Biochemical Estimation of Trace Elements Manganese (Mn), Cobalt (Co),Calcium(Ca) and Iron(Fe) in Patients with Cardiovascular Diseases

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Abstract

background and objectives :

Recent scientific interest has focused on abnormalities in mineral metabolism and those abnormalities may play a role in the pathogenesis of cardiovascular diseases . The hypothesis that trace element status influences the risk of adverse clinical outcomes is worthy of investigation.Therefore, we performed this study on the basis of the existing hypothesis that serum level of Mn,Co,Ca.Fe were inversely associated with prevalence of cardiovascular diseases in 40 patients (20 with hypertension,20 with myocardial infarction), to confirm this possible associations compared with control group (N= 25) , study the sex-effect on the level of these trace elements..

Methods:

This study was done at college of pharmacy/ Hawler Medical University in period between 15/1/2010 – 20 /12 /2010and the concentrations of studied parameters were measured by atomic absorption spectrophotometer in Baghdad / at Ministry of Science and Technology.

Results:

The serum values of Mn, Co, Ca ,Fe in patients group were 0.0113 ug/ml±0.00070, 0.012 ± 0.0014 , 61.4118±10.16 , 0.6721± 0.14956 respectively, compared with the control group , 0.025±0.0032, 0.03 ±0.02 , 90±11 , 1.1±0.12 respectively.The results were significantly decreased in patients group as compared with the control group $P<0.001$. **CONCLUSIONS:** There were a significant decreased in the studied parameters of patients with CVD.

Keywords: Trace Elements

Introduction

Abnormalities associated with trace elements have not received much attention from clinicians in the past .Deficiencies of specific micronutrients can cause heart failure(HF) or may contribute cardiovascular diseases(CVD) .Patients with HF from other causes have a number of risk factors for micronutrient deficiency. They are usually elderly, may have a poor general diet [1]and are prone to excess urinary losses due to diuretic therapy . Epidemiological studies have shown that low plasma levels of antioxidant micronutrients,are associated with increased risk for diseases such as heart diseases[2].

Manganese:

Mn stimulates hepatic synthesis of cholesterol and fatty acids.Mn also seems to play a role in atherosclerosis.Mn is a constituent of the antioxidant enzymes superoxide dismutase and adenylyl cyclase[3].It was found a progressive increase in serum Mn levels corresponding to the severity of the disease.Serum Mn was also positively correlated with blood pressure[4].

Cobalt:

Co is a component of the vitamin B_{12} molecule and it is known to activate hypoxic signaling**,**Co has a relation with atherosclerosis because by increased the blood cholesterol level.Co has been reported to antagonize thyroid activity, thyroid hormones stimulate the adrenergic activity with increase the heart rate & myocardial contractility and increase the sensitivity of the adrenergic receptor to catecholamine**.**Co in high dosages has been

implicated in causing cardiac failure. Potientiate the effectiveness of glucose transport from the blood into body cells ,and increases the assimilation of Fe and the building RBC[5],because Co is the best-known chemical inducer of hypoxia-like responses such as erythropoiesis and angiogenesis in .Co in physiological concentration act as cardioprotective[6] which reduces the heart rate and can reduce the infarct size,[7-8]

Calcium:

There is a link between low Ca intake and higher mortality from ischemic heart disease[9]. Low Ca levels are potentially pro-arrhythmic, and hypocalcemic-associated ventricular fibrillation has been reported .A possible relationship between serum level of Ca and CVD .Chen et al.[10]recorded that ,there were a significant inverse associations of blood pressure with dietary intake of Ca.Several experimental and clinical studies suggest that Ca depletion elevates blood pressure[10].

Iron:

Fe may participate in the Fenton reaction for the production of free radicals,Fe, participate in various enzyme reactions directly related to the regulation of blood pressure and indirectly related to generation of oxidative metabolic energy, alterations in blood lipid levels. The increases in the concentrations of the trace elements Fe in patients with CVD have been shown in several studies because oxidative damage is involved in the pathogenesis of coronary heart disease (CHD) and accelerated atherosclerosis, some

studies have suggested an inverse association between iron and mortality from CVD[11-12]

Subjects:

This study was designed to examine the associations between the serum levels of Mn,Co, Ca,Fe and the incidence of CVD in 40 patients aged 45–67 y of both sexes.

