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ZINC AND COPPER IN CONGESTIVE HEART FAILURE*

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In this study serum zinc (Zn) and copper (Cu) levels in children with congestive heart failure (CHF) were evaluated. The mean serum Zn levels of the patients with CHF were 92.9±18.9 μg/100 ml, and they showed a significant decrease when compared to controls ($p<0.05$). The mean serum Cu levels, which were 173.6±26.6 μg/100 ml, showed a significant increase when compared to controls ($p<0.001$). After digoxin therapy, a significant increase in Zn levels and a significant decrease in Cu levels were observed. *Key words: congestive heart failure, zinc, copper.*

Zinc (Zn) has a key role in many essential enzyme systems including carbonic anhydrase, alkaline phosphatase, carboxypeptidases and glutamic dehydrogenases. It is also essential in the metabolism of nucleic acid, in the synthesis of proteins and collagen, and is concentrated in cardiac tissue[1-3].

Like Zn, copper (Cu) is also an essential trace element. The role of Cu in maintaining collagen integrity is well established and deficiency of this metal has been shown to produce myocardial friability and necrosis. Copper is concentrated in ventricular muscular tissues. In the heart, the major Cu-containing enzyme is cytochrome oxidase[1,3].

In recent years, attention has been drawn towards such trace elements as Cu and Zn in the myocardium which are involved in the maintenance of myocardial integrity. The role of Cu and Zn in acute myocardial infarction in adults has been reported by many workers. In the pediatric age-group there are only a few investigations on the relation of these trace elements to myocardial ischemia and congestive heart failure[4]. The present study was therefore undertaken to explore the diagnostic and prognostic significance of serum Cu and Zn in congestive heart failure (CHF) of children

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Material and Methods

Twenty-nine cases of CHF admitted to the Pediatric Clinic of Dicle University Hospital constituted the material for the present study. Eleven healthy subjects matched according to age and sex served as controls.

The diagnosis of CHF was based on the physical examination. The patients had only received digoxin therapy for CHF. The doses were 0.06 mg/kg for patients under two years of age and 0.04 mg/kg for patients above two years of age. In each case blood was taken to determine the Zn and Cu levels and was kept in a polypropylene tube free of trace elements. After centrifugation the serum was kept at –5°C. In every patient two samples were obtained, one before the initiation of digoxin therapy and the other after the end of the therapy.

Serum Zn and Cu levels were measured by using the Atomic Absorption Method with the Varian Techtron Model 1300 spectrophotometer[1]. The results were expressed as the Mean ± Standard Deviation. Student's *t* test (dependent or independent) was used for statistical analysis[5].

Results

The ages of the patients with CHF ranged between one month and eleven years, with a mean age of 2.3±1.5 years. The ages of the controls were between three months and ten years, with a mean age of 3.1±2.8 years ($p>0.05$). Forty-one percent of the patients were girls and 59 percent were boys. Forty-five percent of the controls were girls and 55 percent were boys ($p>0.05$).

The cause of CHF was pneumonia in twenty patients; cardiomyopathy in three; rheumatic carditis in four, and pericarditis in two. The duration of therapy was between 5-12 days, with a mean 6.8±1.8 days.

The serum Zn and Cu levels of the patients with CHF were evaluated before and after therapy and were compared with the control group (Table I).

The mean serum Zn levels before therapy were 92.9±18.9 μg/100 ml, and they showed a significant decrease in the cases of CHF when compared to the

TABLE I: Serum Zn and Cu Levels* in Patients with CHF Before and After Therapy

Groups	n	Serum Zn** (μg/100 ml)	Serum (μg/100 ml)
t Control	11	107.5±15.7	113.9±16.2
I CHF before therapy	29	92.9±18.9**	173.6±26.6***
II CHF after therapy	29	107.4±17.2***	151.4±27.3***

* Mean±SD
Comparison with controls **$p<0.05$, ***$p<0.001$.

controls ($p<0.05$). After therapy, the mean serum Zn levels were 107.4±17.2 μg/100 ml. No statistically significant difference was observed when compared to the controls ($p>0.05$).

