ORIGINAL ARTICLE

Serum Copper Levels among patients of Ischaemic Heart Disease - An Experience from A Tertiary Care Hospital in Bahawalpur, Pakistan

SHAFQAT NAZIR[†], EHSAN ULLAH[‡], SHAHADAT HUSSAIN CH. [*]

ABSTRACT

Aim: To compare serum copper levels of the patients of coronary artery disease and healthy controls.
Methods: It was a prospective, case control study. A total of 125 male participants were divided into controls (n=25), Ischaemic subjects without infarction (n=50), and Ischaemic subjects with previous or present infarction (n=50). The patients attending outpatient and indoor departments of Cardiology, BVH Bahawalpur were included in the study. The serum was analyzed for copper by atomic absorption spectrophotometery. The accepted reference range for copper in serum is 70-140 ug/dl.
Results: The mean age in the ischaemic heart disease patients without infarction (Group-A) and with infarction (Group-B) was 52.1 ± 1.22 and 50.74 ± 1.12 years respectively. The mean age in control group was 49.36 ± 2.01 years. Family of ischaemic heart disease and history of smoking were more common among disease groups as compared to controls. Serum copper levels were found to be significantly high in study sub-group B-2 (168.28 ± 7.84 micrograms/dL) as compared to control group (141.12 ± 6.43 micrograms/dL) and remaining study groups showed insignificant differences in serum copper levels.
Conclusion: Increased copper level after acute myocardial infarction may be an effect of the disease rather than its cause.
Keywords: Serum copper, ischaemic heart disease, acute myocardial infarction, angina

INTRODUCTION

Ischaemic heart disease (IHD) is on its decline in the Western countries including United Sates of America for last half century[1]. It is still, the single largest cause of death in the developed countries and is one of the leading causes of disease burden in developing countries as well[2,3]. In IHD, myocardial ischemia or infarction occurs because coronary arteries cannot supply enough blood for the metabolic needs of the myocardial muscle. It is also known as ischemic heart disease[4]. Studies on epidemics have demonstrated that IHD is associated with mineral levels in the human body, these mineral elements include calcium, magnesium, sodium, potassium, copper, zinc, iron, selenium, manganese, cadmium, chromium, and vanadium[5].

Many recent studies have found that serum copper is implicated in ischaemic heart diease[6-9]. Researchers from Pakistan have also found that high serum copper levels are associated with greater risk

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[†]Department of Biochemistry, Quaid-e-Azam Medical College Bahawalpur
[‡]Department of Pathology, Quaid-e-Azam Medical College Bahawalpur
[*]Department of Cardiology & CCU, Bahawal Victoria Hospital, Bahawalpur
Correspondence to Dr. Ehsan Ullah, Mobile: +92-333-6390765 Email: e_ullah @yahoo.com

of developing IHD[10]. Investigators have recently urged further research to determine exact role of copper in the IHD[11]. We conducted this study to evaluate serum copper levels in male patients of ischaemic heart disease.

PATIENTS AND METHODS

It was a prospective, case control study. A total of 125 male participants were divided into following groups; Control Group–25 healthy subjects, Group A – 50 Ischaemic subjects without infarction (stable and unstable angina), further divided into A-1 (stable angina) and A-2 (unstable angina), Group B–50 Ischaemic subjects with previous or present infarction further divided into B-1 (post infarction angina) and B-2 (recent acute myocardial infarction). Purposive sampling technique was used to select patients/subjects in various groups and sub-groups. The patients attending outpatient and indoor departments of Cardiology, BVH Bahawalpur were included in the study. Controls were age-matched male relatives of the patients.

About 5ml of venous blood was drawn from the antecubital vein of each patient and control by using a disposable plastic syringe. The clotted blood was poured into distilled-demineralized water centrifuge tubes and centrifuged at 3000 for 10 minutes. Serum

was separated in clean, sterilized, distilled demineralized water plastic capped tubes and stored at -20 degree Celsius. Maximum care was taken to avoid contamination. All the samples were analyzed simultaneously to avoid the effect of alternate freezing and thawing. The serum was analyzed for copper by atomic absorption spectrophotometery[12]. Serum specimens diluted with an equal volume of deionised water were aspirated directly into the atomic absorption spectrophotometer flame and the copper concentrations were calculated against copper standards with a 10ml/dl glycerol matrix to approximate the viscosity of the diluted specimens. The accepted reference range for copper in serum is 70-140ug/dl. Haemolysis is not a great concern for copper determinants, since levels of copper in plasma and red cells are nearly equal.

RESULTS

Amongst the patients of IHD, 56% gave a positive family history of either ischaemic heart disease, hypertension, cerebrovascular accident, diabetes mellitus or combination of any these diseases. In the control group only six individuals (24%) gave a positive family history. The occupation distribution of study group revealed that the largest group comprised of government servants (37%), while the businessmen (20%), the landlords (16%) and labourers (12%) were next to follow. The rest of the patients (15%) belonged to various other professions. The diseased group included 64% smokers as compared to the control group which had only 28% cigarette smokers as compared to the control group which had only 28% cigarette smoker. The mean age in the ischaemic heart disease patients without infarction (Group-A) and with infarction (Group-B)

was 52.1±1.22 and 50.74±1.12 years respectively. The mean age in control group was 49.36±2.01 years.

