MSW MANAGEMENT -Multidisciplinary, Scientific Work and Management Journal
ISSN: 1053-7899
Vol. 33 Issue 2, December – 2023, Pages: 133-141

EVALUATION OF THE EFFECTIVENESS OF ANTICOAGULANT THERAPY IN CORONAVIRUS INFECTION

Boltoeva Feruza Ganjaboevna
Assistant of the Department of Hematology and Military Field Therapy,
Urgench Branch of Tashkent Medical Academy
feruzabaltayeva80@gmail.com

Babajanova Shaira Agzamovna
MD.,Professor of the Department of Hematology,
Transfusiology and Laboratory Work of Tashkent Medical Academy

Kurbonova Zumrad Chutbaevna
PhD,Associate Professor of the Department of Hematology, Transfusiology and Laboratory Work of Tashkent Medical Academy

Annotation. The use of anticoagulants is employed to prevent thrombotic complications in COVID-19, but the optimal anticoagulant therapy strategy has not yet been determined due to varying levels of kinin severity. The purpose of this study was to evaluate the efficacy of anticoagulant therapy in COVID-19 patients. Materials and methods. Clinical trials were conducted in 2021 at the COVID-19 treatment department of the Comprehensive Medical Center in Khorezm region. A total of 187 patients with COVID-19 were examined. Diagnostic indicators were obtained from "Temporary Recommendations for the Treatment of Patients with Coronavirus Infection" for the diagnosis of COVID-19 patients. Research results. Moderate and severe cases of COVID-19 indicate hypercoagulability through decreased levels of APTT, PT, TT, INR, increased PI and fibrinogen. Increased levels of D-dimer, ferritin, C-reactive protein, and procalcitonin were observed in patients with moderate and severe COVID-19. Implementing a complex treatment with low molecular weight heparin in coronavirus infection effectively mitigated hypercoagulability.

Keywords: COVID-19, anticoagulant therapy, hypercoagulability, activated partial thromboplastin time, prothrombin time, thrombin time, fibrinogen, D-dimer, procalcitonin, ferritin, C-reactive protein.

In 2019, the first cases of coronavirus infection (COVID-19) were identified, which quickly spread to many countries and became the cause of a pandemic [6]. Chinese scientists have confirmed that this disease is caused by a new type of beta-coronavirus infection [22]. COVID-19 can damage various organs, including the lungs, heart, blood vessels, liver, intestines, nervous system, and immune system [14, 16].

The pathogenic aspects of COVID-19 are still being studied, and the disease's transmission, clinical manifestations, complications, and treatment strategies are constantly changing [15]. During the acute phase of the disease, mortality rates were high due to the activation of the blood coagulation system, leading to blood clotting and thrombosis [11].

Hypercoagulability has been observed in all components of the blood coagulation system in COVID-19 patients. These changes contribute to the development of thrombosis in many organs, including the lungs and deep veins [4]. Thrombotic events are more common in severe cases of COVID-19, with up to 20-30% of critically ill patients developing thromboembolic complications. COVID-19 differs from other respiratory infections in that it causes a strong thrombotic response [13].

Patients with severe and critical COVID-19 are more likely to be older adults, with 89% of patients aged 50-69 years. These patients are at higher risk of developing thromboembolic complications [4, 10]. Although

MSW MANAGEMENT -Multidisciplinary, Scientific Work and Management Journal
ISSN: 1053-7899
Vol. 33 Issue 2, December – 2023, Pages: 133-141

anticoagulant and antiplatelet therapies are effective in preventing thrombotic events, they are not always successful. Thrombotic events are more common in the heart and brain blood vessels. COVID-19 can cause small blood vessel damage, leading to end-organ damage and death [4].

In response to SARS-Cov-2, the human body produces a large amount of cytokines, including C-reactive protein, ferritin, lactate dehydrogenase, D-dimer, interleukin-1 beta, interleukin-6, interleukin-2, tumor necrosis factor-alpha, and chemokines. This results in a hyperimmune response known as a "cytokine storm," which damages the blood vessels' endothelium and leads to blood coagulation and thrombosis [19].

Currently, the study of genetic risk factors for thrombophilia in various medical fields, especially in response to COVID-19, is a critical task [22].

Thrombophilia gene polymorphisms, such as MTHFR gene A1298C (rs 1801131), C677T (rs 1801133), MTR gene rs1805087, and MTRR gene rs1801394, as well as elevated levels of homocysteine in the Uzbek population, have been studied to help prevent severe complications in patients with genetic susceptibility to thrombosis caused by COVID-19. Changes in MTHFR, MTR, and MTRR genes increase homocysteine levels, which ultimately damage the blood vessel endothelium. The resulting endothelial dysfunction and oxidative stress increase thromboxane A2, leading to platelet aggregation [2, 17, 18].

