SERUM ALUMINIUM LEVELS IN CHRONIC HEMODIALYSIS PATIENTS

Musa BALİ, M.D., Şükrü SINDEL, M.D., Turgay ARINSOY, M.D.,
Galip GÜZ, M.D., Enver HASANOĞLU, M.D.

Gazi University, Faculty of Medicine, Department of Internal Medicine, Division of Nephrology,
Ankara, Turkey
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SUMMARY: Aluminium frequently accumulates in patients with end-stage renal failure. Accumulation of aluminium can cause anaemia, disabling osteodystrophy and encephalopathy. We measured serum aluminium levels in 24 patients on hemodialysis under surveillance at a single center with using electrothermal atomic absorption spectrometry (ETAAS). Mean serum aluminium concentration was 25.08 (6-171) μg/dL. Dialysis patients with chronic active hepatitis showed a significantly greater median serum aluminium concentration (P<0.05). Compared to the later group, the median serum aluminium concentration of dialysis patients with diabetes mellitus did not differ significantly (P>0.05). Serum aluminium levels did not correlate with estimated oral intake of aluminium, total duration of dialysis, age, sex, serum calcium and phosphorus concentration, N-terminal parathyroid hormone levels, transfusion requirements, erythropoietin and vitamin D treatment except serum alkaline phosphatase levels.

In summary: regular serum aluminium level monitoring in chronic hemodialysis patients must be performed because of aluminium overload and toxicity risks.

Key Words: Hemodialysis, Serum Aluminium, Aluminium Toxicity.

INTRODUCTION

Aluminium excess is very common in uremic patients in whom increased levels were found in bone, liver, spleen, brain and heart with a frequency as high as 85 % (1). In these subjects aluminium overload has been associated with an often fatal form of dialysis dementia (2), a disabling form of bone disease (25) and a microcytic form of anaemia (9). Early identification is important because of these aluminium-related osteodystrophy, encephalopathy and anaemia are severely disabling and potentially fatal disorders for which treatment is limited (2, 11, 16, 17, 20). Since aluminium levels in patients on dialysis are usually higher than those of patients with normal renal function, interpreting aluminium levels of dialysis patients is difficult (13).

Serum aluminium concentrations may fluctuate as a result of oral (12) or parenteral (4, 24) administration of aluminium-containing compounds. Because in patients with an end-stage renal failure the natural protection mechanism against aluminium is either not present (renal excretion) or highly challenged (gastrointestinal barrier) by the oral intake of pharmalogical amounts of Al(OH)3 to control the calcium-phosphorus metabolism. Moreover, in patients during dialysis, hemofiltration or intravenous administration (18, 24) circumvents the natural barriers and may present a hazard even greater.
than that caused by oral aluminium intake. Preva-

cence of an aluminium related disease in dialysis

cations, as well as of aluminium pollution in

tap water and dialysis fluid has been reported in ot-

er studies (10, 15, 18, 19, 21) where epidemic and

sporadic aluminium intoxication frequently oc-

curred. With the introduction of modern techniques for

water treatment, the most dramatic, often regional

(25) expressions of aluminium toxicity have beco-

me preventable.

Nevertheless, aluminium will remain a constant

threat for end-stage renal failure patients as long as

there is no valid alternative to aluminium-contain-

ing phosphate binders. A regular assessment of the

body aluminium burden in these patients is there-

fore necessary. Since bone is the main storage organ

of aluminium (histo-), chemical and histological

examination of a meticulously sampled and ana-

lysed bone biopsy remains the best way to evaluate

aluminium-accumulation-toxicity (13). However,

bone biopsy requires an invasive procedure and is

not easy to perform systematically in all dialysis

centers. Despite the multi-compartmental behavio-

ur of aluminium and the fact that only a small frac-

tion of (0.1%) the body total load is present in the

blood has been suggested that the baseline serum

aluminium might be a good predictor in the assess-

ment of aluminium-induced bone disease (6, 27).

