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EFFICACY OF THE ANTIVIRAL DRUG ENISAMY IODIDE IN SEVERE ADULT ACUTE RESPIRATORY INFECTIONS IN THE COVID-19 ERA

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Abstract

Relevance. From 600 thousand to 1.2 million cases of ARVI and influenza are registered annually in Kazakhstan. On the average for the epidemiological season hospitalised with severe and medium - severe course of ARVI - up to 70-80 thousand people, 70% of whom are children under 14 years, including children under 1 year - up to 30-35%, pregnant women -53-55% of the number of pregnant women who fall ill with ARVI, respectively. Treatment of acute respiratory viral infectious disease (ARVI) includes a number of measures and approaches aimed at alleviating symptoms, reducing the duration of the disease and preventing complications. One such drug is enisamia iodide, produced by Pharmak (Ukraine) under the trade name Amizon, registered in the Republic of Kazakhstan as an antiviral agent.

Materials and methods. The study is a cohort, clinical, non-interventional, prospective. In the city infectious diseases hospital of Shymkent, clinical trials were conducted on the effectiveness of the antiviral drug enisamia iodide in severe forms of ARVI in adults, in comparison with a group of patients who did not receive etiotropic treatment from December 2022 to January 2023.

Results and conclusions. As a result of the treatment, progression of normalization of body temperature was observed by the 4th and 5th days (96% and 98%, respectively). In the comparison group, an improvement in the normalization of body temperature by the 3rd day was registered in 60% of patients.

When comparing the main and control groups by bed days, statistically significant differences were established (p=0.049*). Patients with standard therapy stayed in the hospital longer than those who received Amizon additionally. During treatment with Amizon, only 1 case out of 50 developed an adverse event in the form of a minor headache coinciding with the drug intake, which did not require discontinuation of the drug. On the 3rd and 4th days of therapy, statistically significant differences were revealed. Regression of intoxication symptoms (fever, chills, headache, body aches) and catarrhal manifestations occurred much earlier than in the control group. The need to prescribe antibacterial drugs during the use of Amizon was 10%, which indicates its antiviral and antibacterial effect.

Keywords: *acute respiratory infections, antiviral treatment, influenza, enisamia iodide.*

Резюме

ЭФФЕКТИВНОСТЬ ПРОТИВОВИРУСНОГО ПРЕПАРАТА ЭНИСАМИЯ ИОДИД ПРИ ТЯЖЕЛЫХ ФОРМАХ ОРВИ У ВЗРОСЛЫХ В ЭПОХУ COVID-19

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Актуальность. В Республике Казахстан (РК) ежегодно регистрируется от 600 тысяч до 1,2 млн. случаев ОРВИ и гриппа. В среднем за эпидемиологический сезон госпитализируется с тяжелым и средне - тяжелым течением ОРВИ – до 70-80 тысяч человек, 70% из которых составляют дети до 14 лет, в том числе дети до 1 года – до 30-35%, беременные – 53-55% от числа заболевших ОРВИ беременных соответственно. Лечение острого респираторного вирусного инфекционного заболевания (ОРВИ) включает ряд мер и подходов, направленных на облегчение

симптомов, снижение длительности болезни и предотвращение осложнений. Одним из таких препаратов является энисамия иодид, производимый заводом Фармак (Украина) под торговым названием «Амизон», зарегистрированный в РК в качестве противовирусного средства.

Материалы и методы. Исследование является когортным, клиническим, неинтерванционным, проспективным. В городской инфекционной больнице г. Шымкента проведены клинические испытания эффективности противовирусного препарата энисамия йодид при тяжелых формах ОРВИ у взрослых, в сравнении с группой пациентов, не получавших этиотропное лечение с декабря 2022 года по январь 2023г.

Результаты и выводы. В результате проведенного лечения наблюдалась нормализация температуры тела к 4-му и 5-му дню у 96% и 98% больных соответственно. В группе сравнения нормализация температуры тела к 3-му дню зарегистрирована у 60% больных.

При сравнении основной и контрольной групп по койко-дням были установлены статистически значимые различия (p=0,049*). Пациенты со стандартной терапией находились в стационаре дольше, чем те, которые получали Амизон дополнительно. На фоне лечения Амизоном только в 1 случае из 50 развилось нежелательное явление в виде незначительной головной боли, совпадающей по времени с приемом препарата, не потребовавшее отмены препарата. На 3 и 4-й день терапии выявлены статистические значимые различия. Регресс симптомов интоксикации (лихорадка, озноб, головная боль, ломота в теле) и катаральных проявлений происходил значительно раньше, чем в группе контроля. Необходимость в назначении антибактериальных препаратов на фоне применения Амизона составила 10%, что свидетельствует о его антивирусном и антибактериальном эффекте.