Identifying patients with genetic susceptibility to thrombosis and using specific prophylactic and treatment strategies can help prevent severe complications of COVID-19. Studies during the COVID-19 pandemic have shown a link between a history of diabetes mellitus and a higher risk of severe illness. The pathogenesis of diabetes mellitus involves metabolic, hemodynamic, hemostatic, and genetic changes that contribute to endothelial dysfunction and the development of severe thrombotic complications in COVID-19 patients. Changes in the CRP polymorphism of the S3872T gene in patients with diabetes mellitus can also increase the risk of cardiovascular disease [1, 3, 10], especially in those without genetic predisposition to thrombotic complications [7, 8]. Additionally, changes in thrombophilia genes can lead to ischemic stroke in children. Strong hypercoagulation has been observed in patients with changes in thrombophilia genes, and long-term antiplatelet therapy is recommended for these patients [18, 20].

Blood tests not only provide information about the coagulation process but also help identify internal organ damage (such as kidney and liver damage) and determine the severity of illness, which is crucial for determining treatment strategies. COVID-19 patients with leukocytosis, neutropenia, and a left shift in leukocyte count have a higher risk of developing severe complications.Coagulation hemostasis markers remain relatively unchanged in mild COVID-19 cases, but in moderate and severe cases, there is a significant increase in thromboplastin time (25.5-39.5%), prothrombin time (24-37%), thrombin time (22.3-45.2%), and a decrease in prothrombin index (35-62%) and fibrinogen levels (57.6-80.2%). Moderate and severe COVID-19 cases are associated with strong hypercoagulable changes in plasma hemostasis [22].

In addition, COVID-19 increases platelet adhesion and aggregation function while decreasing clot retraction time [5]. Patients with severe COVID-19 have increased platelet aggregation (23-36%) and adhesion (60-98%), while those with mild cases have normal platelet function. The production of thrombus fragments, measured by D-dimer levels, sharply increases in COVID-19. This indicates the presence of hypercoagulable changes in platelet hemostasis[9, 21].

Studies by A. Assiri and colleagues have shown that thrombocytopenia and leukopenia in severe COVID-19 cases are poor prognostic indicators [12].

The use of anticoagulants is employed to prevent thrombotic complications in COVID-19, but the optimal anticoagulant therapy strategy has not yet been determined due to varying levels of kinin severity.

The purpose of this study was to evaluate the efficacy of anticoagulant therapy in COVID-19 patients.

MSW MANAGEMENT -Multidisciplinary, Scientific Work and Management Journal
ISSN: 1053-7899
Vol. 33 Issue 2, December – 2023, Pages: 133-141

Materials and methods. Clinical trials were conducted in 2021 at the COVID-19 treatment department of the Comprehensive Medical Center in Khorezm region. A total of 187 patients with COVID-19 were examined.

All patients were divided into three groups: Group 1 consisted of 56 patients with mild kinin severity, Group 2 consisted of 61 patients with moderate to severe kinin severity, and Group 3 consisted of 70 patients with severe kinin severity. A control group of 30 healthy individuals with matching gender and age was also included in the study.

Diagnostic indicators were obtained from "Temporary Recommendations for the Treatment of Patients with Coronavirus Infection" for the diagnosis of COVID-19 patients. All patients in the study were diagnosed as positive for SARS-Cov-2 virus markers through immunoassay and polymerase chain reaction.

Of the 187 patients, 195 (55.7%) were female and 150 (44.3%) were male. The average age of the patients was 56.4 ± 15.3 years, ranging from 18 to 74 years. Patients with additional diseases such as diabetes mellitus, arterial hypertension, oncological diseases, liver and kidney diseases were not included in the study.

Diagnosis was based on complaints, medical history, clinical signs of the disease, and laboratory data using the "Temporary Recommendations for the Treatment of Patients with Coronavirus Infection" version 10. The age range of patients was from 20 to 72 years.

General blood analysis is an important part of clinical laboratory diagnostics, which is necessary for determining the number of platelets and monitoring their treatment. General blood analysis was performed using Sysmex XN-550 (Japan) automatic hematological analyzer with Sysmex (Japan) reagents.

Plasma coagulation tests were used to describe the hemostasis phase: activated partial thromboplastin time, prothrombin time, prothrombin index, international normalized ratio, thrombin time, fibrinogen and D-dimer. Coagulogram indicators were determined using Sysmex CA-660 (Japan) automatic coagulometer with Sysmex (Japan) reagents.

