Is endothelial dysfunction a driving force of COVID-19 induced coagulopathy?

O. Dukhin[1], A. Kalinskaya[1], I. Molodtsov[2], A. Maltseva[1], D. Sokorev[2], A. Elizarova[1], K. Glebova[1], D. Stonogina[1], S. Shakhidzhanov[3], I. Spiridonov[3], F. Ataullakhanov[4], L. Margolis[5], A. Shpektor[1], E. Vasilieva[1]

[1]Moscow State University of Medicine and Dentistry, Moscow, Russian Federation; [2]Clinical City Hospital named after I.V. Davydovsky, Moscow, Russian Federation; [3]Center for Theoretical Problems of Physico-Chemical Pharmacology RAS, Moscow, Russian Federation; [4]University of Pennsylvania, Philadelphia, United States of America; [5]National Institutes of Health, Bethesda, United States of America

Funding Acknowledgement: Type of funding sources: None.

Background/Introduction: There are numerous reports regarding the direct endothelial damage by the SARS-CoV-2 that can lead to activation of both plasma hemostasis and platelet aggregation. However, the mechanism of interaction between endothelium and haemostasis in COVID-19 remains unclear.

Purpose: The aim of our study was to assess the relationship between each link of clot formation process (endothelial function, plasma coagulation, platelet aggregation) with the severity of the disease.

Methods: 58 COVID-19 patients were included in our study. Patients were divided into moderate (n=39) and severe (n=18) subgroups. All patients underwent a flow-mediated dilation (FMD) test, impedance aggregation, rotational thromboelastometry, thrombodynamics and von Willebrand factor antigen (vWF: Ag) quantification. All measurements were repeated on days 3 (point 2) and 9 (point 3) of hospitalization.

Results: COVID-19 patients demonstrated the enhanced plasma coagulation (clotting time, s 613,0 [480; 820], clot growth rate, μm/min 32,75 [29,3; 38,7]). At point 1 no significant difference in parameters of plasma coagulation between patients' subgroups was noted. At point 2 a significant decrease in the size (CS, μm 1278.0 [1216.5; 1356.5] vs 965.0 [659.8; 1098.0], $p<0,01$) and clot growth rate (μm/min 32,4 [29,2; 35,0] vs 17,7 [10,3; 24,4], $p<0,01$) under the influence of anticoagulants in the moderate subgroup compared with point 1 was observed. We didn't observe such phenomenon in severe subgroup.

There was no significant difference in platelet aggregation between subgroups at point 1. During the course of the disease the patients in the moderate and severe subgroups demonstrated a significant increase in platelet aggregation induced by arachidonic acid and ADP (severe: AUC ARA 48,0 [25,0; 59,0] vs 77,5 [55,8; 92,7], p=0,04; AUC ADP 44,0 [41,0; 56,0] vs 58,0 [45,5; 69,0], p=0,04; moderate: AUC ARA 31,5 [19,8; 50,7] vs 56,0 [39,0; 76,0], p=0,01; AUC ADP 43,0 [20,0; 59,0] vs 56,6 [50,3; 70,5], p=0,04;), in moderate subgroup the significant increase in TRAP-induced aggregation was also noted (AUC TRAP 58,0 [41,0; 69,5] vs 76,0 [58,3; 81,5], p=0,048). There were no significant differences in the FMD-test results between the patient subgroups. FMD-test results were predominantly within the reference ranges (7,1 [4,0; 8,8]).

Patients in the severe subgroup had significantly higher levels of vWF: Ag (228,0 [205,3; 240,7] vs 232,0 [226,0; 423,0], p=0,03).

Conclusion: SARS-CoV-2 infection was characterized by increased levels of vWF:Ag, that could represent the local endothelial damage, meanwhile there was no generalized endothelial dysfunction assessed via FMD-test in moderate to severe patients. At the same time the enhanced plasma coagulation in COVID-19 patients was observed.