CHANGES IN COPPER AND ZINC IN CHRONIC HAEMODIALYSIS PATIENTS

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Summary

We studied the behaviour of copper (Cu) and zinc (Zn) during haemodialysis (HD) in 65 chronic renal failure patients. Serum Cu, Zn and total protein were measured before and after dialysis. The dialyser membrane contained Cu and Zn. However, when the dialyser was washed with normal saline, Zn was removed, while Cu was liberated from the membrane during HD. We conclude that during HD serum Cu and Zn concentrations increased significantly (p<0.01), Cu from 98 to 120μg/dl by haemoconcentration and liberation from the membrane, and Zn from 78 to 91μg/dl by haemoconcentration.

Introduction

Abnormalities in copper (Cu) and zinc (Zn) metabolism have been described in chronic haemodialysis patients [1–5]. Copper intoxication causes copper fever, haemolytic anaemia and liver diseases; clinical symptoms of chronic Zn deficiency in chronic haemodialysis patients are hypogonadism in males, anorexia, and impair wound healing. The mechanisms of the abnormality of these trace metal concentrations in the serum of chronic dialysis patients are not well understood. Therefore, we studied the behaviour of Cu and Zn during haemodialysis.

Materials and methods

We examined 65 chronic renal failure patients (40 males, 25 females, average age 39±16 years) who were undergoing 5-hour haemodialysis (HD), three times a week, by various kinds of dialysers. Serum Cu, Zn total serum protein (TP) were measured before and after dialysis. Ultrafiltrate fluid (UF) was obtained by extracorporeal ultrafiltrate method (ECUM) at five minutes after the start of HD and concentrations of Cu and Zn in the ultrafiltrate fluid (Cu(uf), Zn(uf))
were measured. At 30 minutes after the beginning of HD, we measured serum Cu, Zn and TP (Cu(in), Zn(in), TP(in)) in the blood, Cu and Zn (Cu(Din), Zn(Din)) in the dialysate at the inflow site of the dialyser, serum Cu(out), Zn(out) and TP(out) in the blood, and Cu(Dout) and Zn(Dout) in the dialysate at the outflow site of the dialyser. The dialyser membrane contains Cu and Zn. However, Zn was removed by washing with 500ml normal saline. We examined the amount of Cu liberated from the membrane during HD. Copper values in normal saline (1,500ml) were measured before and after the saline was used to wash dialysers of various kinds. After 5-hour dialysis, the dialyser membrane was washed out with 100ml normal saline, and the copper in the saline measured. We also studied the copper concentration in saline after fresh dialysers were washed out with 1,000ml normal saline and then filled with normal saline for five hours to determine how much copper was liberated from the dialyser membranes. On examination days, patients ate only after HD was completed. The average BUN, serum creatinine, and haematocrit values of the 65 patients were 85±15µg/dl, 9.2±1.6µg/dl and 23.6±1.8% before HD, respectively. No patients were receiving zinc or vitamin supplements, or blood transfusions in the month prior to examination. Serum, ultrafiltrate fluid and dialysate were all handled in the same manner. Cu and Zn concentrations were determined by a standard dilution method using a flameless atomic absorption spectrophotometer (Hitachi, Japan). We used Student’s ‘t’ test, regarding a 95 per cent level of confidence (p<0.05) as significant.

Results

In our patients, we obtained the following results for copper:

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\begin{align*}
\text{Cu(b)} & \quad 98 \pm 10\mu\text{g/dl} \\
\text{Cu(a)} & \quad 120 \pm 13\mu\text{g/dl} \\
\text{Cu(uf)} & \quad 6.3 \pm 0.8\mu\text{g/dl} \\
\text{Cu(in)} & \quad 99.6 \pm 8.4\mu\text{g/dl} \\
\text{Cu(out)} & \quad 118 \pm 11\mu\text{g/dl} \\
\text{Cu(Din)} & \quad 2.7 \pm 0.4\mu\text{g/dl} \\
\text{Cu(Dout)} & \quad 3.3 \pm 0.5\mu\text{g/dl}
\end{align*}
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for zinc:

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\begin{align*}
\text{Zn(b)} & \quad 78 \pm 5.0\mu\text{g/dl} \\
\text{Zn(a)} & \quad 88.9 \pm 6.4\mu\text{g/dl} \\
\text{Zn(uf)} & \quad 8.2 \pm 0.9\mu\text{g/dl} \\
\text{Zn(in)} & \quad 79.4 \pm 4.4\mu\text{g/dl} \\
\text{Zn(out)} & \quad 86 \pm 3.6\mu\text{g/dl} \\
\text{Zn(Din)} & \quad 10.8 \pm 1.1\mu\text{g/dl} \\
\text{Zn(Dout)} & \quad 9.8 \pm 1.0\mu\text{g/dl}
\end{align*}
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for total serum protein:

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\begin{align*}
\text{TP(b)} & \quad 6.2 \pm 0.6\text{g/dl} \\
\text{TP(a)} & \quad 7.0 \pm 0.5\text{g/dl} \\
\text{TP(in)} & \quad 6.3 \pm 0.5\text{g/dl} \\
\text{TP(out)} & \quad 6.9 \pm 0.4\text{g/dl}
\end{align*}
\]
Copper liberation from dialyser membranes: after dialyser was washed with 1,000ml normal saline, 700±300μg/1m²; after dialysis, 500±200μg/1m²; during 5-hour examination of fresh dialyser, 1,500±400μg/1m².

