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DOES DESFERRIOXAMINE INDUCE ALUMINIUM LOAD IN PATIENTS ON CHRONIC HAEMODIALYSIS?

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Summary

We have measured plasma aluminium by atomic absorption before and 44 hours after infusion of 2000mg desferrioxamine in nine patients on maintenance haemodialysis (mean duration of haemodialysis 28 months). In addition, the aluminium content of three different batches of commercially provided desferrioxamine (Desferal, Ciba) was determined.

The mean ± SEM pre-infusion plasma aluminium level was 1.77±0.53μmol/L and increased significantly ($p<0.05$) to 3.67±1.12μmol/L after desferrioxamine. The aluminium content of Desferal ranged from 0.15 to 1.4μmol/2000mg. We conclude that commercial desferrioxamine contains large amounts of aluminium. The marked elevation of plasma aluminium after desferrioxamine infusion is not only due to binding of body stores of aluminium but also due to the administration of aluminium containing desferrioxamine.

Introduction

Aluminium accumulation in patients on chronic intermittent haemodialysis may lead to dialysis encephalopathy [1], vitamin-D-resistant osteomalacia [2] and anaemia [3]. The major sources of aluminium load in dialysis patients are aluminium transfer from the dialysate and intestinal absorption from aluminium-containing antacids used as phosphate binders. Aluminium is stored in the tissues and causes toxicity.

Desferrioxamine is a weak base with high affinity for iron and aluminium. It was first described in the therapy of dialysis encephalopathy in 1980 [4]. As plasma aluminium does not reflect local aluminium accumulation, it has been recommended to perform a so-called 'Desferal' test [5]. The increase in plasma aluminium induced by desferrioxamine correlates well with bone aluminium. [6]. We have performed such a 'Desferal' test in nine patients on maintenance haemodialysis and in addition have determined whether Desferal itself gives an aluminium load to the patients.

Methods

In nine patients (mean age 55 years, range 45 to 74 years) on chronic intermittent haemodialysis (mean duration 28, range 2 to 72 months), plasma aluminium was determined before haemodialysis. At the end of dialysis, 2000mg desferrioxamine (dissolved in 250ml saline) were infused over 30 minutes. Previous intake of phosphate binders was not restricted. After 44 hours, at the beginning of the next haemodialysis, plasma aluminium was measured again. In addition, the aluminium content of three different batches of Desferal (Ciba) was determined. Aluminium was measured by atomic absorption spectroscopy.

Differences were tested by Student's 't' test, and a p value <0.05 was considered significant.

Results

Baseline plasma aluminium ranged from 0.45μmol/L to 4.36μmol/L with a mean of 1.77±0.53μmol/L (x SEM) (Figure 1). There was no significant correlation between the baseline value and the duration of haemodialysis treatment. The infusion of 2000mg desferrioxamine resulted in a significant ($p<0.05$) increase in plasma aluminium 44 hours later. Post-infusion aluminium ranged from 0.4μmol/L to 8.6μmol/L with a mean of 3.62±1.12μmol/L (x SEM) (Figure 1).