Ключевые слова: *острые дыхательные инфекции, противовирусная терапия, грипп, энсамия йодид*

Түйіндеме

COVID-19 ДӘУІРІНДЕГІ ЕРЕСЕКТЕРДЕГІ ЖРВИ-ДІҢ АУЫР ФОРМАСЫНДА ЭНИСАМИЯ ЙОДИД ПРЕПАРАТЫНЫҢ ВИРУСҚА ҚАРСЫ ТИІМДІЛІГІ

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Өзектілігі. Қазақстанда жыл сайын ЖРВИ мен тұмаудың 600 мыңнан 1,2 млн-ға дейінгі жағдайы тіркеледі. Орта есеппен эпидемиологиялық маусымда ЖРВИ-дің ауыр және орташа ауыр ағымымен - 70-80 мың адамға дейін ауруханаға жатқызылып, оның 70% – 14 жасқа дейінгі балалар болса, оның ішінде 1 жасқа дейінгі балалар – 30-35% –ға дейін, жүкті әйелдер ЖРВИ-мен ауыратындар санының тиісінше 53-55% құрайды. Жедел респираторлық вирустық инфекциялық ауруды (ЖРВИ) емдеу симптомдарды жеңілдетуге, аурудың ұзақтығын азайтуға және асқынулардың алдын алуға бағытталған бірқатар шаралар мен тәсілдерді қамтиды. Осындай препараттардың бірі-Қазақстанда вирусқа қарсы әсер ететін, "Амизон" сауда атауымен тіркелген, Фармак (Украина) зауыты шығаратын энисамия йодиді.

Материалдар мен әдістер. Зерттеу когорттық, клиникалық, интервенциялық емес, перспективалық болып табылады. Шымкент қалалық жұқпалы аурулар ауруханасында 2022 жылдың желтоқсанынан 2023 жылдың қаңтарына дейін этиотропты ем қабылдамаған науқастар тобымен салыстырғанда ересектердегі ЖРВИ ауыр түрлерінде энизамия йодидінің вирусқа қарсы препаратының тиімділігіне клиникалық сынақтар жүргізілді.

Нәтижелер мен қорытындылар. Емдеу нәтижесінде 4-ші және 5-ші күндері дене температурасының қалыпқа келуінің үдеуі байқалды (тиісінше 96% және 98%). Салыстыру тобында 3-ші тәулікте дене температурасының қалыпқа келуінің жақсаруы науқастардың 60% -ында тіркелді.

Негізгі және бақылау топтарын төсек күндері бойынша салыстырған кезде статистикалық маңызды айырмашылықтар анықталды (p=0,049*). Стандартты терапиясы бар емделушілер Амизонды қосымша қабылдағандарға қарағанда ауруханада ұзақ болды. Амизонмен емдеу кезінде 50 жағдайдың 1-інде ғана препаратты қабылдаумен сәйкес келетін, препаратты қабылдауды тоқтатуды қажет етпейтін аздаған бас ауруы түріндегі жағымсыз құбылыс дамыды. Терапияның 3 және 4-ші күндерінде статистикалық маңызды айырмашылықтар анықталды. Интоксикация симптомдарының регрессиясы (қызба, қалтырау, бас ауруы, дененің ауыруы) және катаральды көріністер бақылау тобына қарағанда әлдеқайда ертерек байқалды. Амизонды қолдану кезінде бактерияға қарсы препараттарды тағайындау қажеттілігі 10% құрады, бұл оның вирусқа қарсы және бактерияға қарсы әсерін көрсетеді.

