Prevention of aluminium exposure through dialysis fluids. Analysis of changes in the last 8 years

Jose L. Fernández-Martín, Alejandra Canteros, Mercedes Serrano, Angeles González-Carcedo, Carmen Díaz-Corte and Jorge B. Cannata Andía

Bone and Mineral Research Unit, Hospital Central de Asturias, Instituto Reina Sofía de Investigación, Oviedo, Spain

Abstract Despite extensive measures to control aluminium exposure, chronic and acute episodes of aluminium intoxication still occur. The objective of this study was to analyse the changes in the aluminium content of dialysis fluid and the effect on serum aluminium in different dialysis centres in Spain in the last 8 years. For this purpose, the aluminium content in dialysis fluid and serum samples (N=5,609) from 17 dialysis centres was analysed for >8 years (from the last quarter of 1988 to 1996). In that period of time, the percentage of dialysis fluid samples with acceptable concentrations of aluminium (<2 μg/l) increased from 0% in 1988 to 80% in 1996. The percentage of dialysis fluid samples with high aluminium levels (>6 μg/l) ranged between 37.5% in 1988 and 2.3% in 1996. The improvement in the quality of the dialysis fluid resulted in lower values of serum aluminium. The percentage of serum samples with low aluminium (<20 μg/l) increased from 16.5% in 1988 to 54.2% in 1996. The mean serum aluminium correlated with the mean dialysis fluid aluminium (r=0.55, P<0.001). A higher correlation was found when the aluminium in dialysis fluid ranged between 4 and 10 μg/l (r=0.802, P<0.001), and no correlation was found when the aluminium in dialysis fluid was <4 μg/l. Even taking into account that the dialysis fluid is not the only source of aluminium for dialysis patients, our study clearly demonstrated a close relationship with the serum aluminium content. Therefore, we must emphasize the necessity for controlling the aluminium content in dialysis fluid more often than is done at present.

Key words: aluminium exposure; dialysis fluid; haemodialysis; quality of dialysis

Introduction

There are many reports indicating that the most important source of aluminium exposure in dialysis patients is contaminated dialysis fluid [1–3]. At the end of the 1970s and the beginning of the 1980s, dialysis patients were heavily overloaded with aluminium. Nowadays, except for accidental cases of massive exposure [4], most the dialysis units have controlled the sources of aluminium contamination. This has been achieved thanks to the reduction in aluminium hydroxide intake and to the widespread use of adequate water treatment systems [5–7]. However, the risk of aluminium toxicity has not disappeared, and there are still many patients who have a moderate but chronic exposure to this metal, due to both dialysate contamination with a low concentration of aluminium and the oral intake of aluminium-containing phosphate-binding agents. In addition, sporadic massive aluminium contamination also still occurs [4,8,9].

The removal of aluminium by dialysis is not easy because almost 85–90% is protein-bound aluminium [10–12], thus only a small amount of aluminium (10–15%) is diffusible and ultrafiltratable [13,14]. Consequently, prevention of aluminium exposure is still one of the most important goals in the management of renal patients.

Unfortunately, nowadays, many centres still used the norms adopted 15 years ago when the magnitude of aluminium contamination was extremely high, and consequently the threshold agreed for prevention of aluminium exposure via the dialysis fluid was greater than the limits we should use today. As the degree of aluminium exposure has decreased with time, the mean value of serum aluminium in haemodialysis patients has also reached lower values. Therefore, values previously accepted in Europe as a ‘safe’ limit for aluminium contamination in dialysis fluids (10 μg/l) are now considered inadequate and unsafe.

The aim of this study was to analyse (i) the changes in the concentration of aluminium in dialysis fluids in different dialysis units of Spain from October 1988 to December 1996 and (ii) the possible effect of these changes on the serum aluminium of dialysis patients.

Materials and methods

The study was carried out in our unit with samples received from different Spanish dialysis units obtained.
from routine monitoring during the last 8 years. We included in the study only those units that had sent us samples during a period of more than three consecutive years (17 units from different regions of Spain).

From October 1988 to December 1996, aluminium was measured in the 5626 samples from the 17 units. We excluded 17 samples with very high aluminium (\(>500\) mg/l), suspected of being contaminated. At the end of the study, 5609 samples were analysed (410 samples of dialysis fluids and 5199 serum samples).

Aluminium was measured by electrothermal atomic absorption spectrometry with a graphite furnace (Mod. HGA-600) coupled with an atomic absorption spectrophotometer (Mod. Z-3030) using Zeeman background correction [15].

**Results**

In Table 1, mean values of aluminium in serum and dialysis fluids from each year studied are shown. The mean aluminium in the dialysis fluids gradually decreased, except in 1993, when we found important increments of values with a parallel increase in serum aluminium [16]. The increase in aluminium in the dialysis fluid was due to an accidental exposure to aluminium due to a failure in the water treatment system in one of the renal units included in the study. A similar trend was observed in the serum aluminium, reaching 25.7 mg/l at the end of the study.

As can be seen in Figure 1, throughout the last 10 years the percentage of samples with serum aluminium \(<20\) mg/l has increased, reaching 55% in 1996. On the contrary, those samples with values \(>60\) mg/l have decreased. During the same period, we have also observed an increase in the percentage of dialysis fluid samples containing \(<2\) mg/l aluminium (Figure 2). In 1996, 80% of the samples had reached values \(<2\) mg/l.

