Received: 28 June 2021 / Accepted: 02 August 2021 / Published online: 31 August 2021

DOI 10.34689/SH.2021.23.4.001

UDC 616.40:615.7

CLINICAL EFFICACY OF THE ANTIVIRAL DRUG FAVIPIRAVIR IN THE COMPLEX TREATMENT OF PATIENTS WITH COVID-19 CORONAVIRUS INFECTION

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Abstract

Introduction. It is known that most patients with COVID-19 have a disease of mild to moderate severity and can be treated at home. A potential etiotropic drug in the treatment of such patients is favipiravir. To finally decide on the inclusion of this drug in the international recommendations for the treatment of COVID-19, further studies are needed to assess its effectiveness and safety in patients with COVID-19.

The aim of the study was to study the clinical efficacy of favipiravir in the complex therapy of patients with moderate-severity COVID-19 coronavirus infection.

Materials and methods. A retrospective analysis of 468 medical records of an inpatient patient with a moderate form of coronavirus infection COVID-19, who were treated at the State Clinical Hospital at the Multi-Specialty Medical Center of the Akimat of Nur-Sultan, the Semey Infectious Diseases Hospital, for the period August-October 2020, was carried out.

The experimental (main) group consisted of 40 patients with COVID-19 of moderate severity, who, in addition to standard therapy in accordance with the Clinical Protocol for Diagnosis and Treatment "COVID-19 Coronavirus infection (10th edition with changes from 15.07.2020), were prescribed oral favipiravir at a dose of 1600 mg/12 h on day 1, then 600 mg/12 h on the following days, for a total of 7 days. The comparison group (control group) consisted of 40 patients with moderate CVI who did not receive favipiravir.

Descriptive statistics were performed with the calculation of the mean (M) and standard deviation (SD) for quantitative variables; percentages were calculated for qualitative variables. Statistical analysis was performed using Microsoft Excel and IBM SPSS Statistics 20.0. $P < 0.05$ was considered statistically significant.

Results and discussion. The present study showed that the early initiation of antiviral therapy with Favipiravir, compared with standard therapy without an antiviral drug, in patients with a moderate form of COVID-19 is associated with a statistically significant clinical improvement and a large percentage of virus elimination from the mucous membranes of the upper respiratory tract according to molecular genetic research. In the group of patients receiving favipiravir, complete remission of the disease with normalization of the main clinical parameters and the absence of complaints for 7 days of hospitalization was significantly more often than in the comparison group.

Conclusions. The results obtained showed that Favipiravir is an effective antiviral drug in the complex treatment of COVID-19 coronavirus infection of moderate severity. Early administration of the drug in patients with a moderate form of the disease can prevent the progression of the disease to a more severe condition and the development of complications that require additional medical interventions.

Keywords: *coronavirus infection COVID-19, SARS-CoV-2, antiviral drug, favipiravir.*

Резюме

КЛИНИЧЕСКАЯ ЭФФЕКТИВНОСТЬ ПРОТИВОВИРУСНОГО ПРЕПАРАТА ФАВИПИРАВИР В КОМПЛЕКСНОМ ЛЕЧЕНИИ ПАЦИЕНТОВ С КОРОНАВИРУСНОЙ ИНФЕКЦИЕЙ COVID-19

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Введение. Известно, что большинство пациентов с COVID-19 имеют заболевание от легкой до средней степени тяжести и могут лечиться дома. Потенциальным этиотропным препаратом в лечении таких пациентов является фавипиравир.

Целью исследования было изучить и провести анализ историй болезней пациентов с коронавирусной инфекцией COVID-19 средней степени тяжести, применявших фавипиравир в комплексной терапии для определения клинической эффективности фавипиравира.

Материалы и методы исследования. Проведен ретроспективный анализ 468 медицинских карт стационарного пациента с умеренной формой коронавирусной инфекции COVID-19, находившегося на лечении в ГКП на ПХВ «Многопрофильном медицинском центре» акимата города Нур-Султана, Инфекционной больнице г. Семей, за период август-октябрь 2020 года.

Экспериментальную (основную) группу составили 40 пациентов с COVID-19 средней степени тяжести, которым в дополнение к стандартной терапии в соответствии с Клиническим протоколом диагностики и лечения «Коронавирусной инфекции COVID-19» (10-е издание с изменениями от 15.07.2020) был назначен пероральный фавипиравир в дозе 1600 мг/12 ч в 1-й день, затем 600 мг/12 ч в последующие дни, в общей сложности 7 дней. Группа сравнения (контрольная группа) состояла из 40 пациентов с КВИ средней степени тяжести, которые не получали фавипиравир.

