INTRODUCTION

For implementing of the Federal Law “On the Development of Agriculture”, the Russian Federation Government has set goals for increasing the livestock breeding productivity while obtaining high-quality products. The profitability of livestock breeding directly depends on the absence of parasitic diseases, since they cause significant economic losses to the livestock by reducing the productivity and quality their byproduct, deteriorating the breeding value, increasing the cost of cattle feeding and high cost for treatment of parasitoses (Kuzmichev et al., 2006; Mkrtchyan et al., 2015).

Parasitic diseases of animals still have an effect on the animal husbandry within the Russian Federation, especially gastrointestinal fascioliasis (Fasciola hepatica) and strongylatoses (Chabertia ovina, Haemonchus contortus, and Bunostomum trigonocephalum) that are the most widespread causing significant economic losses (Kononova, 2009; Shatokhin et al., 1997; Demidov and Berezkina, 1986; Mkrtchyan and Klimova, 2013; Mkrtchyan et al., 2013).

Previous studies have shown that prolonged parasitism of the pathogens of mono and mixed invasions results in deep and persistent metabolic disorders, which manifested by retarded growth, loss of productivity, deterioration of the
breeding properties, while in case of high infestation rate, can lead to death of the animal (Kosyaev, 2003; Kuzmichev et al., 2006; Shatokhin et al., 1997; Mkrtchyan et al., 2013; Musayev et al., 2017; Safullin and Ustinov, 2010; Safullin and Khromov, 2009; Guralp and Tinar, 1984; Leaning et al., 1983; Wamae et al., 1998).

The pathogens of the parasitic diseases have direct and indirect effect on the animal, thus significantly reduce its overall resistance (Safullin and Khromov, 2009). The direct effect of helminths on the cattle is determined by their mechanical, toxic, trophic, inoculatory, and allergic effects (Kononova, 2009; Kosyaev, 2003; Kuzmichev et al., 2006; Guralp and Tinar, 1984; Leaning et al., 1983). For effective dehelmintization for cattle, weshould bear in mind that comprehensive measures to control cattle parasites which result in completeremoval of both helminths and their metabolic byproducts from the host (Kosyaev, 2003).

The success to control helminthoses depends mainly on the availability of highly effective, low-toxic, and affordable drugs (Mkrtchyan et al., 2013; Mkrtchyan et al., 2015; Musayev et al., 2017). So, the choice of effective anthelmintic should be based not only on high efficiency but also on its safety. Currently, in the world veterinary practice, over 2,000 anthelmintic drugs in various dosage forms are used (Krucohenko and Bondarevsky, 2016; Demidov and Berezkina, 1986; Mkrtchyan and Klimova, 2013; Mkrtchyan et al., 2013, 2015; Musayev et al., 2017; Safullin and Ustinov, 2010; Safullin and Khromov, 2009; Guralp and Tinar, 1984; Leaning et al., 1983; Maingi et al., 2002; Meaney et al., 2002; Stear et al., 2007; Stepek et al., 2005; Traversa and von Samson-Himmelstjerna, 2016).

The current research aims to study the epizootic situation in terms of parasitoses at farms in the Udmurt Republic, assessing the therapeutic efficacy of anthelmintic drugs against mono- and mixed invasions gastrointestinal fascioliasis and strongylatoses in cattle, and estimating the possible economic losses caused by these helminthoses.

**MATERIALS AND METHODS**

Fecal samples were collected from spontaneously infected animals a total of 780 animals were examined. The degree of the animal infection was determined with the use of conventional coproovoscopic methods and incomplete helminthological dissection of the liver and intestines for animals at slaughterhouses. The fecal samples were taken individually and examined using the flotation and successive swabs methods.

The prevalence rate of fascioliasis and strongylatoses in the gastrointestinal tract of cattle was calculated between 2016 and 2019 at farms in the Votkinsk, Grakhovo, Kez, Malaya Purga, and Uva districts of the Udmurt Republic. In 2016 – 2017, of the total number of animals studied (780 heads), 200 samples, respectively, were taken rectally. In 2018, 210 samples were taken; in the last year (2019), 170 samples of faeces were examined. In order to study the epizootic situation of the previously mentioned helminthiases, groups of dairy cows from 3 to 6 years old of black-and-white Holsteinized breed (68–75%) were formed. The conditions for keeping animals in all areas were stall-walking, every year cows were grazed on pastures.