To evaluate the degree of inflammation, procalcitonin, ferritin and C-reactive protein were measured using Maglumi X3 (China) automatic immunoassay and immunoluminescence analyzer with Maglumi (China) reagents.

Research results. A total of 187 patients with coronavirus infection were examined in the clinical study. To study plasma hemostasis indicators, activated partial thromboplastin time (APTT), prothrombin time (PT), prothrombin index (PI), international normalized ratio (INR), fibrinogen, thrombin time (TT), D-dimerwere determined. Ferritin and C-reactive protein, which are also markers of inflammation, were also tested.

In COVID-19 patients with thromboembolic complications, APTT was measured to investigate the first stage of plasma hemostasis. The following results were obtained: in group 1, APTT was 25.2 ± 2.1 sec, in group 2 it was 20.2 ± 1.8 sec*, and in group 3 it was 16.1 ± 1.4 sec***. The control group had an APTT of 27.4 ± 2.2 sec. In conclusion, APTT was normal in group 1, while groups 2 and 3 showed a decrease in APTT, indicating activation of the blood clotting system.

To investigate the second stage of plasma hemostasis, PT, PI, and INR were measured. Similar changes were observed in these indicators: in group 1, PT was 11.1 ± 0.9 sec, in group 2 it was 9.3±0.7 sec*, and in group 3 it was 8.2 ± 0.7 sec**. The control group had a PT of 12.0 ± 1.2 sec. PI is calculated based on PT. In group 1, PI was 108 ± 8.8%, in group 2 it was 129 ± 8.2%*, and in group 3 it was 150 ± 12.3%*. The control group had a PI of 98.0 ± 6.6%.

INR is an indicator of the effectiveness of anticoagulant therapy, and it is necessary to monitor this indicator during treatment. In the control group, INR was 1.0 ± 0.08, while in group 1 it was 0.92 ± 0.06, in group 2 it was 0.77 ± 0.06*, and in group 3 it was 0.68 ± 0.05**.

To investigate TT in COVID-19 patients, which is an indicator of hypercoagulability, the following results were obtained: in group 1, TT was 14.9 ± 1.1 sec***, in group 2 it was 11.2 ± 1.0 sec***, in group 3 it was 9.4 ± 0.7 sec***, and in the control group, TT was 22.6 ± 1.6 sec.

MSW MANAGEMENT -Multidisciplinary, Scientific Work and Management Journal
ISSN: 1053-7899
Vol. 33 Issue 2, December – 2023, Pages: 133-141

Fibrinogen is an indicator of the first stage of plasma hemostasis, and its decrease is a marker of hypercoagulability in COVID-19 patients. In group 1, fibrinogen was 3.86 ± 0.33 g/l, in group 2 it was 4.62 ± 0.51 g/l*, and in group 3 it was 6.14 ± 0.68 g/l***. The control group had a fibrinogen level of 2.54 ± 0.28 g/l (table 1).

Table 1.

Plasma hemostasis indicators in COVID-19 patients.

Groups	Monitoring group (n=20)	Group 1 (n=100)	Group 2 (n=150)	Group 3 (n=100)
APTT, sec	27,4±2,2	25,2±2,1	18,2±1,8**	14,1±1,1***
PT, sec	12,0±1,2	11,1±0,9	9,3±0,7*	8,2 ± 0,7**
PTI,%	98,0±6,6	108±8,8	129±8,2*	150±12,3*
INR	1,0 ±0,08	0,92±0,06*	0,77±0,06*	0,68±0,05**
TT	22,6±1,6	14,9±1,1***	11,2±1,0***	9,4±0,7***
Fibrinogen	2,54±0,28	3,86±0,33	4,62±0,51**	6,14±0,68***

Note: * - indicates a significant difference compared to the control group (*-P<0.05; **-P<0.01; *** - P<0.001).

D-dimer is a marker of thrombus degradation and is related to the formation and fragmentation of thrombi. In group 1, the D-dimer level was 251 ± 20 ng/ml, in group 2 it was 483 ± 32 ng/ml***, and in group 3 it was 665 ± 48 ng/ml***, while in the control group it was 196 ± 16 ng/ml.

Ferritin and C-reactive protein (CRP) are inflammatory markers, and an increase in their levels reflects the degree of inflammation. In group 1, ferritin was 295 ± 31 µg/mL*, CRP was 8 ± 0.7 mg/l*, in group 2, ferritin was 512 ± 42 µg/ml***, CRP was 22 ± 1.8 mg/l***, and in group 3, ferritin was 784 ± 65 µg/ml***, CRP was 62 ± 4.9 mg/l***. In the control group, ferritin was 180 ± 16 µg/ml and CRP was 6.2 ± 0.4 mg/l.

