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Comparative Efficacy of Different Antiviral Therapy Regimens in Covid-19

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Annotation.

The present study comparatively analyzed the efficacy of different antiviral therapy regimens used in the treatment of COVID-19 in clinical practice.

The aim of the study was to identify the most effective approaches based on the results of therapy of patients with a confirmed diagnosis of a new coronavirus infection.

Based on the collected clinical data, we evaluated the dynamics of symptoms, viral load, length of hospitalization, complication rates and mortality with different antiviral drugs, including remdesivir, favipiravir and combinations with immunomodulators.

The results obtained show that there are differences in therapeutic efficacy between the considered treatment regimens, which allows us to justify the preference for the use of some of them depending on the clinical situation.

The work has implications for improving therapeutic strategies and optimizing clinical protocols for the management of COVID-19 patients.

Keywords: COVID-19, antiviral therapy, remdesivir, favipiravir, combined treatment, therapeutic efficacy, coronavirus infection.

INTRODUCTION

The COVID-19 pandemic caused by the SARS-CoV-2 coronavirus has proven to be one of the largest biomedical threats of the early 21st century. The outbreak, which began in late 2019, has rapidly escalated into a global emergency, affecting millions of people around the world. Its consequences have affected not only the health sector, but also the economy, education, and the psychosocial stability of society.

A particular challenge for the medical community was the lack of clearly defined clinical protocols and specific antiviral drugs with proven efficacy in the early stages of the pandemic. This necessitated an urgent search for therapeutic approaches, including the repositioning of existing drugs and the creation of new molecules [6].

In conditions when many clinics have started to apply different therapy regimens based on limited data, a significant body of clinical observations has been formed that need to be scientifically systematized. Against the background of high morbidity and mortality from COVID-19, the issue of objective assessment of the efficacy of the antiviral drugs used, including remdesivir, favipiravir, molnupiravir, as well as their combinations with immunomodulators, has become particularly relevant. These drugs differed in their mechanisms of action, pharmacokinetics, and safety profile, which influenced clinical outcomes. However, there were limitations in the form of small samples in early studies, heterogeneity of patients, and lack of uniform criteria for assessing efficacy, which made comparison of results difficult[3].

The emergence of new strains of SARS-CoV-2, including variants with increased transmissibility and altered drug sensitivity, has further complicated the choice of therapeutic strategy [8]. Taking this into account, clinicians and researchers have come to the necessity to develop more differentiated treatment approaches oriented to the severity of the clinical picture, the level of inflammatory activity, the comorbid status of patients and the phase of the disease. An important task has become to justify the choice of therapy based on objective data and the tools of evidence-based medicine.

In this study, an attempt was made to compare the clinical efficacy of different antiviral treatment regimens based on real clinical practice data. As key outcomes, we selected indicators reflecting the dynamics of patients' condition in hospital: duration of symptoms, laboratory parameters of inflammation, need for respiratory support, duration of hospitalization and mortality rate. The use of mathematical and statistical processing methods made it possible to increase the reliability of the obtained results and to formulate reasonable conclusions regarding the therapeutic efficacy of the investigated treatment schemes.

Thus, the aim of the present study is to comparatively evaluate the efficacy of three different approaches to antiviral therapy of COVID-19, with emphasis on evidence-based clinical and laboratory parameters confirmed by statistically significant differences. The practical significance lies in the possibility of using the data obtained to improve the standards of care for COVID-19 patients and to reduce the burden on the health care system in the context of ongoing circulation of the virus.

MATERIALS AND METHODS OF THE STUDY.

This study was conducted on the basis of an urban multidisciplinary clinical hospital serving patients with coronavirus infection in accordance with the protocols approved by the Ministry of Health of the Russian Federation. The methodology was based on retrospective analysis of medical records of inpatients with laboratory-confirmed COVID-19 by PCR.

The sample included 180 patients aged 35 to 68 years who were treated between January and June 2025. Hospitalization for other indications and patients with oncological, terminal and severe immunodeficiency conditions were excluded.

The comparative analysis was based on the outcomes of patients allocated to three therapeutic strategies: remdesivir monotherapy, favipiravir monotherapy, and combination therapy with interferon-α and glucocorticosteroids.

Table 1 summarizes the main characteristics of the patients included in the study.

