DESFERRIOXAMINE INDUCED ALUMINIUM REMOVAL IN HAEMODIALYSIS

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Summary

This study evaluates if the use of high flux membranes and the type of dialysate influences aluminium removal in haemodialysis. Aluminium kinetics and dialysance were determined in baseline conditions and after infusion of desferrioxamine. The free diffusible fraction of plasma aluminium correlated significantly with the plasma aluminium post desferrioxamine, independently of the type of membrane or dialysate used. Aluminium removal therefore depends on the plasma concentration reached and the dialysate concentration. High flux membranes do not improve aluminium removal in vivo.

Introduction

Aluminium (Al) accumulates in patients on chronic haemodialysis [1], and causes dialysis encephalopathy, Vitamin D resistant osteomalacia and a non-specific toxicity syndrome [2]. It has proved possible to remove significant quantities of aluminium by haemodialysis following desferrioxamine (DFO) chelation [3,4], but only a very small number of studies have reported dialysance of aluminium post DFO. Since acrylonitrile membranes have demonstrated far superior dialysance of the chelate ferrioxamine [5] and that the difference in the pH of dialysis fluid can increase the solubility of aluminium, we have carried out studies to investigate aluminium removal post DFO in acetate and bicarbonate haemodialysis using cuprophan and acrylonitrile membranes.

Methods

After informed consent, ten patients on chronic haemodialysis (HD) for four hours thrice weekly, were studied. Mean duration of dialysis was 69 months. All patients had taken oral Al-containing phosphate binders and were dialysed with deionised tap water. None had evidence of aluminium toxicity. Throughout the study, oral Al-hydroxide was withheld.
Aluminium was determined by atomic absorption spectrophotometry using graphite furnace (Instrumentation Laboratory, IL-551). Samples were collected under acid conditions.

We evaluated aluminium kinetics (plasma Al, free diffusible plasma Al fraction, dialysate Al) as published elsewhere [6]. Dialysance (ml/min) was calculated by:

\[ D = Q_D \frac{C_D - C_{DI}}{C_A} \]

where \( Q_D \) is dialysate flow rate (ml/min), \( C_D \) is dialysate aluminium efflux (\( \mu g/L \)), \( C_{DI} \) is dialysate aluminium influx (\( \mu g/L \)), \( C_A \) equals aluminium concentration in blood and \( D \) equals dialysance.

Aluminium kinetics were studied before and 48 hours after an intravenous infusion of 2g desferrioxamine (DFO). DFO was administered to all patients after a baseline haemodialysis.

Measurements were performed at dialysate flow rates of 500ml/min in acetate and bicarbonate single pass dialyses. Half of the patients were dialysed with acetate dialysate and the other half with bicarbonate. Two membranes were evaluated: cuprophan (CF 15.11, Travenol) and acrylonitrile AN-69 (H-12.10, Hospal).

Student's test for paired data and linear regression analysis were employed for statistical analysis. Data are expressed as average values and the standard error of the mean.

Results

Basal plasma aluminium was within 'safe' limits in all patients (mean plasma Al = 70 ± 7\( \mu g/L \)).

During baseline dialysis, a significant increase in plasma aluminium was observed and can be accounted for by plasma concentration by ultrafiltration. Baseline aluminium dialysance was 0ml/min (Table I and Figure 1).

| TABLE I. Value of measurements before and after desferrioxamine (DFO) haemodialysis (HD) |
|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|
| Plasma aluminium \( \mu g/L \) | Free diffusible plasma aluminium % (\( \mu g/L \)) | Dialysate aluminium influx \( \mu g/L \) | Aluminium dialysance ml/min |
| start | 70±7 | 19 (13.3±1.3) | 13.1±1.2 | 13.1±1.8 | 0 |
| end | 92±9 | | | | |
| Baseline HD | | | | | |
| start | 143±34* | 37.5 (53.7±26.8)* | 14.3±1.5 | 14.9±1.5 | 2.1* |
| end | 90±7 | | | | |
| Post-DFO HD | | | | | |

* p<0.001 in relation to initial values
The significant decrease in plasma aluminium during post DFO dialysis demonstrates aluminium removal (post DFO Al dialysance = 2.1ml/min) (Table 1).

The plasma aluminium reached at the end of haemodialysis was similar in baseline and post DFO dialysis, and depends on the concentration of aluminium in the dialysate (Figure 1).

The free diffusible plasma aluminium fraction (which is the Al content of in vivo obtained ultrafiltrate) was 19 per cent of total plasma aluminium in baseline haemodialysis with both cuprophan and acrylonitrile membranes, and rose to (24–53%) (mean 37.5%) of total plasma aluminium post DFO (Table 1). The free diffusible plasma aluminium fraction correlated significantly with the plasma aluminium reached post DFO ($r = 0.79$, $p<0.01$), independently of the type of membrane used (Figure 2).

There was no difference in any of the measurements made between the patients dialysed with acetate or bicarbonate.

**Discussion**

In all patients with a safe plasma aluminium administration of 2g DFO caused a 100 per cent increase in plasma aluminium concentration due to tissue mobilisation. This was accompanied by an increase in the free diffusible plasma
aluminium fraction, raising the effective concentration gradient between dialysate aluminium and the free diffusible aluminium. Therefore aluminium dialysance which was zero in baseline conditions rose to a mean of 2.1 ml/min post DFO.

Using standard dialysis baths, with a constant dialysate aluminium there was no significant difference in aluminium kinetics between acetate or bicarbonate.

The free diffusible aluminium fraction correlated significantly with plasma aluminium reached post DFO. There was no significant difference between cuprophan or acrylonitrile membranes. In consequence, aluminium kinetics post DFO suggest that aluminium removal is more dependent on the free plasma aluminium fraction than on DFO-Al chelates.

We conclude that the main factors that influence aluminium removal in haemodialysis are dialysate aluminium and the plasma aluminium reached post DFO and are independent of the bath or type of membrane used. The main goal should be to obtain a high effective concentration gradient.

Acknowledgments

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References

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Open Discussion

BAILLOD (London) Could some indication of clinical use of desferrioxamine be made, such as dosage and frequency. Has anyone any comments on the clinical side effects including hyperkalaemia which I have noted in my patients?

MONTOLIU Desferrioxamine was given as a single injection and no side effects or hyperkalaemia were noted.

HABIBUR-RAHMAN (Newcastle upon Tyne) We think that the protein bound aluminium cannot be removed by desferrioxamine as was shown by equilibrium dialysis and ultrafiltration after DFO in vitro. The optimum time of dialysis after DFO infusion would be at the time of maximum aluminium concentration. The serum aluminium peaks after 48 hours and remains the same for 72 hours. So, dialysis after 48 hours of DFO infusion seems to be logical.

MONTOLIU I agree with your first comment. Our experimental protocol was designed to reproduce a kinetic model and not to obtain maximum aluminium estimation.

BRANCACCIO (Milan) I have promoted a protocol similar to yours and I want to tell you that I have obtained aluminium clearances higher than those presented by you. The reason is likely to be due to the fact that the aluminium in our dialysate was always low, about 5μg/L.

MONTOLIU As previously stated our dialysate aluminium was approximately 13μg/L and this probably explains the difference between your results and mine.