Brief Note

Changes in Serum Metal Levels after a Single Hemodialysis Treatment of the Patients of Chronic Renal Failure with Long-Term Hemodialysis

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SUMMARY When patients with chronic renal failure were treated with long-term hemodialysis, serum cadmium and lead levels were increased and chromium was decreased. The change in serum metal levels after a single treatment of hemodialysis was measured. The results are as follows: 1) Serum cadmium and lead values increased during a single hemodialysis but the levels per serum protein were unchanged. The change in serum cadmium and lead levels during the treatment depended on each metal concentration in dialyzing fluid. 2) When the dialyzing fluid was sampled periodically, cadmium and lead levels in the dialyzing fluid were shown to decrease throughout the treatment. These results show that serum cadmium and lead do not flow from the dialyzing fluid into the blood, but rather from the blood to the dialyzing fluid.

3) The chromium levels and chromium per protein ratio in serum tended to decrease during a single hemodialysis treatment. The chromium level in the dialyzing fluid increased after treatment, peaking 1 hour after the treatment. It is hypothesized that chromium was excreted from the serum to the dialyzing fluid. Serum chromium levels in the patients with the long-term hemodialysis treatment were similar to that in diabetic patients. Therefore, it is supposed that the metal levels in the dialyzing fluid control the serum metal levels and that cadmium and lead accumulate in the patients undergoing long-term hemodialysis causing toxic symptoms.

Introduction

Patients with chronic renal failure treated with hemodialysis demonstrate many metabolic disturbances. In this study, the serum level of metal in these patients was checked. Many reports suggest that serum and blood metal concentrations are changed after hemodialysis treatment. However, these reports have not paid much attention to the possible influx and efflux of metals during hemodialysis treatment, with the exception of some metals: aluminum, calcium, and iron.

We have already reported that serum cadmium and lead levels increased and serum chromium values decreased when hemodialysis treatment was prolonged. In
this study, we investigated the mechanisms whereby each serum metal content alters during long-term hemodialysis treatment.

Materials and Methods

Blood samples were obtained from the Ohno General Hospital (Osaka, Japan), and an experimental group was composed of four sub-groups.

The hemodialysis patients were treated with hemodialysis 3 times a week, for a period of 5 hours each time. The dialyzing fluid was ‘Renosal’, purchased from Midori Juji Co. Ltd. Japan, diluted thirty-fold by de-ionized water. In a single treatment, 300 ml/min. of blood was drawn and the dialyzing fluid drained 500 ml/min.

Subjects

Group I (HD group)

Forty-one patients (18 men and 23 women, aged 23-74 yrs, mean age 47 yrs) with chronic renal failure on hemodialysis treatment formed this first group. Serum creatinine and BUN were elevated (creatinine ; mean 10.8 mg/dl, range 7.2-15.2 mg/dl, BUN ; mean 75 mg/dl, range 47.1-103.9 mg/dl) and they had been treated with hemodialysis for 3-10 years. None of the patients had the diabetic symptoms.

Group II (HD-D group)

Group II comprised sixteen chronic uremia patients (9 men and 7 women, aged 36-77 yrs, mean 52 yrs) with diabetic symptoms. They had been treated with hemodialysis(0.3-8.5 years) and their blood sugar levels before a single treatment ranged from 115 to 311 mg/dl (mean 208 mg/dl).

Group III (DM group)

The nineteen patients constituting this group (7 men and 12 women, aged 39-61 yrs, mean 50 yrs) had diabetes mellitus but were not receiving hemodialysis treatment.

Controls

Fifty-four healthy subjects (21 men and 33 women, aged 20-57 yrs, mean 33 yrs) served as controls.

Methods

Blood was obtained before and after the hemodialysis treatment. 50 ml of dialyzing fluid was collected in a volumetric flask at the following intervals; immediately before treatment, and 15 min., 30 min., 1 hour, 2 hours and 5 hours after the treatment. After freeze-drying, the fluid was dissolved with 1 ml of conc. HNO₃ and increased to 5 ml by adding re-distilled water.

Metal contents in serum and dialyzing fluid were measured by Zeeman-effect atomic absorption spectrophotometry (170-70 HITACHI Co. Ltd., Japan) after wet combustion following the procedure mentioned in our previous report⁷. Serum protein was measured by the Biuret method⁹.

Statistical analysis was performed using Student's t-test.

Results

Table I shows the metal contents in the treatment group collected before and after the hemodialysis. When the values before and after the treatment were com-
Changes in Serum Metal Levels after a Single Hemodialysis Treatment of Chronic Renal Failure with Long-Term Hemodialysis

Table I Serum metal contents before and after a single hemodialysis treatment

<table>
<thead>
<tr>
<th></th>
<th>Before Hemodialysis</th>
<th>After Hemodialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cd</td>
<td>ppb</td>
<td>ng/mg §</td>
</tr>
<tr>
<td></td>
<td>1.50±0.64</td>
<td>0.02±0.01</td>
</tr>
<tr>
<td>Pb</td>
<td>ppb</td>
<td>ng/mg §</td>
</tr>
<tr>
<td></td>
<td>149.75±79.80</td>
<td>224.49±135.50**</td>
</tr>
<tr>
<td></td>
<td>2.63±1.65</td>
<td>2.69±1.58</td>
</tr>
<tr>
<td>Cr</td>
<td>ppb</td>
<td>ng/mg §</td>
</tr>
<tr>
<td></td>
<td>9.25±6.09</td>
<td>7.50±4.45</td>
</tr>
<tr>
<td></td>
<td>0.13±0.10</td>
<td>0.10±0.07</td>
</tr>
<tr>
<td>Protein</td>
<td>g/dl</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7.31±0.61</td>
<td>8.00±0.88**</td>
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</table>

§ indicates the serum metal levels per serum protein.
*P<0.05, **P<0.01, VS before hemodialysis. The values are expressed as mean±S.D.