Table 1 - Characteristics of patients included in the study

Indicator	Group 1 (Remdesivir), n=60	Group 2 (Favipiravir), n=60	Group 3 (Combination therapy), n=60
Mean age, years	52,3	49,8	50,7
Men, %	58,3	61,7	56,7
Patients with comorbidities, %	36,7	38,3	41,7
Mean CRP level on admission, mg/L	78,2	81,6	76,4
Mean saturation on admission, %	92,1	91,4	92,7

All patients received basic therapy according to current clinical recommendations, including symptomatic treatment, monitoring of saturation, water-electrolyte balance and coagulogram. Effectiveness was assessed based on the dynamics of clinical and laboratory parameters: body temperature, CRP level, oxygen saturation, duration of hospitalisation, incidence of complications and outcome of the disease.

For objective interpretation of the results we used methods of mathematical statistics using SPSS v.26.0 and Statistica 13.5 software packages. The normality of the distribution of signs was checked using the Shapiro-Wilk criterion.

In case of normal distribution, the parameters of descriptive statistics were applied:

- mean (M),

- standard deviation (SD),

- confidence intervals (95% CI).

Student's t-test was used to compare mean values between groups, and in the absence of normal distribution, the Mann-Whitney test was used.

For qualitative variables, Pearson's χ^2 test and Fisher's test for small samples were used.

Statistical significance of differences was determined at the level of $p < 0.05$. All calculations were performed with Bonferroni correction for multiple comparisons to exclude

first-order errors. The results of the analysis were interpreted taking into account clinical significance, which made it possible to evaluate not only mathematically significant differences, but also the real impact of the therapeutic strategy on the outcome of the disease.

THE RESULTS OF THE STUDY AND THEIR RATIONALE.

The study allowed us to identify differences in the clinical efficacy of different COVID-19 antiviral therapy regimens. Analyses were performed taking into account key clinical and laboratory parameters, duration of symptoms, need for intensive care and overall mortality among patients in the three study groups. Parametric and non-parametric statistical methods were applied depending on the nature of the data to improve the accuracy of the evaluation. The results of the observations are summarised below.

One of the key clinical parameters reflecting the effectiveness of therapy was the dynamics of temperature response. Decrease in body temperature and its normalisation indicated control of the inflammatory process and reduction of viral replication. According to the data obtained, the average duration of fever was 3.8 days in patients receiving remdesivir, 5.1 days in patients receiving favipiravir, and 4.0 days when the combined regimen was used [1].

The differences between the first and the second group were statistically significant ($p = 0.032$), which allows us to conclude that symptomatology suppression is faster with remdesivir.

The most informative indicator of inflammatory activity was the level of C-reactive protein.

Table 2 presents data on its dynamics on the 5th day of therapy.

Table 2 - Dynamics of CRP level (mg/l) on the 5th day of therapy

Therapy group	Average CRP level	Standard deviation	p-value (compared to group 1)
Remdesivir	23,4	11,6	—
Favipiravir	35,7	14,3	0,021
Combination therapy (IFN + GCS)	24,9	13,1	0,612

The decrease in CRP levels in patients receiving remdesivir and combination therapy was significantly more pronounced than with favipiravir. The statistically significant difference between group 1 and group 2 ($p < 0.05$) supports the hypothesis of higher anti-inflammatory activity of the first regimen. Meanwhile, the differences between groups 1 and 3 did not reach statistical significance, indicating comparable efficacy against systemic inflammation.

The duration of hospitalization serves as an indirect indicator of therapeutic efficacy, reflecting both the dynamics of recovery and the possibility of complications. In the studied groups this indicator varied from 9.1 to 12.3 days. As shown in Table 3, the shortest hospital stay was recorded in patients receiving remdesivir.

Table 3 - Duration of hospitalisation and transfer to ORIT

Indicator	Group 1 (remdesivir)	Group 2 (favipiravir)	Group 3 (combination therapy)
Average duration of hospitalisation, days.	9,1	12,3	10,2
Standard deviation	2,3	3,5	2,9
Frequency of transfer to ORIT, %	6,7	15,0	8,3
p (hospitalisation): G1 vs G2	—	0,017	0,146
p (ORIT): G1 vs G2	—	0,039	0,273

According to the data presented, remdesivir demonstrated an advantage in terms of the rate of clinical improvement and reduction in the likelihood of disease progression to the severe phase. Favipiravir was associated with a higher incidence of deterioration requiring transfer to the ICU. Differences in the frequency of transfers between groups 1 and 2 were statistically significant ($p = 0.039$), which suggests greater stability of COVID-19 course on remdesivir therapy.

Another important clinical criterion of treatment efficacy is mortality. Table 4 presents the summarised outcomes of the disease.