Түйінді сөздер: *ЖРВИ, вирусқа қарсы ем, тұмау, энисамия йодиді.*

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Relevance. From 600 thousand to 1.2 million cases of ARVI and influenza are registered annually in Kazakhstan [2]. On average for the epidemiological season hospitalised with severe and moderate course of ARVI - up to 70-80 thousand people, 70% of whom are children under 14 years old, including children under 1 year - up to 30-35%, pregnant women -53-55% of the number of pregnant women who became ill with ARVI, respectively. Thus, as of 1 February 2023, 1,027,000 patients with acute respiratory infections were registered in the RK, 3078 were diagnosed with influenza [2]. Among non-influenza respiratory viral infections, parainfluenza, RSV infection, rhinovirus, adenovirus, bocavirus, metapneumovirus infections are registered in the country. COVID-19 coronavirus infection has been identified in 2,780 cases since 1 January 2023 and 1,405,917 cases since the beginning of the pandemic [11,14,19]. There are also cases of mixtinfection, when during sentinel epidemiological surveillance in patients with an episode of acute respiratory viral infections, simultaneous registration of influenza virus and SARS-CoV2, MS virus and SARS-CoV2, or all three viruses was detected by laboratory, which fits the term "tridemic" that has recently appeared in the world scientific literature [11].

The clinic of influenza is known to be characterised by the following symptoms: high fever above 38°C lasting several days, intense headache which is one of the first symptoms, general weakness and fatigue, muscle and joint pain, sore throat and difficulty swallowing, dry cough, nasal congestion, runny nose, loss of appetite, some patients may experience dizziness. It should be noted that the symptoms of influenza may vary depending on the age, general health and immune system of the patient [15].

ARVI is characterised by nasal congestion, sneezing, profuse nasal mucus discharge, sore and irritated throat, difficulty in swallowing, dry cough or cough with little sputum, moderate pain in the forehead and temples, moderate body temperature, chills or general weakness, discomfort and pain in muscles and joints, redness of the eyes, lacrimation, itching or discomfort. Symptoms of acute respiratory infections may also vary depending on the specific virus, the patient's age, immunity and other factors [15].

In the case of mixtinfection, it can be quite difficult to assume the etiology of the disease, but the need to prescribe an antiviral drug with a wide range of indications as an etiotropic agent is of particular relevance.

Treatment of acute respiratory viral infectious disease (ARVI) includes a number of measures and approaches aimed at alleviating symptoms, reducing the duration of the disease and preventing complications. According to the clinical guidelines approved in the Republic of Kazakhstan, etiotropic therapy with antiviral drugs from the group of neuraminidase inhibitors is used only for the treatment of pregnant women with severe forms of influenza [15]. The main aspects of treatment of acute respiratory infections are: maintaining hydration, symptomatic treatment: medications for headache, fever and muscle aches (e.g. paracetamol or ibuprofen), and vasoconstrictor drops to relieve nasal congestion [8,18,20].

A number of antiviral drugs with different mechanisms of action are registered in the Republic of Kazakhstan and recommended according to their instructions for use in acute respiratory viral infections [18,20]. The drugs used in acute respiratory viral infections (ARVI) include the following classes: Neuraminidase inhibitors - oseltamivir, zanamivir, which block the enzyme neuraminidase, which is necessary for the virus to spread in the body; polymerase inhibitors, which affect viral RNA polymerase and prevent viral RNA synthesis (remdesivir, molnipiravir); immunomodulators - interferons, which stimulate the body's immune system to fight viral infection [10,16].

WHO in 2013 made a BRAVE recommendation that treatment options for acute respiratory infections should be expanded with the development of effective antiviral drugs for the most significant pathogens [3].

One such drug is enisamia iodide, produced by Pharmak (Ukraine) under the trade name Amizon, which is registered in the Republic of Kazakhstan as an antiviral agent[5]. Amizon is a drug containing the active ingredient tilorone, which stimulates immune system functions by acting on various cells including natural killer cells (NK cells), macrophages and dendritic cells [6]. It also enhances the production of interferons, which play an important role in the body's defence against viral infections [5]. Amizon also has anti-inflammatory properties and helps to normalise the immune response, which helps in the fight against various viral and bacterial infections [1].

Indications for its administration are both treatment and prevention of influenza and acute respiratory viral infections, viral-bacterial pneumonias, tonsillitis [15,13-16].

The mechanism of its action is a direct inhibitory effect on the process of viral penetration through the cell membrane, increasing the concentration of endogenous interferon (interferon alpha and interferon gamma) in blood plasma 3-4 times. As a consequence, acute clinical manifestations of viral intoxication are reduced, the duration of the disease is shortened. The scheme of treatment with Amizon may vary depending on the specific disease and individual characteristics of the patient. The following regimen is usually recommended: adults are prescribed 1-2 tablets (250 - 500 mg) of Amizon 3 times a day for 5 days [5,13].