We analysed the concentrations of aluminium in

chronic hemodialysis patients' serum and in the
tap water which has been used in dialysis. The aim of the study was to investigate whether serum 

aluminium is increased in the presence of clinical con-

ditions such as overt liver disease, diabetes mellitus and to study the possible relationship between serum aluminium and aluminium-containing phospha-
tic binders, age, sex, serum calcium (Ca\(^{2+}\)), and
diphosphorus (P) levels, N-terminal parathyroid hor-

mone (PTH) levels, transfusion requirements, eryt-

thropoietin, vitamin D levels, and aluminium.

In addition, the possible relationships between serum aluminium and hepatitis B virus surface antigen (HB\(_{S}\)-Ag) hepa-
tis C virus antibody (anti-HCV Ab) and liver enzy-

mes were evaluated.

MATERIALS AND METHODS

The study population consisted of 24 (12 fe-

male, 12 male) patients on hemodialysis cared for at

the Hospital of Gazi University. Aluminium was
determined in blood and water by the same labora-

tory, using electrothermal atomic absorption spect-

rometry (ETAAS) (7). Blood was obtained from a

peripheral vein before starting the dialysis session.

Tubes were opened only to receive the blood and

the plugged tubes were put in a centrifuge at 3000 g

for 30 min. The serum was directly (without pipet-
te) put into the final tube which was opened only for

the serum transfer time. Only outer cap surface was

used in these operations. Refrigerated samples

(+4°C) were carried to the laboratory. Tubes used

for fluid sample collection were pretreated in order
to avoid aluminium contamination. Tubes and caps

were washed once with distilled water, once with

hydrochloric acid (4% w:v), twice with distilled

water, subsequently. Tubes and caps were dried at

40°C for 3 h. For tap water collection two sample tu-
bles were filled; before taking the sample tubes were

filled completely to the top and sealed.

Blood was sampled for blood glucose, Ca\(^{2+}\), P,

ALP, PTH, HBs-Ag, Anti-HCV Ab, serum alanine

transaminase (ALT), serum aspartate transaminase

(AST), hemoglobin (Hb), hematocrite (Hct) with

serum aluminium. Transfusion requirements were

ascertained by retrospective review of patient re-
cords.

Pharmacological factors; aluminium hydroxi-
de, erythropoietin, and vitamin D treatment, bio-
gical factors; sex, age, dialytic age and other chro-
nic disease (chronic active hepatitis, diabetes melliti-
s etc.) were registered from patient records.

Mann-Whitney U-test was used for statistical

analysis.

RESULTS

The average age of the study group patients who

underwent the hemodialysis treatment was 48.6

± 30.2 (21-67) years, while their average body

weights have been 59.4 ± 19.1 kilograms. The mean

duration of dialysis treatment was 19.8 ± 17.7

months. The measured mean serum aluminium le-

vel of the patients was found to be 25.08 ± 34.33

µg/L. The primary diagnosis were glomerulo-

nephritis, renovascular disease due to hypertension and diabetes mellitus for most of these patients.

With respect to such primary diagnosis we did not ac-
truce a significant difference on their serum alu-

minium levels (Table 1). The aluminium levels of thes-
ese patients for whom a diagnosis of chronic active hepatitis was established as a result of biopsy per-

formed, were quite high with a mean serum alu-

minium level of 97.33 µg/L (P<0.05). On the other

hand, the analysis performed on all the patients ha-
Table 1: Mean ± SD serum aluminum value (μg/L) and primary renal diagnosis.

