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SHORT COMMUNICATION

ZINC COUNTERACTS EXPERIMENTALLY - INDUCED CIRRHOTIC CHANGES IN RATS

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Abstract : In the present study, cirrhosis was induced in rats by administration of carbon tetra chloride for 8 weeks. In these animals $ZnSo_4$ (equivalent to 100 and 200 µg of zinc) was administered orally and liver function tests and plasma zinc (Zn) estimations were carried out after 2 and 4 week intervals. The results revealed that Zn supplement counteracts cirrhotic changes in liver.

Key words : cirrhosis zinc liver function tests

INTRODUCTION

Role of trace elements like zinc (Zn) has received considerable attention during last few decades in various physiological processes. The discovery of Zn in many highly purified enzymes has revealed the diversity of its functions in Protein and Carbohydrate metabolism. Several Zn dehydrogenases have been discovered in the liver which led to the study of Zn metabolism in cirrhosis. It has also been reported that serum Zn concentration is lowered in cirrhosis (1). Hence it was proposed to induce cirrhosis experimentally in albino rats and to evaluate the effect of Zn on these animals.

METHODS

Male albino rats (n = 42) weighing 100 – 150 gm were used in this study. They were fed on a diet which contained 10 gms of rice and bengal gram. The dietary Zn value was estimated to be 140 µg by atomic absorption Spectrophotometry. The animals were administered carbon tetra chloride ($CC1_4$) in a dose of 0.15ml/100 g bw (2) mixed with equal volume of liquid paraffin, orally for 8 weeks on alternate days. A separate group of control animals (n = 6) received only liquid paraffin. At the end of 4 weeks, blood was collected from 6 animals to assess the liver function and the plasma Zn value was determined. $CC1_4$ administration was continued till 8 weeks. At the end of 8 weeks 6 animals were sacrificed and SGOT (3) SGPT (4) ALP (5) and Plasma Zn (6) were measured to test liver function. Liver was subjected for histopathological examination. The remaining animals (n = 30) were divided into 3 groups. Group I (n = 12) received 100 µg Zn per day orally and Group II (n = 12) 200 µg Zn. At the end of 2nd week, 6 animals were sacrificed in each group and all the above estimations were carried out. In the rest of the animals Zn administration was continued for two more weeks and the above said parameters were repeated. The III Group of animals (n = 6) left without Zn therapy, were sacrificed at the end of 4th week and the liver function tests were carried out.

RESULTS AND DISCUSSION

Oral administration of $CC1_4$ produced definite cirrhotic changes in rats. This was evident from the elevated levels of SGOT, SGPT, ALP, observed in these animals, compared to the vehicle treated control group. The plasma Zn level was also significantly reduced in these animals (Table I). Histological examinations also revealed diffused inflamatory infiltration and fibrotic changes (not shown).

After oral Zn administration, there was a restoration in these enzyme levels. This restoration was

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TABLE I : Effect of CCl_4 on liver functions and plasma zinc.

Group	SGOT (IU/L)	SGPT (IU/L)	ALP (IU/L)	Plasma zinc (μg/100 ml)
Control (n = 6)	62 ± 1.92	45.1 ±1.34	54.8 ± 1.98	101.9 ± 5.25
Cirrhotic 4th Wk (n = 6)	145.6 ± 3.34***	157.8 ± 4.34***	207.7 ± 3.1***	66.0 ± 1.13***
8th Wk (n = 6)	207 ± 3.79***	209.5 ± 3.45***	280.2 ± 4.78***	48.1 ± 2.52***

ALP = Alkaline Phosphatase ; Values represent Mean ± SEM

time and dose dependent. The return of these enzyme levels to near normal values was achieved after 4 weeks of 200 μg Zn treatment. However, the restoration was of lesser magnitude with 100 μg Zn (Table II). Histology not shown.

concomitant rise in plasma zinc levels. Histological examination after 4 weeks of 200 μg Zn supplementation revealed improvement in liver cytology - picture not shown.

With the available data, it may not be possible to

TABLE II : Effect of oral zinc on liver functions after CCl_4 induced cirrhosis.

Group		SGOT (IU/L)	SGPT (IU/L)	ALP (IU/L)	Plasma Zinc (μg/100 ml.)
Cirrhotic Control	2 Wk	200 ± 2.0	192 ± 3.0	272 ± 2.4	44.6 ± 1.8
	4 Wk	193 ± 7.0	186 ± 6.3	234 ± 3.2	52.1 ± 3.2
100 μg Zn	2 Wk	111.3 ± 3.95	105.89 ± 3.9	186.22 ± 2.64	75.56 ± 1.31
	4 Wk	62.25 ± 1.53*	62.75 ± 2.1*	179.0 ± 1.96*	133.75 ± 2.87*
200 μg Zn	2 Wk	85.56 ± 1.51*	78.23 ± 1.0*	157.33 ± 2.61*	90.78 ± 1.21*
	4 Wk	52.38 ± 1.74*	48.88 ± 1.44*	136.63 ± 1.47*	161.0 ± 1.85*

ALP = Alkaline Phosphatase ; Figures denote mean ± SEM
*P < 0.001 – compared to corresponding values observed in cirrhotic control group at respective intervals.

When CCl_4 is administered in rats to produce cirrhosis, the reversibility of the disease depends on the number and the interval of the doses. With more than 20 doses given at short intervals an irreversible cirrhosis is produced (7). The cirrhotic changes are reflected in the elevations of the levels of various enzymes and a deficient state of Zn is noted. Zn supplement appears to reverse this cirrhotic process as evidenced by the decrease in the enzyme levels and a define the exact role of Zn in restoring normal liver functions. There are evidences (8) that Zn may exert its effect by improving inflammatory reaction and (or) increase the rate of cellular mitosis and protein synthesis due to enhanced activity of DNA polymerase and reverse transcriptase (Zn containing enzymes) involved in cell mitosis.

Thus Zn may be a tool in ameliorating the symptoms of liver disorders due to cirrhosis.

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