Описательная статистика проводилась с расчетом среднего (M) и стандартного отклонения (SD) для количественных переменных; для качественных переменных рассчитывались проценты. Статистический анализ проводился с использованием Microsoft Excel и IBM SPSS Statistics 20.0. P <0,05 считался статистически значимым.

Результаты и обсуждение. Настоящее исследование показало, что раннее начало противовирусной терапии Фавипиравиром по сравнению со стандартной терапией без противовирусного препарата у пациентов с умеренной формой COVID-19 связано со статистически значимым клиническим улучшением и большим процентом элиминации вируса со слизистых оболочек верхних дыхательных путей по данным молекулярно-генетических исследований. В группе пациентов, получавших фавипиравир, полная ремиссия заболевания с нормализацией основных клинических показателей и отсутствием жалоб в течение 7 дней госпитализации наблюдалась достоверно чаще, чем в группе сравнения.

Выводы. Полученные результаты показали, что Фавипиравир является эффективным противовирусным препаратом в комплексном лечении коронавирусной инфекции COVID-19 средней степени тяжести. Раннее введение препарата пациентам с умеренной формой заболевания может предотвратить прогрессирование заболевания в более тяжелое состояние и развитие осложнений, требующих дополнительных медицинских вмешательств.

Ключевые слова: *коронавирусная инфекция COVID-19, SARS-CoV-2, противовирусный препарат, фавипиравир.*

Түйіндеме

ФАВИПИРАВИР ВИРУСҚА ҚАРСЫ ПРЕПАРАТЫНЫҢ COVID-19 КОРОНАВИРУСТЫҚ ИНФЕКЦИЯСЫ БАР ПАЦИЕНТТЕРДІ КЕШЕНДІ ЕМДЕУДЕГІ КЛИНИКАЛЫҚ ТИІМДІЛІГІ

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Кіріспе. COVID-19 пациенттерінің көпшілігінде жеңілден орташа ауырлыққа дейін ауру бар және оларды үйде емдеуге болатындығы белгілі. Мұндай пациенттерді емдеудегі потенциалды этиотропты препарат фавипиравир болып табылады.

Зерттеудің мақсаты фавипиравирдің клиникалық тиімділігін анықтау үшін кешенді терапияда фавипиравирді қолданған орташа ауырлықтағы COVID-19 коронавирустық инфекциясы бар пациенттердің ауру тарихын зерттеу және талдау болды.

Зерттеу материалдары мен әдістері. 2020 жылдың тамыз-қазан айлары аралығында Нұр-сұлтан қаласы әкімдігінің ШЖҚ "Көпбейінді медициналық орталық" МКК-да, Семей қаласының жұқпалы аурулар ауруханасында емделіп жатқан COVID-19 коронавирустық инфекциясының орташа нысаны бар стационарлық пациенттің 468 медициналық картасына ретроспективті талдау жүргізілді.

Эксперименттік (негізгі) топты ауырлығы орташа дәрежедегі COVID-19 бар 40 пациент құрады, оларға "COVID-19 Коронавирустық инфекциясын" диагностикалау мен емдеудің клиникалық хаттамасына (15.07.2020 жылғы өзгерістерімен 10-шы басылым) сәйкес стандартты терапияға қосымша 1-ші күні 1600 мг/12 сағ, одан кейін 600 мг/12 сағ дозада, жалпы алғанда 7 күн ішінде пероральді фавипиравир тағайындалды. Салыстыру тобы (бақылау тобы) фавипиравир алмаған 40 орташа КВИ пациенттерінен тұрды.

Сипаттамалық статистика сандық айнымалылар үшін орташа (M) және стандартты ауытқуды (SD) есептеумен жүргізілді; сапалық айнымалылар үшін пайыздар есептелді. Статистикалық талдау Microsoft Excel және IBM SPSS Statistics 20.0 көмегімен жүргізілді. P <0,05 статистикалық маңызды болып саналды.

Нәтижелер мен талқылау. Осы зерттеу COVID-19 орташа нысаны бар пациенттерде вирусқа қарсы препаратсыз стандартты терапиямен салыстырғанда Фавипиравирмен вирусқа қарсы терапияның ерте басталуы статистикалық маңызды клиникалық жақсарумен және молекулалық-генетикалық зерттеулерге сәйкес жоғарғы тыныс жолдарының шырышты қабаттарынан вирустың жойылуының үлкен пайызымен байланысты екенін көрсетті. Фавипиравир қабылдаған пациенттер тобында негізгі клиникалық көрсеткіштердің қалыпқа келуімен және ауруханаға жатқызудың 7 күні ішінде шағымдардың болмауымен аурудың толық ремиссиясы салыстыру тобына қарағанда едәуір жиі байқалды.

