Impaired Endogen Fibrinolysis in Patients with Chronic Ischemic Heart Disease

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Abstract
Cardiovascular disease is one of the main causes of mortality all of the world. Hypercoagulability is one of the pathogenetic mechanisms for the development of coronary heart disease. In our study, the main goal was to evaluate new markers of hypercoagulability and to establish the relationship between risk factors for coronary heart disease. Our results showed that The TAFI level in patients was authentically increased by 2.3 more time in patients compared to healthy individuals. At the same time, we found strong correlation between TAFI and the main risk factors of ischemic heart disease such as ADS, AH, obesity.
Key words: *Ischemic heart disease, hypercoagulation, Thrombin-activatable fibrinolysis inhibitor (TAFI), risk factors.*
Results. Cardiovascular Diseases (CVD) represent a larger socially important problem as take the leading place in structure of a mortality, loss of disability and an invalidism of able-bodied population [16]. Hypercoagulability, a condition in which the hemostatic balance is tilted towards thrombus formation, increases the risk of arterial thrombosis. Due to its role in the balance between coagulation and fibrinolysis, thrombin activatable fibrinolysis inhibitor (TAFI) may be involved in the development of cardiovascular diseases [17,18]. The data obtained in the study reflected the total content of the biomarker in the blood, its relationship with risk factors of coronary heart disease.
Conclusion. Assessment of the results obtained in this study researches can this essential life on the assumption that the early development of coronary heart disease, especially at untimely eliminate the dominant risk factors, as established by correlation relationship of TAFI with smoking, obesity, ADS and cholesterol.

Introduction

Worldwide mortality due to cardiovascular disease is the dominant cause of death. Among cardiovascular illnesses, ischemic heart disease (IHD) ranks as the most prevalent [1]. An increasing number of individuals with non-fatal IHD live with chronic disabilities and impaired quality of life [2]. According to the World Heart Federation, the global cost of CVD in 2010 was approximately US$863 billion, which is expected to rise to more than US$1 trillion by 2030. In countries like the United States, the cost of IHD is approaching 1%-1.5% of the gross domestic product (GDP), with costs per episode of IHD of more than $5,000 (7,13). Notably, the median total cost of IHD care in low and middle-income countries (LMIC) country-specific health expenditure per capita was 10% of the total healthcare expenditure [3].

Noncommunicable diseases including CVDs share various modifiable behavioral risk factors such as unhealthy diet, tobacco use, excess alcohol consumption and physical inactivity which lead to metabolic syndromes [4]. The primary pathological process that leads to IHD is atherosclerosis, an inflammatory disease of the arteries associated with lipid deposition and

metabolic alterations due to multiple risk factors. More than 70% of at-risk individuals have multiple risk factors for IHD, and only 2%-7% of the general population have no risk factors [5].

Reduced fibrinolytic capacity is presumed to be involved in the development and/or progression of atherosclerotic plaque, but its pathogenetic role is not fully established. This may be due in part to complex interrelations of fibrinolysis with lipoproteins, with insulin or insulin like peptides, and with different cell types in the normal and atherosclerotic vessel wall. Specific assays for antigen and activity levels of the main components of the fibrinolytic system have recently made it possible to establish an association between low fibrinolytic activity and atherothrombosis [6]. The physiological importance of the fibrinolytic system in humans is demonstrated by associations between impaired fibrinolysis and thrombotic events and between excessive fibrinolysis and bleeding complications. Clinical and epidemiological studies suggested that impairment of fibrinolytic activity, resulting in enhanced fibrin deposition, is a significant contributor to the development of atherothrombosis [7]. Hyperfibrinolysis can result in uncontrolled bleeding, as in the case with disseminated intravascular coagulation (DIC) where systemic inflammation causes increased consumption of fibrin and clotting factors. In a healthy individual, fibrinolysis is regulated by inhibiting plasminogen activator or antagonizing plasmin through α-2-antiplasmin. Plasminogen activator inhibitor (PAI) has been found to work on both tPA and uPA [8,9]. Thrombin-activatable fibrinolysis inhibitor (TAFI) is a glycoprotein which works by reducing activation of plasminogen [8]. Thrombin-activatable fibrinolysis inhibitor is a fibrinolysis inhibitor that is converted into its active form, TAFIa, during coagulation after thrombin cleavage. It acts by reducing plasminogen binding to fibrin leading to increase in lysis time [10,11.]. Its generation is dependent on thrombin levels and greatly potentiated by thrombomodulin [11,12]. TAFI and PAI-1 remained associated with thrombosis after extensive adjustment. Plasminogen, TAFI, PAI-1, and t-PA are associated with venous thrombosis. However, plasminogen and t-PA levels may reflect underlying risk factors. [13]

Most people with IHD do not have symptoms at an early age [14]. Indeed, IHD is acknowledged as an important threat to sustainable development in the 21st century [15].