Procalcitonin is a prohormone used as an early diagnostic marker for bacterial infection. In group 1, procalcitonin was 0.4 ± 0.03 ng/ml**, in group 2 it was 0.72 ± 0.05 ng/ml***, and in group 3 it was 1.4 ± 0.11 ng/ml***, while in the control group it was 0.3 ± 0.02 ng/ml.

In conclusion, patients with severe COVID-19 showed no significant changes in blood coagulation and inflammatory markers in group 1, but significant hypercoagulable changes and inflammatory processes were observed in all stages of plasma coagulation in groups 2 and 3. Standard antiviral, antiplatelet, and symptomatic treatments were provided to patients, and anticoagulant therapy was administered to groups 2 and 3 to improve hemostasis and prevent hypercoagulability.

In group 2, 30 patients and in group 3, 33 patients were recommended to receive Heparin 5000 IU subcutaneously 4-6 times a day according to body weight. Enoxaparin 6000 IU was recommended to be administered subcutaneously twice a day to 31 patients in group 2 and 37 patients in group 3.

Heparin is a parenteral anticoagulant and is produced in a 5 ml vial containing 25,000 IU. Each mL contains 5000 IU of heparin sodium, 9 mg benzyl alcohol, 3.4 mg sodium chloride, and water for injection.

Heparin is a medium molecular weight heparin and acts as an anticoagulant by binding to antithrombin III and inhibiting the formation of fibrin. Antithrombin III is an inhibitor of active thrombin, IXa, Xa, XIa, and XIIa factors and exerts its effect within 15-30 minutes when administered intravenously, within 20-60 minutes when administered subcutaneously, and reaches its therapeutic dose in 4-5 hours. It is bound to 95% plasma

MSW MANAGEMENT -Multidisciplinary, Scientific Work and Management Journal
ISSN: 1053-7899
Vol. 33 Issue 2, December – 2023, Pages: 133-141

proteins and is not rapidly metabolized from the vascular system. Due to its effect on platelet antigens and its association with endothelial and mononuclear-macrophage cells, its duration of action is short, i.e., 4-6 hours.

Enoxaparin is also a parenteral anticoagulant and is available in a 1 ml syringe containing enoxaparin sodium 6000 IU and distilled water.

Enoxaparin is a low molecular weight heparin that acts as an anticoagulant by binding to antithrombin III and inhibiting the formation of fibrin. Antithrombin III is an inhibitor of active thrombin, IXa, Xa, XIa, and XIIa factors and exerts its effect within 15-30 minutes when administered intravenously, within 20-60 minutes when administered subcutaneously, and reaches its therapeutic dose in 4-5 hours. It is bound to 95% plasma proteins and is not rapidly metabolized from the vascular system. Due to its effect on platelet antigens and its association with endothelial and mononuclear-macrophage cells, its duration of action is short, i.e., 4-6 hours.

The effectiveness of anticoagulant therapy was evaluated before and on days 5-10 of treatment.

In COVID-19 treatment, the evaluation of APTT showed the following changes: when therapy was conducted with heparin, in group 2, before treatment, APTT was 18.2 ± 1.8 sec, and after 5 days of therapy, it reached 23.6 ± 1.7 sec$^{\wedge}$, and after 10 days, it was 28.9 ± 2.8 sec$^{\wedge\wedge}$. When anticoagulant therapy was conducted with enoxaparin, the evaluation of APTT showed the following results: in group 2, before treatment, APTT was 18.2 ± 1.8 seconds, and after 5 days of therapy with enoxaparin, it reached 27.8 ± 2.3 seconds$^{\wedge\wedge}$, and after 10 days, it was 29.0 ± 1.9 seconds$^{\wedge\wedge\wedge}$(note: $^{\wedge}$- indicates a significant difference compared to indicator before treatment ($^{\wedge}$-P<0.05; $^{\wedge\wedge}$-P<0.01; $^{\wedge\wedge\wedge}$ - P<0.001).

In Group 3 withCOVID-19, APTT was 14.1 ± 1.4 sec before treatment, by day 5 when treated with heparin, the rate extends to 20.4±2.0 sec$^{\wedge}$, and on day 10 to 24.1±2.1 sec$^{\wedge\wedge\wedge}$. Treatment with enoxyparin has shown that the effectiveness of small molecular heparin has been much higher: at 14.0 ± 1.3 sec before treatment, on day 5, APTT extends to 26.4 ± 2.1 sec$^{\wedge\wedge\wedge}$, and on day 10 to 34.6 ± 2.9 sec$^{\wedge\wedge\wedge}$.

In summary, treatment of groups 2 and 3 demonstrated that enoxaparin, a low molecular weight heparin, showed higher efficacy compared to heparin in increasing the APTT indicator.

