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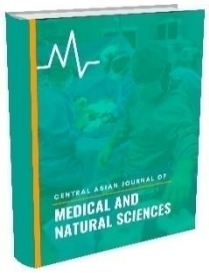

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Impact of Thromboembolism Prevention of Anticoagulant Therapy on the Course and Outcome of Covid-19

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Abstract: This article focuses on the impact of thromboembolism prevention on the course and outcome of anticoagulation therapy in COVID-19, and provides effective ways to manage and treat patients with coronavirus.

Key words: COVID-19, lung ventilation, thromboembolism, anticoagulant therapy, hospitalization.

Intrroduction.

Analysis of the features of the pathogenesis of a new coronavirus infection (COVID-19) demonstrates a significant impact of microcirculation disorders and thrombus formation on its course and outcomes. The results of an assessment of 2773 cases of the disease in hospitalized patients who were on artificial lung ventilation (ALV) showed that among those receiving anticoagulant therapy, mortality was 2 times lower: 29.1% compared with 62.7% in the absence of prevention of thrombotic complications. - ny [1]. This trend is confirmed by previously published data [2, 3]. However, if the need for the use of parenteral direct-acting anticoagulants is obvious today in the severe course of the disease under consideration, then in practice, in mild forms, the question often arises of the tactics of antithrombotic therapy. In addition, with a significant number of cases of mild and obliterated COVID-19 at present, including in people over 65 years of age, the number of refusals from hospitalization and the proportion of those receiving treatment at home are increasing. The

appointment of parenteral therapy on an outpatient basis is often undesirable. At the same time, taking into account the peculiarities of the course of this infection with the possibility of a rapid increase in symptoms and worsening of the condition over several hours [4], the tactics of outpatient management of patients, as a rule, should be quite active. All its components must be carefully verified.

Material and methods

A considerable number of patients receive previously selected therapy due to concomitant somatic pathology; their number is increasing among the elderly. At the same time, chronic diseases of the cardiovascular system are associated with the risk of severe course and deaths not only with COVID-19, but also with other infectious diseases. In this regard, in each case, it is necessary to study the interaction and mutual influence of various components of a comprehensive treatment program, assess the benefits of the medical intervention used and its potential risks.

In accordance with the current recommendations, a significant proportion of patients have indications for the constant use of anticoagulant drugs: persistent and paroxysmal forms of atrial fibrillation (AF), venous thrombosis, a history of pulmonary embolism, mobility restrictions due to injuries, some surgical interventions, diseases of the nervous system. Nevertheless, it must be stated that at present there is no generally accepted approach to prescribing and correcting antithrombotic therapy regimens in the outpatient treatment of COVID-19. The purpose of this work is to evaluate the effect of the activity of the coagulation system on the course of a new coronavirus infection and to substantiate the tactics of managing comorbid patients receiving oral anticoagulants (DOACs) in previously selected doses according to existing somatic indications.

We analyzed 76 cases of confirmed new coronavirus infection in people who received initial anticoagulant therapy on an outpatient basis. The analysis of medical documentation, clinical picture, results of laboratory tests and computed tomography (CT) of the lungs in the patients we observed was carried out by the method of continuous screening. The main group consisted of 26 patients who received DOACs (rivaroxaban, apixaban, dabigatran); 50 participants were included in the comparison (control) group, in which drugs that affect blood clotting were not prescribed prior to the COVID-19 episode. According to another therapy selected earlier in connection with chronic pathology, both groups were comparable (Table 1).

Table 1. Medications of maintenance therapy regimens had been regularly administered to patients in the compared groups

Medication	Main group n (%)	Control group n (%)
Rivaroxaban 16 (62)*		–
Dabigatran 5 (19)*		–
Apixaban 5 (19)*		–
Clopidogrel 3 (12)		9 (18)
Acetylsalicylic acid 0*		19 (38)
Beta blockers 7 (27)		16 (32)
Class I calcium channel blockers 1 (4)		5 (10)
Class II calcium channel blockers 3 (12)		14 (28)
Angiotensin converting enzyme inhibitors 4 (15)		7 (14)
Angiotensin 2 receptor antagonists type 12 (46)		16 (32)
Statins 20 (77)		29 (58)
Imidazoline receptor agonists 3 (12)		5 (10)
Not taking regular medications 0*		7 (14)

In the first group, 38% of patients received acetylsalicylic acid at a prophylactic dose of 100 mg per day, and 14% did not regularly take any drugs. After evaluating complaints, anamnesis and physical examination, all patients were prescribed treatment in accordance with the version of the Interim Guidelines "Prevention, Diagnosis and Treatment of Novel Coronavirus Infection (COVID-19)" that was current at the time of initiation of therapy

https://static0.minzdrav .gov.ru/system/attachments/attaches/.