Тұжырымдар. Алынған нәтижелер Фавипиравирдің орташа ауырлықтағы COVID-19 коронавирустық инфекциясын кешенді емдеуде тиімді вирусқа қарсы препарат екенін көрсетті. Препаратты аурудың орташа формасы бар науқастарға ертерек енгізу аурудың неғұрлым ауыр жағдайға түсуіне және қосымша медициналық араласуды қажет ететін асқынулардың дамуына жол бермейді.

Түйінді сөздер: *COVID-19 коронавирустық инфекциясы, SARS-CoV-2, вирусқа қарсы препарат, фавипиравир.*

Bibliographic citation:

Kulzhanova Sh.A., Aukenov N.E., Konkayeva M.E., Smagulova Z.K., Tuleshova G.T., Maukaeva C.B., Beisenbieva N.Ye., Turebaeva G.O., Nurakhmetova G.A., Utegenova A.M. Clinical efficacy of the antiviral drug Favipiravir in the complex treatment of patients with COVID-19 coronavirus infection // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2021, 4 (Vol.23), pp. 6-15. *doi 10.34689/SH.2021.23.4.001*

Кулжанова Ш.А., Аукенов Н.Е., Конкаева М.Е., Смагулова З.К., Тулешова Г.Т., Маукаева С.Б., Бейсенбиева Н.Е., Туребаева Г.О., Нурахметова Г.А., Утегенова А.М. Клиническая эффективность противовирусного препарата Фавипиравир в комплексном лечении пациентов с коронавирусной инфекцией COVID-19 // Наука и Здравоохранение. 2021. 4 (Т.23). С. 6-15. *doi:10.34689/SH.2021.23.4.001*

Кулжанова Ш.А., Аукенов Н.Е., Конкаева М.Е., Смагулова З.К., Тулешова Г.Т., Маукаева С.Б., Бейсенбиева Н.Е., Туребаева Г.О., Нурахметова Г.А., Утегенова А.М. Фавипиравир вирусқа қарсы препаратының COVID-19 коронавирустық инфекциясы бар пациенттерді кешенді емдеудегі клиникалық тиімділігі // Ғылым және Денсаулық сақтау. 2021. 4 (Т.23). Б. 6-15. *doi:10.34689/SH.2021.23.4.001*

Relevance

The question of effective and safe etiotropic treatment of COVID-19 caused by the new SARS-CoV-2 coronavirus remains open to date [27]. The disease is a newly emerged one, scientific data on the use of antiviral drugs are constantly updated and supplemented, and the recommendations and treatment protocols are revised. Therefore, systematic reviews and meta-analyses are required to justify their application [7].

The global pandemic of coronavirus infection (COVID-19), which has been going on for more than a year, has put the need for the world medical community to develop an effective comprehensive treatment. As is known, the creation of new etiotropic drugs for the treatment of a specific new infection is a long process that takes several years under the best circumstances. Therefore, the main strategy was to study the effectiveness of existing antiviral drugs with proven efficacy and safety against other viruses that could potentially be effective, taking into account their mechanism of action, on the SARS-CoV-2 virus, whose genetic material is represented by a single-stranded RNA molecule identical to other single-stranded RNA viruses [3, 24, 25, 6].

Favipiravir is a new antiviral drug, (T-705; 6-fluoro-3-hydroxy-2-pyrazine carboxamide) is an antiviral drug, an analog of purine nucleoside, which selectively inhibits the RNA-dependent RNA polymerase of the virus [9]. Previously, the effectiveness of favipiravir in the treatment of Ebola and influenza A was proven [23, 29]. There are also data on the antiviral activity of favipiravir against viruses from the genus Arenaviridae [11, 12], Bunyaviridae [12], Flaviviridae [16, 22], Togaviridae [17], Picornaviridae [9], and Caliciviridae [28]. Also, like the above-mentioned viral agents, the causative agent of COVID-19-SARS-CoV-2 is an RNA-containing virus, which indicates the possible potential use of favipiravir in the treatment of COVID-19. Shiraki and Daikoku (2020) indicate that favipiravir will become an important therapeutic agent for the treatment of severe infections caused by RNA viruses for which standard treatment methods are not available [29]. Delang, Abdelnabi, and Neyts, noting the high barrier to favipiravir resistance, indicate that it is necessary to study the safety and efficacy problems in more detail before this drug can be used in the treatment of a large group of patients [5]. In clinical practice, the dosage of favipiravir used is 1600 mg/12 h on day 1, then 600 mg/12 h on the next 2-7 days, administered orally, however, an intravenous route of administration is also being developed [36, 15].