Aims Of The Study:

The aims of this study were to measure the changes in serum levels of Mn, Co,Ca, and Fe in patients with CVD as comparing with the control group,and to find –out the sex effect on the serum levels of the previous parameters in patients group.Furthermore,compared the serum levels of previous parameters between the studied groups myocardial infarction(MI) and hypertension groups(HT).

Material And Methods:

A total of 40 patients were enrolled in present study. The patients were divided into two groups 20 patients with HT and the other 20 had MI.In addition ,matched – age twenty five apparently healthy adult individuals were randomly selected and involved in this study as a healthy control group ,the median age > 45 years. The exclusion criteria diabetes ,muscular disease, kidney stone, growth failure by depending on the personal, clinical , and biochemical data to prevent the overlapping with the results of the present study because of these diseases have also serum trace elements disturbances.

Methods:

Serum concentration of Mn ,Co , Ca ,Fe ions were measured by flame atomic absorption spectrophotometer.

Results:

The serum values of Mn, Co, Ca ,Fe in patients group with CVD were 0.0113 ug/ml±0.00070, 0.012 ± 0.0014 , 61.4118±10.16 , 0.6721± 0.14956 respectively.

Table 1: The serum levels of Mn,Co,Ca and Fe in patients with CVD group

CVD			Mn	Co	Ca	Fe
	N	valid	40	40	40	40
Mean			0.0113	0.0120	61.4118	0.6721
Median			0.0110	0.0120	63.5000	0.6300
±SD			0.00070	0.00140	10.16863	0.14956
Minimum			0.01	0.01	43.00	0.47
Maximum			0.01	0.02	78.00	0.95
Percentile		25	0.0110	0.0110	51.0000	0.5350
		٥٠	0.0110	0.0120	63.5000	0.6300
		75	0.0120	0.0130	68.5000	0.8000

The serum values of Mn, Co, Ca ,Fe in patients group with MI were0.0112 ± 0.00054, 0.0116±0.00096, 52.6471±5.25525, 0.5460 ± 0.04795respectively.

Table 2: The serum levels of Mn,Co,Ca and Fe in patients with MI group

MI group			Mn	Co	Ca	Fe
	N	valid	20	20	20	20
Mean			0.0112	0.0116	52.6471	0.5460
Median			0.0110	0.0115	51.0000	0.5450
SD			0.00054	0.00096	5.25525	0.04795
Minimum			0.01	0.01	43.00	0.47
Maximum			0.01	0.01	65.00	0.63
Percentile		25	0.0110	0.0110	49.0000	0.5100
		٥٠	0.0110	0.0115	51.0000	0.5450
		75	0.0118	0.0120	55.5000	0.5775

The serum values of Mn, Co, Ca ,Fe in patients group with HT were0.0115 ± 0.00083, 0.0124 ±0.00168, 70.1765±4.73333 , 0.8122 ±0.08135 respectively

Table 3: The serum levels of Mn,Co,Ca and Fe in patients with HTgroup

HT group			Mn	Co	Ca	Fe
	N	valid	٢٠	٢٠	٢٠	٢٠
Mean			0.0115	0.0124	70.1765	0.8122
Median			0.0115	0.0120	68.0000	0.8000
SD			0.00083	0.00168	4.73333	0.08135
Minimum			0.01	0.01	62.00	0.68
Maximum			0.01	0.02	78.00	0.95
Percentile		25	0.0110	0.0110	67.0000	0.7500
		٥٠	0.0115	0.0120	68.0000	0.8000
		75	0.0120	0.0130	75.0000	0.9100

Table 4: Comparison between the control and CVD groups regarding the values of serum Mn,Co,Ca and Fe

Parameters	Control	±SD	CVD group	±SD	p
Mn	0.025	0.0032	0.013	0.00070	P<0.001
Co	0.03	0.02	0.012	0.0014	P<0.001
Ca	90	١١	61.41	10.16	P<0.001
Fe	1.1	0.12	0.67	0.14	P<0.001

There were statistical significant differences of serum Mn, Co, Ca, Fe, values in patients with CVD as compared with the control group P<0.001.

