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The Comparative Study of Plasma Homocysteine Levels in Patients with Acute Coronary Syndrome in Terms of Being Smoker and Diabetic

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Smoking and diabetes are risk factors for coronary artery disease which increase homocysteine level. In this study, the role of homocysteine in patients with acute coronary syndrome with a history of cigarette smoking and risk of diabetes was examined. One-hundred ninety three (193) patients with acute coronary syndrome (unstable angina, STEMI and non-STEMI) referred to the Heart Center of Imam Ali (AS) Hospital in Kermanshah were studied. Diabetic patients who were active smokers were selected as study group. Non-diabetic patients who had no history of smoking or at least six months passed since they left smoking were considered as controls. Blood samples were taken during fasting and then homocysteine levels were measured by ELISA method. The mean serum homocysteine level in patients who were only smokers was 19.5±11.4 mg/dl. This was 19.2±9.2 mg/dl in patients who only had diabetes. The homocysteine level in patients who were still smoking and also had diabetes was 17±9.6 mg/dl. This was 19.1±2.10 mg/dl in patients who did not use cigarette and did not have diabetes. The statistical analysis did not show any significant differences between different categories of patients (p: 0.609). The results of the present study showed that although the homocysteine level has increased in patients with acute coronary syndrome, diabetes or smoking does not influence the elevated levels of homocysteine in patients with acute coronary syndrome.

Key words: Acute Coronary Syndrome, Diabetes, Smoking, Homocysteine.

The high prevalence of ischemic heart disease is remarkable around the world and includes about one-fifth causes of death. According to previous studies, heart cardiovascular disease is the most common cause of death in Iran so that about 46% of deaths are due to this disease[1]. So far a number of factors including age, family history, abnormal blood lipids, high blood pressure, diabetes, a history of heart disease have been known as effective factors in causing this disease[2] . For example, the use of drugs like other risk factors can serve as an independent risk factor for coronary artery disease and its association with other risk factors increase the risk of ischemic heart disease[3,4].

Although, many factors are involved in the development of coronary artery disease, it is not yet clear which factor has a more major role in the development of atherosclerosis[5]. Although, homocysteine is involved in natural metabolism, its elevated levels cause some risks. Homocysteine is a risk factor, because its elevated levels interfere with collagen formation.

Homocysteine affects the arteries in different ways. It damages the internal layer of arteries by producing hydrogen peroxide and superoxide. The active form of homocysteine called thiolactanehomocysteine affects platelet aggregation. The changes in coagulation factors facilitate clotting formation and make prone the small arteries to obstruction by preventing

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arteries dilation. Hyperhomocysteinaemia has both mitogen and toxic and thrombogen effects on the muscles of arteries walls. Besides being a risk factor, high levels of homocysteine accelerates the atherosclerosis trend[6].

Several factors contribute to the increase in blood homocysteine levels. These factors include: genetic abnormality, folate deficiency, age, lifestyle factors and drug interactions. Given that smoking and diabetes are risk factors for coronary artery disease which lead to increased homocysteine levels, the present study aims to determine the role of homocysteine in acute coronary syndrome by conducting a case-control study on smoker-diabetic patients with acute coronary syndrome and comparing them with nonsmoker-non-diabetic patients.

METHODS

One-hundred ninety three (193) patients with acute coronary syndrome (unstable angina, STEMI and non-STEMI) referred to the Heart Center of Imam Ali (AS) Hospital in Kermanshah were studied. Diabetic patients who were active smokers were selected as study group. Non-diabetic patients who had no history of smoking or at least six months passed since they left smoking were considered as controls. Criteria for the presence of diabetes were (BS e" 200) and (FBS e" 126). Exclusion criteria included: Chronic kidney disease, pernicious anemia, hyperthyroidism, and certain cancers such as breast cancer, ovarian and pancreatic cancers, history of chemotherapy, and the use of methotrexate, theophylline and phenytoin. After obtaining informed consent, 3-4 ml of blood were taken during fasting. The blood samples were centrifuged in less than 30 minutes at a temperature of 4 °C and were then quickly frozen. The samples were held at -80 °C until studying the serum level of homocysteine. Homocysteine levels were measured by ELISA method. The normal amount of this amino acid is 5-10 µmol/l; accordingly, hyperhomocysteinaemia was defined as follows:

Slight increase: 10-15 µmol/l
Mild increase: 15-30 µmol/l
Moderate increased: 30-100 µmol/l
Sharp increase: more than 100 µmol/l

Descriptive data were analyzed using the numeric parameters such as mean, standard deviation and frequency distribution tables. One-way ANOVA and post-hoc Tukey test were used to analyze the different homocysteine levels in different survey groups. Data analysis was performed using the SPSS 16.

