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Crescent Journal of Medical and Biological Sciences
Vol. 5, No. 4, October 2018, 377–380
eISSN 2148-9696

Zinc Level in Non-Cirrhotic Chronic Liver Disease and Cirrhosis: A Brief Report

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Abstract

Objectives: In this report, it was intended to evaluate the zinc serum level in cirrhotic patients (with or without encephalopathy) and patients with non-cirrhotic chronic liver disease.

Materials and Methods: In the current analytic cross-sectional study, 75 patients were studied including 25 non-cirrhotic patients with chronic liver disease, 25 patients with liver cirrhosis, and 25 cirrhotic patients with hepatic encephalopathy. Then, the serum zinc levels of their blood samples were measured by spectrophotometry.

Results: The average of zinc level was significantly lower in those patients who consumed diuretics or those with ascites ($P<0.0001$). In addition, the average of zinc level concentration was lower in patients with hepatic encephalopathy than patients without encephalopathy and non-cirrhotic chronic liver disease. Generally, the average of zinc in cirrhotic patients was lower than non-cirrhotic patients and in the group of child A it was higher than child B ($P=0.025$) and child C ($P=0.003$).

Conclusions: In overall, the serum level of zinc was lower in patients with cirrhosis and those who consumed diuretics as compared to non-cirrhotic patients. The reduction of zinc in these patients may be due to less consumption of meat compounds as a rich source of zinc and also the consumption of diuretics that causes increased urinary excretion of the zinc.

Keywords: Cirrhosis, Ascites, Hepatic encephalopathy, Zinc, Diuretics

Introduction

With regard to the high prevalence of cirrhosis, doing any research in this context and achieving useful results could encompass the whole range of patients. Many clinical symptoms of zinc deficiency such as decreased appetite, protein metabolism disorder, dysfunction of immune system, and delayed healing wounds are similar to clinical symptoms of cirrhosis (1).

The reduction of zinc disrupts the recovery and regeneration of liver cells. Zinc improves the protein synthesis of hepatic cells (1). Considering the effect of zinc on stability of membrane, zinc deficiency can cause dysfunction of the blood-brain barrier, facilitate crossing ammonia, and provide hepatic encephalopathy (2). Zinc plays a role in ammonia detoxification in the liver and muscles, so that zinc has a cofactor role for the enzyme glutamine synthetase in muscles and for the enzyme ornithine transcarbamylase in the liver (3); therefore zinc deficiency is expected to disrupt the process of ammonia detoxification which accordingly can provide a circumstance for hepatic encephalopathy (4). Additionally, it is believed that the serum levels of zinc are low because the consumption of protein compounds especially meat as a rich source of zinc, is less in these patients. Since there is a misconception that protein compounds can provide encephalopathy through increasing the level of ammonia. Besides, congestive gastroenteropathy in cirrhotic patients disrupts the intestinal absorption of zinc. More importantly, the consumption of diuretics is prescribed for eliminating the edema and ascites which results in increasing the urinary excretion of zinc and therefore reducing plasma level of the zinc (5). Therefore, in this study, attempts have been made to check the zinc level in cirrhotic patients with or without encephalopathy and patients with non-cirrhotic chronic liver disease.

Materials and Methods

After approval of the proposed project by Research Assistance of Tehran Medical University and Medical Ethics Committee, 75 patients from Imam Khomeini hospital of Tehran were studied (during October 2015 to 2016). This study was an analytic cross-sectional research. The main variable of the study is zinc serum level of fasting blood in patients. Patients were divided into 3 groups; patients

Received 1 September 2017, **Accepted** 20 April 2018, **Available online** 9 July 2018

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with non-cirrhotic chronic liver disease (n = 25), those with hepatic cirrhosis without encephalopathy (n = 25), and patients with overt hepatic encephalopathy (n = 25). Then, their venous blood samples were stored at -70°C and after completing the samples with Alycon 300 USA by spectrophotometric method, serum levels of zinc were measured and compared with each other. At first, normal distribution of the quantitative data was measured by one sample from Kolmogorov–Smirnov method. The analysis of variance (ANOVA) was used for quantitative data of these 3 groups. With regard to the significant difference, for pairwise comparison Scheffe method was applied. For comparison of a quantitative variable in qualitative groups and the relationship between quantitative variables *t* test (Mann-Whitney test was run to check if there was an abnormal distribution and chi-square methods were used, respectively.

