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CORRELATION ANALYSIS OF THE INCIDENCE OF POSTVIRAL SYNDROME WITH COMPARATIVE DATA OF ANTIVIRAL DRUGS

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Abstract. In this article, we performed a correlation analysis between the incidence of postcovirus syndrome and the use of antiviral drugs in patients. Comparative data on the use of antiviral drugs in different groups of patients, with different clinical manifestations in patients hospitalized with this pathology were used. This analysis allowed us to detect a non-significant correlation between groups with the use of different antiviral drugs. Moreover, our results confirmed the importance of early use of antiviral therapy to prevent the development of postviral syndrome. The results obtained are an important step in increasing the efficiency of diagnosis and treatment of post-Covid syndrome, and also contribute to the more effective use of antiviral therapy in clinical practice.

Key words: correlation analysis, post-Covid syndrome, frequency of occurrence, antiviral drugs, comparative data.

Introductions

Post-Covid syndrome (PCS) is a set of physical and psychological symptoms that some people experience after they have had COVID-19. Studying the relevance of post-Covid syndrome is a complex multidisciplinary task that requires the interaction of specialists from different fields of science. Among the disciplines that are now actively involved in the study of post-Covid syndrome are medicine, psychology, neurobiology, epidemiology and sociology. As part of studying the relevance of post-Covid syndrome, it is important to determine not only the physical symptoms, but also the mental health problems that patients face. Typical symptoms of post-Covid syndrome include severe fatigue, pain, sleep disturbances, memory loss, anxiety and depression. However, even though post-Covid syndrome has long attracted the attention of the medical community, the creation of effective methods for diagnosing and treating this syndrome

is still an urgent problem. Recent research suggests that post-Covid syndrome may remain symptomatic for a long time, and this is a future area of study. Therefore, the study of post-Covid syndrome is an important area of science, which requires continued research to develop new diagnostic methods and effective treatment, as well as improve people's quality of life.

In the treatment of coronavirus disease at the beginning of the pandemic, drugs such as ribavirin, interferon, favipiravir, remdesevir and corticosteroids were recommended for use in patients with ARVI or MERS infections, although the effectiveness of some drugs remains controversial[1]. In this study, we assessed the comparative effectiveness and impact on clinical parameters of two antiviral drugs approved in 2021. Ministry of Health of the Republic of Uzbekistan - Favipiravir and Remdesivir [2].

The first drug we will consider is Favipiravir. This drug was developed in Japan and was used as an antiviral drug for influenza [3]. This drug has high activity against RNA-containing viruses, but it has no effect on DNA-containing viruses (cytomegalovirus, adenovirus, herpes simplex virus type 1). Since its principle of action is based on the inhibition of viral RNA-dependent RNA polymerase, the drug is effective against influenza virus, respiratory syncytial virus, rhinovirus and 2019-nCoV virus [4].

In laboratory conditions, when tested on animals, Favipiravir showed activity against many RNA viruses. Clinical trials have been conducted with this drug in humans with diseases such as rabies, fever with thrombocytopenia syndrome, Ebola and Lassa fever. At the moment, there is no data on the emergence of resistance to the drug [3]. Favipiravir In Uzbekistan, it began to be used with the advent of the Coronavirus pandemic and was prescribed according to the scheme depending on the patient's weight: Patients weighing less than 75 kg: 1600 mg (8 tablets) 2 times a day on the 1st day and then 600 mg (3 table) 2 times a day from days 2 to 5 of treatment. Patients weighing 75 kg or more: 1800 (9 tablets) mg 2 times a day on the 1st day, then 800 mg (4 tablets) 2 times a day from days 2 to 5 of treatment. 600-1800 mg on day 1, then 600-800 mg on days 2-10, depending on the patient's weight. [5]

The second antiviral drug is Remdesivir, which is an antiviral drug that inhibits RNA-dependent RNA polymerase. This enzyme is necessary for the replication of many RNA viruses [6]. Its mechanism of action consists of inhibition of a special enzyme in virus-containing cells, which is necessary for virus replication, therefore this drug has high activity against many RNA virus-induced diseases (including MERS and SARS viruses) [7][8][9]. In our Republic, the drug Remdesivir is prescribed according to the regimen of 200 mg on the 1st day of treatment, followed by a dose reduction, respectively, 100 mg from 2 to 5 days of treatment [5].