In an earlier period in the Republic of Kazakhstan, clinical trials on the efficacy of enisamium iodide in the complex treatment of moderately severe forms of acute respiratory viral infections were conducted on the basis of large infectious diseases hospitals in Almaty and Astana. The results of the trials demonstrated that enisamium iodide (Amizon) is an effective and safe antiviral drug and can be used as an etiotropic drug in the complex treatment of acute respiratory viral infections, its use allows to reduce, and in some cases completely abandon the use of symptomatic therapy in influenza and acute respiratory viral infections, reduce the cost of treatment and reduce the risk of side effects of therapy [3,15].

The aim of our study was to evaluate the efficacy of enisamium iodide in the complex treatment of severe acute respiratory viral infections.

Materials and methods. Clinical trials of the efficacy of antiviral drug enisamiya iodide in severe forms of acute respiratory viral infections in adults, compared with a group of patients who did not receive etiotropic treatment, were conducted for the first time in the City Infectious Diseases Hospital of Shymkent. Our study was cohort, clinical, non-interventional, prospective, took place during the epidemic season of influenza and ARVI 2022-2023 and lasted from December 2022 to January 2023.

Inclusion criteria for patients with severe acute respiratory viral infectious disease (ARVI) in the study were: severity of symptoms with significant clinical manifestations, such as high body temperature, severe sore throat or chest pain, difficulty breathing, significant general malaise and/or progressive respiratory failure; need for hospitalization, i.e. patients requiring inpatient treatment and observation due to severe ARVI; established according to diagnostic criteria; and inclusion of patients with severe acute respiratory viral infectious disease (ARVI) in the study. *Exclusion criteria* for patients with severe acute respiratory infections: pregnancy and lactation, use of other etiotropic drugs, presence of serious systemic complications, age below 18 years and non-compliance with the inclusion criteria.

The course of the study was agreed and approved by the management of the City Infectious Diseases Hospital of Shymkent. Moreover, according to the obtained results of the study was made introduction to the clinic, formalised in the form of an act of introduction.

Enisamium iodide with the trade mark "Amizon" in a dose of 250 mg was administered in the main group *(n=50)* by 2 tablets 3 times a day, a course of 5 days, simultaneously with pathogenetic and symptomatic therapy. Patients from the comparison group *(n=50)* received only pathogenetic and symptomatic therapy in the form of antipyretic, anti-inflammatory and detoxifying, expectorant drugs.

Ethics. The study was approved at the meeting of the local ethics committee of JSC UKMA. Protocol No. 4 dated 03/10/2022). Informed consent was obtained from all patients.

Statistical analysis. Statistical processing was performed using IBM SPSS 26.0 programme. Quantitative data were described using median and interquartile range. The Mann-Whitney test was applied. Categorical data were described with absolute values and percentages. Comparison of percentages in the analysis of four-field contingency tables was performed using Pearson's chi-square test.

Results.

Out of 50 patients of the main group admitted with severe ARVI 62% (31 patients) were aged 30-39 years, 20% (10 patients) - 20-29 years, 12% (6 patients) - over 60 years and 6% (3 patients) - 15-19 years. Men treated with Amizon were 18(36%), 32(64%) women. 88% of patients were residents of Shymkent city, the rest were rural residents. Most patients had concomitant pathology: chronic pyelonephritis - in 26% of patients, chronic bronchitis - in 24%, arterial hypertension - in 18%, chronic tonsillitis and encephalopathy - in 10%, chronic gastritis - in 6%, diabetes mellitus, chronic sinusitis, bronchiectasis and chronic hepatitis - in 2% of patients. When analyzing the duration of hospitalization. It was found that 58% of patients were admitted to the hospital bed on the 3rd day of the disease, 24% - on the 1st or 2nd day of the disease, and in 16% of cases there was a late hospitalization, i.e. on the 4th day of the disease. hospitalization, i.e. on days 4-5 of the illness (Figure 1).