The serum Zn levels of the patients with cardiac failure showed a significant increase after therapy when compared to the levels before therapy ($p<0.001$; Figs. 1 and 2).

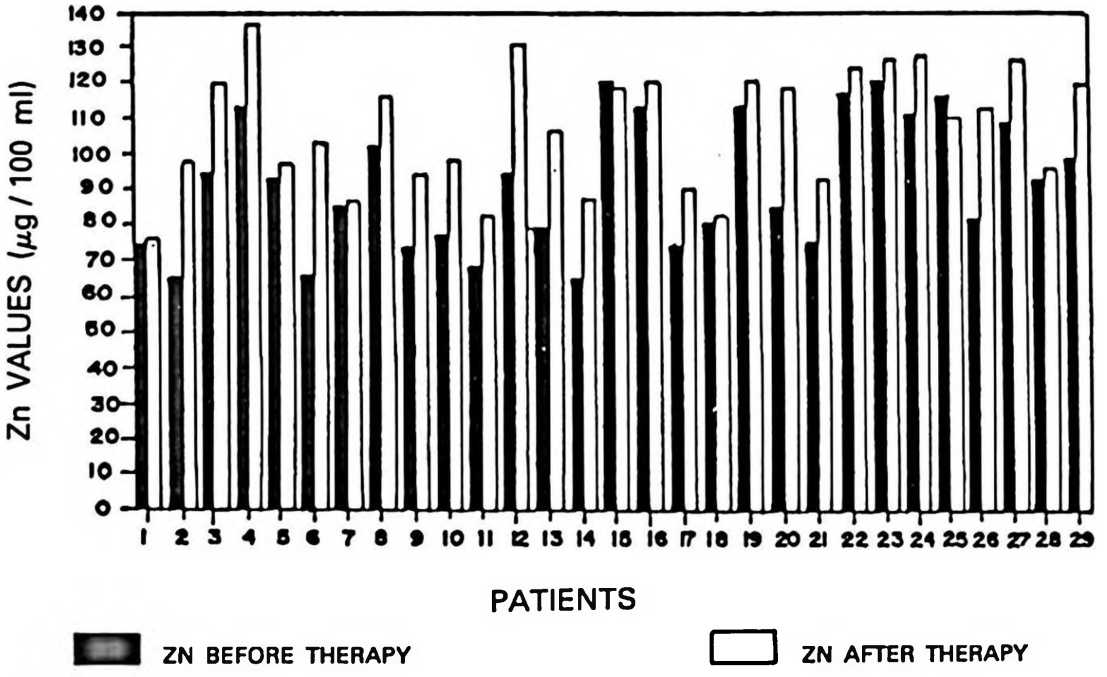

Fig. 1: Zn levels before and after therapy

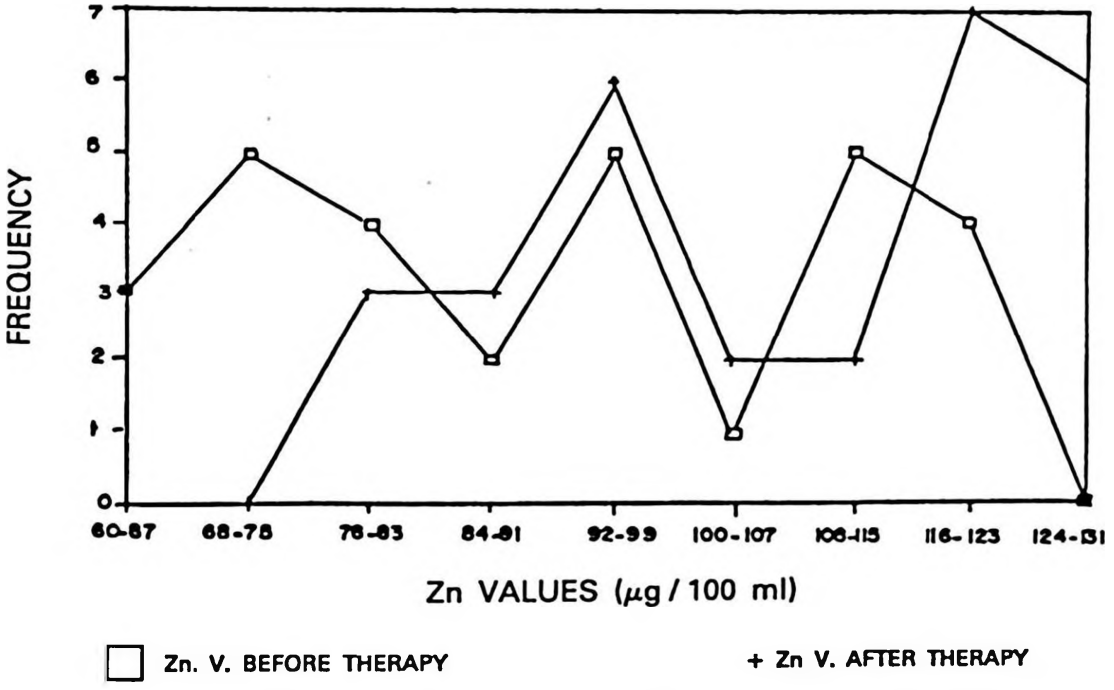

Fig. 2: Distribution of Zn levels before and after therapy

The mean serum Cu levels of the patients with CHF before digoxin therapy were 173.6±26.6 μg/100 ml. The mean serum Cu levels were significantly elevated when compared to the controls ($p<0.001$). After the therapy the mean serum Cu levels were 151.4±27.3 μg/100 ml. A significant difference was still present when compared to the controls ($p<0.001$). The serum Cu levels showed a significant decrease in the patients with CHF after therapy when compared to the levels before therapy ($p<0.001$). Copper levels before and after therapy, and the distribution of Cu levels are given in Figs. 3 and 4.