When faced with this pandemic, it became clear that patients do not always disappear from symptoms over time. Some of them persist for quite a long time, and in some cases even new complaints are added. Cardiac injury and elevated troponin levels are associated with a high risk of death in patients hospitalized with acute COVID-19 infection[10,11]. People with post-Covid syndrome often experience persistent disorders of the cardiovascular system. Cohort studies have shown cardiac damage, myocardial inflammation, and elevated troponin levels in many COVID-19 patients 71 days after diagnosis[12]. At 60.3 days after the onset of COVID-19 symptoms, 21.7% of the 143 patients studied reported chest pain possibly caused by myocarditis[13].

Individuals at low risk of severe COVID-19, including young competitive athletes, have been shown to have residual myocarditis long after recovery from COVID-19 [14]. In addition to complaints of cardiac problems, studies in humans following COVID-19 infection have also noted a tendency to develop previously absent postural orthostatic tachycardia (POT) syndrome due to autonomic nervous system dysfunction [15–16].

The purpose of this study is to determine the correlation between post-Covid syndrome and the use of different antiviral drugs.

Materials and methods.

The materials were obtained in a retrospective study of medical records of 168 patients who received treatment with Remdesivir and Favipiravir as the main method of antiviral therapy in the 2nd Zangiota specialized hospital for the treatment of patients with coronavirus. Inclusion criteria for the study were PCR positive for COVID-19, moderate and severe cases of the disease. Exclusion criteria were concomitant diseases in the stage of decompensation. The average age of the patients was 54.5 years, of which 81 were men and 87 women. All study patients were carefully diagnosed and treated based on the clinical recommendations of the Ministry of Health of the Republic of Uzbekistan. The criterion for assessing the effectiveness of the drug was objective and subjective clinical indicators. Computed tomography was performed using a CT scanner before and after treatment. All biochemical blood tests were examined using mindray BC-20s analyzers and the SYSMEX CA-600 series analyzer. The patients were divided into 2 groups: One group consisted of 81 patients and they received Remdesevir according to the regimen in accordance with the protocol for the management of patients with coronavirus infection: on the 1st day 200 mg IV, then on days 2-5 100 mg IV V. Group number two consisted of 87 patients and received the drug Favipiravir, also according to the scheme (6.7)

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When studying post-Covid syndrome, a special questionnaire was developed by doctors at the 2nd Zangiota specialized hospital for the treatment of patients with coronavirus. The questionnaire reveals the patient's condition as much as possible and has separate cells for filling out on the patient's side if they wish to describe the condition in more detail or provide additional information. The survey was conducted after 12 weeks. During the re-examination, laboratory examinations were carried out such as: CBC, Biochemical analysis, coagulogram, immunogram and instrumental studies - electrocardiography.

Research results:

The average duration of treatment (hospitalization) was 10.25 in both groups, 6.8 and 13.7 days, respectively, in the study groups. At admission, patients had lung damage 29.5%, 33% for the first and 26% for the second group, respectively. 10 (6 in the 1st group, 4 in the 2nd) patients needed oxygen in the CPAP mask mode, 124 (64 and 60, respectively, in groups) patients in nasal oxygen, while 34 patients did not need additional oxygen support. (11 and 23, respectively, by group). In 76 patients (87.3%) of the 2nd group, nausea was observed, while in the 1st group, nausea was detected only in one patient (1.25%). In 74 (97.4%) patients, nausea was relieved by the use of metoclopramide 3 times a day before the end of the course of treatment. In 2 (2.6%) patients, ondosetron 8 mg was used intravenously 2 times a day for 3 days, with a further transfer to metoclopramide tablets 1 tab 3 times a day. When analyzing laboratory data in the 2nd group, a sharp jump in the levels of liver enzymes was observed: ALT by 1.88 times and AST by 1.55 times compared with the first day of hospitalization. Patients were recommended to take drugs L - ornithine and L - aspartate on an outpatient basis.

Table 1. Biochemical blood parameters of patients during hospitalization and on the last day of therapy.

Blood parameters	**First group**		**Second group**	
	Before treatment	After treatment	Before treatment	After treatment
ALT	34,85	37,12	32,44	**60,96**
AST	37,42	41,52	30,64	**47,52**
Creatinine	84,99	99,34	99,52	100,09

Urea	4,98	6,14	5,02	5,14
Blood glucose	7,7	6,41	9,02	9,23

All subjects in both groups had a negative PCR test for COVID-19 at discharge. Quantitative analysis for immunoglobulins G and M in the first group varied as follows: for IgG - 0.01 Ng/ml to 2.43, on average 0.78 Ng/ml, for M 0.16 to 1.22 Ng/ml, on average 0.65 Ng/ml. Similar indicators can be seen in group 2: for IgG 0.08 to 2.71 Ng/ml, average 1.52, for M 0.05 to 3.09, average 1.81. (Fig.1)