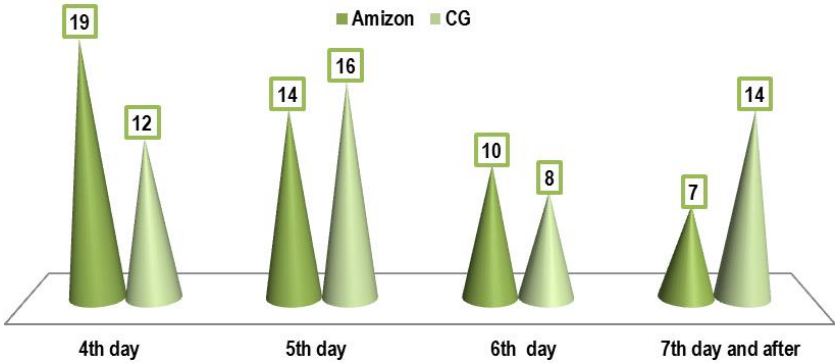

Figure 1. Day of discharge from hospital of patients with severe acute respiratory infections.

Table 1 shows that the patients' complaints showed signs of pronounced intoxication and catarrhal syndromes: increased body temperature and headache - in 100% of patients, dry cough - in 92% of patients, sore throat and nasal congestion - in 88% of patients, chills - in 65% of patients, body aches - in 57% of patients. On objective examination in the emergency room the condition of all patients condition of all patients was assessed as severe, in 72% of cases there was revealed hyperaemia of the pharynx, and in 42,5% of cases - lymphatics. 42.5% of cases - lymphadenopathy.

Figure 2 shows that the treatment resulted in normalisation of body temperature by day 2 from the start of treatment in 38% of patients in the test group, by day 3 - in 80%, by day 4 - in 96% and by day 5 - in 98% of patients. In the comparison

group normalisation of body temperature by day 2 from the beginning of treatment was observed in 18% of patients, by day 3 - in 60%, by day 4 - in 90% and by day 5 - in 96% of patients.

The cessation of chills in patients from the test group was observed in 54% on the 2nd day of treatment, in 92% on the 3rd day of treatment and in 100% on the 4th day of treatment, whereas in the comparison group chills stopped on the 2nd day of treatment in 64%, in 78% on the 3rd day of treatment and in 100% on the 5th day of treatment (Table 1).

Table 1.

Comparative characterisation by complaints in patients.

Complain ts	Main group (n=50)				Control group(n=50)				p	ODDS; 95% CI
	Day 2	Day 3	Day 4	Day 5	Day 2	Day 3	Day 4	Day 5		
Body temperature	9	30	45	48	19	40	48	49	>0,05	
Headache	6	18	33	41	3	14	23	38	0.035* (day 4)	(2.8 DI 1.02-5.11)
Sore throat	4	17	41	46	10	20	36	43	>0,05	
Nasal congestio n	10	10	35	44	8	13	26	46	0.05*(day 4)	(2.16 DI 0.95-4.89)
Chills	32	39	49	49	39	27	46	50	0.006*(day 3)	(3.6 DI 1.52-8.97)
Dry cough	1	3	11	32	3	11	28	38	0.041*(day 3)	(2.5 DI 0.92-7.08)

** - differences of indicators are statistically significant (p<0.05)*

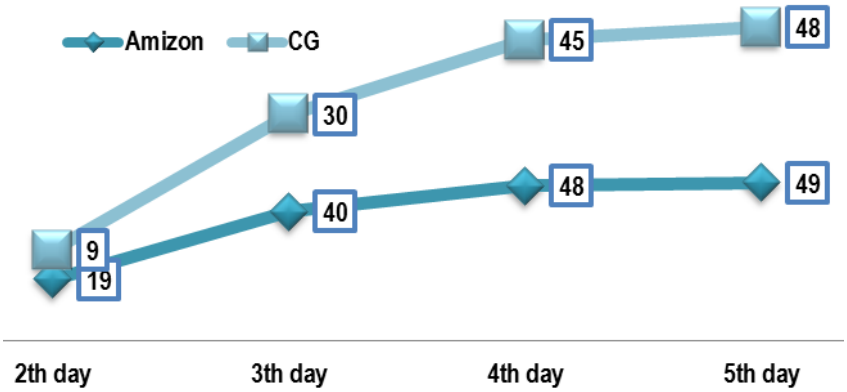

Figure 2. Dynamics of normalisation of body temperature on the background of the conducted treatment cures.

When comparing the main (Me=5[4-6]) and control groups (Me=5[5-7]) in terms of bed-days, statistically significant differences were found (p=0.049*). Patients with standard therapy stayed in hospital longer than those who received Amizon additionally (minimum number of bed-days were 4 and 2 days, respectively). The Mann-Whitney test was used.