The inclusion criteria for cirrhosis was the diagnosis based on biopsy; and for overt hepatic encephalopathy the diagnosis was based on clinical findings and ruling out the metabolic and traumatic causes. Fasting plasma level of zinc was measured through normal values in males (72.6-127) and females (70-114). Ages of patients ranged from 18 to 80 years.

The exclusion criteria for the study was the consumption of zinc supplements, malignant diseases, acute renal failure and hepatic fulminant, grave function of renal (GFR <60 cc/min), patients with known zinc deficiency, and those with alcoholic liver disease (chronic consumption of alcohol).

In this study, no intervention or therapy was conducted on patients and the only additional diagnostic procedures was to measure the zinc level which was performed per day for the patients during taking their blood samples.

Results

There was not any significant difference between the 3 groups in terms of gender ($P = .2$) and age ($P = 0.17$) and the comparison of zinc level average did not show a significant difference across the genders (99.5 mg/dL in men compared with 92.4 in women) (Table 1). The comparison of zinc level average in terms of diuretics consumption by separating the 2 groups of cirrhotic showed a significant difference. In both groups, zinc average was less especially in the group that had consumed diuretics (Table 2). The comparison of zinc level average showed a significant difference in terms of diuretics consumption in all cirrhotic patients, so that in the group that had diuretic consumer, it was lower (104 compared with 7.07; $P < 0.0001$). The comparison of zinc level average displayed a significant difference in terms of ascites by separating both cirrhotic groups. Considering both groups, zinc average was less in the group that had ascites. The comparison of zinc level average showed significant differences in terms of the presence or absence of ascites in all of cirrhotic patients, so that in the group with ascites it was lower (102.5 compared with 76.8; $P < 0.0001$) (Table 3). The comparison of zinc level average did not show a significant difference (105.5 compared with 100; $P = 0.6$) in terms of the presence or absence of ascites in the case that the patients did not consume diuretics, (Table 4). The comparison of zinc level average showed a significant difference in terms of child; in pairwise comparison it was found that zinc average was more in child A group than child B group ($P = 0.025$) and child C ($P = 0.003$) (Table 1). Zinc average in child B had not a significant difference between both cirrhotic groups ($P = 0.10$). In addition, zinc level average in child C did not show a significant difference between the 2 cirrhotic groups ($P = 0.6$). Zinc level average, in terms of child, was

Table 1. Characteristics of the Evaluated Groups

	Non-cirrhosis	Non-encephalopathic Cirrhosis			Encephalopathic Cirrhosis		
The number of patients	25	25			25		
Average in terms of age	45	41.8			48		
Number in terms of gender							
Man (zinc level average)	14 (112)	9 (96.4)			14 (70.2)		
Woman (zinc level average)	11 (111.4)	16 (99.8)			11 (87)		
The average of zinc concentration, mg/dL	111.7	99.6			77.7		
Child- Pugh		A	B	C	A	B	C
		9	10	6	0	14	11
The consumption of diuretics							
No	0	15			11		
Yes	0	10			14		

Table 2. The Effect of Using Diuretics on Zinc Level in Patients With and Without Encephalopathy.

Group	Consumption of Diuretics	Number	Average of Zinc Level	*P*
Cirrhotic without encephalopathy	No	15	111	<0.0001
	Yes	10	79.8	
Cirrhotic with encephalopathy	No	11	94.8	0.003
	Yes	14	64	

Table 3. The Effect of Ascites on Zinc Level in Patients With Using Diuretics.

Ascites	Number	Average of Zinc Level	*P*
No	22	102.5	<0.0001
Yes	28	76.8	

Table 4. The Effect of Ascites on Zinc Level in Patients With0ut Using Diuretics.

Ascites	Number	Average of Zinc Level	*P*
No	20	105.5	0.6
Yes	6	100	

not different in the group that did not consume diuretics ($P=0.1$). The comparison of zinc average in terms of child in cirrhosis without hepatic encephalopathy showed a significant difference and in group B was less than A ($P=0.01$), but did not reveal a difference in patients with hepatic encephalopathy ($P=0.6$). In pairwise comparison it was shown that there was a difference between child A and C ($P=0.007$).