Table 5: Comparison between the mean serum levels of Mn,Co,Ca and Fe in female and male patients with hypertension

	Sex	N	Mean	Std. Deviation	P
Mn	Female	5	0.0112	0.00084	0.784
	Male	15	0.0116	0.00084	
Co	female	5	0.0120	0.00183	0.581
	Male	15	0.0125	0.00169	
Ca	Female	5	67.2000	1.09545	0.014
	Male	15	71.4167	5.14266	
Fe	Female	5	0.8140	0.10807	0.113
	Male	15	0.8115	0.07403	

There was significant difference regarding serum level of calcium between females and males in patients with hypertension p < 0.05,while, the other parameters there were no significant differences p> 0.05 .

Table 6: Comparison between the mean serum levels of Mn,Co,Ca and Fe in female and male patients with MI

	Sex	N	Mean	Std. Deviation	P
Mn	Female	5	0.0114	0.00055	0.447
	Male	15	0.0111	0.00054	
Co	female	5			0.173
	Male	15	0.0115	0.00082	
Ca	Female	5	54.0000	4.63681	0.781
	Male	15	52.0833	5.58339	
Fe	Female	5	0.5420	0.05263	0.953
	Male	15	0.5473	0.04818	

There were no significant differences regarding serum level of studied parameters between females and males in patients with MI p > 0.05

Table 7: Comparison between the HT and MI groups regarding serum levels of Mn , Co , Ca and Fe

Parameters	Group	N	Mean	±SD	P
Mn	HT	20	0.0115	0.00083	0.030
	MI	20	0.0112	0.00054	
Co	HT	20	0.0124	0.00168	0.180
	MI	20	0.0116	0.00096	
Ca	HT	20	70.1765	4.73333	0.822
	MI	20	52.6471	5.25525	
Fe	HT	20	0.8122	0.08135	0.056
	MI	20	0.5460	0.04795	

Table 8:Comparison between the mean serum levels of Mn,Co,Ca and Fe in female and male patients with CVD

	Sex	N	Mean	Std.	P
Mn	Female	10	0.0113	0.00067	0.759
	Male	30	0.0113	0.00073	
Co	Female	10	0.0119	0.00145	0.401
	Male	30	0.0120	0.00141	
Ca	Female	10	60.6000	7.64780	0.048
	Male	30	61.7500	11.18326	
Fe	Female	10	0.6780	0.16424	0.853
	Male	30	0.6700	0.14712	

There was significant difference regarding serum level of calcium between females and males in patients withCVD p < 0.05,while, the other parameters there were no significant differences p> 0.05.

Discussion:

The hypothesis of the current study was that the trace elements status influences the risk of adverse clinical outcomes in patients with CVD which was worthy to investigate. Deficiency of many micronutrients is associated with the development ofCVD increased loss induced by diuretic therapy .They were usually an elderly patients and may have a poor general diet[13]. The serum values of Mn, Co, Ca ,Fe in patients group were 0.0113 ug/ml±0.00070, 0.012 ± 0.0014 , 61.4118±10.16 , 0.6721± 0.14956 respectively, compared with the control group , 0.025±0.0032, 0.03 ±0.02 , 90±11 , 1.1±0.12 respectively.The results were significantly decreased in patients group as compared with the control group *P*<0.001. The major finding of the present study was the detection of a strong negative correlation between Mn,Co,Ca,Fe in serum patients and prevalence of CVD.In agreement with current study,it was reported that, Mn deficiency were associated with CVD[14] .In addition, I thought the decrease level of serum Mn , Mn is a constituent of the antioxidant enzymes superoxide dismutase[3],and CVD are considered as a stress factor which made all the body's Mn consumed for the synthesis of this enzyme and lead to reduce the serum level of Mn. Moreover, it was found that, vitamin B_{12} deficiency symptoms, including an accumulation of serum homocysteine , can be attenuated by Co, that was mean Co reduce the deficiency of B_{12}[13] .This conclusion supported the hypothesis that Co in clinical dose acted as cardio-protective agent,it is well known that hyperhomocysteinaemia is considered a risk factor for incidence of CVD[18].Co is beneficial because it is part of vitamin B_{12},so deficiency of serum Co lead to deficiency of B_{12},and at the same time there were an significant inverse relation ship between total homocystein and B_{12} , and it is well known that increase level of homocystein are considered as a risk factor for prevalence of CVD[18]. Accordingly,there was a significant negative correlation between total homocystein and B_{12} , B_6, folate in patients with CVD[19].Several investigators have since reported a significant relation between elevated plasma homocysteine concentrations and atherosclerosis in the coronary, cerebral, and peripheral vasculature.In consistence   with our hypothesis, in current study find out   that, CVD induce hypocalcemia and this finding was in

