Original Article

Fructosamine 3-Kinase in Erythrocytes for Myocardial Infarction Patients

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Abstract

Background: Fructosamine-3-kinase (FN3K) enzyme appears to protect proteins from nonenzymatic glycation. **Objectives:** The current study aimed to establish the activity of FN3K in serum and erythrocyte lysate. **Methods:** The activity of FN3K were estimated in (30) healthy individuals and compared to values in (35) non-diabetic myocardial infarction patients. **Results:** The results showed that there was a significant increase in the activity of enzymes in the lysate of erythrocytes, compared with the activity of enzymes in serum for both the control groups and the patients group. The results also showed a significant increase in the activity of the FN3K enzyme in the serum of patients compared to the control group. The activity of enzymes is not affected by gender for both groups. A group of biochemical variables related to myocardial infarction were measured. The result showed a negative significant relationship between the activity of the enzyme and the level of total antioxidant capacity a positive significance in glycated hemoglobin in the control group, and patients positive significance between the activity of the enzyme and the level of Zn. **Conclusion:** The activity of FN3K enzyme is affected by age, uncontrol blood glucose levels, and oxidative stress in healthy patients.

Keywords: Heart, Myocardial Infarction, Glycation, FN3K, Deglycation, AGEs.

Introduction

Myocardial Infarction (MI), is a main cause of death all over the world this term reflects the death of the cells due to a deficiency of cardiac ischemia that takes place when the blood is impeded from flowing to the heart muscle and it occurs mostly, due to accumulation of fats, cholesterol and other materials, these fat deposits that contain cholesterol are called plaques and the process of plaques accumulation is called atherosclerosis.[1-4] Myocardial ischemia initiates inflammatory signalling, which attracts immune cells and produces reactive oxygen species as well as molecular damage.[5-9] The risk factors of MI include age and gender, Smoking, obesity, alcohol and genetic family history. [10] Preventing the incidence of this disease might be through controlling the diet system, pattern of life and maintaining a healthy body weight.[11] The human body's tissues and organs contain a complex set of chemicals known as advanced glycation end-products (AGEs) their focus sharpens as they get older. Glycation fundamentally causes AGEs to develop in the human body. In this non-enzymatic process, a molecule of glucose, lipid or nucleic acids combined with an amine group from free amino acids or proteins to create a Schiff base, which then undergoes a rearrangement to produce a fructosamine known as the Amadori product. Through additional chemical processes including oxidation and dehydration, this comparatively stable molecule can produce a variety of AGEs. These can be found in intracellular proteins, serum albumin-like plasma proteins, long-lived extracellular matrix proteins, and long-lived plasma proteins. Glycation is categorized in each of those situations as a non-enzymatic post-translational alteration of proteins[12] this non-enzymatic alteration of protein changes not just its structure but also its biological characteristics.[13] Glucose concentration and protein half-life are the two conventional parameters that are known to cause glycation of proteins in vivo,[14] however, research has shown that many non-diabetic diseases are associated with higher levels of glycoprotein.[15] In non-diabetic patients who have experienced MI, glycation is a risk factor for short-term mortality and can have a negative impact on biological systems.[16] The deglycation process is one of the most crucial systems that repair these damages, therefore,

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organisms attempt to lessen the damaging consequences of the glycation process through their natural defence system as these interactions negatively affect the activities of key molecules.[17] Fructosamine 3-Kinase (FN3K) [EC 2.7.1.171], is one of the deglycation enzymes that control the non-enzymic glycation reactions (natural defence system) inside the cells to resist the negative effects of the glycation process.[18] The FN3K phosphorylate fructosamine compound (fructoselysin) transforms it into Fructoselysin-3-phosphate (FL3P), which is an unstable compound that decomposes spontaneously to produce the 3-Deoxyglucosone (3DG) and non-organic phosphates.[19] The highest activity of the enzyme was spotted in the brain, heart, kidneys and muscles.[20] Elevated levels of advanced glycation endproducts (AGE) increase the risk of cardiovascular disease comorbidity and mortality, the FN3K enzyme reduces risk by lowering AGE levels.[21] Early studies indicate that FN3K might play a vital role in reducing the formation of Advanced glycation end products (AGEs) which is related to the damage of various tissues including the heart.[22] The research aims to study the activity of FN3K in healthy people from two different sources serum and red blood cells, in addition to determining the activity of enzyme FN3K in patients with MI and its relationship to occurrence and development of disease.

