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## USE OF THE ANTIVIRAL DRUG «ARBIMECTIN» IN THE TREATMENT REGIMEN FOR CALICIVIRUS IN CATS

### ANNOTATION

The article discusses the possibility of using the antiviral drug "Arbimectin" in the treatment regimen for cats suffering from a viral disease - calicivirus. Data are presented confirming the effectiveness of Arbimectin in all forms of calicivirus in cats. Some issues of the pharmacodynamics of Arbimectin in the treatment of intracellular viruses are considered. The given treatment regimen makes it possible to increase the effectiveness of calicivirus therapy in sick animals.

The use of Arbimectin, which has the ability to penetrate into affected cells and block the synthesis of viral ribonucleic acid, significantly reduces the duration of the disease and mortality among cats. Arbimectin promotes a more complete release of the body from the virus, which is confirmed by a reduction in the time it takes for the viral antigen to be released from the body of animals. Studies have shown that the inclusion of Arbimectin in the treatment regimen for various forms of calicivirus significantly increases the percentage of recovery, with the exception of the nervous form, in which the drug is not effective. Thus, Arbimectin is recommended for use in complex therapy of feline calicivirus to improve its outcomes.

**Key words:** *Feline calicivirus, Arbimectin, therapy, complex use, effectiveness.*

**Introduction:** Relevance of the study: Currently, felinology of various cat breeds is intensively developing in Kazakhstan. Thus, according to data from the leading felinological organization of Kazakhstan, the Union of Felinologists of Kazakhstan, the average annual increase in the number of purebred cats in Kazakhstan is 9,8%. In 2023, 95 kittens were received, while in 2024 – 215. In general, in Kazakhstan, the same growth dynamics are observed in 2024, as can be seen in the example of the Felinologists Club, Semey. So, in 2023, 95 high-breed kittens were registered in the “Book of Breeding”, and in 2024 there are already 215 kittens. Thus, the number of purebred cats susceptible to various infectious diseases increases every year.

Calicivirus is a widespread infectious disease in cats manifested by an increase in body temperature, ulceration of the mucous membranes of the oral and nasal cavities, conjunctivitis and even lameness. Sick cats and virus carriers can secrete the pathogen with discharge from the oral and nasal cavities, with lacrimal secretions, feces, urine, for several months. Infection occurs alimentally, through direct contact, aerogenically, through clothing and care items. The disease is more common in the cold season. Young kittens aged from 1 month to 2 years are the most susceptible. Feline caliciviruses are mildly virulent and the disease often occurs in a latent form, but when combined with other agents (bacteria, viruses), calicivirus infection can cause death in more than 80% of cats. It is believed that calicivirus infects only cats, but similar diseases have been isolated in dogs with vesicles on the genitals

Treatment of feline calicivirus is currently based on the use of specific hyperimmune serums in combination with antibiotics, vitamins and symptomatic agents. However, the widespread use of hyperimmune serums and interferon is limited to about a week from the moment the animal becomes ill, the moment when viral particles are in the blood. When viruses are no longer detected in the blood, being predominantly detected in tissues, the effectiveness of serum use drops sharply. In addition, the use of serums and immunomodulators at later stages of the disease can lead to a deterioration in the condition of patients. For example, gamma interferon promotes damage to nerve cells through the activation of cytotoxic T cells, so immunostimulants that increase its

synthesis very often aggravate the course of a severe form of the disease in cats or accelerate the onset of this stage of the disease. The use of only antimicrobial drugs and symptomatic agents significantly lengthens the healing period of the animal, does not always lead to its recovery, and is also quite expensive.

Treatment of patients with feline calicivirus using known methods is not effective enough due to the fact that the drugs used are not able to penetrate inside the cell affected by the virus, where viral reproduction occurs, thereby affecting only the virus that has emerged from the destroyed cell into the intercellular space, resulting in the release of the body lengthened by the virus.

The use of the antiviral drug Arbimectin in the treatment regimen of cats with the viral disease calicivirus, confirming the effectiveness of the use of Arbimectin in all forms of the course of calicivirus in cats. The above treatment regimen makes it possible to increase the effectiveness of calicivirus therapy in sick animals.