Table 1 shows mean serum copper levels in control subjects and patients of ischaemic heart disease, both group-A and group-B, according to different age decades. Mean±S.E.M. serum copper levels in the control group, group-A and group-B were 141.12±6.43ug/dl, 135.56±4.77ug/dl and 148.94±5.59ug/dl respectively. The comparison between mean serum copper values of group A (135.56±4.77ug/dl) and group B (148.94±5.59ug/dl) with that of control group (141.12±6.43ug/dl) showed no statistical difference. Similarly the comparison of mean serum copper values among different age groups was also non-significant (P>0.05). But statistically a highly significant (P <0.001) difference was observed when mean serum copper level of group A and group B were compared with the mean serum copper values in the age group 30-39 years as shown in Table1.

The mean values of serum copper in both sub-groups, A1 and A2, were 135.04±6.03ug/dl and 136.08±7.64ug/dl respectively (Table 2). These values showed no statistical difference (P>0.05) as compared to normal control mean values (141.12±6.43ug/dl). The mean serum copper levels in both sub-groups B1 and B2 were 129.60±6.14ug/dl and 168.28±7.84ug/dl respectively (Table 2). The comparison between mean serum copper levels of sub-group B1 and control group showed no statistical difference (P<0.05) but statistically a significant difference (P<0.02) was noted when mean serum copper concentration of sub-group B2 was compared with that of the control group.

Table1. Comparison of serum copper levels among study groups according to age strata

Age Groups	Serum Copper Levels (micrograms/dL)			P value
	Control Group	Group-A	Group-B	
30 – 39 Years	125±15.61 (n=05)	121.60±4.86 (n=05)	129.75±10.56 (n=04)	N.S
40 – 49 Years	148.00±12.40 (n=08)	138.20±8.98 (n=15)	148.15±8.27 (n=20)	N.S
50 – 59 Years	141.28±10.67 (n=07)	134.61±8.20 (n=18)	159.18±9.65 (n=17)	N.S
60 – 69 Years	145.60±15.51 (n=05)	143.66±10.71 (n=12)	148.78±15.64 (n=09)	N.S
Total	141.12±6.43 (n=25)	135.56±4.77 (n=50)	148.94±5.59 (n=50)	N.S

Table2. Comparison of serum copper levels between control and various study subgroups

Comparison between Control and sub-groups	Serum Copper Levels (micrograms/dL)		P value
	Control Group	Study Sub-Groups	
Control vs. A-1	141.12±6.43	135.04±6.03 (A-1)	N.S
Control vs. A-2	141.12±6.43	136.08±7.64 (A-2)	N.S
Control vs. B-1	141.12±6.43	129.60±6.14 (B-1)	N.S
Control vs. B-2	141.12±6.43	168.28±7.84 (B-2)	0.001

DISCUSSION

In the present study the level of serum copper the level of serum copper ranged between 111-170ug/dl in maximum number of healthy controls while the mean value of the whole group was found to be 141.12±6.43ug/dl. This is slightly high as compared with the levels reported both in Pakistan and abroad[13,14]. The variations in normal values among different communities may be due to their different socio-economic conditions and patterns of food. Some earlier studies have shown no influence of age on the mean serum copper level in men between 3rd and 5th decade of life[15,16]. The present study also did not show any significant change in mean serum copper levels in case of controls and patients of different age groups, ranging between 30-65 years. In accordance with few earlier workers, the mean values of serum copper in this study among the patients of ischaemic heart disease without infarction (Group-A) or with infarction (Group-B) were not different statistically as compared to the mean values in control group[17,18,19].

The mean serum copper levels in patients of sub-group A1 and A2, suffering from stable angina pectoris and unstable angina pectoris respectively, were not different statistically (P > 0.05) when compared with mean serum values of control group (Table2). However, the mean serum copper level in patients who had experienced attack(s) of myocardial infarction in the past (Group-B1) was not statistically different from the mean values in case of normal controls; while the mean serum copper level in patients of a recent acute myocardial infarction attack (group-B2) was statistically higher (P < 0.05) when compared with mean values of control group (Table 2). As elevated serum copper is found only in recent AMI group, it can be said that this rise in serum copper level after acute myocardial infarction could be an effect of the disease rather than its cause. The precise origin of the increase in the serum copper in myocardial infarction is not known. Anoxic injury leading to the release of copper from the necrosed myocardium is one explanation but the myocardial copper stores can't explain such significant rise. Increased synthesis or decreased break down of ceruloplasmin by the liver has also been put forward as an explanation. The serum ceruloplasmin being an acute phase reactant may rise as a non specific reaction to the tissue injury from the stores elsewhere in the body[20].

CONCLUSION

Increased copper level after acute myocardial infarction may be an effect of the disease rather than its cause.

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