Wang and co-authors demonstrated in vitro activity of favipiravir against SARS CoV-2 [21]. Moreover, at the moment, more than 15 clinical trials have been registered to determine the effectiveness of favipiravir in the treatment of patients with COVID-19, registered in the US National Library of Medicine, the Chinese Register of Clinical Trials, the Indian Register of Clinical Trials and the Japanese Register of Clinical Trials

The currently available information on the effectiveness and safety of using favipiravir in the treatment of patients with COVID-19 is ambiguous. Thus, Sreekanth Reddy and Lai (2021) note that, compared with other antiviral drugs, favipiravir is cheap and can serve as an option for emergency use in the treatment of patients with COVID-19 [32]. Udwadia and co-authors (2021) indicate a significant reduction in the time to clinical cure when using favipiravir compared to standard treatment, also noting that favipiravir may be useful in mild to moderate COVID-19 [33]. Evaluating the pathogenetic mechanisms of COVID-19, it is known that favipiravir can partially control inflammatory mediators, although it cannot fully control them or the respiratory status of patients [35]. Taking into account such indicators as mortality and days of hospitalization, Ghasemnejad-Berenji and Pashapour (2021) conclude that favipiravir may be crucial for ensuring effective treatment [11]. Mortality in the favipiravir group was approximately 30% less than in the control group, but this result is not statistically significant [17].

The main advantages of favipiravir are that it is administered orally and can be prescribed to patients who are not subject to hospitalization. Since the majority of patients with COVID-19 (85%) have a mild to moderate disease and can be treated at home, this drug can potentially be used for a large number of patients. As with any antiviral drug, it should be emphasized that favipiravir should be prescribed immediately after the onset of symptoms, so that it is effective in reducing viremia [1,20]. It is also noted that after treatment with favipiravir, there is a significant clinical improvement compared to standard treatment without significant differences in viral clearance, oxygen support requirements and side effect profiles [31].

Scientists from Turkey in a cohort study concluded that favipiravir is a safe drug without serious side effects and deserves further study [6]. Moreover, Nasir and co-authors (2020) in a systematic review indicate that the side effects caused by favipiravir are mild and treatable [26].

Currently, favipiravir is a potential agent in the treatment of patients with mild to moderate COVID-19. However, further studies are needed to evaluate the clinical efficacy and safety of the use of favipiravir. As noted by Łagocka and co-authors (2021), there is a need to confirm the effectiveness of favipiravir in viral infections in a multicenter randomized double-blind clinical trial on a large group of patients [18].

In the Republic of Kazakhstan, the use of favipiravir in the complex treatment of COVID-19 patients is allowed within the framework of clinical trials (CP "COVID-19 Coronavirus infection", 10th edition with amendments from 15.07.2020) [4].

The aim of the study was to study the clinical efficacy of favipiravir in the complex therapy of patients with moderate-severity COVID-19 coronavirus infection.

Materials and methods of research. The data of 80 medical records of an inpatient patient with a moderate form of COVID-19 coronavirus infection were analyzed. The study was approved by the Local Ethics Committee of the NAO "Astana Medical University" (extract from Protocol No. 10 of November 26, 2020).

All patients whose medical records were included in the study met the following inclusion criteria:

- SARS-CoV-2 infection was verified by polymerase chain reaction (PCR);
- changes according to CT of the chest organs corresponded to a viral lesion of the lungs of minimal or medium volume (CT 1-2);

- moderate course of the disease [CP "Coronavirus infection COVID-19"].
- Criteria for exclusion from the study:
- severe or extremely severe COVID-19;
- decompensated chronic diseases of the kidneys, liver and heart, diabetes mellitus, severe obesity;
- pregnancy and lactation;
- conditions associated with impaired functioning of the immune system (HIV, cancer, autoimmune diseases), immunosuppressive therapy;
- the patient has hypersensitivity to favipiravir or any other component of the drug;
- elderly age.

The study was conducted in accordance with the task of the Ministry of Health of the Republic of Kazakhstan as part of a clinical study to study the effectiveness of favipiravir in the complex treatment of patients with COVID-19 coronavirus infection and is an open retrospective study. The experimental (main) group consisted of 40 patients with a moderate form of CVI, who, in addition to standard therapy in accordance with the Clinical Protocol for Diagnosis and Treatment "COVID-19 Coronavirus infection" (10th edition with changes from 15.07.2020), were prescribed the drug favipiravir at a dose of 1600mg x 2p/day on the 1st day, then 600mg x 2p/day, 7 days, by the decision of the council.