Statistically significant differences were found when comparing the main and control groups in terms of pharyngeal hyperaemia on day 3. The odds of regression of this complaint in patients of the main group increased 1.4 times (95% CI: (0.17- 1.01) compared to the control group. There was a medium correlation (V =0.478) between the compared features.

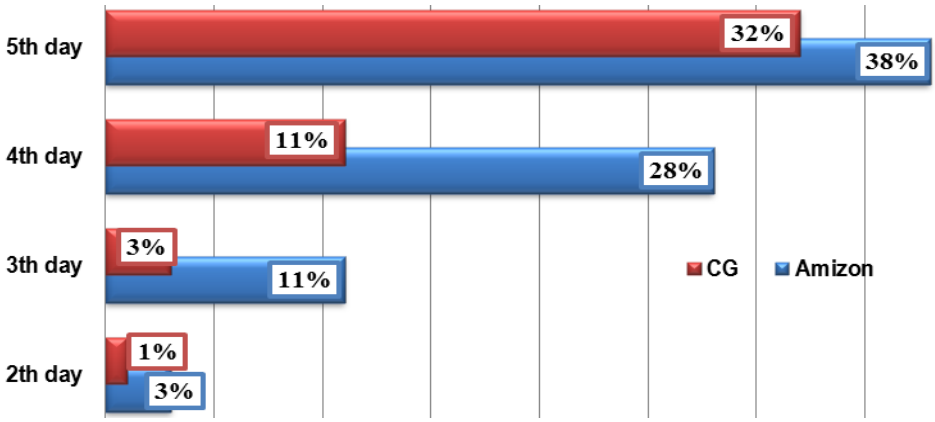

Figure 3: Dynamics of dry cough regression in patients with severe acute respiratory infections.

Discussion.

In our study, 62% (31 patients) of the main group receiving the drug were aged 30-39 years. Statistically significant differences were revealed on the 3rd and 4th day of therapy. In the work of Guo M. et al analysed the timing of normalisation of body temperature of patients (below 37ºC) on the 2nd, 3rd, 4th and 5th day of the study. The study by Cocking D et al involved patients from 18 to 50 years old, among them 73% were older than 35 years [9]. Analysis of temperature normalisation by day did not show statistical significance. But it should be noted, in 38% of patients from the main group normalisation of body

temperature was observed by day 2, by day 3 - in 80%, by day 4 - in 96% and by day 5 - in 98% of patients. On day 3, the number of patients with normal temperature in the main group was 23 (34.33%) versus 7 (10.45%) in the comparison group, and on day 4, this figure was 56 (83.58%) and 44 (66.67%) patients, respectively [12].

Against the background of Amizon treatment, only 1 case out of 50 developed an adverse event in the form of a minor headache coinciding in time with the drug intake, which did not require cancellation of the drug. Significant positive dynamics was observed in the group of patients treated with Amizon and in such parameters as duration of dry cough, headache, sore throat and nasal congestion.

Antibacterial therapy was additionally prescribed in 5 cases: in 2 cases - for exacerbation of chronic sinusitis, in 2 cases - for exacerbation of chronic pyelonephritis, in 1 case - for exacerbation of chronic bronchitis. In the comparison group, antibacterial drugs were also needed in 5 cases: for chronic bronchitis, sinusitis and pyelonephritis. According to various authors [12,13,17] When assessing the proportion of patients who required antibiotic therapy due to complications, the following data were obtained: 2 (3.0%) patients in the main group required additional therapy compared with 8 (11.9%) patients in the control group.

The drug Amizon has a high efficacy compared to the group of patients who did not take it. Other sources also confirm this [12,13,17]. It has demonstrated the following main benefits: reduced duration of illness, which allows patients to recover faster and return to normal activity; reduced severity of symptoms such as fever, headache, runny nose, sore throat and other manifestations of acute respiratory infections; improved general condition, reduced fatigue and increased performance; safety and low risk of undesirable side effects.

The advantage of this study is that for the first time in Kazakhstan the efficacy and safety of the drug was evaluated in a group of patients with severe course of acute respiratory viral infections, including comorbid, with the presence of concomitant pathology. The disadvantage of the study is the lack of virological control of the elimination of the pathogen itself, which is due to the lack of a research laboratory.

Conclusions.

1. The drug Enisamium iodide (Amizon) demonstrated its clinical efficacy in the treatment of severe acute respiratory viral infections, including in comorbid patients: 66% of patients were discharged from hospital with recovery on the 4th-5th day from the beginning of treatment.