Materials and Methods

The study was conducted using human blood specimens and samples collected from April to June 2023 in cooperation with the Mosul Center for Cardiac Medicine and Surgery and Blood Bank in Mosul City. The groups were distributed as follows:

Control group: 30 specimens were collected from healthy persons; (15) of them from males and (15) of females whose ages ranged from 40 to 70 years old.

MI Group: 35 specimens of blood were taken from individuals who suffer from MI. The specimens included (16) males and (19) females with ages ranging from 40 to 70 years old.

Erythrocytes Separation: To separate erythrocytes from other components of blood, firstly uncoagulated blood is obtained as the blood taken from the person is put in a tube that contains the anticoagulant ethylene di-amin tetra acetic acid (EDTA).[23] After that red blood cells are separated the uncoagulated blood is put in the centrifuge with a speed of (3000Xg) for ten minutes to ensure obtaining the red blood cells only. The plasma and the white layer are removed and the red cells are washed with sodium chloride (0.9%) three times.[24]

Hemolysis erythrocytes preparation: The erythrocytes hemolysis results from the breaking of the red blood cells by Osmoticlysis. One volume of erythrocytes was prepared in the previous paragraph and they were incubated in (4°C for at least 4 hours. After that, the erythrocytes are put in the centrifuge for 20 minutes at a speed of (9000×g) for the purpose of sedimentation of the membranes of red blood cells.[25]

Fructosamine-3kinase enzyme measured using the ELISA technique as per manufacturer instruction using Kit supplied by Sunlong company (China).[26] Iron and zinc measured atomic spectrophotometry technique as per manufacturer instruction using Kit supplied by the Solarbio Company(Chinese).[27,28] Total Antioxidant Capacity using the spectrophotometry technique and the analysis kit manufactured by Biohermes company.[29] The Glycated haemoglobin HbA1c and activity of Creatine Kinase enzyme was estimated using the analysis kit manufactured by Roche German Company using the Cobas device.[27,30] Moreover, the concentration of glucose, total cholesterol, Triglyceride, Low-density lipoprotein cholesterol. High-density lipoprotein cholesterol and lactate dehydrogenase (LDH) were estimated using the analysis kit made by BioLabo company using a spectrophotometer.[31]

Result

Activity of FN3K enzyme was estimated in erythrocytes lysate in MI and control groups, results showed a very high significant increase in activity of FN3K in the MI group (590±10.6ng/l) at P≤0.001 compared to the control group (387.7±3.2 ng/l) as shown in Figure 1 and activity of FN3K not affected by gender for both groups in erythrocytes lysate. The activity of FN3K enzyme also was estimated in serum in MI and control groups, results showed a very high significant increase in the activity of FN3K in MI patients (263.5±2.17ng/ l) at P≤0.001 compared to the control group (182.3±7.36) as shown in Figure 2 and activity of FN3K not affected by gender for both groups in serum, The results indicated a highly significant increase in activity of the enzyme in erythrocytes lysate compared to serum

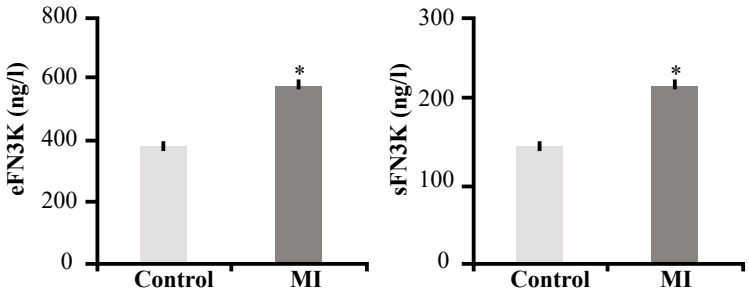

Figure 1: Activity of FN3K in Erythrocytes Lysate and Serum of Control and MI Groups. Data Expressed as mean±SD, *Indicates Significantly Higher at p<0.05 Using Independent Sample t-test. eFN3K=Erythrocyte Fructosamine 3-kinase, sFN3K=Serum Fructosamine 3-kinase, MI=Myocardial Infarction.

Results of the research indicated that there was an increase in levels of FBS, HbA1c and a very high significant increase in activity of CK and LDH in the MI group compared with the control group and decreased levels of TAC and Zn in the MI group also, increase in levels of Fe in patients compared with control group, results show increase in TC, TG, LDL-C, VLDL-C, TG on HDL, TG on LDL and decrease in HDL in MI group compared with control group (Table 1).