When anticoagulant therapy was performed with heparin, similar changes were observed in PT tests in group 2: before treatment, the PT was 9.3 ± 0.7 sec, while after 5 days of therapy it increased to 11.2 ± 1.0 sec and up to 12.5 ± 1.3 sec$^{\wedge}$ after 10 days. When anticoagulant therapy was performed with enoxaparin, the following results were obtained when testing the PT in these groups: before treatment, the PT was 9.1 ± 0.8 sec, while after 5 days of therapy with enoxaparin it increased to 12.8 ± 1.1 sec$^{\wedge\wedge}$ and up to 15.2 ± 1.3 sec$^{\wedge\wedge\wedge}$ after 10 days.

In group 3, before treatment, the PT was 8.2 ± 0.7 sec, while after 5 days of therapy with heparin it increased to 10.3 ± 0.9 sec and up to 12.2 ± 1.0 sec$^{\wedge\wedge}$ after 10 days. In group 3, before treatment with enoxaparin, the PT was 8.1 ± 0.8 sec, while after 5 days of therapy it increased to 12.3 ± 1.1 sec$^{\wedge\wedge}$ and up to 14.0 ± 1.2 sec$^{\wedge\wedge\wedge}$ after 10 days.

The PTI tests showed that in patients in the 2 group who had been treated with heparin prior to therapy, the PTI was 129 ± 10% before treatment, 107 ± 9% on the fifth day of therapy, and 96 ± 7%$^{\wedge\wedge}$ on the tenth day of therapy. Inpatients in the second group who had been treated with enoxaparin, the PTI tests yielded the following results: 131 ± 1.1% before treatment, 93 ± 8%$^{\wedge\wedge}$ after five days of therapy, and 78 ± 8%$^{\wedge\wedge\wedge}$ after ten days of therapy.

In group 3, patients treated with Heparin had a PTI of 146 ± 11% before therapy, which decreased to 116 ± 10%$^{\wedge}$ on day 5 of therapy and further decreased to 98 ± 8%$^{\wedge\wedge\wedge}$ on day 10. In contrast, patients treated with Enoksiparin in group 3 had a PTI of 148 ± 12% before therapy, which decreased to 97 ± 8%$^{\wedge\wedge\wedge}$ on day 5 of therapy and further decreased to 85 ± 7%$^{\wedge\wedge\wedge}$ on day 10.

In the group treated with heparin, in group 2, before treatment, INR was 0.77 ± 0.06 sec, and after 5 days of therapy, it reached 0.93 ± 0.07 sec, and after 10 days, it was 1.04 ± 0.08 seconds$^{\wedge\wedge}$. In the group

MSW MANAGEMENT -Multidisciplinary, Scientific Work and Management Journal
ISSN: 1053-7899
Vol. 33 Issue 2, December – 2023, Pages: 133-141

treated with enoxaparin, in group 2, before treatment, INR was 0.75 ± 0.06 sec, and after 5 days of therapy, it reached 1.06 ± 0.08 seconds$^{\wedge\wedge}$, and after 10 days, it was 1.26 ± 0.1 sec$^{\wedge\wedge\wedge}$.

In patients of group 3, before treatment with heparin, INR was 0.68 ± 0.05, and after 5 days of therapy, it reached 0.85 ± 0.8$^{\wedge}$, and after 10 days, it was 1.01 ± 0.09$^{\wedge\wedge\wedge}$. In patients of group 3, before treatment with enoxaparin, INR was 0.67 ± 0.05, and after 5 days of therapy, it reached 0.97 ± 0.08$^{\wedge}$, and after 10 days, it was 1.16 ± 1.0$^{\wedge\wedge\wedge}$.

The treatment regimen with heparin in group 2 resulted in an improvement in fibrinogen levels. Before treatment, the fibrinogen level was 4.65 ± 0.55 g/l, after 5 days of heparin therapy, it became 4.03 ± 0.32 g/l, and after 10 days, it decreased to 3.26 ± 0.23 g/l$^{\wedge}$. In the COVID-19 treatment regimen with enoxaparin, there was a normalization of fibrinogen levels within 5 days. Before treatment, the fibrinogen level in group 2 was 4.60 ± 0.48 g/l, and after 5 days of therapy, it decreased to 3.15 ± 0.30 g/l$^{\wedge}$, and after 10 days, it further decreased to 2.66 ± 0.22 g/l$^{\wedge\wedge\wedge}$.