2.Regression of intoxication symptoms (fever, chills, headache, body aches) and catarrhal manifestations occurred significantly earlier than in the control group.

3. The need for antibacterial drugs against the background of Amizon use was 10%, which indicates its antiviral and antibacterial effect.

4. The drug showed good tolerability: no serious adverse events were observed, only 1 patient noted headache associated with the drug administration.

5. The drug is an effective agent for the treatment of acute respiratory viral infections and influenza, promoting rapid recovery, reduction of symptoms and improvement of general well-being of patients and can be recommended for use in the treatment of severe forms of acute respiratory viral infections both in outpatient and inpatient settings, including in comorbid patients.

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Literature:

1. *Баранов А.М., Шкрабов А.В., Шустер А.М., Галкина И.В.* Клинико-экономическая эффективность применения Амизона при лечении гриппа и ОРВИ у детей // Российский вестник перинатологии и педиатрии. 2013. 58(3):82-86.

2. Данные комитета по санитарно-эпидемиологическому контролю Республики Казахстан, 2024 https://rk-ncph.kz/ru/sanepidem/ezhemesyachnaya-situatsiya (Дата обращения: 15.01.2024)

3. *Кулжанова Ш.А., Нурахметова Г.А., Конкаева М.Е., Смагулова З.К.* Клиническая эффективность препарата энисамия йодид в комплексном лечении ОРВИ // Медицина (Алматы). 2020. №5-6 (215-216). С. 32-37. DOI: 10.31082/1728-452X-2020-211-215-216-5-6-32-37

4. *Медведева И.В., Калинина Л.А., Сухомлинов А.В., и др.* Применение Амизона у детей с хроническими респираторными заболеваниями // Педиатрия. Журнал им. Г.Н. Сперанского. 2014. 93(1):34-39.

5. *Петров В.А., Злотникова Е.И.* Экспериментальное исследование антивирусной активности Тилорона (Амизона) в отношении гриппа A/H5N1 и других возбудителей ОРВИ // Вопросы вирусологии. 2008. 53(6):38-42.

6. *Сазонова М.А., Дудкин В.А., Старостина Е.Г., и др.* Иммуномодулирующий препарат Амизон у детей с рецидивирующими респираторными вирусными инфекциями // Клиническая педиатрия. 2012. 2:31-35.

7. *Boltz D., Peng X., Muzzio M. et al.* Activity of enisamium, an isonicotinic acid derivative, against influenza viruses in differentiated normal human bronchial epithelial cells // Antivir Chem Chemother. 2018. No 26. 2040206618811416. DOI: 10.1177/2040206618811416.

8. *Casanova J.L., Abel L.* The human model: a genetic dissection of immunity to infection in natural conditions // Nat. Rev. Immunol. 2004. Vol. 4 (1). P. 55–66. DOI: 10.1038/nri1264

9. *Cocking D., Cinatl J., Boltz D.A.* Antiviral effect of a derivative of isonicotinic acid enisamium iodide (FAV00A) against influenza virus // Acta Virol. 2018. 62(2):191-195. doi: 10.4149/av_2018_211

10. *Frolov A.F., Frolov V.M., Bukhtiarova T.A., Danilenko V.F.* Clinical aspects of the use of Amizon // Ukrainian Medical Journal. 2004. 1(39):69–74.

11. *Shaimerdenova G., Abuova G.N., Serikbayeva S.* Antiviral Therapy in Pregnant Women with COVID-19 Archives of Clinical Infectious Diseases. 2023. 18 (1)e132803 https://doi.org/10.5812/archcid-132803 (Дата обращения: 12.01.2024)

12. *Guo M., Ni J., Yu J.* Antiviral Activity of Benzoic Acid Derivative NC-5 Against Influenza A Virus and Its

Neuraminidase Inhibition // Int J Mol Sci. 2019 Dec 12;20(24):6261. doi: 10.3390/ijms20246261

13. *Jones J.C., Marathe B.M., Lerner C.* Novel Endonuclease Inhibitor Exhibits Broad-Spectrum Anti-Influenza Virus Activity In Vitro // Antimicrob Agents Chemother. 2016 Aug 22. 60(9):5504-14. doi: 10.1128/AAC.00888-16

14. Governments continue discussions on pandemic agreement negotiating text. World Health Organization (WHO) https://www.who.int/com (Дата обращения: 12.01.2024)

15. Klinicheskie protokoly Ministerstva zdravookhraneniya Respubliki Kazakhstan – 2019: Gripp i ORVI (Kazakhstan). [Clinical protocols of the Ministry of Health of the Republic of Kazakhstan - 2019: Influenza and ARVI]. [Kazakhstan] https://diseases.medelement.com/disease/16085 (Дата обращения: 12.01.2024).