Umifenovir, which is part of it, specifically suppresses various viruses (rhinovirus, adenovirus, parainfluenza virus, calcevirus).

According to the mechanism of action, it refers to inhibitors that interact with the hemagglutinin of the virus and prevent the fusion of the lipid membrane of the virus and cell membranes.

Arbimectin stimulates cellular and humoral immune responses: increases the number of lymphocytes in the blood, especially T cells, increases the number of T helper cells, normalizes the immunoregulatory index, stimulates the phagocytic function of macrophages and increases the number of natural killers (NK cells).

With viral infections in animals, the duration and severity of the disease and its main symptoms decrease, and also reduces the incidence of complications associated with viral infection in the form of exacerbations of chronic bacterial diseases. Arbimectin is rapidly absorbed and distributed to organs and tissues. It is metabolized in the liver. About 40% is excreted unchanged, mainly with yellow and in small amounts by the kidneys.

Arbimectin belongs to the semi-synthetic macrocyclic lactones obtained from the soil actinomycete *Streptomyces avermitilis*., which has an antiviral effect. The probable mechanism of antiviral action is associated with inhibition of the transport of viral proteins into the nucleus of the host cell. Reduces viral load, reduces the severity of the disease and the risk of further spread of infection without causing toxic damage to cells.

Arbimectin is rapidly absorbed in the gastrointestinal tract, reaching its maximum plasma concentration after 4-5 hours. It is widely distributed across tissues. It is excreted almost exclusively with faeces. The medicinal product Arbimectin, according to the degree of exposure to the body, belongs to moderately dangerous substances (hazard class 3 according to GOST 12.1.007-76), in recommended doses it does not have a locally irritating and sensitizing effect.

**Purpose and objectives of the study:** The purpose of our research was to study the epizootic features of the course of feline calicivirus among cats in the Abay region of Kazakhstan, as well as to improve the system of anti-epizootic measures against calicivirus among cats in terms of prevention, diagnosis and treatment of this disease.

To achieve the intended goal, it was necessary to solve the following as one of the tasks: to improve the treatment regimen for calicivirus in cats and determine its effectiveness.

To solve this, it was necessary to develop a method for treating calicivirus that would allow simultaneously influencing the virus both coming out of the affected cells and inside them, using the antiviral drug Arbimectin, widely known to veterinary specialists, and determining the effectiveness of its use. There was no information in the literature available to us about the use of Arbimectin for the treatment of feline calicivirus.

**Materials and methods.** The experimental part of the work was carried out at the Department of Veterinary Medicine of the National Academy of Sciences of the Shakarim University of Semey and the private veterinary clinic CVM Dr. Vet. The diagnosis of calcivirosis in cats was made comprehensively, taking into account clinical signs, the results of microscopic examination of smear prints from ulcerative lesions of the oral cavity. And the final diagnosis was made based on the results of PCR diagnostics performed by the ZooVita veterinary laboratory. In addition to clinical examinations before the start of treatment and five days after the recovery of cats, morphological and biochemical blood parameters were examined on an automatic biochemical analyzer using appropriate diagnostic kits. At the same time, the state of the respiratory, cardiovascular, digestive, nervous and genitourinary systems, skin, visible mucous membranes, and the presence of outflows from the oral and nasal openings were taken into account. Previously, we developed a new method of treating feline calicivirus, which differs from the traditional use of the drug Arbimectin, which has the property of blocking the synthesis of viral ribonucleic acid in affected cells, as a

result of which the body is freed from the virus faster and more completely, which allows for increased efficiency.

To study the effectiveness of this drug, experimental and control groups were formed, consisting of animals with manifestations of clinical signs of feline calcivirus. The animals were monitored for 14 days, noting any changes in their condition. Recovery was defined as the disappearance of all clinical signs of the disease and the absence of relapse within 2 days. Before administration of the drug, blood serum samples were taken from the animals in order to clarify the diagnosis of the disease.

In the experimental group, sick animals, simultaneously with polyvalent hyperimmune serum against feline calcivirus, symptomatic, restorative and antimicrobial drugs, were administered intramuscularly with Arbibectin in the form of a 7% aqueous solution at a dose of 0.0035 g per 1 kg of animal weight twice with an interval between injections of 24 hours. Further treatment was carried out without Arbibectin with polyvalent hyperimmune serum against feline calcivirus in combination with symptomatic, restorative and antimicrobial drugs. Animals in the control group were treated without the use of Arbibectin.