The comparison group (control group) consisted of 40 patients with a moderate form of COVID-19 who received pathogenetic and symptomatic therapy without favipiravir in accordance with the clinical protocol. The compared groups of patients did not differ significantly by age, gender and by the main clinical manifestations of COVID-19. The age of the patients ranged from 51 to 56 years (men-50%, women-50%). All patients had clinical signs of COVID-19: respiratory manifestations (runny nose, nasal congestion, lack of smell, sore throat, cough, chest pain, shortness of breath during exercise), symptoms of intoxication (headache, joint pain, body aches, weakness, sweating, chills). The duration of the disease in patients from the moment of the first signs of the disease to hospitalization in the hospital was from 5 to 8 days. The most frequent concomitant diseases were arterial hypertension (AH) (38.8%), diabetes mellitus (DM) (12.5%), compensated form and chronic diseases of the respiratory system (10%). The distribution of concomitant diseases was similar between the two comparison groups (Table 1).

Table 1.

Demographic and clinical characteristics of COVID-19 patients at the time of hospitalization.

Characteristics	Total (n=80)	Experimental group (n=40)	Control group (n=40)	χ^2	P
Age, years (*M±SD*)	52,35±7,4	53,6±8,79	51,1±6,01	-	0,154
Male gender, cases (%)	40 (50)	21 (52,5)	19 (47,5)	0,2	0,655
Day of hospitalization (*M±SD*)	6,45±2,54	6,25±2,75	6,65±2,32	-	0,484
DM, cases (%)	10 (12,5)	5 (12,5)	5 (12,5)	0	1,0
AH, cases (%)	31 (38,8)	17 (42,5)	14 (35,0)	0,474	0,491
Hr. RS diseases, cases (%)	8 (51,2)	5 (12,5)	3 (7,5)	0,55	0,456

The effectiveness of favipiravir was evaluated on the basis of clinical criteria (the duration of the main clinical signs of the disease against the background of treatment), while taking into account the timing of the disappearance of symptoms of intoxication, respiratory failure, the timing of the reverse development of catarrhal symptoms, the duration of stay in the hospital), the onset of rehabilitation from the SARS-CoV-2 virus according to the results of PCR of the nasopharynx and oropharynx mucosa by the time of discharge from the hospital.

Descriptive statistics were performed with the calculation of the mean (M) and standard deviation (SD) for quantitative variables; percentages were calculated for qualitative variables. Statistical analysis was performed using Microsoft Excel and IBM SPSS Statistics 20.0. P <0.05 was considered statistically significant.

The results of the study.

The analysis of the medical records of COVID-19 patients showed that the positive dynamics of the symptoms of the disease was more often registered in patients receiving favipiravir. Thus, on the 7th day of hospitalization, there was a decrease in the frequency of cases of chest pain (2.5% vs. 17.9%, p<0.05), dry cough (35% vs. 40%, p>0.05). The data obtained indicate a predominant clinical effect of complex therapy, including favipiravir, in comparison with standard therapy (Table 2).

Table 2.

Effect of favipiravir on the incidence of symptoms (in %) in patients with moderate COVID-19 on days 1, 7 and 14 of hospitalization.

The symptom	Experimental group(n=40)			Control group(n=40)			p 1	p 2	p 3
	1	7	14	1	7	14			
Weakness	100	29,0	2,0	100	30,0	4,0	>0,05	> 0,05	>0,05
Dry cough	26,0	14,0	1,0	32,0	16,0	2,0	<0,05	>0,05	>0,05
Chest pain	12	1,0	0	23	7	1	<0,05	<0,05	>0,05
p1 – the significance of differences in the compared groups on day 1, p2 – on day 7, p3 – on day 14 of hospitalization									