consistente with the finding established by other researchers[15].The studies point to the fact that Ca absorption was reduced in people over 70 years of age because the gut may be less sensitive to calcitriol[16]and also because of lower renal synthesis of calcitriol.Older people make less vitamin D in the skin after exposure to ultraviolet light[17]. Older adults are at greater risk for nutritional deficiencies due to physiologic changes associated with aging, acute and chronic illnesses, medications. Among the micronutrients, the significant ones that may be associated with deficiencies in elderly adults include vitamin B_{12},Ca,Fe,and other vitamins and trace minerals. Oral health status, that may not fit properly,that will interfere with consumption of a well-balanced diet,GIT problems due to, a decrease in hormone and enzyme production.There was a link between low calcium intake and higher mortality from ischemic heart disease. There was significant difference regarding serum level of calcium between females and males in patients withCVD $p < 0.05$, 67.2±1.09545,   71.4167±5.14266 .This occured meight be because all the females in the current study were menopause, and due to the deficiency of estrogen , estrogen effect on Ca homeostasis and long term of estrogen depletion is associated with

bone resorption   increase stress fracture & post menopausal osteoporosis. Similarly, as in case of HT group ,there was significant difference regarding serum level of calcium between females and males.while ,in case of MI group there were no significant differences between females and male P>0.05,this was occur ,meight be need large number of patients to validate this findings.Usually, anemia associated with age is due to chronic bleeding in the gastrointestinal tract. It seems that the metabolic changes that occur with aging would have some impact on trace element needs, Like us, many investigators published that,there were a significant inverse relationship between iron and the prevalence of coronary atherosclerosis[11-12, 19].

Conclusion:

This conclusion was supported by previous investigations, which was in agreement with our hypothesis. Alterations in the serum levels of some trace elements may be utilized as an additional markers in the assessment of CVD.

Recommendation:

 Prospective cohort studies are required to clarify the clinical relevance of serum levels of Mn.Co,Ca and Fe in patients with CVD.

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التقدير الكيموحيوي للعناصر النزرة المغنيسيوم والكويلت والكالسيوم والحديد في مرضى العضلات القلبية

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الملخص

ركزت الاهتمامات العلمية حديثا على دور العناصر النزرة لحدوث الكثير من الامراض ومنها امراض القلب والاوعية الدموية . لقد وجدت الدراسة الحالية ان هناك علاقة عكسية بين تركيز الدم للعناصر الاتية Mn, Co, Ca, Fe فى الدم وحدوث امراض القلب والاوعية الدموية فى مجموعة مرضى عددهم ٤٠ مريض اعمارهم بين (٤٥- ٦٧) من كلا الجنسين. ، ٢٠ مريض منهم مصاب بارتفاع ضغط الدم و ٢٠ مريض مصاب باحتشاء العضلة القلبية ومقارنة النتائج مع المجموعة الضابطة (٢٥ شخص طبيعى خالى من الامراض) ومن الاهداف الاخرى لهذه الدراسة ، معرفة تاثير الجنس على تركيزالعناصرالنزرةاعلاه فى الدم ، ومعرفة الفرق بين ارتفاع ضغط الدم ومرض احتشاء العضلة القلبية فيما يتعلق بتركيز تلك العناصر .

حيث كانت تركيز العناصر الاتية Mn, Co, Ca, Fe فى الدم للاشخاص المصابين بامراض القلب والاوعية الدموية على التوالى

0.0113 ug/ml±0.00070, 0.012 ± 0.0014 , 61.4118±10.16 , 0.6721± 0.14956

اما تركيز تلك العناصر للمجموعة الضابطة فهى على التوالى

0.025±0.0032, 0.03 ±0.02 , 90±11 , 1.1±0.12

هناك فرق احصائى ملحوض بين كلا المجموعتين P<0.001

اما تركيز تلك العناصر لمجموعة المصابين بارتفاع ضغط الدم فهى على التوالى

0.01150±00083 , 0.0124±0.00168, 70.1765 ± 4.73333 , 0.81220± 08135

بينما تركيز تلك العناصر لمجموعة المصابين بمرض احتشاء العضلة القلبية فهى على التوالى

0.0112±0.00054 , 0.0116±0.00096 , 52.6471±5.25525 , 0.5460 ±0.04795