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Clinical Pharmacological Approach To The Treatment Of Infectious Diseases With Antiviral Drugs

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Abstract. The clinical efficacy and safety of riamilovir were assessed based on the results of a study of 150 patients in three compared groups, 50 patients in each. Patients received etiotropic antiviral therapy with riamilovir, 1 capsule (250 mg) 3 times a day for 5 days in the first group, in the second group patients received riamilovir in the “off label” regimen, 1 capsule (250 mg) 5 times a day for 5 days, and the third group consisted of 50 patients who received only pathogenetic treatment. The etiotropic antiviral drug riamilovir demonstrated clinical efficacy when used in both treatment regimens in patients with ARVI and a good safety profile.
Keywords: acute respiratory viral infections, acute respiratory diseases, riamilovir, nucleoside analogues, influenza.

INTRODUCTION

The events of recent years have clearly demonstrated the scale of the threat of the spread of new and emerging viral infections: overcoming the interspecies barrier has led to outbreaks of Ebola fever, Middle East respiratory syndrome, and the global spread of infection caused by SARS-CoV-2. In addition, urbanization, global warming, and the expansion of the geography and activity of air traffic also have a significant impact on the epidemiological situation, contributing to the expansion of viral infections from endemic regions. In particular, this is how the active spread of the dengue fever virus began, which, according to estimates by the World Health Organization (WHO) for 2024, has infected more than 350 million people in more than 120 countries around the world, and the Zika fever virus, which caused the largest outbreak of infectious fever in South and Central America, recorded in 2015.

MATERIALS AND METHODS

Viral infections are recognized as one of the global challenges in the field of biological safety, requiring the search for modern solutions to meet the ongoing need for effective and safe antiviral drugs: with the existing diversity of viral threats, approved pharmaceutical drugs of direct antiviral action are available for the treatment of only 10 of these viral infections [1, 2]. A special place among them is occupied by pharmacological substances that act on viral enzymes, in particular on viral proteases and polymerases (Figure). Drugs of this group show high efficiency against hepatitis C and HIV viruses, and the experience of the active phase of the COVID-19 pandemic has opened up prospects for the use of RNA-dependent RNA polymerase inhibitors for the treatment of respiratory infections, which continue to occupy a leading place in the general structure of infectious pathology. This group of infections causes significant economic damage to the state budget due to the high incidence of disability among the population [3, 4]. According to expert estimates, respiratory viral diseases during epidemic periods affect from 10 to 20% of the country's population, annually causing economic damage exceeding 10 billion rubles. When analyzing the main drugs for the treatment of acute respiratory viral infections, it is necessary to note a number of existing shortcomings: a narrow spectrum of antiviral action, the development of resistance, the need for early initiation of drug use (no later than the first 2 days of the disease), toxicity and the development of side effects, the lack of more effective drugs for the treatment of severe forms of influenza infection and a limited choice of drugs for the treatment of acute respiratory viral infection (ARVI) of non-influenza etiology [5].

RESULTS AND DISCUSSION

Men constituted 92.67% of the study population. Patients from the group who did not receive antiviral therapy were younger than patients who received riamilovir ($p<0.05$).

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The average duration of hospitalization of patients included in the study was 9.14±3.31 days.

The duration of hospitalization of patients who received antiviral therapy with riamilovir was statistically significantly shorter than that of patients who did not receive etiotropic treatment ($p<0.05$), with the shortest duration of inpatient treatment observed in patients who received riamilovir 5 times a day for 5 days ($p<0.05$).

The duration and severity of AIS in patients, regardless of the dosage regimen of the study drug throughout the entire period of hospitalization, were statistically significantly lower than in patients from the group where antiviral therapy was not prescribed ($p<0.05$). The total duration of fever was statistically significantly different between all compared groups of patients: the shortest duration was recorded among individuals receiving riamilovir at a regimen of 1250 mg per day for 5 days ($p<0.05$). The duration of febrile fever was statistically significantly shorter in the groups of patients receiving antiviral therapy regardless of the daily dosage ($p<0.05$).

The duration of objective and subjective signs of pharyngitis and rhinitis was statistically significantly shorter in patients from the group receiving riamilovir at a dose of 1250 mg per day compared to patients taking the standard dosage of the drug and not receiving etiotropic treatment ($p<0.05$).