To identify the economic damage caused to the farms by fascioliasis and strongylatoses invasions, the actual loss was calculated following the Methodological Recommendations for Determining the Economic Efficacy of Veterinary Measures (Shatokhin et al., 1997). These losses include decreased milk production, direct rejection of the cattle live at meat processing plants, and the cost of dehelmintization drugs.

The therapeutic efficacy of anthelmintic drugs was studied on 675 animals, which were divided by the principle of analogs into groups; 45 animals per each. The anthelmintic efficacy of the drugs was determined following the Guidelines of the World Association for the Advancement of Veterinary Parasitology (1995) based on coproovoscopic studies of the animals. Before mass dehelmintization, each drug had been previously tested on a small group of five to ten animals and treatment of the entire group was started within three days in the absence of complications.

For studying the therapeutic efficacy of anthelmintic drugs against fascioliasis in cattle, the following drugs were chosen: Klozantin 20 %, Alvet granules, Closaverm, Santomectin, and Albendazole. In addition to their efficacy, the main requirement for the anthelmintic drugs used at agricultural farms is their reasonable price (Table 1). The first series for the experiment was performed on the animals spontaneously infected with fascioiiae. For this purpose, six groups of cattle were included: the first group was dehelmintized with Klozantin 20 % at the dosage of 1.25 ml per 50 kg of the bodyweight; the second group received Alvet granules (3.75 g per 100 kg of the bodyweight), the third group received injectable Closaverm was used at the dosage of 1 ml per 50 kg of the bodyweight, the fourth group received injectable Santomectin was injected at the dosage of 1 ml per 50 kg of the bodyweight, the fifth group received injectable Albendazole at the dosage of 15 ml per 50 kg of the bodyweight while the sixth group had been infected but not dehelmintized as control group.

The second series of the experiment was performed on the animals that had been spontaneously infected with strongylata. For this purpose, six groups of cattle were
included: the first group received Alben pills at the dosage of one pill per 35 kg of the bodyweight, the second group received injectable Klozantin 20 % at the dosage of 1.25 ml per 50 kg of the bodyweight, the third group received injectable Ivermec at the dosage of 1 ml per 50 kg of the bodyweight, the fourth group received injectable Novomec at the dosage of 1 ml per 50 kg of the bodyweight, the fourth group received injectable Albendazole at the dosage of 15 ml per 50 kg of the bodyweight while the sixth group did not receive antiparasitic drugs as control.

Table 1: The comparative characteristics of the anthelmintic drugs recommended for the treatment of fascioliasis in cattle.

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Cost</th>
<th>The cost of a single dose</th>
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<tbody>
<tr>
<td>Klozantin 20%</td>
<td>100 ml — 685 rubles</td>
<td>77 rubles</td>
</tr>
<tr>
<td>Alvet granules</td>
<td>500 g — 580 rubles</td>
<td>20 rubles</td>
</tr>
<tr>
<td>Closaverm</td>
<td>100 ml — 430 rubles</td>
<td>39 rubles</td>
</tr>
<tr>
<td>Santomectin</td>
<td>50 ml — 296 rubles</td>
<td>53 rubles</td>
</tr>
<tr>
<td>Albendazole</td>
<td>1 liter — 625 rubles</td>
<td>84 rubles</td>
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In the third series of the experiment, the animals infected with a combination of fasciolae and strongylata. For dehelmintization, two broad-spectrum drugs with trematocide and nematocidic effects were used according to the recommendations: Klozantin 20 % and Albendazole at the above dosages. The rate of animal infestation was determined by the method of studying fecal samples with the use of the flotation and sequential swabs methods before and after the antiparasitic treatments (15, 30, and 90 days after dehelmintization). After the antiparasitic treatment of the animals, measures were taken for disinfecting the environment.

RESULTS AND DISCUSSION

In the Udmurt Republic, all necessary climatic conditions are optimal for completing the biological cycle of cattle helminths. Our results revealed that in the studied areas, both monoinvasions and mixed invasions with gastrointestinal fasciolae and strongylatoses and their associations were reported. During studying the invasion rate, it was found that gastrointestinal strongylatoses more dominant over fascioliasis which their invasion degree varies from 33.07 % to 59.59 %. Their high invasion rate is explained by many factors including the population of adult animals (cows, heifers) in the epizootic process of gastrointestinal strongylata is important as a primary source of the invasion pathogen and the biological cycle of the pathogen directly depends on the environmental conditions, such as temperatures, air humidity, and oxygen content. Therefore, the conditions for the development of soil-transmitted helminths are favorable.