16. *Kruker A.T., Krause M.* Oseltamivir-induced delirium // Ther Umsch. 2010 Dec. Vol. 67 (12). P. 613-5. DOI: 10.1024/0040- 5930/a000106

17. *Moscona A.* Global transmission of oseltamivir-resistant influenza // N Engl J Med. 2009 Mar 5;360(10):953-6. doi: 10.1056/NEJMp0900648

18. *Ramos I., Fernandez-Sesma A.* Modulating the innate immune response to influenza A virus: potential therapeutic use of antiinflammatory drugs // Frontiers in immunology. 2015. No 6. P. 361. DOI: 10.3389/fimmu.2015.00361

19. *Shaimerdenova G., Abuova G., Yelshibek G., Zhuparbek A., Bakytzhan G., Ashtayeva S. et al.* The use of Remdesivir in pregnant women with COVID-19 // J Clin med kaz. 2023. 20(1):31-4. https://doi.org/10.23950/jcmk/12911 (Дата обращения: 13.08.2023)

20. *Spencer S., Nguyen H., Elal A.A. et al.* Surveillance for Oseltamivir Resistant Influenza A (H1N1) pdm09 Virus Infections During 2016–2017 and 2017–2018, United States // Open Forum Infectious Diseases. 2018. Vol. 5 (Suppl. 1). P. S267-S268. DOI: 10.1093/ofid/ofy210.752

References:

1. Baranov A.M., Shkrabov A.V., Shuster A.M., Galkina I.V. Kliniko-ekonomicheskaya effektivnost' primeneniya Amizona pri lechenii grippa i ORVI u detei [Clinical and economic effectiveness of Amizon in the treatment of influenza and ARVI in children]. *Rossiiskii vestnik perinatologii i pediatrii* [Russian Bulletin of Perinatology and Pediatrics]. 2013. 58(3):82-86 [in Russian]

2. Dannye komiteta po sanitarno-epidemiologicheskomu kontrolyu Respubliki Kazakhstan, 2024 [Data from the Committee for Sanitary and Epidemiological Control of the Republic of Kazakhstan] https://rk-ncph.kz/ru/sanepidem/ezhemesyachnaya-situatsiya [in Russian]

3. Kulzhanova Sh.A., Nurakhmetova G.A., Konkaeva M.E., Smagulova Z.K. Klinicheskaya effektivnost' preparata enisamiya iodid v kompleksnom lechenii ORVI [Clinical effectiveness of the drug enisamium iodide in the complex treatment of ARVI]. *Meditsina* (Almaty) Medicine]. 2020. №5-6 (215-216). pp. 32-37. DOI: 10.31082/1728-452X-2020-211-215-216-5-6-32-37 [in Russian]

4. Medvedeva I.V., Kalinina L.A., Sukhomlinov A.V., i dr. Primenenie Amizona u detei s khronicheskimi respiratornymi zabolevaniyami. Pediatriya [Application of Amizon in children with chronic respiratory diseases]. *Zhurnal im. G.N. Speranskogo* [Pediatrics. Journal named after G.N. Speransky]. 2014. 93(1):34-39. [in Russian]

5. Petrov V.A., Zlotnikova E.I. Eksperimental'noe issledovanie antivirusnoi aktivnosti Tilorona (Amizona) v otnoshenii grippa A/H5N1 i drugikh vozbuditelei ORVI [Experimental study of the antiviral activity of Tiloron (Amizon) against influenza A/H5N1 and other pathogens of ARVI]. *Voprosy virusologii* [Questions of Virology]. 2008. 53(6):38-42. [in Russian]

6. Sazonova M.A., Dudkin V.A., Starostina E.G., i dr. Immunomoduliruyushchii preparat Amizon u detei s retsidiviruyushchimi respiratornymi virusnymi infektsiyami [Immunomodulatory drug Amizon in children with recurrent respiratory viral infections]. *Klinicheskaya pediatriya* [Clinical Pediatrics]. 2012. 2:31-35. [in Russian]

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