For the treatment (in complex therapy) of infectious diseases of viral and bacterial etiology, the drug Arbibectin is used in cats 2 times a day, for 5-7 days, then 1 time a day, for 5 days.

For the prevention of viral diseases, the drug is used in animals 1 time a day, for 3-4 days.

To reduce the viral load and reduce complications in cats with calcivirus, the drug Arbibectin is recommended to be used 2 times a day, for 10-14 days.

The peculiarities of action during the first use of the drug or during its withdrawal were not revealed. Violations of the doses and course of use of the drug should be avoided, as this may lead to a decrease in its effectiveness. In case of missing the next application of the drug, it should be applied as soon as possible in the same dose and according to the same scheme.

**Research results.**In total, Arbibectin was used on 50 cats with calcivirus. In the control group, 24 sick cats were treated. The results obtained during the treatment of cats in the experimental and control groups are presented in Table 1.

Table 1 – Results of treatment for feline calcivirus

Treatment method and stages of the disease	Number of samples	Average duration of illness (days)	Number of recovered people	% recovery
Without Arbibectin	24	8	18	75
Initial stage	7	4	6	85,7
Expressed symptoms	11	8	8	85,7
Protracted current	6	14	4	66,6
<b>With Arbibectin</b>	<b>50</b>	<b>6</b>	<b>44</b>	<b>88,0</b>
Expressed signs	27	4	27	100
Protracted current	23	11	17	73,9

Analyzing the data presented in Table 1, it can be noted that without the use of Ar-bimectin for feline calcivirus, 7 samples were taken at the initial stage with an average duration of the disease of 4 days, the number of recovered 6 cats.that is, 85.7 percent recovery.

Pronounced signs were observed in 11 cats, and a prolonged course in 6 cats, with a recovery of 66.6%.

After the use of Arbibectin, pronounced signs were observed in 27 cats, recovery began on the 4th day with a 100% recovery. When a prolonged course with the use of arbibectin was observed in 23 cats, and recovery was 73.9%.

The use of Arbibectin reduces the duration of the disease, its lethality, and, consequently, the effectiveness and cost of the treatment itself. This effect of the use of Ar-bimectin can be explained by its pharmacological features. Arbibectin is a drug that affects intracellular parasites by suppressing the synthesis of their nucleic acids. Due to its chemical formula, Arbibectin penetrates into almost all types of cells of the animal's body (pore diameter in cell membranes from 0.4 nm in erythrocyte membranes

and in intestinal epithelium up to 4 nm in capillary endothelium), interrupts the chain of reproduction of the virus, thereby suppressing its spread in the body.

The average duration of cat disease during treatment without Ar-bimectin is 8 days, with a recovery rate of 75%. When Ar-bimectin is included in the animal treatment regimen, these indicators are 6.6 days and 88%, respectively. The obtained indicators indicate the effectiveness of the use of Arbimectin in the treatment of feline calcivirus. At the same time, compared with the control group, the duration of the disease and mortality are reduced.

It should be noted that in the experimental group, the death of sick animals was observed in the nervous form of the disease. In this regard, in our further studies, the effectiveness of the use of Arbimectin in various forms of the course of feline calcivirus was verified. For this purpose, Arbimectin was used in the treatment regimen of cats. The research results are presented in Table 2.

Table 2 – Results of the use of Arbimectin in the treatment of various forms of calcivirus in cats

Flow form and pattern calcivirus treatment	Number of samples	Treatment results	
		Number of recovered	% recovery
Treatment without Arbimectin	60	47	78,3
Treatment with Arbimectin	130	113	86,9

As can be seen from the data presented in Table 2, 60 blood samples were taken from sick cats. The effectiveness of treatment of feline calcivirus without the use of Arbimectin is 78.3%, that is, 47 the number of cats recovering. With the use of Arbimectin.

The results of Arbimectin treatment showed that out of 130 samples taken, the number of recovered cats was 113, and the percentage of recovery was 86.9%, respectively.