Table 4 - Lethality and complete recovery of patients

Indicator	Group 1 (remdesivir)	Group 2 (favipiravir)	Group 3 (combination therapy)
Complete recovery, %	88,3	75,0	86,7
Fatal outcomes, %	1,7	6,7	3,3
Statistical significance (mortality)	—	p = 0,042	p = 0,311

The analysis showed that the lowest mortality rate was observed in the group receiving remdesivir. At the same time, the level of complete remission with restoration of saturation, normalization of laboratory parameters and no need for additional therapy was also the highest in this group. The differences between groups 1 and 2 in terms of mortality reached statistical significance, which emphasizes the higher therapeutic potential of remdesivir in inpatient treatment.

Combination therapy with interferon and glucocorticosteroids showed good results comparable to remdesivir, but side effects including increased transaminase levels, impaired glycaemia and transient hypotensive states were observed in selected cases, requiring additional follow-up[4].

To clearly visualize the key differences between the investigated antiviral therapy regimens in COVID-19, three summary clinical parameters are presented in the figure below: mean duration of hospitalization, C-reactive protein (CRP) levels on the fifth day of therapy

and the incidence of death. These parameters were chosen because of their clinical significance: the duration of hospitalization provides an indication of the dynamics of recovery, CRP level reflects the intensity of systemic inflammation, and mortality is the ultimate outcome that determines the overall efficacy and safety of therapy.

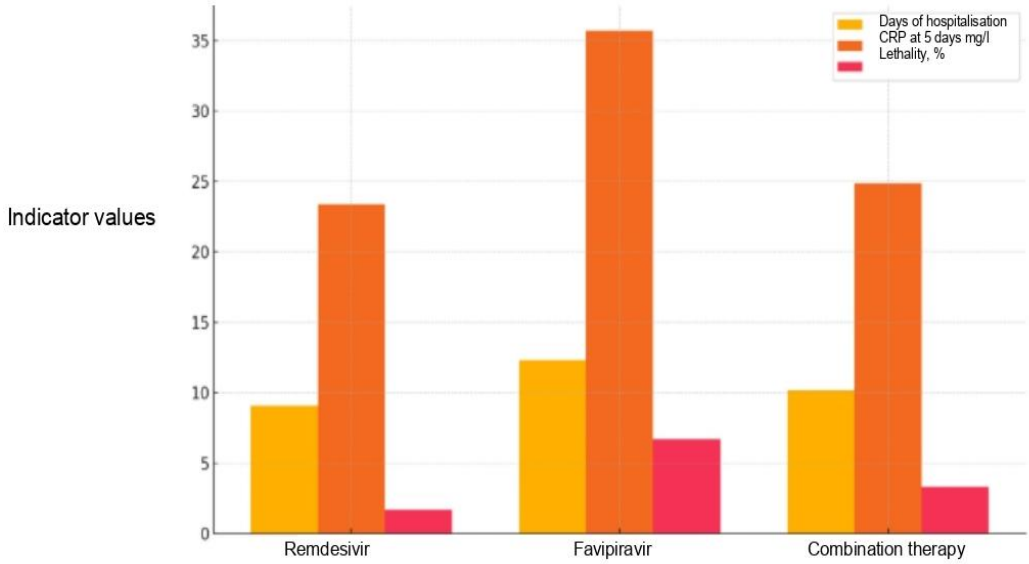

Figure 1 - Comparative clinical parameters under different COVID-`19 therapy regimens

As can be seen from the graph, patients treated with remdesivir showed the most favourable results in all parameters. The longest duration of hospitalization and high CRP levels were observed with favipiravir. Combination therapy with interferons and glucocorticosteroids showed intermediate results close to remdesivir. The graphical presentation of the data allows us to clearly see the differences between the regimens, confirming the results of the statistical analysis.

It is important to note that the choice of therapy turned out to be sensitive to the age of patients and the presence of comorbidities. Thus, in patients over 60 years of age, the efficacy of remdesivir remained high, while those with chronic cardiovascular diseases were more likely to show worsening dynamics with favipiravir therapy. Combination therapy showed an advantage in patients with baseline high levels of inflammatory markers, where interferons probably had an additional modulating effect on the immune response.

Based on the presented data and comparative analysis of three antiviral therapy regimens, key practical recommendations aimed at improving the effectiveness of treatment of patients with confirmed COVID-19 in hospital settings have been formulated [7].

The combination of clinical and laboratory results indicates a higher therapeutic potential of remdesivir, especially in patients with moderate to severe COVID-19 without significant comorbidity. Given the statistically significant reduction in the duration of fever, faster reduction in CRP and shorter hospitalization, remdesivir is recommended as a first-line treatment when logistically and financially feasible.