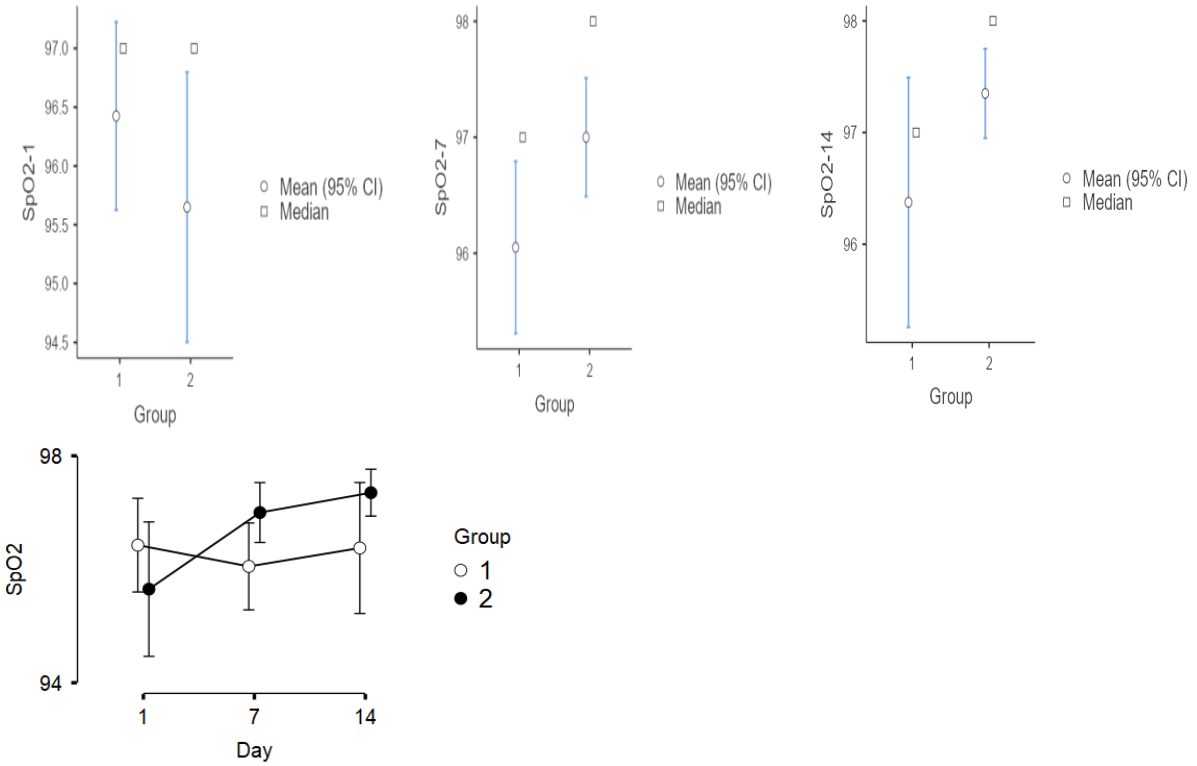
The average severity of the COVID-19 coronavirus infection is characterized by the following criteria: shortness of breath during physical exertion, respiratory movement rate (BPD) 20-22 per minute, oxygen saturation SpO2 in the range of 94-96 %, CT 1-2 (lung lesion volume up to 50%) (CP "COVID-19 Coronavius infection").

On the first day of hospitalization, saturation was reduced in patients of the two comparison groups and corresponded to the average severity of the disease (Table 3). Against the background of the use of favipiravir on the 7th and 14th days of hospitalization, an increase in oxygen saturation indicators was observed, whereas in the comparison group this indicator slightly decreased on the 7th day, reaching the initial indicators on the 14th day (Figure 1), while significantly differing from the oxygen saturation indicators in the experimental group.

Table 3.

Indicators of oxygen saturation (SpO2) in patients treated with and without favipiravir on the 1st, 7th, 14th day of hospitalization.

Day of hospitalization	Comparison group	N	Mean	Median	SD	SE
SpO2-1 day	Control (1)	40	96.4	97.0	2.58	0.408
	Experienced (2)	40	95,7	97.0	2.70	0.586
SpO2-7 day	Control (1)	40	96.0	97.0	2.40	0.379
	Experienced (2)	40	97.0	98.0	1.65	0.261
SpO2-14 day	Control (1)	40	96.4	97.0	3.61	0.570
	Experienced (2)	40	97.3	98.0	1.29	0.204



Note: 1 is the control group, 2 is the main group.

Figure 1. Dynamics of oxygen saturation indicators on days 1, 7, 14 of hospitalization of patients with COVID-19.

The respiratory rate had a positive trend in the two compared groups without statistically significant differences between the comparison groups on days 7 and 14 of hospitalization (Table 4, Figure 2).

Table 4.

Indicators of BPD in COVID-19 patients who received favipiravir and without it on the 1st, 7th, 14th day of hospitalization.

Day of hospitalization	Comparison group	N	Mean	Median	SD	SE
RR -1 day	Control (1)	40	22.4	21.0	3.73	0.589
	Experienced (2)	40	21.4	20.0	3,35	0,529
RR -7 day	Control (1)	40	20.7	20.0	2.66	0.421
	Experienced (2)	40	19.6	20.0	1,33	0.263
RR -14 day	Control (1)	40	19.6	19.0	2.19	0.347
	Experienced (2)	40	19.1	19.0	1.14	0.181

The following criteria for the moderate course of COVID-19:shortness of breath during exercise and DN 0-1 (Table 5).

