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Compared levels of specific divalent trace elements in hyperlipidemia and hepatitis sera patients

Namama S. Hamad[1], Dler. M. Salh[1], Avan A. Ahmed[2].

1. Chemistry Department, School of Science, Faculty of Science and Educational Science, Sulaimaniyah University, Kurdistan Region, Iraq.
2. Ministry of Health. Central Lab. Sulaimani.

Corresponding Author E-mail: dlerchem@yahoo.com

Abstract

Patients with hepatitis infection can also have hyperlipidemia. Sera of both hepatitis (40) and hyperlipidemia (40) were collected from the central lab of Sulaimaniyah-Kurdistan region/ Iraq. Age, sex, duration of infection, medication used and lipid profile using computerized database program, as characteristics information of patients were done. The levels of Cr, Cu, Zn, Mn, V and Se were determined in sera of both patients and compared with healthy controlled (n=30), using Inductively Coupled Plasma-Optical Emission Spectrometry (ICP-OES). Hepatitis samples yielded concentration in ppb of (7.34±0.01) Cr, (171.7±2.51) Cu, (138±3.41) Zn, (1.309±0.99) Mn, (184.7±6.12) V and (218.9±3.14) Se respectively, while hyperlipidemia samples yielded concentration (ppb) of (5.22±0.45) Cr, (197.01±2.34) Cu, (160.3±4.01) Zn, (0.068±1.91) Mn, (247.01±0.65) V and (185.5±3.11) Se respectively. Controlled samples reflects the following concentrations (ppm), (5.324±1.34) Cr, (131.2±4.34) Cu, (216.6±0.83) Zn, (0.024±1.75) Mn, (235.3±0.18) V and (223.2±3.15) Se respectively.The aim of the study focused on evaluating metal ions physiological role in the body, and as liver was responsible for synthesizing lipid , thus lipid profiles where suggested to be investigated along the study.

Key words: hepatitis, hyperlipidemia, trace elements, ICP-OES technique

1. Introduction

Hepatitis and hyperlipidemia become a major human health problem worldwide (Sankaraya,S,S. *et al.*2004). It is not clear what the prevalence of hyperlipidemia is and how often hyperlipidemia is treated in patients with hepatitis. In addition, in those patients receiving cholesterol-lowering medication, it is not clear whether it is associated with worsening of liver synthetic function or not. In 1978, a comprehensive compilation of literature values (Iyengar GV. *et al* 1978). It served as a guideline for approximate concentrations of many elements in numerous tissues (Woittiez JRW 1983). exclusively investigated the problem of establishing reference values for 28 elements in human serum. Trace elements such as Cr, Cu, Zn, Mn, V and Se are essential nutrients for humans and are required in very small amounts for many physiological functions, including immune, antioxidant function, growth and reproduction (Cunnane,S,C. 1988). It has been determined that humans need nearly 72 trace elements, including very low concentration of heavy metals, such as Cu, Se, V, Cr, Mo, Mn and Co. Most metals are toxics at high concentrations, while other provokes deleterious effects at low concentrations (Rizk,SL 1984). For evample, Vanadium (VI) revealed a biological interest due to its biotoxicity (Rojas,E *et al* 1996). The significance of the biochemical and nutritional roles of trace elements is widely recognized, since metals are found as constituent components of many metalloproteins and metalloenzymes. Some trace elements such as Copper act as cofactors against hepatic fibrosis in chronic liver diseases. Trace elements also affect many aspects of lipids metabolism through enzymes action and have modulator effects on the synthesis and metabolism of lipids (Suzuki K. *et al* 1996). Zinc for example, functions as an antioxidant and stabilizes membranes; Selenium is an essential micronutrient for human health (Koo,I; % Williams D.A. 1981, Shankar AH, & Prasad AS. 1998, Rayman M.P 2000). The human body contain approximately ten milligrams of Mg most of which is found in the liver, bone and kidneys, it is a cofactor for a number of important enzymes, including arginase, pyruvate carboxilase and several phosphatase, peptidases and glycosyl transferase, Low levels of Mg has been associated with Atherosclerosis (Blaurock-Busch E 1997). We conducted a study to assess the relationship and changing of some trace elements between hyperlipidemia and hepatitis.

2. Material and Methods

The randomly selected study group comprised 40 patients with hepatitis that included 25 males and 15 females (aged 30±15.2), ranging between 25 and 60 years. Forty patients with hyperlipidemia were also included, 23 male and 17 females (aged 35±12.3) years. The control group comprised 30 healthy control groups, which included 19 male and 11 females aged between 20 and 63 years. Sera of patients and control were isolated from blood at the central lab (Sulaimaniyah- Kurdistan region/ Iraq). All sera were collected in the morning after fasting 8 hours. Patients with hepatitis were diagnosed based on clinical, biochemical and histological. Serum with hyperlipidemia also diagnosed based on increased concentration of cholesterol, triglyceride, HDL and LDL. Standard solution of the metals (1000 µg/ml of Cr, Cu, Mn, Zn, V and Se were prepared. Other chemicals were purchased from Fluka. Standard solutions were prepared freshly from the stocks, with diluted nitric acid (3 %v/v). In order to achieved ICP-OES responses, the experiments were performed using different concentration levels.