In further studies, the timing of detection of the antigen of the feline calcivirus virus in the secretions and excreta of recovered cats was studied. To this end, after the disappearance of clinical signs of the disease, cats previously exposed to treatment against feline calcivirus both with and without Arbimectin were daily sampled of faeces, nasal and oral effluents and examined in serological reactions to detect the virus antigen. The studies continued until the detection of the viral antigen was stopped. The results of these studies are presented in table 3.

Table 3 – Time frame for detection of the feline calcivirus virus antigen in the secretions and excreta of recovered cats

Test material	Number of samples	Time frame for antigen detection during treatment	
		with Arbimectin	without Arbimectin
Feces	20	3,2±0,4	5,8±1,2
Nasal discharge cavities	20	3,6±0,6	6,9±1,7
Discharge from the mouth cavities	20	2,1±0,3	4,3±0,9

As can be seen from the data presented in Table 3, the timing of isolation of the feline calcivirus virus from the body of sick cats in the case of using a treatment regimen with Arbimectin is 1.5-2 times less than the same indicator for treatment without Arbimectin.

The number of feces taken from 20 samples. The detection time of the antigen with Arbimectin is  $3.2 \pm 0.4$ , without Arbimectin is  $5.8 \pm 1.2$ .

Nasal discharge samples taken from 20 cats with Arbimectin were  $3.6 \pm 0.6$ , without Arbimectin  $6.9 \pm 1.7$ .

Samples taken from the oral cavity also in 20 cats showed the results of the detection of antigen with Arbimectin  $2.1 \pm 0.3$ , without Arbimectin  $4.3 \pm 0.9$ .

The results obtained confirm our assumption that Arbibectin blocks intracellular viral reproduction, thereby reducing the number of virions in the body of a sick animal.

**Conclusions:** Based on the data obtained, we can summarize that the treatment of feline calicivirus is currently based on the use of specific hyperimmune serums in combination with antibiotics, vitamins and symptomatic agents. But the widespread use of hyperimmune serums is limited by about a week from the moment of the animal's disease, the moment when the viral particles are in the blood. Further, the virus ceases to be detected in the blood, mainly being detected in tissues, and the effectiveness of the use of serums drops sharply. In addition, the use of serums and immunomodulators at a later stage of the disease can lead to a deterioration in the condition of patients. For example, gamma interferon contributes to damage to nerve cells by activating cytotoxic T cells, therefore immunostimulants that increase its synthesis very often exacerbate the course of severe disease in cats or accelerate the onset of this stage of the disease. The use of antimicrobial drugs only and is symptomatic

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The inclusion of Arbibectin in the treatment regimen of feline calicivirus in cats reduces the duration of the disease and its lethality. At the same time, the effectiveness of treatment of calicivirus coli with Arbibectin is up to 100;

The timing of isolation of the feline calicivirus virus from the body of sick cats in the case of a treatment regimen with Arbibectin is 1.5-2 times less than the same indicator for treatment without Arbibectin.

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## ТҮЙІН

Алынған деректерге сүйене отырып, қазіргі уақытта мысықтың кальцивирусын емдеу антибиотиктермен, витаминдермен және симптоматикалық агенттермен бірге қолданылатын арнайы гипериммунды сарысуларды пайдалануға негізделген деп қорытынды жасауға болады. Дегенмен, гипериммунды сарысуларды қолдану жануар ауруының алғашқы аптасымен шектеледі, өйткені осы кезеңде вирус бөлшектері қанға түседі. Кейіннен вирус қаннан анықталмай, негізінен тіндерден табылатындықтан, сарысуларды пайдалану тиімділігі күрт төмендейді. Сонымен қатар, аурудың кейінгі сатысында сарысулар мен иммуномодуляторларды пайдалану пациенттердің жағдайын нашарлатуы мүмкін. Мысалы, гамма-интерферон цитотоксикалық Т жасушаларын белсендіру арқылы жүйке жасушаларының зақымдалуына ықпал етеді, сондықтан оның синтезін арттыратын иммуномодуляторлар мысықтардағы ауыр аурудың ағымын жиі нашарлатады немесе аурудың осы сатысының ерте басталуына әкеледі. Антимикробтық препараттарды қолдану тек симптоматикалық сипатқа ие.

