Silicon and aluminium interactions in haemodialysis patients

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Abstract

Background. Aluminium toxicity in dialysis patients is well described. Aluminium has a close chemical affinity with silicon. Silicon may have a role in protection against aluminium toxicity.

Methods. We measured serum aluminium and silicon levels from haemodialysis patients from four different centres.

Results. Though no relationship was seen across all centres combined, in one centre there was a reciprocal relationship in patients on home haemodialysis (who did not require reverse osmosis). Median (range) aluminium levels were higher, 2.2 (0.4–9.6) µmol/l when serum silicon was less than 150 µmol/l, and lower, 1.1 (0.2–2.8) µmol/l when serum silicon levels were greater than 150 µmol/l (P = 0.03).

Conclusions. In patients treated by haemodialysis without reverse osmosis high serum silicon concentrations were associated with lower serum aluminium concentrations than those with low serum silicon. Further work needs to confirm a preventative role for silicon in the accumulation and subsequent toxicity of aluminium in dialysis patients.

Key words: aluminium; aluminium absorption; aluminium toxicity; end-stage renal disease; haemodialysis; silicon

Introduction

Aluminium toxicity in dialysis patients is well described. It can cause severe bone disease, encephalopathy and resistant anaemia. Aluminium has a close chemical affinity with silicon, the two elements interacting in an aqueous environment to form hydroxyaluminosilicates [1]. In many dialysis patients the major source of aluminium exposure is from aluminium-containing phosphate binders as this may remain the only binder that can effectively control hyperphosphataemia and consequent renal osteodystrophy.

Silicon is the second most common element in the earth’s crust. Over the past 20 years its biological importance has become increasingly recognized and investigated. It is claimed to be required in bone, cartilage and connective tissue metabolism [2]. The major importance of silicon is thought to relate to its role in limiting the bioavailability of aluminium [3]. Modest levels (100 µmol/l) of silicic acid in water can protect against aluminium toxicity in fish [4,5]. The major effect relates to the limitation of aluminium absorption by silicon due to hydroxy-aluminosilicate formation, though internal silicic acid may also have a protective role against the cellular toxicity of aluminium [3]. With these facts in mind we decided to look at the serum concentrations of silicon in relation to those of aluminium in haemodialysis patients from different regions. Our aim was to see if there was any correlation between the two and any protective effect of silicon against aluminium toxicity.

Subjects and methods

Random single serum samples were taken predialysis from haemodialysis patients from London (n = 105), 37 of these home patients), Leeds (n = 39), Liverpool (n = 33), and Portsmouth (n = 73). Except for the London home haemodialysis patients, all were using reverse-osmosis units in the preparation of their dialysate fluids. All centres used calcium-based phosphate binders as the default preference, with aluminium hydroxide binders added where phosphate control was deemed inadequate. Data on individual aluminium phosphate binder intake was not available. Serum and tap water samples were analysed for silicon by direct current plasma emission spectrometry [6]. Dialysate measurements were limited to the London home patients not on reverse osmosis, as our own studies as well as previous studies [7] have shown that such treatment effectively reduces silicon levels to less than 2 µmol/l. Aluminium levels (in serum and tap water)
were measured by flameless atomic absorption spectrometry [8,9]. Statistical analysis of grouped data expressed as median (range) was by Mann–Whitney U-test, and linear regression analysis was used to examine the relationship between normally distributed paired data [10].

**Results**

The median serum aluminium and silicon concentrations were 0.93 (0.09–9.63) μmol/l and 77 (22–375) μmol/l respectively. The variation between the four centres is shown in Figure 1a, b. Tap water concentrations of silicon were respectively 161, 42 (24–213), 20, and 155 μmol/l in the Portsmouth, Liverpool, Leeds, and London unit-based patients; and 77 (13–332) μmol/l in the London home patients. Dialysate aluminium concentration was <0.1 μmol/l in the Portsmouth, Liverpool and Leeds patients; and 0.24 (0.019–1.0) in the London home patients.

There was no clear relationship between the serum levels of the two elements across the centres, but there was a significant difference (Figure 2) in serum aluminium concentrations in the London home haemodialysis patients when grouped according to low (<150 μmol/l) or high (≥150 μmol/l) serum silicon, 2.2 (0.4–9.6) vs 1.1 (0.2–2.8) μmol/l respectively (P = 0.03). This ‘threshold’ level was chosen as a result of unpublished studies performed by Birchall et al. to determine the dose dependent nature of silicon protection from aluminium toxicity. Dialysate silicon concentration—with a dialysate prepared from tap water with no reverse osmosis treatment—appeared to be an important factor (r = 0.86, P < 0.0001) in determining serum concentrations of the element in home haemodialysis patients in London not requiring reverse osmosis (Figure 3). There was no significant difference in dialysate aluminium concentrations between the high and low silicon patients. There was no evidence that sustained high levels of silicon were associated with any adverse effects. No patient (all centres) had serum aluminium concentrations above 2.5 μmol/l if their serum silicon concentration was above 150 μmol/l, although this did not reach statistical significance. The incidence of aluminium toxicity was too low to allow statistical testing. However, no cases of clinical aluminium toxicity presented in the London...
group in the 10 years leading up to this study, whereas there were sporadic cases in both Leeds and Liverpool.