In the current study, cattle infestation with fasciolae within the examined regions is mainly due to the constant acting regular transmission of the pathogen within the animal species population. A significant number of waterlogged pastures, bottom-land meadows, and prolonged suitable temperatures contributing in developing and spreading of the intermediate host; Galba truncatula. The most favorable conditions for the development of F. hepatica are noted in the Central Uva district, where the invasion rate reaches 49.22 % while the lowest percentage of adult livestock infection was noticed in the northern Kez district of the Udmurt Republic 16.77 % which proven that even a slight decrease in the ambient temperature adversely influences the development of fasciolae.

The mixed invasions with gastrointestinal fasciolae and strongylata showed a slightly different pattern; the minimum invasion rate was observed in the northern Kez region 5.59 %, while the maximum rate for infected animals (22 %) was observed in the southern Malaya Purga district.

In parallel with the coprologic studies, incomplete helminthological dissection of the carcasses of the animals infected with fasciolae and strongylata in the digestive tract was made. Studying the liver of the cattle showed that it was enlarged and had extended biliary passages with thickened walls; after incision, thick yellow-green liquid with a large number of parasites was released. During the helminthological study for the gastrointestinal tract of cattle, the catarrhal-hemorrhagic inflammation of the abomasum and the small intestine was observed.

Studying the cattle fascioliasis invasion rate after dehelmintization showed that on the 15th day, the degree of infestation with fasciolae had decreased significantly in all the treated groups especially in groups 3 and 4, where the efficiency of the drugs exceeded 93 % and 95 %, respectively. Within that, as early as three months after dehelmintization, the eggs of fasciolae were not found in the animals in the first, third, and fourth groups.

The farms in the Udmurt Republic are continuously affected by gastrointestinal strongylatoses. Therefore, one of the main tasks is to choose the most affordable and effective drugs (Table 2).

Our results revealed that in case of nematodes monoinvasion, the most effective antiparasitic drugs are Klozantin 20 % (the cost of one dose per animal is 77 rubles) and Ivermectin (the cost of dehelmintization of a single animal does not exceed 40 rubles). Meanwhile, Alben in the form of pills had the lowest efficacy (75.5 %).
in dehelminthization that was possibly due to the dosage form and the drug resistance as this drug had been used at the studied farms for several years. In the mixed invasions of gastrointestinal fascioliasis and strongylatoses in the cattle, two broad-acting drugs were used: Albenazoled and Klozantin 20 %. The determination of the therapeutic efficacy of the antiparasitic drugs for the animals invaded by mixed helminths showed that Klozantin 20 % had the highest efficiency of 93.3 %, but it only manifested by the 90th day after dehelminthization.

Table 2: The comparative characteristics of the anthelmintic drugs intended for the treatment of gastrointestinal strongylatoses in cattle.

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Cost</th>
<th>The cost of a single dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alben — pills</td>
<td>1 pill – 10 rubles</td>
<td>130 rubles</td>
</tr>
<tr>
<td>Klozantin 20%</td>
<td>100 ml — 685 rubles</td>
<td>77 rubles</td>
</tr>
<tr>
<td>Ivermec</td>
<td>50 ml — 193 rubles</td>
<td>35 rubles</td>
</tr>
<tr>
<td>Novomec</td>
<td>100 ml — 420 rubles</td>
<td>38 rubles</td>
</tr>
<tr>
<td>Albendazole</td>
<td>1 liter — 625 rubles</td>
<td>84 rubles</td>
</tr>
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</table>

The choice of antiparasitic drugs individually for each farm; it is necessary not only to focus on the cost but also on the time of the drug removal from milk and its limitation in meat consumption that would allow the usage of anthelmintic drugs for the simultaneous treatment of the entire livestock and ensuring efficacy against mixed invasions since mixed invasions were found at the farms during the studies. The economic losses for cattle breeding in various regions of the Udmurt Republic by gastrointestinal fascioliasis and strongylatoses and their association was calculated that include loss from diagnostic slaughtering, underproduction of milk, liver rejection, and dehelminthization cost. The surveillance was made on 675 animals that had been spontaneously infected with gastrointestinal fascioliasis, strongylatoses, as monoinvasion.

The economic damage from milk underproduction was studied for 120 days; during the study, 12 check milkings were made.

The loss caused by decreased milk productivity due to cattle fascioliasis was as follows: 

$L = M_s * (B_h - B_a) * T * P,$

where $M_s$ was the number of affected animals, $B_h$ and $B_a$ were the average daily productivities of healthy and affected animals, per animal, kg, $T$ was the average duration of observing the changes in the productivity of the animals, days, and $P$ was the average sales price of one kg of the product, rubles. 