The average of zinc concentration in patients with hepatic encephalopathy (87 mg/dL average) was lower than cirrhotic patients without encephalopathy (88.1 average) and non-cirrhotic patients (112 average), so that in pairwise comparison the difference was significant between zinc average in cirrhosis with encephalopathy and cirrhosis with non-encephalopathy ($P=0.007$), and also there was a significant difference between zinc average in cirrhotic patients with encephalopathy and non-cirrhotic patients ($P=0.0001$).

Discussion

The results obtained in the present study are consistent with the findings of the study by Chiba et al, in Japan. They founded that in cirrhotic patients, treatment with diuretics increased zinc excretion by suppressing its renal reabsorption, which may result in zinc deficiency (5). Sengupta et al, also founded that zinc deficiency was widespread in Child-Pugh score B or C, and with MELD score ≥15 cirrhotic patients. Disease severity had been also related to the zinc deficiency (6). Anber et al found this relation with cirrhosis caused by hepatitis C virus (HCV) (7).

In our study, comparing the concentration of zinc in non-cirrhotic patients with cirrhotic patients (a total of 50 cirrhotic patients with and without hepatic encephalopathy), it was concluded that zinc average was higher in non-cirrhosis (111 mg/dL) than cirrhosis (88.1 mg/dL).

Another question and secondary goal of the project was the comparison of zinc average in patients based on consumption or non-consumption of diuretics (a total of 50 patients with cirrhotic, 24 patients had consumed diuretics and 26 patients did not consume diuretics). Comparing zinc average it was revealed that there was a significant difference between both groups (104.2 mg/dL in comparison with 70.7, $P<0.0001$). In other words, zinc average was significantly lower in group of diuretics consumers. This case was not evaluated in previous studies. A total of 50 patients with cirrhosis were 28 patients with ascites and 22 patients without ascites that the average of zinc concentration in them had a significant difference (70.7 mg/dL in comparison with 102.5; $P<0.0001$), specifically, in the group with ascites zinc level of plasma was significantly lower which is similar to the results of Rahelic et al (8).

However, the important point is that the recent comparison is taken without the consumption of diuretics as a confounding factor and therefore, for solving this problem, zinc levels were compared in cirrhotic patients with ascites and cirrhotic patients without ascites that did not consume diuretics. It was found that there was no significant difference (105 in comparison with 100; $P=0.6$). Conversely, in examining the average of zinc concentration the following results were obtained based on Child-Pugh classification. Zinc level average in child-A group was significantly higher than child-B group ($P=0.25$) and child-C group ($P=0.003$).

It seems that one of the factors reducing the level of zinc in child B and child C is the consumption of diuretics as a confounding factor since none of the 9 patients consumed diuretics in group A. Therefore, to solve this problem, patients of child A, B, and C groups who did not consume diuretics were compared, and no significant difference was observed between 3 groups (child A = 112 average, child B = 100, and child C = 92). To confirm this subject, the average of zinc concentration showed no significant difference in child-B in both cirrhotic patients (with and without hepatic encephalopathy) ($P=0.1$; 96 mg/dL in comparison with 79) and also zinc level average did not show a significant difference in child-C in both cirrhotic patients (with and without hepatic encephalopathy) as well ($P=0.6$; 81 mg/dL in comparison with 78).

Conclusions

In overall, the serum level of zinc in patients with cirrhosis is lower than non-cirrhotic patients and its level is lower in diuretics consumers. The reduction of zinc in these patients may be due to less consumption of meat compounds as a rich source of zinc and also the consumption of diuretics that causes increased urinary excretion of zinc.

Suggestions for Further Research

The practical purpose of this study was to provide a basis for future research projects, therefore, it is suggested that in future researches the zinc compounds be given to patients with hepatic encephalopathy during the interventional study and their effect be evaluated in

preventing or reducing the likelihood of future attacks of hepatic encephalopathy.

Conflict of Interests

None.

Ethical Issues

The proposed project was approved by Research Assistance of Tehran Medical University and Medical Ethics Committee.

Financial Support

The present study has been supported by Tehran University of Medical Sciences.

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