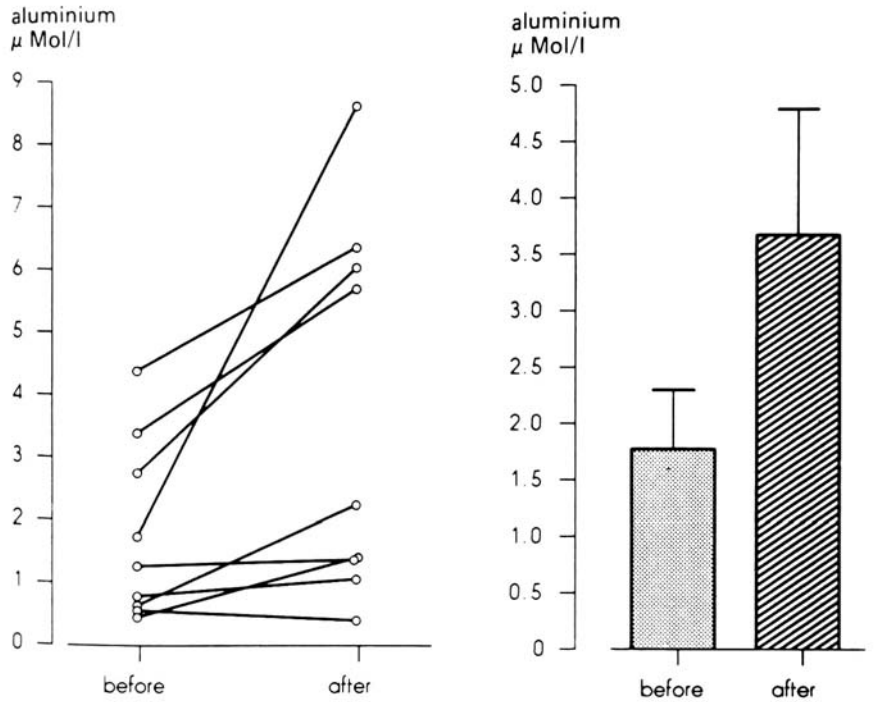

Figure 1. Plasma aluminium before and 44 hours after the application of 2000mg desferrioxamine (mean ± SEM)

In one patient with considerable residual renal function and only on haemodialysis for two months the post-infusion aluminium value declined. In the other patients the increase in plasma aluminium ranged from 0.05μmol/L to 6.87μmol There was no correlation between the increase and the duration of haemodialysis treatment.

The aluminium content of the three examined batches of Desferal (Ciba) ranged from 0.15μmol to 1.4μmol per 2000mg desferrioxamine. Repeated measurements of one batch showed only a small range from 0.76μmol to 0.84μmol per 2000mg desferrioxamine (Figure 2).

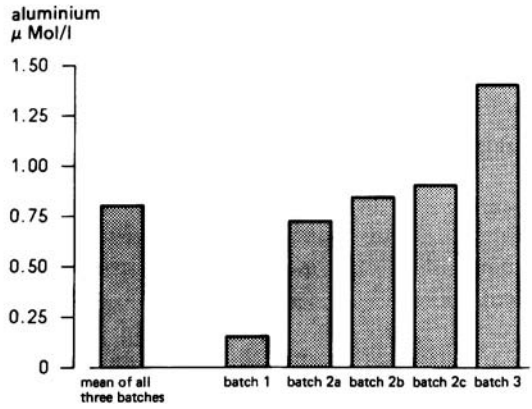

Figure 2. Aluminium content of three different batches of desferrioxamine (2000mg)

Discussion

It is generally accepted that desferrioxamine administration to patients on chronic haemodialysis leads to a mobilization of tissue aluminium and alters aluminium kinetics, allowing a substantial increase in aluminium removal by haemodialysis [7]. Clinical experience supports this hypothesis [4,8]. Our results also show that the administration of desferrioxamine leads to an increase in plasma aluminium. This increase may in part be due to the fact that commercially available desferrioxamine contains variable amounts of aluminium. At an estimated plasma volume of 2.5L, the desferrioxamine infusion with the greatest aluminium content of 1.4μmol may lead to an increase in plasma aluminium of 0.5μmol/L, and thus in our patients 10 to 100 per cent of the increase in plasma aluminium after Desferal may have been due to the load from the test substance. Therefore, we would recommend that the desferrioxamine test should be indicated only for patients with strong clinical evidence of aluminium toxicity. Since the aluminium content of different batches of Desferal varies considerably, while the aluminium content of the same batch is relatively constant, we recommend determining the aluminium content of each batch before administration to patients.

References

1 Alfrey AC, Le Condre GR, Kuchny WD. *N Engl J Med 1976; 294:* 184
2 Ward MK, Feest TG, Ellis HA. *Lancet 1976; i:* 841
3 Elliot HL, Macdougall AL. *Proc EDTA 1978; 15:* 157
4 Ackrill P, Ralston AJ, Day JP et al. *Lancet 1980; ii:* 692
5 Milliner DS, Nebeker HG, Ott SA et al. *Kidney Int 1984; 25:* 149
6 Fournier A, Fohrer P, Leflon P et al. *Proc EDTA-ERA 1984; 21:* 371
7 Stummvoll H-K, Graf H, Meisinger V. *Mineral Electrolyte Metab 1984; 10:* 263
8 Botella J, Gallego JL, Fernandez-Fernandez I et al. *Proc EDTA-ERA 1984; 21:* 403