Fig. 1 Metal levels in the dialyzing fluid.
Vertical line: metal concentration in the dialyzing fluid.
Horizontal line: the time of the hemodialysis treatment, "0" means before the treatment.
Results are expressed as mean±S.D. obtained from 8 samples.
Each value is compared with the value of 0 time. *P<0.05.

pared, the serum cadmium and lead levels after the treatment were significantly higher than before; but these values per serum protein were unchanged. The chromium levels between serum and per serum protein were lower after treatment than before, but the difference was not significant. We subsequently measured the metal contents in the dialyzing fluid. The cadmium and lead in the dialyzing fluid tended to decrease during dialysis treatment (Fig. 1 (1) and (2)). However, the
Table II  Serum chromium levels in the control, HD, HD-D and DM groups  
The values were expressed as mean±S.D.

<table>
<thead>
<tr>
<th></th>
<th>Male(ppb)</th>
<th>Female(ppb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>28.33±19.66</td>
<td>30.19±16.84</td>
</tr>
<tr>
<td>HD group</td>
<td>10.41±4.04**</td>
<td>10.75±7.69**</td>
</tr>
<tr>
<td>HD-D group</td>
<td>10.23±6.16**</td>
<td>13.63±10.42**</td>
</tr>
<tr>
<td>DM group</td>
<td>13.05±5.41**</td>
<td>9.94±6.04**</td>
</tr>
</tbody>
</table>

**P<0.01 vs control value.

Chromium levels collected at 15 min., 1 hour and 2 hours were significantly higher than in the dialyzing fluid before treatment (Fig. 1 (3)).

Table II shows the serum chromium level in the control, HD, HD-D and DM groups. The serum chromium levels in the three groups were identical but lower than the control value.

**Discussion**

It is reported that aluminum influx from the dialyzing fluid causes Alzheimer syndrome\(^{10}\) and \(\delta\)-Amino levulinate dehydratase activity is inhibited by lead accumulation\(^{11}\). However, understanding the influx and efflux mechanisms of metals in hemodialysis treatment is not sufficient to explain why metal accumulation occurs.

We have already reported that the longer the duration of the hemodialysis treatment, the higher the concentration of cadmium and lead, both of which are harmful Metals\(^{7}\), while chromium, which is a necessary glucose tolerance factor\(^{12}\), is lower\(^{7}\). In this study, we investigated the mechanisms whereby the level of the serum metals differs depending on the kind of metal in patients with long term dialysis. Bogden et al.\(^{13}\) showed the release of considerable amount of Zn from disposable coils into the dialysis fluid, but they did not show the detectable release of cadmium and lead. Salvadeo et al.\(^{13}\) have also claimed that cadmium and lead were released from dialyzing fluid into the blood to cause harmful metal accumulation.

We have shown that cadmium and lead in the dialyzing fluid decreased in a time dependent manner (Fig 1). We suggest that this phenomena is not caused by the influx of cadmium and lead from the dialyzing fluid, but by disturbance of the excretion of these harmful metals, as evidenced by the fact that the cadmium and lead values per serum protein were the same before and after the treatment (Table I).

Gidden et al.\(^{14}\) found that cadmium bound strongly to protein, and chromium was slightly bound to protein in normal and dialyzed uremic serum. In our experiments, chromium tended to decrease during treatment in both the serum and the serum protein (Table I). Furthermore, when the chromium level in the dialyzing fluid was measured, it was significantly higher than before treatment, reaching its peak 1 hour after the beginning of treatment (Fig. 1 (3)). These results show that chromium was transported from the serum to the dialyzing fluid.

Rudolph et al.\(^{15}\) showed that cadmium was accumulated in skeletal muscle in dialyzed uremias, while Meredith et al.\(^{15}\)
Changes in Serum Metal Levels after a Single Hemodialysis Treatment of Chronic Renal Failure with Long-Term Hemodialysis

found that lead in red blood cells from hemodialysis patients was elevated and δ-amino levulinate dehydratase activity in the erythrocyte was inhibited.

The serum chromium levels in the HD, HD-D and DM groups were lower than in the control, but there were no significant differences among these three groups (Table II).

From these results, it is supposed that the metal levels in the dialyzing fluid deserve attention, when the period of hemodialysis treatment is longer. Therefore, we conclude that harmful metals, such as cadmium and lead, are not excreted, but accumulated in the patients with long-term hemodialysis and that chromium, which is necessary to glucose tolerance, is excreted into the dialyzing fluid.

References

3) A. Salvadeo, C. Minoia, S. Segagni and G. Villa: Intern. J. Art. Organs, 2, 17 (1979)
12) O. Wada, S. Manabe, H. Matsui and M. Nagahashi: Metabolism and Disease, 20, 625 (1983)