In the absence of laboratory results confirming the presence of SARS-CoV-2 at the time of initialization of treatment, drugs recommended for the treatment of acute respiratory viral infections and influenza were used. The compared groups were comparable in terms of gender, severity at the start of treatment, the time of onset of the first symptoms of coronavirus infection, as well as the nature of the prescribed initial therapy. The age of the patients ranged from 42 to 96 years. Among the participants in both groups, women slightly dominated: 58% in the main group and 56% in the control group. The period from the onset of the disease to the initialization of drug intervention ranged from 1 to 5 days. A mild form of COVID-19 was registered in 6 (23%) patients of the main group and in 10 (20%) patients in the control group.

Signs of lung tissue damage (from 3 to 25% of the volume) (CT-1) were detected in 20 (77%) patients in the main group and in 40 (80%) in the control group. Umifenovir, interferon alfa-2b, imidazolylethanamide pentanedioic acid, lopinavir/ritonavir, riamilovir, inosine pranobex were prescribed as etiotropic treatment. According to indications, paracetamol was used to reduce body temperature. Antibacterial (azithromycin, amoxicillin clavulanate or levofloxacin) and mucolytic (acetylcysteine, ambroxol) drugs were used for signs of pneumonia. As an additional therapy, some patients received enterosorbents (with clinically significant manifestations of intoxication) and vitamin-mineral complexes.

All subjects were monitored daily for clinical symptoms, body temperature, blood oxygen saturation. On the 1st–3rd day, and subsequently, in the presence of changes or other indications, a CT scan of the lungs, a clinical blood test, and a study of the concentration of D-dimer were performed; according to indications - a biochemical blood test with the determination of the activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST), levels of creatinine, C-reactive protein, troponin I.

To assess the effect of treatment, the number of hospitalizations, deaths, and additionally, the progression of symptoms by the end of the 1st week of the disease were taken into account, and the need to correct the initial therapy regimen was determined.

Comparison of indicators was carried out using the program Statistica v.12. Mean values, standard deviation, Z-test were evaluated. Differences were considered significant at $p < 0.05$.

A comparison of the outcomes of a new coronavirus infection in both groups is presented. It can be seen that, against the background of previously selected anticoagulant therapy, the disease generally proceeded favorably, despite the large number of risk factors for a severe course and the presence of deaths due to respiratory infections. Among the participants of the main group, there was not a single case of death and severe respiratory and/or renal failure requiring oxygen therapy and/or hemodialysis, which significantly differs from the indicators in the control group ($p < 0.05$). This fact emphasizes the high importance of selecting an adequate antithrombotic drug intervention for concomitant somatic pathology in comorbid patients in order to prevent complications of COVID-19.

The obtained results confirm the significant contribution of disorders of coagulation mechanisms in the pathogenesis of infection caused by SARS-CoV-2, and the role of hemorheological disorders in its progression. At the same time, these observations indicate the possibility of outpatient management of

such individuals and the absence of the need to adjust doses and regimens for taking anticoagulants in mild cases of COVID-19. In further studies, it is necessary to establish the possible role of antiplatelet therapy and the effect of each of the components of maintenance treatment on the course of the infectious process in comorbid patients. Given the risk of bleeding when taking drugs of this class, the data presented cannot indicate the need and safety of their prophylactic use in other groups of patients who do not have direct indications for it. The importance of individual determination of the benefit-risk ratio is obvious when deciding whether to prescribe a particular drug, as well as assessing its effectiveness and safety.

Of course, in all cases of the presence of chronic diseases, especially in people over 65 years of age, careful monitoring of clinical symptoms is required, adequate correction of therapeutic regimens, taking into account the characteristics of the course of infectious and somatic pathology, monitoring the condition of patients at least 1 time per day, including including and in outpatient management of patients with a mild form of a new coronavirus infection.

Conclusion.

1. Taking DOACs in accordance with indications for concomitant somatic pathology reduces the likelihood of a severe course and adverse outcomes in the development of a new coronavirus infection, which indicates a significant contribution of disorders in various parts of the blood coagulation system to the pathogenesis of COVID-19.

2. In patients who received adequate outpatient treatment with drugs of the indicated pharmacological group against the background of a mild infection caused by SARS-CoV-2, there were no indications for changing drugs and correcting anticoagulant therapy regimens.

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