Effect of Hemodialysis on Serum Copper and Zinc Levels in Renal Failure Patients

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ABSTRACT
For human beings trace elements are essential nutrients with a gamut of functions. Available data regarding trace element status in hemodialysis patients are contradictory. The present study was aimed to investigate possible existence of trace element disturbances in uremic patients undergoing dialysis treatment. Blood samples of forty hemodialysis patients and twenty healthy controls were analyzed for quantitation of copper and zinc. The study revealed that serum copper and zinc concentrations in hemodialysis patients are distinctly decreased compared to that of healthy controls. Abnormalities of trace elements are primarily the result of uremia, and they may be further exacerbated by the dialysis procedure.

Key words: Copper, zinc, hemodialysis.

INTRODUCTION
Uremia is characterized by functional and biochemical disturbance that result primarily from the diseased kidney’s diminished capacity to remove organic solutes from the body. Most research on uremic toxicity has focused on retention and removal of these organic compounds. However, subtle changes in the concentration of inorganic compounds, including trace elements, may also cause functional or biochemical disturbance (1).

Hemodialysis (HD) removes uremic toxins primarily by allowing equilibration of plasma and dialysate across a semipermeable membrane. Substances that have lower concentrations in dialysate than in blood tend to be removed by dialysis. Although this is appropriate in the case of uremic toxins, it may lead to depletion of biologically essential substances. Substances present in dialysate but not in blood will tend to accumulate in the patient, and the lack of renal clearance in hemodialysis patients might theoretically lead to toxicity of ingested trace elements even when they are not present in dialysate. Thus, hemodialysis patients are at theoretical risk for both deficiency and accumulation of trace elements, depending on dietary intake, removal by dialysis, the composition of the source water used for hemodialysis, and residual kidney function (2-4).
Disproportionate accumulation or depletion of trace elements are both known to have adverse consequences in the general population (5,6) and may have significant clinical implications, including increasing risk for cancer, cardiovascular disease, immune deficiency, anemia, and renal function impairment and bone disease (7). While very little is known about trace element concentration and metabolism in healthy individuals, even less is known about the physiology of trace elements in uremia.

Although not established, it is plausible that disordered trace element status (if present) would contribute to morbidity and mortality among hemodialysis patients. However, the incidence of abnormal trace element status in dialysis patients has not been comprehensively studied. The present study was aimed to evaluate the possible alterations in copper (Cu) and zinc (Zn) levels in uremic patients undergoing hemodialysis.

MATERIALS AND METHODS

The present study was carried out in the Department of Biochemistry, Dr. V. M. Govt. Medical College, Solapur and SCSM General Hospital, Solapur. A total of 60 subjects were included in the study. Out of these 20 were healthy controls and 40 were hemodialysis patients.

Inclusion criteria

Healthy controls: Twenty healthy volunteers were selected and matched for age, sex and socio-economic background. Only those who proved to be in a good state of health and free from any sign/s of chronic disease/s or disorder/s were included.

Study group subjects: Acute kidney disease (AKD) and chronic kidney disease (CKD) patients in the age group of 35 to 60 years undergoing hemodialysis were selected. The patients were diagnosed on the basis of detailed clinical history, clinical examination, and other relevant biochemical investigations. All patients had four hours dialysis sessions with polysulfone dialysis membrane.

Exclusion criteria

The patients suffering from other diseases, such as diabetes, inflammatory diseases, hepatic or respiratory diseases as well as smokers and alcoholics were excluded from study.

The distribution of subjects in the present study was as follows: Control; Healthy subjects (n:20), Group I; AKD patients undergoing hemodialysis (n:20), Group II; CKD patients undergoing hemodialysis (n:20)

Informed consent was obtained from each participant in the study. The study was cleared by institutional ethical committee. Four ml blood was collected in plain bulb, both before and after hemodialysis from each patient. The serum was separated within 2 hours after blood withdrawal, by centrifugation at 3000 rpm for 10 minutes at room temperature. Serum creatinine was estimated by using Jaffe’s reaction in which creatinine react with picric acid to form creatinine picrate (8,9). Serum samples were diluted with deionized water and Cu and Zn levels were then measured on atomic absorption spectrophotometer. The concentrations of Zn and Cu in serum were reported as mg/dl after necessary corrections were made. The values are expressed as mean±SD. Student’s ‘t’ test was done for comparison of data.