From the presented data, it can be seen that shortness of breath during physical exertion on days 7 and 14 of hospitalization was less common in the group of patients receiving favipiravir, but without significant differences. Respiratory failure of the 1st degree on the background of favipiravir regressed better in comparison with the control group without significant differences.

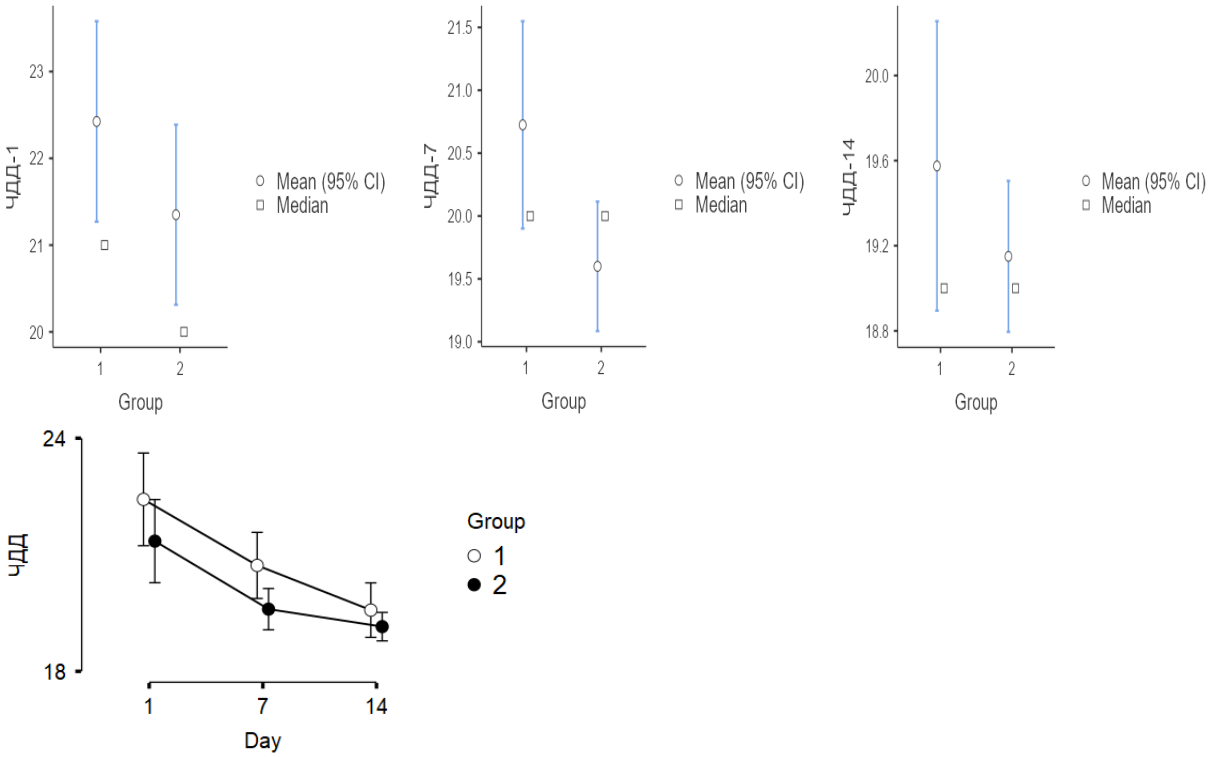


Figure 2. Dynamics of BDD indicators on the 7th, 14th days of hospitalization of patients with COVID-19.

Table 5.

Effect of favipiravir on the incidence of symptoms (in %) in patients with moderate COVID-19 on days 1, 7 and 14 of hospitalization.

The symptom	Experimental group(n=40)			Control group(n=40)			p 1	p 2	p 3
	1	7	14	1	7	14			
Shortness of breath during exercise	30,0	16	1	21	10	3	>0,05	>0,05	>0,05
RF 0-1	19	4	0	10	6	1	>0,05	> 0,05	>0,05
p1 – the reliability of differences in the compared groups on day 1, p2 – on day 7, p3 – on day 14 of hospitalization									

In the group of patients receiving favipiravir (Table 6), complete remission of the disease with no complaints was observed in 92.5% of patients on 7 days of hospitalization, and in 100.0% of patients on 12-14 days of hospitalization. In the control group, a complete improvement in the condition on the 7th day of hospitalization was observed only in 37.5% of patients, on the 14th day of hospitalization, an improvement in the condition was noted in 52.5% of patients, only 90%.