Table 1: Results of Some Variables in MI Patients Compared to the Control Group.

Variables Groups	Control Group (Mean±SE)	MI (Mean±SE)
FBS(mg/dl)	94.8±2.3	117.2±2.2
HbA1c	4.8±0.1	6.7±0.9
CK(U/L)	11.06±0.3	40.17±2.1
LDH(U/L)	186.36±7.4	354.25±7.5
TAC(µmol/ml)	1.31±0.4	0.94±0.8
Zn(µg/dl)	91.03±1.3	44.4±1.2
Fe(µg/dl)	121.8±1.1	189.2±1.6
TC(mg/dl)	130.9±3.2	190.6±1.6
TG(mg/dl)	144.3±4.9	198.6±2.6
HDL-C	41.7±0.2	30.2±1.09
LDL-C	88.9±5.8	134.1±1.3
VLDL-C	27.1±9.09	37.05±1.03
TG on HDL	3.4±0.1	6.86±0.2
TG on LDL	1.9±0.1	1.48±0.02

The result shows there was an inverse relationship between the activity of FN3K and HbA1c and direct relationship between TAC and FN3K activity in the MI group and a highly significant inverse relationship between Zn and FN3K in the control group (Table 2).

Table 2: Linear Correlation Coefficients of Some Variables with FN3K in the MI Group.

Parameters	Groups		r
HbA1c	MI	FN3K	-0.74
TCA			0.58
Zn	Control		-0.44

Discussion

The present study demonstrated an increase in the activity of the FN3K enzyme in erythrocytes lysate in both groups, control and MI. This is consistent with the researchers' findings.[32] The reason can be attributed to enzyme activity is associated more with intracellular glycation than with plasma protein glycation. This would lead us to suppose that the main effect of FN3K is to deglycate intracellular proteins.[33] The results also showed a significant increase in enzyme activity in the MI group compared to the control group. The reason can be attributed to concentrations of glycated haemoglobin being dramatically elevated in MI patients, it appears on the borderline in comparison to healthy subjects.

Results also demonstrated that no significant correlation between blood sugar with glycated haemoglobin. In the line with this finding, Gosavi *et al.*[34] reported an increased level of Hb_{A1C} in non-diabetic with acute MI.[34] The glycation induce As glycation can jeopardize physiological pathways and is a destructive biomarker for short-term mortality following acute MI in non-diabetic patients.[35] Moreover, glycation reciprocally correlated with lipid peroxidation markers.[36] Redox imbalances encourages glycation and potentiates induction of MI perhaps in non-diabetic patients providing clear evidence of glycation role in the precipitation of cardiovascular ailments due to presence of some biogenic factors, perhaps the activity of FN3K.[37] Data represented elevated blood sugar level was not high and was within acceptable limits in patients with MI, and the reason is attributed to the fact that increased glucose in serum increases the risk of heart disease including MI, as a result of disrupting the normal endothelial function of blood vessels by oxidative stress that increase in thickness of arteries which leads to death or damage to the heart muscle.[38] The results also showed that there was a very high significant increase in the activity of both CK and LDH enzyme in MI patients compared to the control group the reason for the increase in two enzymes is due to damage or defect in the heart muscle and this is consistent with Harahap and Margata[39], a very high significant decrease in concentration of total antioxidants capacity(TAC) in patients and this decrease reduces the important role of TAC as an antioxidant in protecting the heart muscle from lipid peroxidation products[40] results also showed that there was a decrease in the level of Zn in MI compared to the control group, the decrease in zinc reduces its role as an antioxidant and then increases oxidative stress and inflammation, which causes damage to the heart muscle[28,41] and a very high significant increase in the level of iron in serum of patients with M compared with control group, and this is consistent with Ahmed *et al.*[42] where the level of iron increases in patients which leads to its accumulation in the walls of blood vessels. The results in Table 1 also showed a very high significant increase in concentration of TC, TG, LDL-C, and VLDL-C and

a very high significant decrease in HDL concentration in the patient group compared to the control group, this is consistent with Noreen *et al.*[43], where the excessive concentration of cholesterol and fats in the blood leads to an imbalance in the blood flow to and from the heart, and increase ratio TG/HDL-C and TG/LDL-C in MI is a potential risk factor for prediabetes and associated with insulin resistance and cardiovascular disease.[44,45]

Conclusion

The present study concluded that fructosamine 3-kinase in erythrocytes served as a diagnostic tool for diagnosis and follow-up of patients with myocardial infarction patients.

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