

Serum Levels of Copper, Zinc, Iron and Magnesium in Iraqi`s Patient with Chronic Hepatitis C

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Abstract

Objective: This study was conducted to determine the alterations in serum trace elements, including zinc (Zn), copper (Cu), iron (Fe), and magnesium (Mg) in patients with chronic hepatitis C and to compare the results with those of age and sex matched healthy individuals.

Methods: The study was carried out in Medical Research Unit, College of Medicine, Al-Nahrain University from 2009-2010. One hundred and ten subjects, 60 patients with chronic hepatitis C and 50 healthy individuals were included in this study. The serum zinc, copper, iron and magnesium concentrations were measured by using atomic absorption spectrophotometry.

Results: Serum zinc, copper, iron and magnesium concentrations were found to be 1.081 ± 0.08 , 1.143 ± 0.025 , 0.0819 ± 0.0188 and 27.455 ± 0.409 mg/L respectively in patients with chronic hepatitis C and 1.086 ± 0.4680 , 1.103 ± 0.326 , 0.0339 ± 0.0066 and 16.80 ± 0.56 mg/L in healthy individuals, respectively. Serum iron was exhibited to be elevated significantly ($p < 0.01$) and magnesium was observed to be decreased significantly ($p < 0.01$) in patients when compared with those of the control group. However zinc and copper remained without significant variants.

Keywords Zinc; Copper; Iron; Magnesium; Hepatitis C

المخلص

الأهداف: كان الهدف من الدراسة: تعيين التغيرات في تراكيز العناصر النادرة (النحاس، والزنك، والحديد، والمغنسيوم) في مصول المرضى المصابين بالتهاب الكبد الفيروسي C ومقارنتها بالأشخاص الأصحاء. **الطريقة:** تم إجراء هذه الدراسة في وحدة البحوث- كلية الطب- جامعة النهرين، خلال الفترة 2009-2010، أخذت عينات مقدارها مئة وعشر أشخاص: ستون مصابا بالفيروس C؛ وخمسون من الأصحاء. تم قياس مستويات العناصر في مصول الدم بواسطة تقنية مطيافية الامتصاص الذري.

النتائج: كانت تراكيز الزنك، والنحاس، والحديد، والمغنسيوم كالتالي: 1.081 ± 0.08 و 1.143 ± 0.25 و 0.0188 ± 0.0819 و 27.455 ± 0.409 ملجم/لتر على التوالي في المرضى. و 1.086 ± 0.4680 و 1.103 ± 0.326 و 0.0066 ± 0.0339 و 16.80 ± 0.56 ملجم/لتر في الأصحاء. التحليل الإحصائي أظهر أن تركيز الحديد والمغنسيوم يرتفع في مصل الدم وبفرق معنوي عند ($p < 0.01$) في المرضى عند مقارنتها بالأصحاء. أما تراكيز الزنك والنحاس فلم تظهر تغييرا معنويا بين المرضى والأصحاء.

Introduction

Trace elements play important roles in diseases caused by virus. The change in trace elements might also be associated with various diseases ⁽¹⁾. The relationship between chronic

hepatitis and trace elements has not been understood clearly ⁽²⁾. Various trace elements are responsible for many biochemical, immunological, and physiological activities. Essential micronutrients are involved in many metabolic pathways in the liver, such as enzymatic functions, protein synthesis, oxidative damage and anti-

oxidant defense, immunological competence, interferon therapy response and alterations of the virus genomes⁽³⁾. Measurement of trace element in serum/plasma is easy and used commonly. Serum metal level has been reported to be highly sensitive in the diagnosis of liver diseases⁽⁴⁾. The concentration of each trace element varies with different types of liver diseases because these elements may have a direct hepatic toxicity or may be decreased as a consequence of the impaired liver function. Trace elements such as Zn, Cu, Fe and Mg are required for the immune system to function efficiently. The present study was undertaken to determine the trace element (Zn, Cu, Fe, and Mg) level in

serum and to compare the results with those of healthy individuals.

Material and Methods

The current study was conducted in the Medical Research Unit, College of Medicine, and Al-Nahrain University in Baghdad, Iraq between 2009 and 2010. The randomly selected study group comprised of 60 patients with chronic hepatitis C (40 males and 20 females) with ages of 39.5 ± 13.6 years. The control group comprised 50 healthy volunteers (24 males and 26 females) with ages of 33.4 ± 14.8 years, *see* in (Table.-1). Blood samples were collected from Al-Khadimiya Hospital- Baghdad-Iraq. All sera were collected in the morning.