In group 3, before treatment with heparin, the fibrinogen level was 6.12 ± 0.70 g/l. After 5 days of heparin therapy, the fibrinogen level became 5.23 ± 0.41 g/l, and after 10 days, it decreased to 4.02 ± 0.33 g/l$^{\wedge\wedge}$. In group 3, before treatment with enoxaparin, the fibrinogen level was 6.17 ± 0.65 g/l. After 5 days of enoxaparin therapy, the fibrinogen level decreased to 4.31 ± 0.35 g/l$^{\wedge}$, and after 10 days, it further decreased to 3.58 ± 0.30 g/l$^{\wedge\wedge\wedge}$.

D-DIMER IS A PRODUCT OF THROMBUS BREAKDOWN AND ITS ELEVATION INDICATES INCREASED FIBRINOLYSIS IN COVID-19. IN GROUP 2, BEFORE TREATMENT, D-DIMER LEVELS WERE 481 ± 31 NG/ML. AFTER 5 DAYS OF HEPARIN TREATMENT, D-DIMER LEVELS DECREASED TO 356 ± 38 NG/ML$^{\wedge}$, AND AFTER 10 DAYS, IT FURTHER DECREASED TO 274 ± 26 NG/ML$^{\wedge\wedge\wedge}$. IN GROUP 2 PATIENTS TREATED WITH ENOXAPARIN, BEFORE TREATMENT, D-DIMER LEVELS WERE 485 ± 33 NG/ML, AND DURING TREATMENT, AFTER 5 DAYS, IT DECREASED TO 314 ± 32 NG/ML$^{\wedge\wedge\wedge}$, AND AFTER 10 DAYS, IT FURTHER DECREASED TO 218 ± 20 NG/ML$^{\wedge\wedge\wedge}$ (TABLE 2).

TABLE 2.

CHANGES IN D-DIMER LEVELS DURING ANTICOAGULANT TREATMENT.

Groups	**2-group**		**3-group**	
Treatment type	Heparin	Enoxaparin	Heparin	Enoxaparin
Before treatment	481±31	485±33	667±46	663±50
5th day	356±38$^{\wedge}$	314±32$^{\wedge\wedge\wedge}$	459± 39$^{\wedge\wedge}$	374± 32$^{\wedge\wedge\wedge}$
10th day	274± 26$^{\wedge\wedge\wedge}$	218± 20$^{\wedge\wedge\wedge}$	276±25$^{\wedge\wedge\wedge}$	218± 20$^{\wedge\wedge\wedge}$

Note: $^{\wedge}$ - indicates a significant difference compared to the control group ($^{\wedge}$-P<0.05; $^{\wedge\wedge}$-P<0.01; $^{\wedge\wedge\wedge}$ - P<0.001).

In group 3, before treatment, D-dimer levels were 667 ± 46 ng/ml. After 5 days of heparin treatment, D-dimer levels decreased to 459 ± 39 ng/ml$^{\wedge\wedge}$, and after 10 days, it further decreased to 276 ± 25 ng/ml$^{\wedge\wedge\wedge}$. With enoxaparin treatment, before treatment, D-dimer levels were 663 ± 50 ng/ml, and during therapy, after 5 days, it decreased to 374 ± 32 ng/ml$^{\wedge\wedge\wedge}$, and after 10 days, it further decreased to 218 ± 20 ng/ml$^{\wedge\wedge\wedge}$.

Ferritin levels before treatment in group 2 were 515 ± 45 μg/ml. After 5 days of heparin therapy, ferritin levels decreased to 378 ± 33 μg/ml$^{\wedge}$, and after 10 days, it further decreased to 220 ± 20 μg/ml$^{\wedge\wedge\wedge}$.

MSW MANAGEMENT -Multidisciplinary, Scientific Work and Management Journal
ISSN: 1053-7899
Vol. 33 Issue 2, December – 2023, Pages: 133-141

With enoxaparin treatment, before treatment, ferritin levels were 510 ± 39 μg/ml, and during therapy, after 5 days, it decreased to 332 ± 31 μg/ml$^{\wedge\wedge\wedge}$, and after 10 days, it further decreased to 165 ± 16 μg/ml$^{\wedge\wedge\wedge}$.

In group 3 patients with COVID-19, before treatment, ferritin levels were 784 ± 65 μg/ml. After 5 days of heparin treatment, ferritin levels decreased to 474 ± 42 μg/ml$^{\wedge\wedge\wedge}$, and after 10 days, it further decreased to 289 ± 26 μg/ml$^{\wedge\wedge\wedge}$. With enoxaparin treatment, before treatment, ferritin levels were 784 ± 65 μg/ml, and during therapy, after 5 days, ferritin levels were 502 ± 48 μg/ml$^{\wedge\wedge\wedge}$, and after 10 days, it further decreased to 321 ± 29 μg/ml$^{\wedge\wedge\wedge}$.