**Discussion**

We have demonstrated a very good relationship between dialysate silicon and serum levels in the London home haemodialysis patients indicating that the dialysate is the major source of silicon for patients not using reverse osmosis. In addition, a serum silicon concentration below 150 μmol/l was, in this subgroup of patients, associated with a significantly higher serum aluminium concentration. In the group as a whole (all centres) no patient had serum aluminium concentrations above 2.5 μmol/l if their serum silicon concentration was above 150 μmol/l, although this did not reach statistical significance. Thus high serum silicon concentrations may help protect patients from the adverse effects of aluminium levels higher than 2.5 μmol/l that have been described previously [11]. It has been suggested from studies of aluminium toxicity to fish [4] that strong interactions between aluminium and silicon require a critical silicon concentration of equal to or greater than 100 μmol/l in water—our study investigated serum concentrations.

Dialysis patients are potentially exposed to aluminium and silicon via two major routes: the dialysate and the gastrointestinal tract. With the increased use of reverse osmosis, this type of water used for dialysate preparation contains negligible amounts of silicon and aluminium. Gastrointestinal exposure to aluminium is also much reduced with the reduction in use of aluminium-containing phosphate binders. Exposure to aluminium and silicon is therefore mainly through food and drinking water, although occasionally dialysate contamination may still occur [12]. Apart from the theoretical grounds [1, 3] and animal studies suggesting beneficial effects of silicon, there is evidence that silicon in water limits the enteral absorption of aluminium from both food and water in man [13] and rats [14], although more recently this has been questioned in further rat studies [15]. One might expect, therefore, a reciprocal relationship between silicon and aluminium levels in dialysis patients if the sole or principal route of absorption is enteral. Thus, patients with very high serum silicon concentrations had lower aluminium levels inferring either a reduced intestinal absorption or increased removal of aluminium through dialysis, by the formation of an aluminium-silicon complex. We would not, however, wish to suggest a potential benefit from the use of non-reverse osmosis treated water for the preparation of dialysate, as reverse osmosis is the only reliable means of excluding aluminium from water used in this process (unless the source water has consistently very low aluminium concentrations).

Dobbie and Smith [7] in 1986 looked at silicon levels in uraemic individuals. They found uraemic patients had significantly higher serum silicon levels than healthy individuals. They examined haemodialysis patients from four different centres and observed that serum silicon levels in these patients correlated with dialysate silicon. Roberts and Williams [6] also found high concentrations of silicon in patients with chronic renal failure compared to healthy subjects. They found that despite reverse osmosis dialysis (dialysate silicon < 1 μmol/l) certain haemodialysis patients had markedly high silicon levels (> 100 μmol/l), suggesting dietary sources to be significant. Our study adds to this observation as many of the patients had significantly elevated silicon levels despite having been exposed only to dialysate prepared from reverse osmosis treated water. Together with more recent evidence from D’Haese et al. [16], our results confirm the importance of both dialysate and dietary sources of silicon in determining plasma concentrations. In fact, the mean plasma silicon concentration in these latter patients on regular haemodialysis was similar to tap water. In the Roberts study the silicon and aluminium concentrations in the plasma of 41 patients were not correlated [6], but these patients did use dialysate prepared with reverse osmosis.

We did observe, however, that there was no evidence of aluminium related disease in London and Portsmouth (high drinking water silicon) but small numbers with this diagnosis in Liverpool and Leeds (low drinking water silicon). The patients in the London group with high serum aluminiums (> 4 μmol/l) all had serum silicon concentrations of 100–150 μmol/l, i.e. above the critical minimum silicon concentration, and therefore may have been protected from possible toxic effects of elevated aluminium. These findings suggest that a serum concentration of silicon—around 100 μmol/l—may exert a protective effect against aluminium accumulation and toxicity, in-keeping with previous animal studies [4, 5]. A high concentration of silicon in the blood appears of itself to have no ill effects.

Further work needs to be done to confirm that silicon, as these findings suggest, plays a preventative role both in the accumulation of aluminium and in aluminium related disease in dialysis patients. The possibility of applying this to therapeutic use by increasing the oral intake of silicon should be considered, for example, to reduce absorption and consequent toxicity of aluminium from aluminium-containing phosphate binders and other dietary sources.

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