Aim. To assess the markers of endogen fibrinolysis in patients with stable angina and with the main risk factors of ischemic heart disease (IHD).

Materials and methods. For the solution of objectives we all examined 67 patients with IHD passing on hospitalization in I-cardiology department of multidisciplinary clinic of Tashkent Medical Academy with the diagnosis ischemic heart disease. Average age of patients made 56,8±6,40 years.

The diagnosis of IHD (stable angina) verificated in compliance with classification of IHD accepted at the IV congress of cardiologists (2000) became criteria of including of patients. Functional class of IHD was established on the basis of classification of stenocardia of the Canadian society of cardiologists (1976) and exciting test veloergometry.

The control group was created from 25 people with risk factors of IHD, but without clinical signs of IHD. Average age of respondents of control group made 48,9±7,08 years.

All of the patients were assessed main risk factors such as arterial hypertension, obesity, anxiety depressive syndrome (ADS) and nicotine dependence. For detection of obesity was calculated the body weight index (BWI) with Quetelet's

formula. ADS was estimated by using Hospital Anxiety and Depression Scale (HADS). Nicotine dependence was estimated by Fagerstrem's test. Plasma level of thrombomoduline and Thrombin-activated fibrinolysis inhibitor were determined by using Human soluble Thrombomodulin elisa kit and imuclone tafielisa.

Statistical data processing.

Obtained in the study data were subjected to statistical analysis on a PC Pentium-IV using the program, many «MicrosoftOfficeExcel-2010" package, including the use of built-in statistical processing functions, as well as the program «STATISTICA 6.0». We used the methods of parametric variation and non-parametric statistics with calculation of the arithmetic mean of the studied indicator (M), standard error of the mean (m), relative-tion values (frequency,%). Statistical significance of the measurement-tion when compared to the mean values was determined by Student's test (t) with the calculation of error probability (P) when checking normality (kurtosis criterion) and the equality of general variances (F- Fisher criterion). For statistically significant changes took confidence level of $p < 0.05$.

Results

Cardiovascular Diseases (CVD) represent a larger socially important problem as take the leading place in structure of a mortality, loss of disability and an invalidism of able-bodied population [16]. Hypercoagulability, a condition in which the haemostatic balance is tilted towards thrombus formation, increases the risk of arterial thrombosis. Due to its role in the balance between coagulation and fibrinolysis, thrombin activatable fibrinolysis inhibitor (TAFI) may be involved in the development of cardiovascular diseases [17,18].

The data obtained in the study reflected the total content of the biomarker in the blood, its relationship with risk factors of coronary heart disease. In the main group's patients 71,6% (48/67) had appreciable high level of TAFI. Average index was 168,1±12,36 ng/ml. This index in control group was 73,5±7,6 ng/ml (table 1).

Table 1

Level of Thrombin-activated fibrinolysis inhibitor (TAFI) and thrombomoduline level in healthy people and COVID-19

Index	healthy people, n=25	Patients with IHD, n=65
TAFI (ng/ml)	73,5±7,6	168,1±12,36*
thrombomoduline (ME)	38,4±4,2	63,8±3,22*

Note: * - $p < 0,05$

We found markedly elevated levels of TAFI and thrombomoduline among patients hospitalized with IHD. The TAFI level in patients was authentically increased by 2.3 more time in patients compared to healthy individuals, and the thrombomoduline level was increased 1.65more time.

The hypercholesterinemia takes place at 21 - 27% of the population, smoking - at 60 - 90%, a hypodynamia - at 22%, excess body weight - at 40-60% that leads to working capacity depression, deterioration in social adaptation, emergence of the interfaced psychological problems [19]. Smoking, according to many researchers, along with arterial hypertension and a dislipoproteidemiya is important risk factor in development and advance of an atherosclerosis including in coronary vessels [20].