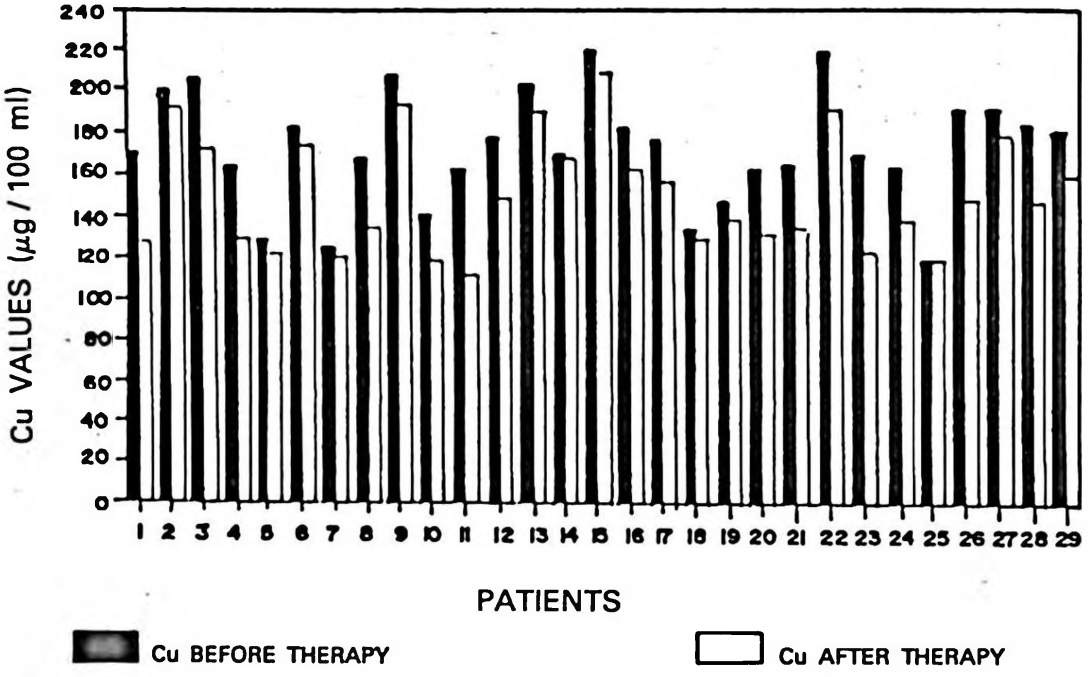

Fig. 3: Cu levels before and after therapy

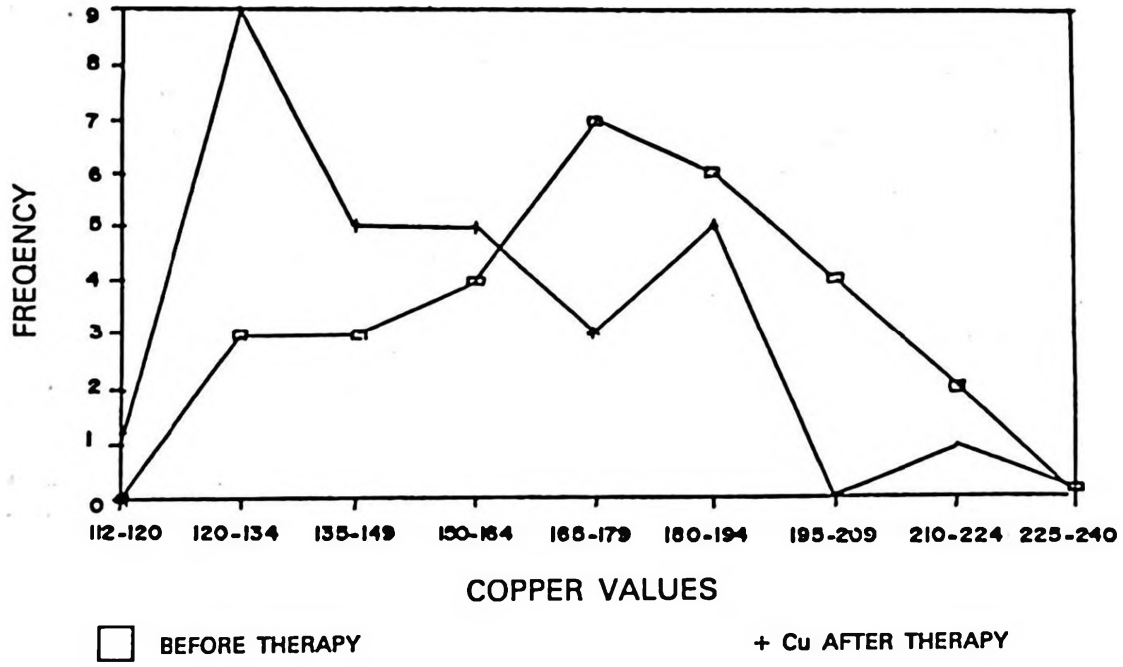

Fig. 4: Distribution of copper levels before and after therapy

Discussion

The role of Zn and Cu in enzymatic reactions has been examined critically as a potential key factor in cardiovascular diseases. In acute myocardial infarction decreased plasma Zn levels have been reported. In myocardial ischemia, however, slightly higher than usual serum Zn levels suggest that the net effect of cardiac ischemia is a release of Zn[1,3,6-9].

However, not much data is available regarding the relationship of Cu with cardiac disease. Elevated Cu levels have been reported in rheumatic heart diseases, CHF and atheriosclerotic heart diseases[1,6,7,10,11].

In the present study, we observed that serum Zn levels were significantly lower in CHF. The precise origin of the decrease in serum Zn concentration following CHF is not known. Hypoxic injury of myocardial tissue may increase the activity of leukocyte endogenous mediator (LEM) which mediates the hepatic uptake and sequestration of circulating Zn[1,3,12]. It is not known whether infectious or inflammatory stress precipitates a drop in circulating Zn levels. In CHF secondary to pneumonia, the reason for the decrease can be explained by infection but Zn levels were also decreased in cases of CHF due to cardiomyopathy and rheumatic carditis.

Serum Cu levels were significantly higher in CHF. Increased synthesis or decreased breakdown of ceruloplasmin by the liver has been suggested as an explanation for the increase of Cu in CHF. A rise in cerulaplasmin and hence serum Cu is related to the passive congestion in the liver[10,13].

Further investigations are needed to explain the variations in serum and tissue Zn and Cu levels in CHF.

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