

## ZINC AND COPPER DEFICIENCY IN MAINTENANCE HEMODIALYSIS PATIENTS WITH END STAGE RENAL DISEASE - Preliminary Report -

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*SUMMARY: Serum zinc and copper levels and erythrocyte zinc contents were studied and a series of 49 randomly chosen patients on maintenance hemodialysis program. All patients were suffering of end stage renal disease for which they were referred to the hemodialysis center. Upon arrival their mean blood urea nitrogen was above 150 µg/dl, serum creatinine levels over 10 mg and creatinine clearance less than 10 ml/min. They were on a specified diet containing 40-50 gr protein per day. Their mean serum zinc levels were found 60.69±1.21 µg/dl, erythrocyte zinc content 1175.28±55.88 µg/dl 10<sup>10</sup> erythrocyte zinc content 11.29±0.24 µg/dl and serum copper levels 88.43±3.36 µg/dl. Each of these figures were significantly below those of a group of normal control subjects (p<0.05). A striking similarity between zinc deficiency symptoms and the complaints of these patients develop on maintenance hemodialysis program (anemia, loss of weight, neuropathy, arthropathy, gonadal dysfunctions alopecia, nail dystrophy) has been observed and its significance discussed.*

*Key Words: Zinc deficiency, copper deficiency, hemodialysis, end stage renal disease.*

### INTRODUCTION

Hemodialysis has been highly successful in prolonging the life of patients with end stage renal disease (ESRD). The time gained enables the patients to wait for extended periods of time for renal transplantation while others live years on maintenance application. It is noteworthy however that during this time, these patients develop certain well defined complaints: Anemia, fatigue, loss of weight, uremic osteodystrophy (osteoporosis), subperiosteal bone resorption, bone cysts), neurological disturbances (polyneuropathy, carpal tunnel syndrome, EEG abnormalities), arthropathy, gonadal dysfunctions (oligospermia, impotence, amenorrhea), alopecia, nail dystrophy etc.) (Table 1). These symptoms have been the subject to many investigations which provided the necessary information for designing the dietary regime and therapeutic measures presently in use. Several attempts to prevent development and even progressive aggravation of these symptoms by the present day regime and hemodialysis therapy have been uniformly unsuccessful (1, 2). Reevaluating the clinical status of these patients we recently observed a striking resem-

blance between the zinc deficiency syndrome which inspired this investigation. The preliminary results of this study is presented in this communication.

### MATERIALS AND METHODS

The study was carried out on 49 patients (32 males and 17 females) all of whom were referred to the Hemodialysis Center of the Ankara Social Security Hospital with the diagnosis of ESRD.

Upon arrival all patients were clinically evaluated and laboratory procedures repeated after which they were accepted for maintenance hemodialysis program.

During their follow up they were given a standard diet and supported with necessary measures and maintenance therapy. They were admitted to the hospital three times weekly on ambulatory basis and after hemodialysis of 4.7 hours they were allowed to return their homes. The group of 49 patients, results of which are presented in this communication were randomly chosen from among the large series on maintenance dialysis therapy regimen taking particular note that none had any special features distinguishing them from the rest and that they were representative of the large group.

Samples were removed from the patients before, during and at the end of the dialysis. After routine washing with water,

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detergents and acid all glassware and equipment used, were additionally rinsed several times with de-ionized water. All procedures were carried out with special precautions to prevent contamination. Trace elements were measured using a Cathode on Alpha-4 atomic absorption spectrophotometer. The results were subjected to statistical analysis.

## RESULTS

### Clinical observations

The patients clinical status improved under the prescribed regime in a few days. They remained ambulatory with no serious clinical complications. At the time of arrival their mean blood urea nitrogen was above 150 mg/dl, serum creatinine over 10 mg/dl and creatinine clearance less than 10 ml/min at the time of their admission. Their other blood parameters were as follows: Ca 7.20 mg/dl, phosphorus 5.9 mg/dl, hemoglobin 9.39 g %, hematocrit 26.80%, serum protein 6.96 g/dl, albumin 3.47 g/dl, transferrin 2.26 g/dl.

Table 1: The number of patients complaining of zinc deficiency symptoms.

