Background. The role of statins in treatment of coronary artery disease cannot be overestimated [1]. This group of medicines is included into the complex therapeutic treatment of patients with unstable angina (UA) [2]. Besides its direct mechanism of action [3], this group is characterized by numerous pleiotropic effects [4], including influence on fibrinolytic potential of blood plasma [5]. However, the data regarding effect of different statins on tissue plasminogen activator (tPA) and its inhibitor (PAI-1) are rather controversial [6,7].

The aim of our study was to compare changes of fibrinolytic potential of blood plasma after short-term treatment with statin (atorvastatin or rosuvastatin) in patients with UA.

Material and methods. 39 patients with UA were included in our prospective observational study. Written consent was obtained from each participating subject after the approval of the local ethics committee.

The inclusion criteria were age of 50-70 years, hospitalization in Kyiv city hospital #12 with UA (progressive), no statin intake within at least 3 months prior to the current study, standardized treatment according to the European Society of Cardiology guidelines, namely enoxaparin 1 mg / kg twice daily 3 days, 0.5 mg/kg twice daily 2 days subcutaneously, acetylsalicylic acid (ASA) once daily, clopidogrel once daily, bisoprolol once daily, angiotensin-converting enzyme inhibitor (ACEi)
(enalapril / ramipril / perindopril), nitrates in infusion once daily and in tablets twice
daily, pantoprazol once daily. It is worth to mention that primarily patients with all
types of UA were enrolled into the study. However, the difference in haemostatic
parameters in patients with different types of UA was found. Consequently, in our
study we included patients only with progressive UA who have already been treated
with ASA, bisoprolol, ACEi but with no statin intake within at least 3 month prior to
the study (mainly because of low compliance).

We divided them into 2 groups which were comparable in age, gender, body
mass index (BMI), lipidogram parameters, levels of blood pressure while admission.
I group was treated with atorvastatin 60 mg once daily, II group – with rosuvastatin
20 mg once daily [8].

The exclusion criteria were the history of myocardial infarction, stroke, heart
defects, persistent atrial fibrillation / atrial flutter, cardiomyopathies, non-ischemic
myocardial injuries, heart failure IIb-III stage, endocrinological disorders, active
infection, chronic diseases in period of exacerbation, blood diseases including
coagulopathies, anemia of II-III stage, glomerular filtration rate less than 60 ml/min./
1,73 m², hepatic dysfunction, malignancy, traumas and bleedings within 6 months
prior to this study, other conditions with known thrombophilic state.

Blood samples were taken before and on the seventh day of the treatment.
Whole blood samples were collected by phlebotomy in sodium citrate and were
centrifugated. Levels of PAI-1, tPA were done by ELISA immune assays with
primary and secondary antibodies according to the manufacturer’s instructions.

Statistical program SPSS v.22 was used for statistical analysis. The type of
distribution was checked by Kolmogorov-Smirnov test. As the distribution was
skewed, numerical variables were presented as the median and interquartile range.
Nominal variables were presented in absolute values (percentage) and compared
using chi-squared test. Wilcoxon test was used for paired samples. P value <0,05
was considered statistically significant.

Results. 39 patients were included in our study with median age of 64,0 (60,0-
69,0) years and BMI of 28,08 (25,71-32,27) kg/m². The levels of general cholesterol,
triglycerides, high density lipoprotein, low density lipoprotein were 5,1 (4,5-6,6)
mmol/L, 2,06 (1,44-2,66) mmol/L, 1,15 (1,00-1,69) mmol/L, 3,35 (2,51-4,04) mmol/L
respectively. All patients had symptoms of typical angina. Ischemic changes were
registered on all ECGs while admission: 37 (95%) patients with ST-segment
depression, 2 (5%) patients with new-onset left bundle branch 20 (51
%) with T wave
variability. The qualitative troponin I test was negative in all patients. Both groups
were comparable in age, gender, BMI, lipidogram parameters, levels of blood
pressure while admission.

The levels of PAI-1 in atorvastatin group before and after 6 days of treatment
were 0,392 (0,343-0,417) U/ml and 0,510 (0,408-0,521) U/ml respectively, and in
rosuvastatin group the same parameters were 0,386 (0,338-0,407) U/ml and 0,497
(0,398-0,528) U/ml. Thus, there was no significant difference in incre
ase of PAI-1
levels between groups.

The tPA levels in atorvastatin group before and after 6 days of treatment were
0,245 (0,194-0,255) U/ml and 0,195 (0,176-0,215) U/ml, whereas in rosuvastatin
group tPA levels were 0,227 (0,214-0,321) U/ml and 0,222 (0,212-0,296) U/ml.
Thus, the significant decrease in tPA level was registered in atorvastatin group
(p=0.042), while tPA level in rosuvastatin group was remained almost at the same level (0.237).

Increase in PAI-1 level in both groups and significant or slight decrease in tPA levels are the signs of thrombotic state activation after 6 days of treatment. However, the background of such trends may be treatment with anticoagulant (enoxaparin) and its discontinuation. Taking into the account this fact abovementioned changes may be connected with protective effects of rosuvastatin on endothelium.

**Conclusions.** Thrombophilic state activation after enoxaparin discontinuation is more pronounced in atorvastatin group. Absence of tPA level changes in rosuvastatin group may be the sign of protective rosuvastatin influence on endothelium. Abovementioned findings call for further researches of statins' pleiotropic effects on hemostasis.

**References:**