Table 1. Age and gender distribution of control and HCV patients group

Group	Age (years)			Gender M/F
	N	Mean \pm SD	Range of years	
Control	50	33.4 ± 14.8	18-65	24/26
Patients (HCV)	60	39.500 ± 13.6	17-54	40/20

The healthy subjects were not alcoholic, or smokers, and free from acute or chronic pathologies, clinically evident at the moment of examination. Sera were collected from patients before drug administration. Patients with chronic hepatitis C were diagnosed through clinical, biochemical, and serological examinations.

Blood samples were taken from all subjects in accordance with standard procedure; five mL of blood was collected from the vein in evacuated tubes without adding any anticoagulants. Patients were newly diagnosed. Collected blood samples were allowed to clot. The blood samples were centrifuged at 3000 g for 10 min; sera were transferred and stored in plastic vials at -4°C until further analysis.

Trace elements analysis

Serum sample preparation

Sera were diluted 10 folds with de-ionized and analyzed by atomic absorption spectrophotometer AA 6200 Shimadzu (Kyoto, Japan) with computer.

Statistical analysis

Statistical analysis was performed using SPSS program, version 11.0. Variables were expressed as mean \pm standard deviation (SD). Data were analyzed using independent sample Student's *t* test. Significance was assigned for *p* values <0.05 with 95% Confident Interval.

Results

The serum Fe and Mg concentrations were found to be (Fe: 0.0819 ± 0.0188 mg/L) and (Mg: 27.455 ± 0.409 mg/L) in patients with viral hepatitis C, which was higher than that of controls (Fe: 0.0339 ± 0.0066 mg/L) and (Mg: 16.80

± 0.56 mg/L). Serum Cu and Zn concentrations remained without significant variations (Cu: 1.143 ± 0.025 mg/L) and (Zn: 1.081 ± 0.080

mg/L) compared with those of healthy individuals controls (Cu: 1.103 ± 0.326 mg/L, Zn: 1.0858 ± 0.4680 , at ($p < 0.05$), see (Fig.-1).

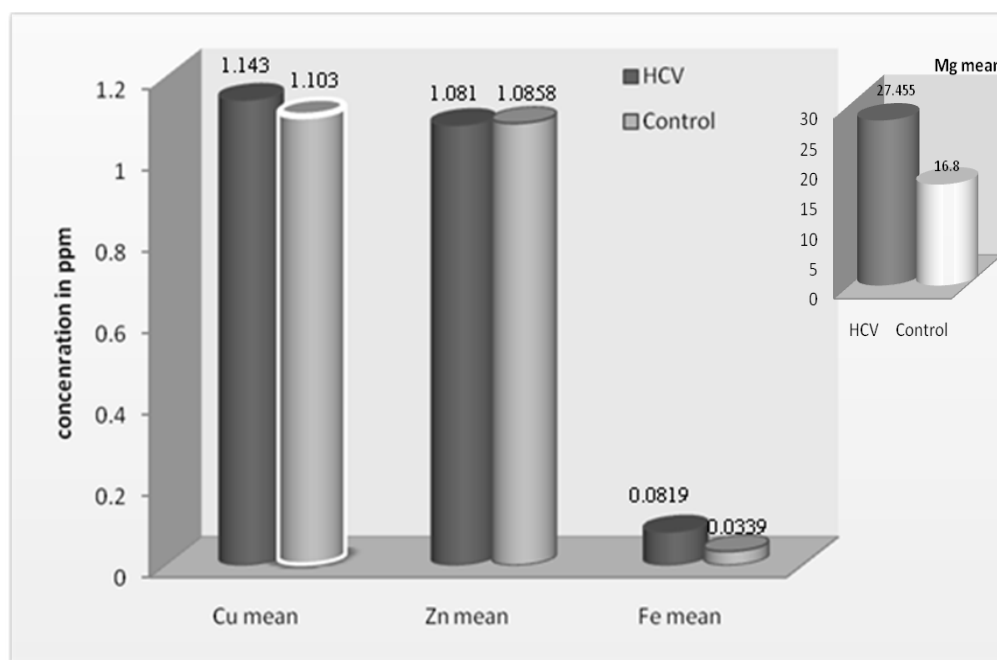


Figure 1. Serum Zn, Cu, Fe and Mg, concentrations (mg/L) in the control (n = 50) and the HCV patients (n = 60) shown as mean \pm SD ($p < 0.05$) and ($p < 0.01$).

