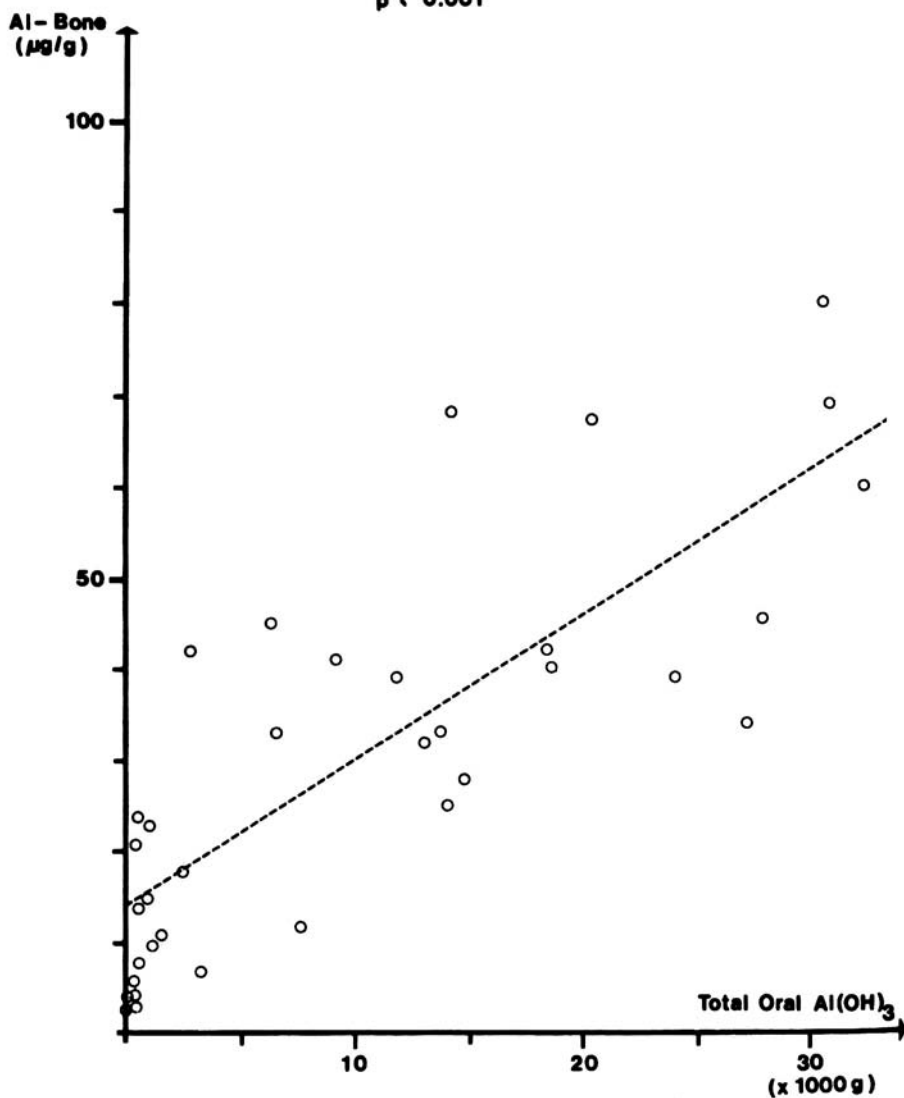


Figure 3. Correlation between bone aluminium and total ingested Al (OH)<sub>3</sub> for patients using reverse osmosis

bone aluminium content of group II with reverse osmosis ( $\bar{X} = 29 \pm 21 \mu\text{g/g}$ ). Due to overlapping standard deviations this difference is not significant (Figure 1). For all 54 patients a slight significant correlation is found between total oral Al (OH)<sub>3</sub> intake and bone aluminium content (Figure 2:  $p < 0.01$ ). The aluminium exposure was also calculated in relation to the body weight (g/kg body weight). The correlation for all 54 patients is not significantly different from that disregarding body weight ( $p < 0.01$ ). Looking at group I and II separately, there is however no statistical relation for these parameters within group I ( $p > 0.1$ ). In contrast there is a highly significant correlation between total oral aluminium intake and the bone aluminium content ( $p < 0.001$ , Figure 3) in group II using reverse osmosis.

## Discussion

It has been clearly demonstrated that aluminium contamination of the dialysate is the most important source for aluminium accumulation in dialysis patients. This is confirmed by our results demonstrating a trend to a higher bone aluminium load in patients using only water softeners for water pretreatment indicating the combined effect of dialysate aluminium and oral medication of aluminium containing drugs on the aluminium content of the bone. The correlation between bone aluminium and total ingested aluminium becomes evident in those patients who had always been dialysed with aluminium free dialysate (group II). Our results demonstrate clearly the aluminium accumulation in the bone is secondary to oral intake of Al (OH)<sub>3</sub>. The bone aluminium load is significantly dependent on the total dose of ingested Al (OH)<sub>3</sub>. Thus intestinal absorption of aluminium from antacids and phosphate binders plays a major role in the aluminium contamination of bone in patients on chronic haemodialysis. The demonstrated impact of oral aluminium producing overload may be helpful in deciding whether to use aluminium containing phosphate binders in uraemic patients. It has been suggested that elevated parathormone concentrations might be toxic in uraemic patients. Whether chronic aluminium intoxication by using conventional phosphorus binders or hyperphosphataemia with the development of secondary hyperparathyroidism, which might be treated surgically, is more harmful for these patients has to be considered.

## References

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