$L = 45 * (14 - 10.5) * 120 * 23 = 434,700$ rubles. Thus, the loss caused by decreased milk productivity due to fascioliasis was around 9,660 rubles per animal; 434,700 rubles per 45 infected animals. For determining the economic loss caused by the deteriorated quality of the animal byproducts were performed by assessing the liver of the cows affected by fascioliasis; according to the results of the examination at the meat processing place, it was found that all affected liver had to be rejected. During the 60 days of the experiment, three animals were slaughtered, and 23 kg or 3,680 rubles worth of liver were rejected: $L = B_a * (P - P_a).$ The total economic losses caused by fascioliasis were determined by the sum of all parts of the economic loss that were 438,380 rubles. The cost of comprehensive measures to control fascioliasis was calculated with regard to the material costs, cost of labor, and the cost of arranging veterinary measures and veterinary activities management. Based on the results, the total cost of using injectable drugs in case of using Klozantin 20 % was 3,234 rubles. In case of using Alvet granules, it was the minimum cost (2,142 rubles), while in case of using Closaver, the cost of treatment was 2,783 rubles, in case of using Santomectin was 3,142 rubles, and the most expensive cost was for Albendazole as 3,680 rubles.

By the results of the animal dehelminthization, the economic loss that prevented through the treatment of affected animals was calculated as follow: 

$L_p = M_t * K * LW * P - L,$

where $M_t$ was the number of affected animals at the farm that received treatment, $K$ was the coefficient of the lethality of the animals, $LW$ was the average bodyweight for animals, kg, $P$ was the price unit of the product as rubles, and $L$ was the actual economic loss as rubles. 

$L_p = 45 * 451 * 23 - 438,380 = 466,785 - 438,380 = 28,405$ rubles. The cost as a result of dehelminthization using different drugs:

- Klozantin 20 % was 25,171 rubles, Alvet granules was 26,263 rubles, Closaver was 25,622 rubles, Santomectin was 25,263 rubles, and Albendazole was 24,725 rubles.

The economic efficacy of the veterinary measures per one ruble of the costs was determined by the following formula: 

$E_r = E_v / C_v = 25,171 / 3,234 = 8$ rubles, where $E_r$ was the economic effect, rubles, and $C_v$ was the cost of veterinary measures, rubles. As a result of dehelminthization, the economic efficacy per one ruble of the costs was eight rubles for Klozantin 20 %; 12 rubles for Alvet granules, nine rubles for Closaver; eight rubles for Santomectin was eight rubles, while the lowest economic efficacy per one ruble of the costs was seven rubles for Albendazole.

The loss from reduced milk productivity caused by gastrointestinal strongylatoses in the cattle was as follows:

$L = 45 * (13 - 9.8) * 120 * 23 = 397,440$ rubles.

Thus, the loss caused by reduced milk productivity due to strongylatoses in cattle was 8,832 rubles per cow; 397,440
rubles per 45 infected animals, which was 828 rubles less, compared to fascioliasis. The cost of comprehensive dehelminthization against gastrointestinal strongylatoses was calculated including the material costs, the labor costs, and the cost of arranging veterinary measures and veterinary activities management. Based on the results, the total cost of using injectable drugs for Klozantin 20 % was 3,234 rubles, Alben was 6,180 rubles, Ivermectin series was 2,345 rubles, Novomec was 2,670 rubles, and Albendazole was 3,680 rubles. After dehelminthization for the infected animals, the economic loss that prevented by the treatment of the cows infected with strongylatoses was calculated as follows: \( P_l = 45 \times 451 \times 23 - 397,440 = 464,715 - 397,440 = 67,275 \) rubles. The economic benefit obtained as a result of dehelminthization using different drugs with for Klozantin 20 % was 64,041 rubles, Alben was 61,095 rubles, Ivermec was 64,930 rubles, Novomec was 64,605 rubles, and Albendazole was 63,595 rubles. The calculation of the economic efficacy for the veterinary measures per one ruble of the costs showed that the economic efficacy of dehelminthization with Klozantin 20 % was 20 rubles, Alben was 10 rubles, Ivermec was 28 rubles, and Novomec was 24 rubles. The economic effect for using medium preparation of Albendazole for treatment of strongylatoses, the economic effect was 17 rubles.