Discussion

Trace elements play important roles in liver disease in particularly liver degeneration. The most important trace elements are zinc and copper⁽⁵⁻⁹⁾. It is reported that hypozincemia develops in cases of advanced liver damage and acute hepatitis⁽⁹⁾. Copper acts as a cofactor against hepatic fibrosis in chronic liver disease, particularly in the biosynthesis of collagen. As the disease progresses from chronic hepatitis to liver cirrhosis, serum calcium, magnesium, phosphorus and zinc concentrations decrease, while the copper concentration increases. These trace element abnormalities may reflect such pathological conditions as liver dysfunction, cholestasis, hepatic fibrosis or liver regeneration⁽⁶⁾. Pramoolsinsap *et al*⁽¹⁰⁾. Serum zinc levels were significantly decreased in patients with chronic active hepatitis,

cirrhosis, and hepatocellular carcinoma, and copper levels were significantly elevated only in patients with hepatocellular carcinoma. It was found that serum zinc levels correlated with bilirubin, albumin, and cholesterol levels, but not with daily urinary zinc excretion. Serum copper levels correlated with alkaline phosphatase and gammaglutamyl transferase. These results suggested that changes in liver cell pathology compounded by functional impairment might alter the metabolism of trace elements, in particular, zinc and copper. Yıldırım and colleagues⁽⁹⁾ compared serum and erythrocyte Zn levels in patients with acute hepatitis, asymptomatic carriers, and healthy control groups. They did not find any significant difference between groups. Kalkan *et al*⁽⁴⁾ determined serum trace elements including selenium (Se), Zn and Cu in sera of patients with viral hepatitis A,

B, C, D, E cases. The serum Cu level was found to be significantly higher in patients with viral hepatitis than in control groups. Both, Se and Zn levels found to be significantly lower in viral hepatitis. There was no difference among viral hepatitis groups classified in regard with agents and clinical manifestation, such as acute hepatitis B, chronic hepatitis B, C, D. They concluded that decreases in Zn and Se levels and elevation of Cu levels are probably result from defiance strategies of organism and were induced by the hormone-like substances. Pharmoolsinsap *et al*⁽¹¹⁾ compared serum zinc and copper levels in patients with acute hepatitis B and healthy groups. The patients had significantly decreased serum zinc but elevated copper levels. Ozbal *et al*⁽¹²⁾ examined the relationship between serum zinc levels and response to interferon-alpha therapy in children with chronic hepatitis B. They found that initial serum zinc and alanine aminotransferase levels were significantly higher in sustained responders than in non-responders. They concluded that serum zinc levels might be used as a factor predicting response to interferon-alpha therapy and may help in identifying those children with a better change of response. Salih *et al*⁽¹³⁾ measured the alterations in serum Zn and Cu in patients with chronic hepatitis C. They found unchanged serum zinc and copper concentrations in patients with chronic hepatitis C.

In our study, the serum level of Fe and Mg was elevated significantly in both HCV patients. These data on the relevance of Fe as a prognostic factor prompted us to ascertain whether HCV-related liver damage is mediated by Fe and Mg accumulation. We have also observed decreased total oxidative activity in both patient groups and hence increases in Fe generate reactive oxygen species

which may exceed the capacity of the antioxidant system and perpetuate oxidative stress to cells. Oxidative stress with the attendant low-grade inflammation is implicated in a number of pathological conditions, including aging, atherosclerosis, and diabetes⁽¹⁴⁾.

Serum Cu and Zn are essential trace elements for several metabolic processes. Regarding Zn, patients with chronic hepatic encephalopathy have been shown to have low serum Zn levels. Moreover, in a controlled study, significant improvement was seen in those patients on oral Zn supplementation⁽¹⁵⁾. In our patients with HCV, have shown both Zn and Cu levels in serum remained unchanged HCV patients. Various studies, both groups showed significantly decreased Zn levels, though content of Zn and selenium in plasma and erythrocytes were significantly lower in hepatitis C patients^(16, 17). Abdul Aziz *et al* have shown both Zn and Cu levels in serum remained unchanged HCV patients⁽¹⁸⁾. Our results show a similar tendency in HCV patients.

In conclusion, this study is the first one evaluating the alterations in serum status of zinc, copper, magnesium and iron in Iraqi's patient with chronic hepatitis C and healthy individuals. We concluded that serum essential trace elements Zn, Cu, Mg and Fe concentrations were probably altered by the some immune system as a defense strategy of organism during HCV infection. Further investigations will be needed to determine trace elements in liver tissue and leukocytes before and after treatment in order that the role of Cu, Zn, Fe, and Mg levels in patients with chronic hepatitis can be established.

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