	Female patients (n = 17)	Male Patients (n = 32)
Anemia	8	15
Alopecia	5	10
Amenorrhea	12	-
Impotence	-	13
Loss of libido	?	6
Anosmia	9	22
Significant loss of weight	9	11

Under the MHP the patients remained in stabilized clinical status with no significant complications. The general complaints enumerated above (anemia, fatigue, osteodystrophy etc.), however supervened despite which they were quite satisfied accepting them phylosophically as the 'realities of life from then on' (Table 1).

Table 2: Laboratory findings of patients while on MHP.

Hemoglobin	9.39±1.61 g/dl
Hematocrit	26.80±1.09 %
Serum total protein	06.96±0.27 g/dl
Serum albumin	03.47±0.10 g/dl
Serum zinc	60.00±1.21 µg/dl
Serum Cu	88.43±3.36 µg/dl
Erythrocyte zinc	1175.28±55.88 µg/dl
10 <sup>10</sup> erythrocyte zinc content	11.29±0.24 µg/dl

### Laboratory findings

Serum zinc level was 60.69±1.21 µg/dl this figure was significantly lower ( $p<0.05$ ) than the normal controls (93.2±1.8 µg/dl). Serum copper levels were 88.43±3.36 µg/dl also significantly lower ( $p<0.05$ ) than control group (103.2±2.4 µg/dl).

10<sup>10</sup> erythrocyte zinc content was 11.29±0.24 µg and erythrocyte zinc was 1175.28±55.88 µg/dl both significantly lower ( $p<0.05$ ) than the control values (13.9±0.5 µg and 1340±46 µg/dl respectively) (Table 2).

### DISCUSSION

Zinc and copper metabolism of patients with end stage renal disease (ESRD) was studied earlier by several investigations (3, 4, 6-10). Their serum levels were mostly found below normal values. Some investigations have observed zinc content of leukocytes, erythrocytes and that of hair below normal values in patients with ESRD (5). Our results confirm these observations recorded in the literature with the only difference that the level of reduction was more exaggerated in our series (Table 1). Zinc deficiency in patients on maintenance hemodialysis thus appears at the present time as a proven fact (11-15). Its pathogenesis, however, has not been clearly uncovered (11, 15, 17). Protein - calorie malnutrition, malabsorption and iatrogenically induced inadequancies, may all be contributing factors (4). The fact however that all of our patients were receiving a diet with limited protein content may be one of the most important factors (17). This diet according to the food analysis tables provides only 10.77 mg elemental zinc, while the advisable optimal daily zinc requirement for adult human is 15 mg (12, 17, 18). Foods such as meat, fish, cheese, chicken, nuts, almonds, parsley which are rich in Zn content were severely limited in their ration (12, 16, 18). It is therefore obvious that whatever other contributors may be dietary restriction appears as the primary cause of Zinc deficiency in our patients.

Serum levels of total blood protein and especially of albumin in patients with ESRD are usually low (19). In our own series serum total protein was also at the lower level of normal and that of albumin was significantly below normal values. Furthermore in our patients Zn levels were reduced in parallel with serum total proteins, serum albumin, hematocrit and hemoglobin ( $p<0.05$ ).

Serum copper levels on the other hand were below normal in 49 patients ( $p<0.05$ ) but not as much reduced as serum Zn, hematocrit and hemoglobin levels.

Our results appear contrary to the findings reported in the literature where an inverse relationship has been observed between copper and zinc (20). We observed in this study and reported (21, 22) in our earlier communications that in many cases a parallel reduction of these two trace metals occurs. We believe this correlated

diminution perhaps reflects the dietary nature of these trace metal deficiencies (12-14, 23).

Review of the literature thus indicates that zinc deficiency is a constant corollary of patients with ESRD maintained on hemodialysis (4, 5, 12). Our patients revealed even lower figures for blood and tissue zinc levels which was probably due to severe dietary limitation.

A more important point concerns treatment of these patient with zinc supplementation. Several investigators have reported successful restoration of zinc values in these patients with ESRD which was commensurate with clinical improvement: Amenorrhea, impotence, loss of libido allow which improved after return of zinc levels to normal (4, 7, 24). There are however in the literature reports stating that despite zinc treatment the clinical status of the patients remained unchanged (25, 26). This point therefore warrants further investigation.

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