The clinical state of the dehelminthized animals was observed; where no adverse effects were observed on animals during the experiments period.

Determining the economic loss from mixed invasion by fascioliasis and strongylatoses, we determined its total amount per 45 animals that was 372,600 rubles. Over the 120 days of the study, the worth of the milk not obtained from a single infected cow with the trematode–nematode invasion was 8,280 rubles; \( L = 45 \times (13 - 9) \times 120 \times 23 = 372,600 \) rubles. The cost of dehelminthization for infected cattle with mixed invasion was 3,234 rubles using Klozantin 20 %, and 3,680 rubles using Albendazole.

The economic loss prevented through the treatment of affected animals was calculated as follow: \( P_l = 45 \times 451 \times 23 - 372,600 = 460,575 - 372,600 = 87,875 \) rubles. The economic effect obtained through dehelminthization using different drugs and toxicity groups was 84,641 rubles for Klozantin 20 %, and 84,195 rubles for Albendazole.

By the results of dehelminthization, the economic efficacy per one ruble of the costs after using Klozantin 20 % was 26 rubles, and after using Albendazole was 23 rubles. Klozantin 20 % showed higher efficacy (93.3%), compared to other drugs. The milk yield increased by 32.5 %, compared to the previous year, when no dehelminthization had been made.

Our results revealed that a high invasion rate for cattle with fascioliasis was 49.22 % and for gastrointestinal strongylatoses was 59.59 % and has been noticed in various regions of the Udmurt Republic because of the optimal climatic conditions are suitable for the regular transmission of the pathogen to susceptible animals. Analyzing the therapeutic efficacy for the anthelmintic drugs, we found that the optimal drugs in terms of efficacy and cost for the treatment of fascioliasis monoinvasion (100 % EE) are Klozantin 20 %, Closaverm, and Santomectin, however compared to the Closaverm will cost two times less, and Santomectin will cost 14 rubles more. For the treatment of gastrointestinal strongylatoses, the 100 % efficiency has been shown by the Ivermectin series with the Closantel. In addition to the efficacy, the Ivermectin series are 50 % cheaper, which makes them significantly more competitive. The measures to control the parasites mixed invasions are significantly aggravated by the process. Here, none of the used drugs has shown 100 % efficiency, while in the experimental group where Klozantin 20 % has been used at the dosage of 1.25 ml per 50 kg of the bodyweight, the it has been noticed increasing the productivity of dairy cows that has been increased by 32.5 %.

The losses caused by fascioliasis include decreased milk productivity by 434,700 rubles or 9,660 rubles per animal. Additional economic losses due to disposal of the liver has amounted to 3,680 rubles. Likewise, treatment of the animals infected with fascioliasis has been 28,405 rubles. The use of Closantel has saved eight to nine rubles, while treatment with Albendazole has cost one ruble less, but has not shown 100 % efficiency in any experimental group.

The economic loss from strongylatoses due to decrease in the milk productivity was 397,440 rubles, which was 828 rubles less than the loss from infected animals with fascioliasis, while the prevented damage in this experimental group is 2.5 times higher. The economic effect per one ruble of the costs for all drugs from dehelminthization of the animals with strongylatoses has been more than 10 rubles, which has been proved by the use of the above-mentioned drugs.

To control the mixed invasions, the therapeutic efficacy of Klozantin 20 % and Albendazole has been assessed. Over the 120 days of the study, the worth of the milk not obtained from a single infected cow with the trematode–nematode invasion has been 8,280 rubles. The prevented economic damage due to the treatment of the animals infected with mixed helminths has been 3.1 times higher than that of the animals with fascioliasis, and 1.3 times higher than that infected animals with strongylatoses. After dehelminthization, the economic efficacy per one ruble of the costs after using Klozantin 20 % has been 26 rubles, and after using Albendazole was 23 rubles.
To fight fascioliasis at farms, it is sufficient to break a single link within the pathogen biological development cycle starting from the affected animal to the mollusk. Within that, it is necessary to promptly identify the affected animals and take measures to control the intermediate host. Cattle strongylatoses are geohelmintoses, which should be considered during their control. Disinvasion of pastures and walking grounds must be performed to disinfect them from nematode eggs, where larvae can develop. The veterinary measures, including anthelmintic treatments, are important for obtaining high-quality products and high monthly weight gains, and for selling products at a high price.

AUTHORS CONTRIBUTION

All authors contributed equally to the manuscript.

CONFLICT OF INTEREST

The authors have declared no conflict of interest.

REFERENCES