Table 6.

Frequency of cases of improvement of the condition (in %) in patients with moderate COVID-19 on days 7 and 14 of hospitalization.

Indicator	Experimental group(n=40)		Control group(n=40)		p 1	p 2
	7	14	7	14		
Improvement of the condition	37,0	40,0	15	36	< 0,05	>0,05

The percentage of patients with negative PCR results at the time of hospital discharge was greater in the group of favipiravir compared to standard group therapy: 34 (85,0%) vs 28 (70,0%, p< 0.05) (table 9).

Table 9.

The influence favipiravir the frequency of occurrence of a negative result of PCR discharge from the mucous membrane of the nasopharynx and oropharynx at the time of discharge from hospital.

Comparison group	Negative PCR	Positive PCR
Experimental group (n=40)	34 (85,0%)	6 (15,0%)
Control group (n=40)	28 (70,0%)	12 (40,0%)
p	< 0,05	< 0,05

Discussion.

Despite a significant number of drugs that have been evaluated to one degree or another and are still being studied for COVID-19, there is still no convincing data on their clinical effectiveness.

The results of international randomized trials have shown the clinical efficacy and safety of favipiravir in the complex treatment of COVID-19 coronavirus infection compared with the use of pathogenetic and symptomatic therapy alone.

Favipiravir belongs to the class of antiviral drugs that inhibit RNA-dependent polymerase, an enzyme necessary for the replication of a number of RNA viruses [19]. Since the inhibition of the enzyme prevents the replication of the virus in infected cells, it exhibits antiviral activity against a number of single-stranded RNA-containing viruses, such as Ebola virus, Marburg virus, human respiratory syncytial virus, Lassa fever virus, and coronaviruses (including MERS and SARS viruses) [21, 13].

Favipiravir is used in the treatment of COVID-19 in various countries, after its antiviral effect against SARS-CoV-2 was demonstrated in vitro [21]. The results of several randomized clinical trials show that patients receiving favipiravir, compared with patients receiving placebo, had a clinical improvement, in addition, the progression of the disease decreased in patients who needed oxygen therapy.

Thus, there are experimental and clinical data regarding the antiviral activity of favipiravir against the SARS-CoV-2 virus. Data from placebo-controlled studies show positive effects for patients with COVID-19. Favipiravir reduces the time to recovery of hospitalized patients who require additional oxygen, and can positively affect the outcomes of mortality, while having a favorable safety profile.

The present study showed that an early start of antiviral therapy with Favipiravir compared with standard therapy without an antiviral drug in patients with a moderate form of COVID-19 is associated with a statistically significant clinical improvement and a large percentage of virus elimination from the mucous membranes of the upper respiratory tract according to molecular genetic research.

The administration of favipiravir contributed to a statistically significant increase in the probability of clinical improvement in the patients' condition in the form of normalization of the condition and the absence of complaints by the 7th day of hospitalization, which reduced the number of bed days, thereby reducing the cost of treating patients.

The data obtained suggest that treatment with favipiravir can prevent the progression of the disease to a more severe condition, as evidenced by the absence of cases of the need for respiratory support among patients who did not need it, and the absence of patients who need a higher level of respiratory support during therapy.

Thus, these results indicate that treatment with favipiravir can not only reduce the burden of the disease, prevent the development of severe, complicated forms of the disease, but also reduce the use of limited health resources during this pandemic. Studies on the clinical efficacy and safety of favipiravir in coronavirus infection COVID-19 require further continuation in order to obtain more reliable data.

Conclusions:

1. Favipiravir is an effective antiviral drug in the complex treatment of COVID-19 coronavirus infection of moderate severity.

2. The early initiation of antiviral therapy with Favipiravir compared with standard therapy without an antiviral drug in patients with a moderate form of COVID-19 is associated with a statistically significant clinical improvement and a large percentage of virus elimination from the mucous membranes of the upper respiratory tract according to molecular genetic research.

Вклад авторов:

Кулжанова Ш.А. – научное руководство, концептуализация и критический анализ проведенного поиска, оформление.

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Конфликт интересов:

Авторы заявляют об отсутствии конфликтов интересов.

Финансирование: При проведении данной работы не было финансирования сторонними организациями и медицинскими представительствами.

Сведение о публикации: результаты данного исследования не были опубликованы ранее в других журналах и не находятся на рассмотрении в других издательствах.

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