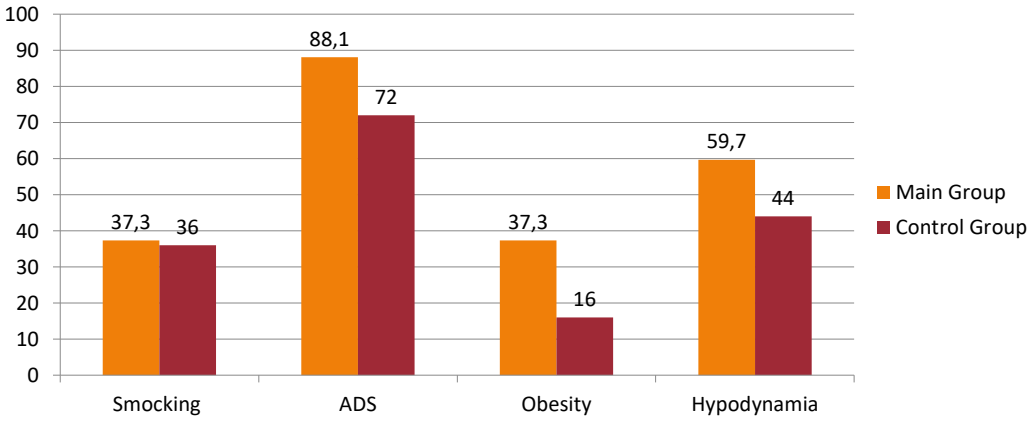

Fig.1. Frequency of risk factors of IHD patients and healthy individuals.

Apparently according to fig.1, in the anamnesis 37, 3% (25/67) of patients of the main group had a smoking, and at 36,0% (9/25) of patients of control group and difference between groups weren't statistically significant (P> 0,05). Patients with CVD had an existence of ADS at 88,1% (59/67) that there was more than in group of healthy faces at 72,0% (18/25) of patients (P<0,05). Patients with CVD with the accompanying obesity in the main group made 37,3% (25/67) and in control group of 16,0% (4/25) (P<0,05). At assessment of physical activity of the studied groups, statistically significant differences between groups (P<0,05) are taped as the hypodynamia prevailed at CVD patients in 59,7% (40/67)cases whereas in control group low physical activity made 44% (11/25) of probands.

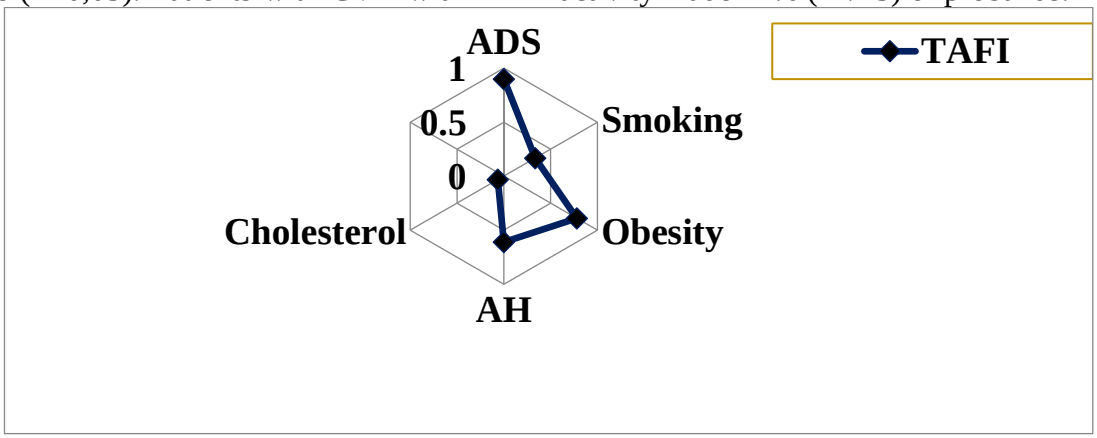

Fig. 2. Correlation between TAFI and the main risk factors of ischemic hear disease

We have already assessed the correlation between TAFI level in plasma and risk factors of IHD such as, anxiety depressive syndrome (ADS), smoking, AH, obesity and cholesterol level. TAFI level was considered to be associated with smoking and cholesterol level weak negative correlation (r=-0,3; r=0,1, respectively). At the same time we found strong correlation between TAFI and ADS,

AH, obesity, r was equal to 0; 0,90; 0,61;0,78 respectively (Figure 2).

Conclusion. Assessment of the results obtained in this study researches can this essential life on the assumption that the early development of coronary heart disease, especially at untimely eliminate the dominant risk factors, as established by correlation relationship of TAFI with smoking, obesity, ADS and cholesterol.

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