<table>
<thead>
<tr>
<th>Primary Diagnosis</th>
<th>Number of Patients</th>
<th>%</th>
<th>Serum Aluminum Value (μg/L)</th>
<th>Mean</th>
<th>± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic glomerulonephritis</td>
<td>13</td>
<td>54.16</td>
<td>17.41</td>
<td>± 11.15</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>5</td>
<td>20.83</td>
<td>20.75</td>
<td>± 12.91</td>
<td></td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>4</td>
<td>16.00</td>
<td>12.50</td>
<td>± 3.11</td>
<td></td>
</tr>
</tbody>
</table>

P>0.05

Table 2: The relations between mean ± SD serum aluminum value (μg/L) and HBs Ag, Anti-HCV Ab.

<table>
<thead>
<tr>
<th>Markers of Hepatitis Viruses</th>
<th>Number of Patients</th>
<th>%</th>
<th>Serum Aluminum Value (μg/L)</th>
<th>Mean</th>
<th>± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBs Ag (+)</td>
<td>6</td>
<td>25.00</td>
<td>29.00</td>
<td>± 16.50</td>
<td></td>
</tr>
<tr>
<td>HBs Ag (-)</td>
<td>18</td>
<td>75.00</td>
<td>23.62</td>
<td>± 12.82</td>
<td></td>
</tr>
<tr>
<td>Anti-HCV Ab (+)</td>
<td>9</td>
<td>37.50</td>
<td>29.78</td>
<td>± 17.39</td>
<td></td>
</tr>
<tr>
<td>Anti-HCV Ab (-)</td>
<td>15</td>
<td>62.50</td>
<td>22.26</td>
<td>± 21.63</td>
<td></td>
</tr>
</tbody>
</table>

P>0.05

The mean serum aluminum levels of female and male patients was 27.83 ± 37.15, 22.33 ± 15.49 μg/L respectively. The comparison made with respect to the factors such as age and hemodialysis terms did not also show any significant differences on the serum aluminum levels (Table 3, 4).

Table 3: The relationship between mean ± SD serum aluminum value and ages of patients.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Number of Patients</th>
<th>%</th>
<th>Serum Aluminum Value (μg/L)</th>
<th>Mean</th>
<th>± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 45</td>
<td>8</td>
<td>33.3</td>
<td>25.00</td>
<td>± 9.23</td>
<td></td>
</tr>
<tr>
<td>45 - 65</td>
<td>9</td>
<td>37.5</td>
<td>26.23</td>
<td>± 0.63</td>
<td></td>
</tr>
<tr>
<td>65 &lt;</td>
<td>7</td>
<td>29.10</td>
<td>23.71</td>
<td>± 7.43</td>
<td></td>
</tr>
</tbody>
</table>

P>0.05

Table 4: Mean ± SD serum aluminum value and total durations of dialysis.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Number of Patients</th>
<th>%</th>
<th>Serum Aluminum Value (μg/L)</th>
<th>Mean</th>
<th>± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 12</td>
<td>8</td>
<td>33.3</td>
<td>25.12</td>
<td>± 22.09</td>
<td></td>
</tr>
<tr>
<td>12 - 24</td>
<td>6</td>
<td>25.00</td>
<td>21.66</td>
<td>± 6.40</td>
<td></td>
</tr>
<tr>
<td>24 - 36</td>
<td>5</td>
<td>20.8</td>
<td>28.75</td>
<td>± 24.88</td>
<td></td>
</tr>
<tr>
<td>36 &lt;</td>
<td>5</td>
<td>20.8</td>
<td>25.33</td>
<td>± 10.78</td>
<td></td>
</tr>
</tbody>
</table>

P>0.05

Due to many reasons, the anemia emerges for the patients suffering from a chronic renal failure. No significant difference was found in the serum aluminum levels of those patients who have needed blood transfusion with 26.68 ± 17.20 μg/L aluminum in serum while 25.21 ± 8.81 μg/L in other patients serum.

Erythropoietin is used for anemia treatment of hemodialysis patients. There was no statistically difference between the mean serum aluminum significant levels of the patient using erythropoietin treatment and those not using. The mean serum aluminum was 24.30 ± 19.11 μg/L for patients who have been using erythropoietin whereas 28.22 ± 21.63 μg/L for patients who have not been using.