Figure 3 shows the correlation between the annual mean serum aluminium and the concentration in the dialysis fluids for each of the participating units. We observed a highly significant relationship between both parameters \((r=0.55; P<0.001)\) even though there are two values clearly different from the others. As most values (except three) were \(<10\) mg/l (reference maximum value accepted in Europe [6]), we plotted all of them, separating those values greater and less than 4 mg/l into two different groups. As can be observed, there is a significant relationship between dialysis fluids

**Table 1.** Aluminium (mean ± SD) found in serum and dialysis fluid throughout the period under study

<table>
<thead>
<tr>
<th>Year</th>
<th>Serum Al Mean ± SD (N)</th>
<th>Dialysis fluid Al Mean ± SD (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988</td>
<td>61.8 ± 47.4 (194)</td>
<td>5.5 ± 2.5 (8)</td>
</tr>
<tr>
<td>1989</td>
<td>52.0 ± 43.1 (633)</td>
<td>5.4 ± 3.1 (50)</td>
</tr>
<tr>
<td>1990</td>
<td>43.8 ± 38.8 (390)</td>
<td>3.2 ± 6.0 (42)</td>
</tr>
<tr>
<td>1991</td>
<td>44.3 ± 41.5 (553)</td>
<td>2.8 ± 5.0 (39)</td>
</tr>
<tr>
<td>1992</td>
<td>45.5 ± 53.1 (623)</td>
<td>3.5 ± 8.5 (44)</td>
</tr>
<tr>
<td>1993</td>
<td>60.5 ± 65.4 (579)</td>
<td>7.3 ± 10.5 (75)</td>
</tr>
<tr>
<td>1994</td>
<td>32.9 ± 29.2 (941)</td>
<td>3.4 ± 3.7 (46)</td>
</tr>
<tr>
<td>1995</td>
<td>33.3 ± 27.8 (629)</td>
<td>4.1 ± 3.1 (30)</td>
</tr>
<tr>
<td>1996</td>
<td>25.7 ± 22.2 (719)</td>
<td>2.5 ± 1.6 (25)</td>
</tr>
</tbody>
</table>

As can be seen in Figure 1, throughout the period of time studied in the 17 dialysis centres.

Fig. 1. Percentage of serum samples at different levels throughout the period of time studied in the 17 dialysis centres.

Fig. 2. Percentage of dialysis fluid samples at different levels throughout the period of time studied in the 17 dialysis centres.

Fig. 3. Correlation between the mean serum aluminium and aluminium in dialys

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and serum aluminium when the aluminium in the dialysis fluid is >4 µg/l (r=0.802; P<0.001); on the contrary, values <4 µg/l do not show any correlation (r = 0.229; P = 0.105, Figure 4).

**Discussion**

Aluminium balance in haemodialysis depends mainly on the gradient of diffusible aluminium, on the type of dialysis membranes, on their surface and thickness and also on many other factors, such as the pH of the dialysate. Among all these factors, undoubtedly the most important is the concentration of aluminium in the dialysis fluids.

In our study, we noticed a decrease in serum aluminium in patients on haemodialysis throughout the last years. In 1996, the mean serum aluminium was 25.7 ± 22.2 µg/l; considering that almost only 10–15% of this aluminium is ultrafiltratable, it seems evident that aluminium in the dialysis fluid should not exceed 3 µg/l [17]. If we go beyond this level, most of the dialysis patients would be at risk of receiving aluminium from the dialysate. On the other hand, if we maintain the dialysate aluminium below this threshold, most of the patients would have the opportunity to remove aluminium [18].

The decrease in the serum aluminium observed in the last decade could also be due partly to the great restriction in the use of oral aluminium hydroxide. However, an important correlation was still observed between aluminium in the dialysate and serum aluminium (Figure 4). When the levels of aluminium in the dialysate were <10 µg/l but >4 µg/l there was a significant relationship between the dialysis fluid and the serum, suggesting a transfer of aluminium from the dialysate to the patient. On the contrary, values of aluminium <4 µg/l in the dialysate showed no correlation with serum aluminium.

These results emphasize that even though values of 10 µg/l of aluminium in the dialysate have been considered for a long time as a 'safe' limit in order to avoid [6] the patient’s contamination from the dialysate, this limit or threshold for safety is no longer useful and we should reduce this figure to at least <4 µg/l. This last figure is almost coincident with the theoretical threshold of 3 µg/l in dialysis fluid mentioned above. If we do not achieve this new 'safe threshold', a large percentage of patients will be slowly, but permanently, exposed to (non-massive) aluminium transfer from the dialysate [19,20].

There is much evidence which demonstrates that despite progress in dialysis procedures, there is still a real risk of aluminium exposure. For example, bone biopsies from dialysis patients who began their dialysis during the last decade in Europe in units that have used adequate water treatment systems and low doses of aluminium hydroxide during the last 15 years show a high aluminium concentration in bone [21,22], indicating that there is still an important and inadvertent transfer of aluminium; this is the main message from Figure 4.

It is important to stress the necessity of periodic control of the water treatment systems and dialysis fluids to guarantee high quality of the water used in haemodialysis. Recent studies show that the frequency of control of dialysis fluids is, on average, extremely low (once or twice per year) [23]. The ideal situation would be to check the dialysis fluids every month in order to detect as soon as possible any failure in the water treatment system, to avoid massive exposure to aluminium. This is a safe and very low cost policy.

Nowadays, the mechanisms involved in aluminium intoxication are better known, but there is still great concern about the danger of aluminium toxicity. As we have the best technology in our hands, we should put all our efforts into minimizing the exposure to this metal in dialysis patients.

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**References**

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