Мысықтардың кальцивирус инфекциясын емдеу схемасына қарсы вирусқа қарсы Арбимектин препаратын қосу оның барлық формаларда тиімділігін дәлелдейді. Жоғарыда аталған емдеу схемасы ауру жануарларда кальцивирус терапиясының тиімділігін арттыруға мүмкіндік береді. Препараттың құрамындағы умифеновир әртүрлі вирустарды (риновирус, аденовирус, парагрипп вирусы, кальцивирус) селективті түрде тежейді.

Деректерді талдай отырып, Арбимектинді қолданбай кальцивируспен ауырған мысықтарда аурудың бастапқы кезеңінде 7 сынама алынып, аурудың орташа ұзақтығы 4 күн болғанда, 6 мысықтың сауығуы байқалды, бұл 85,7% сауығуды құрайды. 11 мысықта айқын белгілер байқалып, 6 мысықта аурудың ұзақ ағымы байқалып, сауығу 66,6% құрады.

Арбимектинді қолданғаннан кейін 27 мысықта айқын белгілер байқалып, 4-ші күні 100% сауығу басталды. Аурудың ұзақ ағымында Арбимектинді қолданған кезде 23 мысық сауықты.

Химиялық формуласының арқасында Арбимектин жануарлардың барлық дерлік орган жасушаларының түрлеріне (эритроциттер мембранасындағы және ішек эпителийіндегі саңылаулардың диаметрі 0,4 нм-ден бастап капиллярлардың эндотелийіндегі 4 нм-ге дейін) еніп, вирус репродукциясының тізбегін үзеді, осылайша оның организмде таралуын тежейді.

Сонымен қатар, ауру мысықтардың қанынан 60 сынама алынды. Арбимектинді қолданбай кальцивирусты емдеу тиімділігі 78,3% құрады, яғни 47 мысық сауықты.

Арбимектинмен емдеу нәтижелері 130 алынған үлгінің ішінде 113 мысықтың сауыққанын көрсетті, сауығу пайызы сәйкесінше 86,9% болды.

Кейінгі зерттеулерде кальцивируспен ауырған мысықтардан алынған антигеннің сауыққан жануарлардың ағзасындағы бөлініп шығу мерзімі зерттелді. Арбимектинді қолданған жағдайда кальцивирус вирусының ағзадан бөліну мерзімі Арбимектинді қолданбай емдеу жағдайына карағанда 1,5-2 есе аз.

Ауыз қуысынан алынған сынамалар антигеннің анықталу нәтижелерін көрсетті: Арбимектин қолданғанда –  $2,1 \pm 0,3$ , Арбимектин қолданбағанда –  $4,3 \pm 0,9$ .

Алынған нәтижелер Арбимектиннің жасушаішілік вирустық репродукцияны блоктайтынын, осылайша ауырған жануарлардың ағзасындағы вирустық бөлшектердің санын азайтатынын растайды.

Мысықтардағы кальцивирусты емдеу схемасына Арбимектинді қосу аурудың ұзақтығын және оның өлім-жітімін төмендетеді.

## РЕЗЮМЕ

В статье рассмотрена возможность применения противовирусного препарата «Арбимектин» в схеме лечения кошек, больных вирусным заболеванием – кальцивирус. Приведены данные, подтверждающие эффективность применения Арбимектина при всех формах течения калицивируса у кошек. Рассмотрены некоторые вопросы фармакодинамики Арбимектина в лечении внутриклеточных вирусов. Приведенная схема лечения позволяет повысить эффективность терапии кальцивируса у больных животных.

Применение Арбимектина, обладающего способностью проникать внутрь поражённых клеток и блокировать синтез вирусной рибонуклеиновой кислоты, существенно уменьшает продолжительность болезни и летальность среди кошек. Арбимектин способствует более полному освобождению организма от вируса, что подтверждается сокращением сроков выделения вирусного антигена из организма животных. Исследования показали, что включение Арбимектина в схему лечения различных форм кальцивируса, значительно повышает процент выздоровления, за исключением нервной формы, при которой препарат не эффективен. Таким образом, Арбимектин рекомендуется к применению в комплексной терапии кальцивируса кошек для улучшения её исходов.