2.1 Sample Digesion:

1ml of serum was transferred to a Teflon beaker and 10ml of concentrated nitric acid and 2.5ml concentration perchloric acid were added. The sample was then brought very slowly to boiling on a hot plate and heated to dryness. If sample blackening occurred during the fuming stage, nitric acid was added drop wise, then the sample was cooled, dissolved again in distilled water and concentrated HCl (10:1) and brought to a volume of 25ml in a volumetric flask. The solution was analyzes against calibration curve (Nakyama,A.H *et al* 2002).

2.2 ICP-OES:

An inductively coupled plasma-Optical Emission Spectrometer has been extensively used in the analysis of major, minor and trace elements in biological material because of its high sensitivity, accuracy, low matrix effect and simpler operation. The presence of various elements in the sample was identified by determining the wavelength of the emitted radiation (Cu: 327.393nm, Se: 196.026nm, Zn: 213.857nm, Cr: 267.716, Mn: 257.610, V: 290.880) and the concentration was calculated by intensity of the radiation, which might be sufficiently low for certain applications with a simple matrix. Sample and standard were analyzed in triplicate (R.Selvaraju, *et al* 2009). Statistical analysis, using STATISTICAL program (statsoft) where applied for data analysis. A p-value of < 0.05 was considered statistically significant (Joaquim P. 2007).

3. Results

Serum concentrations of total cholesterol, HDL, LDL and triglyceride are represented in table (1). Patients with hyperlipidemia shows a significant decrease ($p<0.05$) in Zn serum (160.3±4.01) , (0.068±1.91) Mn and Se (185.5±3.11) ppb respectively compared with controls. While levels of Cu and V increased significantly ($p<0.05$) compared with those of control. No significant changes were found in case of Cr.

Table 1. Characteristics of both patients which shows same features.

No.	parameter	Mean ± SD
1	Body mass (kg)	55-85
2	Duration of disease (month)	5-15
3	S. cholesterol (mg/dl)	265-400
4	S.LDL	160-170
5	S.HDL	60-65
6	S. triglyceride (mg/dl)	200-499

Serum Cr, Cu, and Mn of hepatitis patients were significantly higher (17.53±0.01), (171.7±2.51) and (1.309±0.99) ppb respectively as compared to normal (Cr=5.324±1.34), (Cu=131.2±5.93) and (Mn=0.204±1.75) ppb. The serum Zn, V and Se level was (Zn=138.3±3.41), (V=184.7±6, 12) and (Se=218.9±3.41) ppb in patients with hepatitis which was higher than that of normal (216.6±0.83), (235.3±0.18) and (223.2±3.15) respectively, as shown in table (2). Results of this study have been summarized and show the overall comparison between trace elements in both case hyperlipidemia and hepatitis in figure (1).

Table 2. Concentrations of Cr, Cu, Zn, Mn, V and Se in healthy control hepatitis and hyperlipidemic patients

metals	Normal ppb	hepatitis ppb	Hyperlipidemia ppb
Cr	5.324±1.34	17.53±0.01	5.22±0.45
Cu	131.2±4.34	171.7±2.51	197.01±2.34
Zn	216.6±0.83	138.3±3.41	160.3±4.01
Mn	0.204±1.75	1.309±0.99	0.068±1.91
V	235.3±0.18	184.7±6.12	247±0.65
Se	223.2±3.15	218.9±3.41	185.5±3.11