In Group 2, before treatment, the level of CRP was 21.3 ± 1.8 mg/L. After treatment with heparin, on day 5, it decreased to 15.5 ± 1.3 mg/l$^{\wedge}$, and on day 10, it further decreased to 9.6 ± 0.8 μg/ml$^{\wedge\wedge\wedge}$. For treatment with enoxaparin, the level of CRP before therapy was 22.1 ± 1.8 mg/l, and on day 5 of treatment, it decreased to 11.2 ± 1.1 mg/l$^{\wedge\wedge\wedge}$, and on day 10, it further decreased to 6.1 ± 0.5 mg/l$^{\wedge\wedge\wedge}$.

In group 3, prior to treatment with Heparin, the initial CRP level was 60 ± 4.8 mg/l, while after 5 days of treatment it decreased to 35 ± 4.3 mg/l$^{\wedge\wedge\wedge}$, and after 10 days it further decreased to 14 ± 2.2 mg/l$^{\wedge\wedge\wedge}$. On the other hand, in group 3, prior to treatment with Enoxaparin, the initial CRP level was 64 ± 5.0 mg/l, while after 5 days of treatment it decreased to 26 ± 1.8 mg/l$^{\wedge\wedge\wedge}$, and after 10 days it decreased even further to 8 ± 0.7 mg/l$^{\wedge\wedge\wedge}$.

Procalcitonin before treatment in group 2 was 0.71 ± 0.06 ng/ml, while on heparin therapy it decreased to 0.53 ± 0.04 ng/ml$^{\wedge}$ at 5 days and 0.15 ± 0.02 ng/ml$^{\wedge\wedge\wedge}$ at 10 days. With enoxaparin therapy, procalcitonin was 0.73 ± 0.05 ng/ml before treatment, 0.32 ± 0.03 ng/ml$^{\wedge\wedge\wedge}$ at 5 days, and 0.05 ± 0.01 ng/ml$^{\wedge\wedge\wedge}$ at 10 days. In group 3, procalcitonin before treatment was 1.42 ± 0.13 ng/ml, and after heparin treatment, it increased to 0.96 ± 0.07 ng/ml$^{\wedge\wedge}$ at 5 days and 0.21 ± 0.03 ng/ml$^{\wedge\wedge\wedge}$ at 10 days. With enoxaparin therapy, procalcitonin was 1.39 ± 0.10 ng/ml before treatment, 0.50 ± 0.04 ng/ml$^{\wedge\wedge\wedge}$ at 5 days, and 0.12 ± 1.1 ng/ml$^{\wedge\wedge\wedge}$ at 10 days (table 3).

Table 3

Changes in procalcitonin levels in the blood following the use of anticoagulant medication.

Groups	**2 group**		**3 group**	
Type of treatment	Heparin	Enoxaparin	Heparin	Enoxaparin
Before treatment	0,71±0,06	0,73±0,05	1,42±0,13	1,39±0,10
5 days after treatment	0,53 ±0,02$^{\wedge}$	0,32 ±0,03$^{\wedge\wedge\wedge}$	0,96±0,07$^{\wedge\wedge}$	0,50 ±0,04$^{\wedge\wedge\wedge}$
10 days after treatment	0,15 ±0,02$^{\wedge\wedge\wedge}$	0,05 ±0,01$^{\wedge\wedge\wedge}$	0,21±0,03$^{\wedge\wedge\wedge}$	0,12 ±1,1$^{\wedge\wedge\wedge}$

Note: $^{\wedge}$ - indicates a significant difference compared to the control group ($^{\wedge}$-P<0.05; $^{\wedge\wedge}$-P<0.01; $^{\wedge\wedge\wedge}$ - P<0.001).

Based on the above information, treatment with Enoxaparin showed significant efficacy in normalizing coagulation hemostasis indicators compared to treatment with Heparin. Additionally, treatment with Enoxaparin resulted in noticeable changes in the levels of D-dimer, ferritin, C-reactive protein and procalcitonin.

Conclusions:

1. Moderate and severe cases of COVID-19 indicate hypercoagulability through decreased levels of APTT, PT, TT, INR, increased PI and fibrinogen.

2. Increased levels of D-dimer, ferritin, C-reactive protein, and procalcitonin were observed in patients with moderate and severe COVID-19.

3. Implementing a complex treatment with low molecular weight heparin in coronavirus infection effectively mitigated hypercoagulability.

References.

1. Голдобин В.В. Атеротромботический инсульт: клинические показатели и параметры тромбоцитарного гемостаза у пациентов в остром периоде//Саратовский научно-медицинский журнал.—2012.—Т.8.—№4.—С.954–957.