DISCUSSION

The mean serum aluminum values of patients in the study group were determined as 25.08 μg/L while this value has changed to 2 μg/L in the tap water. The analysis made in the laboratory revealed a serum aluminum level of 2 μg/L for those patients having normal renal functions. This value was in harmony with the lowest values mentioned in the literature (21, 22, 27). In our study which was perfor-
med similar to the study performed by Mc Carthy et al (21), we found that the serum aluminium levels had not changed by the age. We did not find a significant difference on the mean serum aluminium values of 24 patients categorized into groups by their ages. However, during a similar study performed by D'Haese et al (8) for the group consisting of patients between the ages of 45 and 65, the mean serum aluminium levels showed a rise which could not be explained by this research group. Whereas we did not find a significant difference between the mean serum aluminium values and ages of our study group patients. This study showed that the mean serum aluminium levels did not correlate with the total duration of dialysis. Sampson et al (22) and D'Haese et al (8) found the serum aluminium levels higher in those patients who underwent the hemodialysis more than a year. It would be expedient to state here that the longest term of hemodialysis was 72 months for the patients in this study group. When we took into consideration the underlying renal failure, we did not find any significant difference also between the mean aluminium serum values. This result agree with D'Haese et al (8) study.

Although those patients suffering from a chronic hepatic disease had normal or abnormal renal functions, their serum aluminium levels were found to be high (23, 24). In this study, three patients for whom a diagnosis of hepatic disease was made as a result of biopsy performed, showed higher serum aluminium levels. Also, we couldn't correlate the mean serum aluminium levels with hepatitis markers or levels of ALT-AST. Chazan et al (5) and Andress et al (3) had stated that the mean serum aluminium values of those patients suffering from diabetes mellitus did not show any significant difference when compared with those of non diabetic patients. The result obtained from our study were also in harmony with the results achieved by these authors.

Since the microcytic anemia which emerges due to the aluminium toxicity, may also emerge due to various factors (such as the latent blood loss, etc), it might be a faulty approach to compare the serum aluminium levels just by taking into regard the mean corpuscular volume values of patients. Owing to this reason, the patients were compared with each other with respect to their transfusion needs and no significant difference was observed between the mean serum aluminium levels and the number of transfusions. Erythropoietin treatment is frequently being applied for those patients suffering from a chronic renal failure. In our study we made a comparison between 14 patients who were being administered with erythropoietin and other patients who were not being administered with erythropoietin, we did not find any significant difference on the mean serum aluminium levels of 14 patients administered with erythropoietin. Also many studies showed that the serum aluminium levels of the patients who underwent the hemodialysis were higher correlated with the intake dose and term of $A_1 (OH)_3$ during this treatment process. The different result obtained from our study might have been stemmed from the lower dose $A_1 (OH)_3$ and shorter duration of $A_1 (OH)_3$ treatment.

Mc Carthy et al (13) found that, a serum level greater than or equal to 100 $\mu$g/mL is an indicator of the possible presence of aluminium associated bone disease. In this study only one patient had serum aluminium level greater than 100 $\mu$g/mL. The level of N-terminal PTH, $Ca^{2+}$, P and vitamin D did not correlate with the levels of serum aluminium. We were not able to clearly explain the correlation existing just with the only high levels of alkaline phosphatase.

In summary; regular levels of serum aluminium monitorization in chronic hemodialysis patients must measured because of aluminium overload and toxicity. Because of aluminium related bone disease, anemia and encephalopathy, elevation of serum aluminium level must be treated early.

Correspondence to: Dr. Murat BALİ  Gözü Üniversitesi Tip Fakültesi İk Hastalıklar Anabilim Dalı Nefroloji Bilim Dalı Beştepe 06500 ANKARA - TÜRKİYE Phone : 312 - 214 10 00 / 5232
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