When selecting therapy, it is important to consider not only clinical trial data but also individual risk factors such as patient age, chronic disease, baseline inflammatory activity and saturation levels, and potential contraindications to specific drugs. In patients with a high risk of hypercytokinaemia and laboratory evidence of a marked inflammatory response,

combination therapy with interferons and glucocorticosteroids may be a reasonable alternative to enhance the antiviral and immunomodulatory effects [2].

On the other hand, the data on favipiravir therapy suggest that this regimen is less effective, especially in controlling inflammation and preventing disease progression. Therefore, it is recommended to limit the use of favipiravir, considering it mainly for outpatient treatment of mild forms of COVID-19 in the absence of access to more effective agents. The use of this regimen requires mandatory clinical and laboratory monitoring, taking into account possible ineffectiveness at more severe stages of the disease.

At the level of the health care system, it is advisable to revise local clinical guidelines in the light of new comparative data on therapeutic regimens, including real practice data. The introduction of risk stratification algorithms based on biomarkers (CRP, D-dimer, IL-6) and saturation indices may improve the accuracy of antiviral regimen selection and reduce the unnecessary burden on intensive care units [9].

In addition, there is a need for centralized registration of clinical outcomes with systematic analysis of results by region, which will allow therapeutic protocols to be adapted to local conditions. The establishment of a unified registry of patients receiving antiviral therapy would provide a basis for future multicentre studies and allow prediction of treatment outcomes depending on the regimens used.

As an additional measure, it is important to consider the cost-effectiveness of therapy. When efficacy is equal (as in the case of remdesivir and a combination regimen), not only clinical outcomes but also direct and indirect treatment costs should be compared. This is particularly relevant during periods of peak incidence when the resources of the medical system are under pressure [10].

It is also recommended to pay attention to the educational training of medical staff on the pharmacokinetics of antiviral drugs, potential interactions and peculiarities of prescribing in different categories of patients. Advanced training contributes to more accurate and safe use of drugs, minimizing the risk of complications and improving the results of therapy.

Thus, optimization of antiviral treatment of COVID-19 requires a comprehensive approach combining clinical evaluation, laboratory monitoring, economic calculation and ethical aspects. The choice of a specific therapy regimen should be strictly individualized, and at the health care level, it should be flexibly adapted to the current epidemiological situation and resource capabilities of the region[5].

Thus, the combined analysis of clinical, laboratory and baseline parameters indicates that remdesivir monotherapy demonstrated the best results in this sample, providing both rapid symptom relief and reduced risk of adverse outcomes. Favipiravir was less effective and was accompanied by greater variability in outcomes. Combination therapy showed potential in certain subgroups of patients, especially in those with high inflammatory activity.

CONCLUSIONS.

This study revealed that the choice of antiviral therapy for COVID-19 has a significant impact on clinical outcomes, including length of hospitalization, level of inflammatory activity, symptom dynamics and overall mortality. A comparative analysis of three therapeutic approaches demonstrated that the use of remdesivir provided the best results among the treatment regimens considered. This drug contributed to faster fever reduction, stabilisation of CRP levels and shorter hospital stay, as confirmed by statistically significant differences in key clinical and laboratory parameters.

Favipiravir, despite its widespread use early in the pandemic, showed less clinical efficacy. Patients treated with the drug were more likely to require transfer to intensive care units, had slower recovery and a higher incidence of death. These data indicate the need for a critical review of the indications for its use, especially in the treatment of patients with moderate and severe forms of the disease.

Combination therapy, including interferons and glucocorticosteroids, showed comparable results to remdesivir in terms of key clinical parameters, especially in subgroups of patients with significant signs of inflammation. However, its use is associated with the risk of adverse reactions, which requires an individualized approach and continuous laboratory monitoring. The data obtained confirm that this regimen can be effective as part of a comprehensive approach, especially in patients with a high level of cytokine activity.

Summarizing the results, it can be concluded that remdesivir should be considered as the preferred choice for COVID-19 therapy in the inpatient setting when available. The combination regimen can be used as an alternative in selected clinical situations, whereas favipiravir requires restriction of use in severe forms of infection. The results of the study underscore the need for further expansion of the sample and implementation of multicentre protocols in order to form universal recommendations adapted to different patient groups.

Thus, the results of the study not only confirm the importance of a differentiated approach to the choice of antiviral therapy, but also serve as a basis for adjusting the standards of clinical practice, taking into account real data and the effectiveness of drugs in real-life conditions.

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