During the study period, some patients from the groups under consideration developed complications from the paranasal sinuses in the form of acute sinusitis. When analyzing the frequency of detection of this complication, the following data were obtained.

Acute catarrhal sinusitis was detected in 7.33% of patients, purulent sinusitis developed only in 2.67% of patients. There were no statistically significant differences in the frequency of detection of these conditions in patients from the compared groups ($p>0.05$). At the same time, the analysis of the number of acute purulent sinusitis in the compared groups showed that they were not registered in the group of patients receiving riamilovir at a daily dosage of 1250 mg. At the same time, it should be noted that during the study period, other complications of ARVI in the form of pneumonia, myocarditis, etc. were not registered in any of the compared groups.

No statistically significant differences were obtained when comparing the specified indicators upon admission and discharge ($p> 0.05$).

Throughout the study, patients did not report any adverse events that could be associated with taking the study drug. In a laboratory study of 150 primary samples containing nasopharyngeal swabs using the PCR method, pathogens of acute respiratory viral infections were identified in 33.33% of patients; in a study of smears taken on the 6th day of hospitalization, pathogens were detected in 12.67% of patients. The most frequently detected were rhinovirus RNA (7.33% of cases) and influenza A virus RNA (4.66% of cases). Of note is the 100% elimination of pathogens of acute respiratory viral infections in the group of patients receiving riamilovir 5 times a day for 5 days. In the group of individuals receiving riamilovir in a standard dosage, detection of the virus in repeated smears was observed in 2% of cases, namely, only 1 patient out of 50. In the group of patients who did not receive antiviral therapy, the absence of elimination of ARVI pathogens by the 6th day of inpatient treatment was observed in 36% of cases. This significantly exceeded the frequency of detection of pathogens in a control study of nasopharyngeal material in groups of patients who received antiviral therapy with riamilovir ($p<0.05$).

The results of our study emphasized the obvious potential of using nucleoside analogues in the treatment of ARVI in adults. Riamilovir in both dosage regimens demonstrated high efficacy, good tolerability and safety profile. Moreover, the most significant clinical effects were observed when using increased dosages of the antiviral drug. Diseases caused by influenza viruses A and B, human metapneumovirus, respiratory syncytial virus are annually among the leading causes of death, especially among individuals at increased risk (children, the elderly, individuals from organized groups) [1]. One of the key factors in the development of complicated course of the above-mentioned diseases is recognized to be incomplete and/or untimely antiviral therapy, which, in combination with an insufficient systemic immune response due to a short incubation period, high contagiousness of pathogens and involvement of mucous membranes in the pathophysiological cascade, induces a longer persistence of viruses in susceptible tissues. Paradoxical prolongation of virus replication in response to inadequate antiviral therapy is associated with a slowdown in the rate of penetration and subsequent replication of the pathogen in a “partially protected” cell, which indicates the importance of selecting optimal dosing regimens based on the pharmacokinetics and

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pharmacodynamics of drugs [2]. These data are consistent with the results obtained in our study: the maximum reduction in the duration of the disease and 100% elimination of viral pathogens of various etiologies by the 6th day of inpatient treatment were achieved in patients who received riamilovir at a dose of 1250 mg per day for 5 days. The obtained results of the study are of primary importance in relation to the study of options for the use of antiviral drugs in order to achieve maximum clinical efficacy, reduce the incidence of complications and the epidemiological risk of patients. We also consider the absence of laboratory signs of hepato- and/or nephrotoxicity when using riamilovir in both standard and increased dosage regimens to be significant results of the study. According to available data, the search for a therapeutic window for broad-spectrum antiviral drugs is difficult due to the direct and/or indirect effect on the enzymatic structures of the host cells, as well as the lack of a definitive understanding of the mechanisms of action of a number of antiviral compounds and the characteristics of their distribution in specific tissues.

CONCLUSION

Thus, the antiviral drug riamilovir demonstrated high clinical efficacy when used in both treatment regimens in patients with influenza and acute respiratory viral infections and a good safety profile. In addition, the use of riamilovir in a dosage regimen of 1250 mg per day in hospitalized patients led not only to more pronounced clinical effects (lower incidence of complications, shorter duration of the main manifestations of the disease), but also to the complete elimination of acute respiratory viral infections in the study group by the 6th day of hospitalization.

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