Discussion

We examined copper and zinc transfer during dialysis. Approximately 96 percent of the Cu in serum binds to protein; non-protein bound copper in serum is free diffusible copper. The ultrafiltrate copper concentration is equivalent to free diffusible non-protein bound copper in serum. When the dialysate Cu concentration is lower than the free diffusible Cu in serum, Cu moves from blood to dialysate. In our patients non-protein bound Cu in serum was 6.3±0.8μg/dl and the concentrations of Cu in the dialysate (Cu(Din)) 2.7±0.4μg/dl. According to the principle of diffusion, Cu moved from blood to dialysate through the dialyser membrane. Serum Cu at the inflow site of the dialyser (Cu(in)) was 99.6±8.4μg/dl and Cu at the outflow site (Cu(out)) increased significantly to 118±11μg/dl (p<0.01). The total protein value significantly increased from 6.3±0.5μg/dl to 6.9±0.4μg/dl (p<0.01). The values of TP(out)/TP(in) were 1.09±0.04 and those for Cu(out)/Cu(in) were 1.19±0.06. We found a significant difference (p<0.05) between the ratios of TP(out)/TP(in) and Cu(out)/Cu(in). TP(a)/TP(b) ratios were 1.13±0.03 and the Cu(a)/Cu(b) ratios were 1.22±0.05. There was a significant difference (p<0.01) between TP(a)/TP(b) and Cu(a)/Cu(b). At that time the Cu of the dialysate was 2.7±0.4μg/dl at the inflow site and 3.3±0.5μg/dl at the outflow site. There was no significant difference between Cu(Din) and Cu(Dout). The Cu moved from blood to dialysate; however, Cu contained in the dialyser membrane was liberated from the membrane to blood and dialysate. Therefore Cu(out) values were higher than Cu(in) due to haemoconcentration and liberation from the membrane, despite the decrease in serum copper (Cu(out)) at the outflow site due to diffusion. These results indicate that serum copper post-dialyser exceeded the serum copper pre-dialyser because haemoconcentration and liberation had a greater influence than did diffusion. It was for this reason that the serum copper significantly increased (p<0.01) from 98±10μg/dl before HD to 120±13μg/dl after HD (Figure 1).

Ultrafiltrable zinc (non-protein binding zinc in serum) was 8.2±0.9μg/dl and dialysate zinc concentrations were 10.8±1.1μg/dl. The dialysate zinc values were significantly (p<0.05) higher than ultrafiltrable zinc. Therefore, zinc moved from dialysate to blood by diffusion.

There was no significant difference between dialysate zinc concentrations before the dialyser (Zn(Din)=10.8±1.1μg/dl) and after (Zn(Dout)=9.8±1.0μg/dl). Serum zinc pre-dialyser (Zn(in)) was 79.4±4.4μg/dl and post-dialyser 86.0±3.6μg/dl (p<0.05). There was no significant difference between TP(out)/TP(in) (1.09±0.04) and Zn(out)/Zn(in) (1.08±0.06). These results show that the changes in serum zinc concentration mainly depended on haemoconcentration during HD.

There was no difference between the ratio of total serum protein before HD to that after HD (TP(a)/TP(b)=1.13±0.03) and the ratio of Zn(a)/Zn(b) (1.14±0.06).
**Figure 1.** Copper concentrations in ultrafiltrate fluid, dialysate, and serum (at the inflow site and outflow site of the dialyser): ratios of serum copper concentrations before and after HD; and ratios of total serum protein before and after HD

**Figure 2.** The zinc concentrations in ultrafiltrate fluid (Zn(uf)), dialysate and serum (at the inflow site and outflow site of the dialyser; Zn(Din), Zn(Dout), Zn(in), Zn(out)); ratios of serum zinc concentration before and after HD (Zn(a)/Zn(b)); and ratios of total serum protein before and after HD (TP(a)/TP(b))

Serum zinc significantly increased from 78±5.0µg/dl before HD to 88.9±6.4µg/dl after HD, due to haemoconcentration and to a lesser extent to zinc diffusion from dialysate to blood (Figure 2).

**References**

1. Mahajan SK, Gardiner WH, Abbasi AA et al. Trans ASAIO 1978; 24: 50