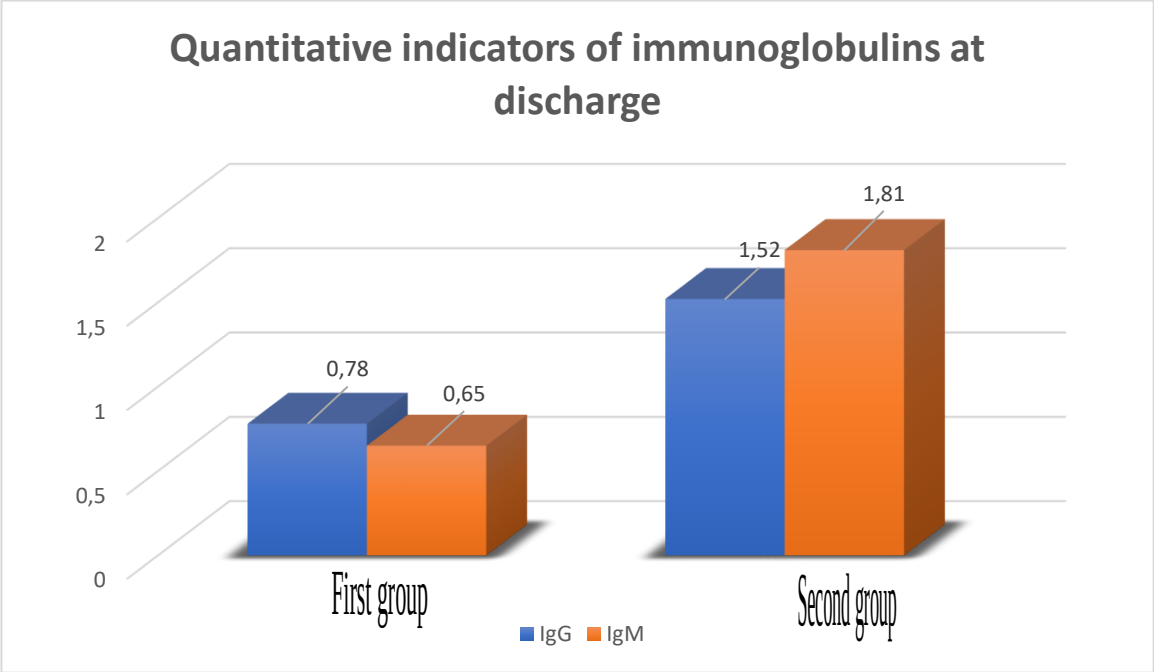

Fig. 1 Indicators of immunoglobulins G and M after the end of treatment.

The frequency of occurrence of various symptoms that were studied 3 months later in patients after discharge from hospitals was as follows in the first group: fatigue (35%), shortness of breath (20%), memory loss (28%), insomnia (26%), decreased quality of life (10%), impaired respiratory function (15%), arterial hypertension (5%), arthralgia (2%), psychoemotional disorders (7%), impaired taste and/or smell (8%).

In the second group: fatigue (38%), shortness of breath (23%), memory loss (19%),

insomnia (32%), decreased quality of life (12%), impaired respiratory function (14%), arterial hypertension (9 %), arthralgia (5%), psychoemotional disorders (10%), impaired taste and/or smell (5%).

It should be noted that the majority of patients did not experience any serious changes in parameters during laboratory and instrumental research methods. However, these results indicate that there are problems in patients after acute coronavirus infection.

Conclusions:

The use of Remdesivir showed the absence of side effects and a relatively short period of hospitalization (6.8-13.7, respectively).

Favipiravir is more hepatotoxic, which leads to manageable unwanted side effects such as nausea, vomiting and a quantitative increase in liver enzymes. Therefore, it would be advisable to include the treatment of hepatoprotectors in the protocol.

The advantage was that the indicators of the value of formed immunity were higher in patients in the Favipiravir group.

Both drugs Favipiravir and Remdesivir have shown effectiveness against coronavirus infection. At the same time, it is necessary to carefully select patients when prescribing both drugs, taking into account the characteristics of the body and the presence of comorbid diseases of the liver and gastrointestinal tract.

A study of patients 3 months after discharge from the hospital showed that the frequency and clinical manifestations in the first group differed little from those of patients in the second group. Thus, we can say that the choice of antiviral drug is not decisive in the development of post-Covid syndrome.

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