RESULTS

Patients with acute coronary syndromes included 127 males and 66 females. The mean age of the patients was 61.2±11.5 years. The men's and women's mean ages were 60±11.8 and 63.4±10.9 years, respectively. Statistical analysis showed no significant difference between men's and women's age (p: 0.059). Among the patients, 80 men and 18 women were consuming cigarettes. There was a significant difference between gender and smoking so that more men were smokers ($p < 0.0001$).

Of the patients, 58 men and 37 women had diabetes. There was no significant difference between the gender and history of diabetes (p: 0.171) (Table 1). Among the patients, 142 people were with unstable angina, 42 patients with STEMI and 27 patients were diagnosed with non-STEMI. Statistical analysis showed no significant difference between the type of acute coronary syndrome (ACS) and smoking ($p = 0.488$). Among the patients with unstable angina, 64 patients had diabetes. Statistical analysis showed no significant difference between the type of ACS and history of diabetes (p: 0.002) so that most of patients with diabetes had unstable angina (Table 2).

The mean age of smokers and non-smokers was 60.4±11.2 and 60±11.2 years, respectively. There was no significant difference between smokers and non-smokers in this regard (p: 0.335). No significant difference was found between smokers and nonsmokers in terms of mean duration of diabetes (p: 0.11). Moreover, there was no significant difference between smokers and nonsmokers in terms of mean homocysteine serum level (p: 0.569) (Table 3).

The mean age of diabetic and non-diabetic patients was 61.3±11.3 and 61±11.8 years, respectively. No significant difference was found between the mean ages of diabetics and non-diabetics (p: 0.893). There was not any significant difference between the mean number of smoked cigarettes among diabetics and non-diabetics (p:

0.852). No significant difference was observed between diabetics and non-diabetics in terms of mean serum homocysteine level (p: 0.412) (Table 4). Statistical analysis revealed no significant difference among the various categories of patients in terms of the mean number of cigarettes smoked per day in patients who only were smokers and patients who were smokers and had diabetes (p: 0.852).

Statistical analysis showed no significant difference between the various categories of patients in terms of the mean duration of diabetes in

Table 1. Number of patients in terms of gender and study group

	Male (n=127)	Female (n=66)	Total (n=193)
Only smoker	43	8	51
Only diabetic	21	27	48
Diabetic and smoker	37	10	47
Non-diabetic and non-smoker	26	21	47

Table 2. The type of ACS in terms of history of diabetes and smoking

	Unstable angina (n=124)	STEMI (n=42)	Non-STEMI (n=27)
Only smoker	32	16	3
Only diabetic	37	4	7
Diabetic and smoker	27	8	12
Non-diabetic and non-smoker	28	14	5

Table 3. Age, duration of diabetes, cigarette consumption per day and homocysteine levels in smokers and non-smokers

	Smoker	Non-smoker	p value
Age	60.4±11.8	60±11.2	0.335
Duration of diabetes	8.4±4.4	7±3.7	0.11
Cigarette consumption per day	23.6±6	-	-
Homocysteine level	18.3±10.6	19.2±9.6	0.569

Table 4. Age, duration of diabetes, cigarette consumption per day and homocysteine levels in diabetics and non-diabetics

	Diabetic	Non-diabetic	p value
Age	61.3±11.3	61±11.8	0.893
Duration of diabetes	7.7±4.1	-	-
Cigarette consumption per day	23.3±5.8	23.5±6.3	0.852
Homocysteine level	18.1±9.4	19.3±10.8	0.412

Table 5. Age, duration of diabetes, cigarette consumption per day and homocysteine levels in the study groups

	Only smoker	Only diabetic	Diabetic and smoker	Non-diabetic and non-smoker	p value
Age	60±12.6	61.7±9.9	60.8±12.6	62.3±12.5	0.772
Duration of diabetes	-	7±3.7	8.4±4.4	-	0.110
Cigarette consumption per day	23.5±6.3	-	23.3±5.8	-	0.852
Homocysteine level	19.5±11.4	19.2±9.2	17±9.6	19.1±10.2	0.609

patients who only had diabetes and those who were smokers and had diabetes (p: 0.110). Statistical analysis showed no significant difference between the mean serum homocysteine levels in patients who only were smokers and just had diabetes and those who were smoker and had diabetes and patients who did not use tobacco nor had diabetes (p: 0.609) (Table 5).