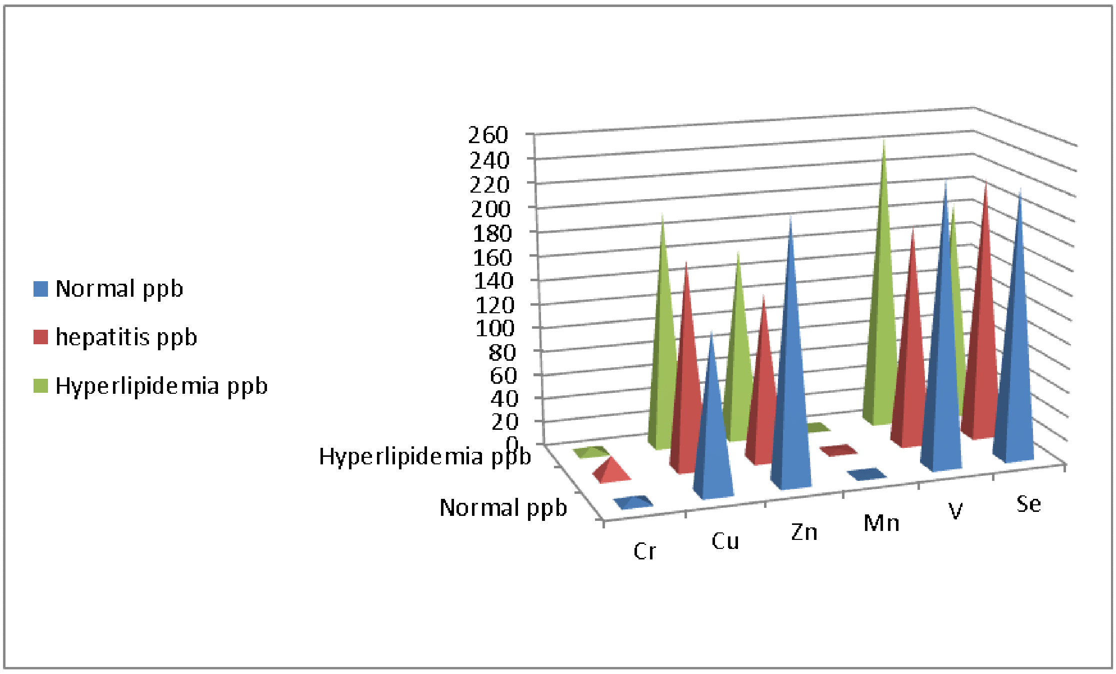

Figure 1.Comparison between hyperlipidemia and hepatitis patients for serum concentration of Cr, Cu, Zn, Mn, V and Se compared with normal sera.

4. Discussion

Damaged of hepato cell can resulted in fluctuation of body cell constituents. Lipid profiles were of important can be affected by liver damaged and the process resulted in variation in lipid levels. Trace elements are used as a diagnosing tool during disease, it is important to know whether the balance is changed in free or bound elements. The results of the present study have shown a significant increase ($p< 0.05$) in Cr, Cu and Mn in hepatitis and Cu and V in hyperlipidemia, while there were no significant changes in serum Cr in hyperlipidemia patients. These metals are members of one of the major subgroups of the micronutrients that have attained prominence in human nutrition and health. The biological role of trace metals, especially serum Zn, Cu, Cr and Mn, in different physiologic conditions has been extensively investigated in recent years (Hambidge M 2000). Similar observations were made (Lin CC *et al*. 2006), and paramoolsinsa PC (Pramoolsinsap C. *et al*.1996). They reported statistically significant decreased levels of serum Mn, Cu and Se in patients with hepatitis. But different observations have been reported (Saghir M. *et al*.. 2011), show that Cu level decreased in hepatitis. It is clear that deficiencies of some trace elements, such as Cu, Cr, Zn and Mn can result in marked alterations in lipid and lipoprotein metabolism (Engle T. *et al.* 2000). To the best of our knowledge, there has been no previous research regarding the correlations of serum trace elements with lipids and lipoprotein in hyperlipidemia patients.Several studies reported an inverse relation between serum Cu and cholesterol in rats during Cu deficiency (Cunnane,S,C. 1988), while Koo and Willams found no significant correlation between the serum Cu and cholesterol levels in non Cu deficient rats (Koo,I;Williams D.A.1981). Decrease in serum Se might indicate the development and progression of hepatitis, it is also links to the disease progress of some viral agents in relation to the biosynthesis of selenoproteins (Banares F.F. *et al.* 2002), and decrease in serum Se significantly increases the risk of cancer mortality , Four-year animal studies showed that dietary supplement of Se reduced the hepatitis infection by 77.2% (Yu. S.Y. *et al.* 1997). El-Hendy et al ,showed that Zn deficiency increases serum cholesterol in a dose-dependent (El-Hendy H.A. *et al.* 2001), Manganese is critical for lipid and lipoprotein metabolism, it has been demonstrated that Mn enhance cholesterol synthesis in the liver.The above results show that serum Cu concentrations of hepatitis patients are higher than normal individual serum concentrations. These elevated serum Cu levels indicate an alteration of Cu metabolism during the acute phase of uncomplicated hepatitis (Hatano R. 2000), it may be explained by the release of copper from damaged necrotic hepatocytes (Taylor E.W. *et al.*1997).

Vanadium has a role in the regulation of the metabolism of lipids and other constituents of importants. The major concern is that excessive levels of vanadium have been suggested to be a factor in manic depression, as increased levels of vanadium is found in hair samples from manic patients, and these values fall towards normal levels with recovery (Goujy,Han CC, & Lin YM.2010).

5. Conclusion

The real mechanism is not known but abnormal results of trace element may damage the liver by oxidative stress. Our study results were suggesting trace element supplementation may be complementary therapy to hyperlipidemia and hepatitis patients, so some of these trace elements might be considered as a marker of normal liver function. Dietary intake of these elements or vegetable and food which consider as rich sources of these elements are necessary to reduce these tow syndromes.

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