2. Деревянчук Е.Г., Александрова А.А., Рымашевский А.Н. Роль гомоцистеина и фолиевой кислоты в развитии гестоза на поздних этапах // Валеология.-2011.-№3.-С.63–66.

3. Зотова И.В. и др. Оценка риска тромбоэмболий при мерцательной аритмии: современное состояние проблемы //Атеротромбоз.—2013.—№1.—С.21–32.

4. Львова О.А. и др. Эпидемиология и этиология инсультов у детей грудного возраста //Неврология. Нейропсихиатрия. Психосоматика.—2013.—№25.—С.50–55.

5. Момот А.П. Состояние тромботической готовности—возможности современной диагностики и перспективы //Медицинский алфавит. Современная лаборатория.—2013.—№1.—С.20–23.

6. Овсянникова А.Н. и др. Клинико-генетическая характеристика больных ишемическим инсультом молодого и среднего возраста //Ульяновский медико-биологический журнал.—2016. —№3.—С.48–58.

7. Ackermann M., Verleden S.E., Kuehnel M. et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19 //NEnglJMed.–2020.№383(2).–P.120–128.https://doi.org/10.1016/10.1056/NEJMoa2015432.

8. Assiri A, Al-Tawfiq JA, Al-Rabeeah AA et al. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study // LancetInfect Dis.- 2013.- №13(9).-b.752–761.

9. Bennett J, Dolin R, Blaser MJ. Principles and Practice of Infectious Diseases. 8thEdition//Elsevier.-2014.-№8(2)-b.3904.

10. Bhimraj A, Morgan RL, Shumaker AH et al. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. ClinInfectDis.2020:ciaa478.doi:10.1093/cid/ciaa478.

11. Chan et al. Simulation of the clinical and pathological manifestations of Coronavirus Disease 2019 (COVID-19) in golden Syrianhamstermodel: implications for disease pathogenesis and transmissibility. //Clin. Infect. Dis. –2020.–№3;71(9).–P.2428-2446.doi:10.1093/cid/ciaa325.

12. Deng Y., Zou J.H., Sun S.S., Liu B.J., Wang L., Shi J.Y., Xiong X.A. andZhang S.F. Tag-based Analysis at the BESIII Experiment. Journal of Physics: Conference Series 1525 (2020) V 314. 012083 IOP Publishing doi:10.1088/1742-6596/1525/1/012083.

13. Harteman J.C. Role of thrombophilic factors in full-terminfants with neonatal encephalopathy //Pediatr.Res.—2013.—№73.—P.80–86.

14. Huang C, Wang Y, Li X et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. // Lancet.-2020.-№395(10223).-b.497–506.

15. Järemo P., Eriksson-Franzen M., Milovanovic M. Platelets, gender and acute cerebral infarction.//JTranslMed.—2015.—№13.—P.267.

16. Inciardi R.M., Lupi L., Zaccone G. et al. Cardiac involvement in a patient with coronavirus

disease 2019 (COVID-19). JAMA Cardiol.2020;5(7):819–24.https://doi.org/10.1001/jamacardio.2020.1096.

17. Inoyatova F.Kh., Kurbonova Z.Ch., Babadzhanova Sh.A. Relationship between MTHFR genes 1801133 and rs1801131 polymorphisms with disease severity of COVID-19 and homocystein levels in uzbek patients. J. Pharm. Negat.Results.2022,13,1879–1888.

18. Inoyatova Feruza Khidoyatovna, Zumrad Chutbayevna Kurbonova, Shaira Agzamovna Babadjanova. Relationship Of Polymorphisms Of MTR Genes1805087, MTRR Gene rs1801394 Hohomocystein Concentration And Covid-19 Severity In Uzbek Patients //Neuroquantology.2022,Vol. 20(12).P. 2061-2075.

19. Klok F., Kruip M., van der Meer N. et al. Confirmation of the high cumulative incidence of thrombotic complications in critically ill ICU patients with COVID-19: an updated analysis //Thromb Res.–2020. №191. – P. 148–150. https://doi.org/10.1016/j.thromres.2020.04.041.

20. Kopyta I. et al. Neonatal arterial ischemic stroke and limbischemia—clinical course and risk factors analysis //GinekolPol.—2016.—Vol.87.—№6.
—P.473–475.

21. Kurbonova Z.Ch., Babadjanova Sh.A. Charakteristics of Coagulation Hemostasis in Corona Virus Infection // Jundishapur journal of Microbiology. –2022.-No2(15).–C.453-460.

22. Xu X., Barth R.F., Buja L.M. A call to action: the need for autopsies to determine the full extent of organ involvement associated with COVID-19 infections. CHEST.2020.doi:10.1016/j.chest.2020.03.060.