The mean homocysteine level in men and women who were still smoking and also had diabetes was 18.5±9.5 and 11.5±8.2 mg/dl, respectively. Statistical analysis showed that the homocysteine levels are significantly higher in men than women (p: 0.040). The mean homocysteine level in men and women who only were smokers was 20.6±12 and 14±5.7 mg/dl, respectively. Statistical analysis did not show any significant difference between males and females (p: 0.138)

The mean homocysteine level in men and women who only had diabetes was 20.5±8.8 and 18.2±9.5 mg/dl, respectively. Statistical analysis did not show any significant difference between males and females (p: 0.395). The mean homocysteine level in men and women who were non-smokers and non-diabetics was 22.1±10.9 and 15.3±8 mg/dl, respectively. Statistical analysis showed that the homocysteine level is significantly higher in men than women (p: 0.021)

DISCUSSION

The results showed that homocysteine levels increased in patients with acute coronary syndromes. The results of this study are consistent with other studies. For example, Deihim et al investigated the relationship between blood homocysteine levels and the risk of arterial thrombosis diseases. In this study, 100 patients with arterial thrombosis and 68 people were selected as study group and controls, respectively. Mean homocysteine level in study and control groups was 23.58±18.4 and 11.45±3.4 µmol/l, respectively. The observed difference in homocysteine levels between the two groups was statistically significant. Finally, they concluded that homocysteine can be considered as a risk factor for thrombosis. For this reason, it seems that measuring the homocysteine level is necessary in patients with a history of atherosclerosis, thrombosis or vascular diseases or those who have one of these diseases in their immediate family.

The results showed that there is no significant difference between the type of ACS and smoking. The results of the present study are inconsistent with most previous studies. For example, in a comprehensive study on 7599 people, Venn et al found that even being passive smoker can increase the levels of risk markers for cardiovascular disease (such as fibrinogen and homocysteine) twice the rate for other people[7]. In a study by Virtanen et al. on 802 men, it was found that the increase in homocysteine levels in men who had a history of smoking increased risk of death[8]. Factors such as geographical conditions and genetics, number of samples and being smoker or non-smoker (number of cigarettes smoked per day) may contribute to difference of our results with the results of other studies.

The results of the present study showed a significant difference between the type of ACS and diabetes. These results are consistent with the results of some studies such as Zakeri et al. Zakeri et al. studied 33 diabetic patients with acute or old myocardial infarction as well as 34 patients with negative OGTT with acute or old myocardial infarction in the control group. They found that plasma homocysteine levels in diabetic patients with coronary heart disease are higher than non-diabetics. The observed difference between the mean fasting serum homocysteine in study group (16.2±4.8) and controls (10.6±4.8) was significant (P<0.05).

However, the results of the present study are inconsistent with some studies such as Haji Sadeghi et al. They found no significant difference between plasma homocysteine levels in study group (151 patients with type 2 diabetes without nephropathy) and controls (P: 0.44) [9]. The results showed that although the homocysteine level has increased in patients with acute coronary syndrome, no significant difference was observed between the mean serum homocysteine levels in patients who only were smokers and just had diabetes. Furthermore, no significant difference was found between patients who were still smoking and also had diabetes as well as in non-smokers and non-diabetics.

CONCLUSION

The results showed that despite the increase of the homocysteine level in patients with acute coronary syndromes, diabetes or smoking is not effective in the increase of homocysteine level in patients with acute coronary syndrome.

Suggestions

Although no correlation was found between homocysteine level and the presence of diabetes or smoking, more extensive tests, especially with regard to young patients and without risk factors are recommended. Furthermore, conducting trials to investigate the effects of folic acid on reduction of homocysteine levels and its consequences on the outcome of patients with acute coronary syndrome is necessary.

REFERENCES

1. M.R.Biravand, M.A.A., dyslipidemia and acute coronary syndrome. *Pahouhande Journal of Shahid Beheshti University of Medical Sciences,* 2006; **54**.
2. Braunwald, E., D. Zipes, and P. Libby, Heart disease: a textbook of cardiovascular disease. Heart Disease: A Textbook of Cardiovascular Disease, 2001.
3. Abbasi, S.D.a.A., The correlation of ischemic risk factors with left main tract disease *Jornal of Isfahan Medical School*, 2008. **11**(3).
4. Handin, R., *et al*., Harrison's principles of internal medicine. Harrison's principles of internal medicine, 2005.
5. Kamran Pourmand, M.S., Hamid Sanei, Elaheh Refaee, Fahimeh Akrami, Mohammad Talaei, Which mejot atherosclerosis' risk factors represents the extent of coronary artery disease? *Journal of Isfahan Medical School*, 2007; **25**(85).
6. Herrmann, W., et al., *Total homocysteine, vitamin B12, and total antioxidant status in vegetarians.* Clinical chemistry, 2001; **47**(6): p. 1094-1101.
7. Venn, A. and J. Britton, Exposure to secondhand smoke and biomarkers of cardiovascular disease risk in never-smoking adults. Circulation, 2007; **115**(8): p. 990-995.
8. Virtanen, J., et al., Homocysteine as a risk factor for CVD mortality in men with other CVD risk factors: the Kuopio Ischaemic Heart Disease Risk Factor (KIHD) Study. *Journal of internal Medicine*, 2005; **257**(3): p. 255-262.
9. Homocystein level in patients with coronary artery disease in type 2 diabetes mellitus wihout nephropathy. *Iranian Heart Association*, 2009; **10**(4).