RESULTS

Table 1 indicates serum creatinine levels in healthy controls and hemodialysis patients. Before hemodialysis in AKD and CKD patients serum creatinine levels were significantly increased (p<0.001) as compared to healthy controls. The serum creatinine levels were significantly higher (p<0.001) in CKD patients as compared to AKD patients. Table 2 exhibit serum copper levels in hemodialysis patients and healthy controls. There was significant decline in serum copper levels in both AKD and CKD patients as compared to healthy controls (p<0.001) which further decreased significantly after hemodialysis (p<0.05). Table 3 illustrate serum zinc levels in hemodialysis patients and in healthy controls. There was significant decline in serum copper levels in both AKD and CKD patients as compared to healthy controls (p<0.001) which further decreased significantly after hemodialysis (p<0.05). Table 3 illustrate serum zinc levels in hemodialysis patients and in healthy controls. Before hemodialysis the levels of serum zinc were significantly lower in AKD and CKD patient when compared to healthy controls (p<0.001), which further declined significantly after hemodialysis (p<0.001). Before hemodialysis serum copper and zinc levels were significantly lower in group II patients than group I patients (p<0.05).

DISCUSSION

Though trace elements occur in very low concentrations in the body, their role in the maintenance of undisturbed biological functions is nonetheless highly important. The present study reports significantly lowered serum cop-
per levels in both AKD and CKD patients as compared to healthy controls (p<0.001) which further declined significantly after hemodialysis (p<0.05). In some studies, serum Cu levels were higher in hemodialysis patients(10), while in others the serum Cu levels in patients with CKD were within normal ranges or lower(11). The results of the present study do agree with the latter.

In this study, there was significant reduction of serum zinc levels in AKD and CKD patients when compared to healthy controls (p<0.001), which further decreased significantly after hemodialysis (p<0.001). Our results are in contrast to Hosokawa et al who reported that in uremic patients serum Zn levels were increased after HD (12).

The concentration and toxicity of trace elements in body fluids can be affected by multiple factors such as inadequate intake (e.g. malnutrition low income diet, alcoholism etc.), malabsorption (e.g. intestinal dysfunction), altered distribution (due to changes in transport, changes in receptor etc.)(13). Most of these factors cause a decrease rather than an increase in trace element concentration. In uremia, the concentrations of trace elements are modified partly as a consequence of endogenous toxicities and of impaired renal function, partly due to dietary restriction and, last but not least, due to therapeutic measures (i.e. conservative and modern instrumental therapy).

In hemodialysis patients trace element decreases mainly occur through losses to the dialysate and through urinary losses. However, the most important factor affecting trace element concentration in uremic patients is the degree of kidney disease (13). In the present study also serum copper and zinc levels were significantly lesser in CKD patients than AKD patients (p<0.05).

Both zinc and copper are vital elements for normal metabolism. Zinc deficiency is a leading cause of disease in developing countries (5), and is associated with delayed wound healing (14), and immune deficiency characterized by impaired cell proliferation, abnormal T-cell function, defective phagocytosis, and abnormal cytokine expression (15,16), all of which might contribute to the excess risk of infection observed in hemodialysis patients (17). Zinc deficiency may also cause or contribute to a number of relatively non-specific conditions commonly observed in hemodialysis patients, including anorexia, dysgeusia, and impaired cognitive function (18, 19). The biochemical changes, particularly increased plasma ammonia and ribonuclease activity, which have been reported in experimentally induced zinc deficiency in human beings and animals(20,21) have been reported in patients on hemodialysis with low serum zinc concentrations(22). Copper deficiency may be associated with anemia which may be megaloblastic or sideroblastic and leucopenia (24).

In summary, we found that average blood concentrations of biologically important trace elements like copper and zinc were substantially different in hemodialysis patients, compared with healthy controls. Since both deficiency and excess of trace elements are potentially amenable to therapy, the hypothesis that trace element status influences the risk of adverse clinical outcomes appears worthy of investigation. Further studies are needed to elucidate the clinical importance and long-term effects of imbalances of these trace elements.

**REFERENCES**


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**Table 3. The levels of Serum creatinine (mg/dl), copper (μg/dl) and zinc (μg/dl) in healthy controls, ARF and CRF patients undergoing Hemodialysis (HD)**

<table>
<thead>
<tr>
<th>Serum</th>
<th>Healthy Control</th>
<th>Group I</th>
<th>Group II</th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.87±0.13</td>
<td>9.06±1.32A1</td>
<td>12.46±2.39A1,C1</td>
<td>5.57±0.58A1,B1</td>
<td>5.90±0.72A1,B1</td>
</tr>
<tr>
<td>Copper (μg/dl)</td>
<td>118.29±11.04</td>
<td>103.06±13.26A1</td>
<td>97.35±11.02A1,C2</td>
<td>96.93±10.68A1,B2</td>
<td>89.70±9.96A1,B2</td>
</tr>
<tr>
<td>Zinc (μg/dl)</td>
<td>104.15±7.83</td>
<td>90.06±6.06A1</td>
<td>86.83±5.12A1,C2</td>
<td>85.62±5.43A1,B1</td>
<td>82.39±5.14A1,B1</td>
</tr>
</tbody>
</table>

A1: Comparison with controls (p<0.001), B1: Comparison with PreHD (p<0.001), B2: Comparison with PreHD (p<0.05), C1: Comparison with Group I-preHD (p<0.001) C2: Comparison with Group I-preHD (p<0.05)