



Effect of Deltamethrin (Delcide) on the Reproductive Capacity of Laboratory Mice

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Abstract

The key to successful research on laboratory animals is their quality. In the conditions of the domestic market of laboratory animals, there are a number of limiting factors, and it is practically impossible to buy animals in the necessary volume. In this regard, our preclinical center is engaged in breeding 11 types of laboratory animals. When preparing laboratory animals, we pay special attention to their health, including preventive measures including insectoacaricide treatment. This paper considers a spontaneously recorded practical case of the negative impact of deltamethrin (Delcide) on the reproductive function of outbred and BALB/c mice. Delcide was used in our test mode for insectoacaricide treatment of mice.

After the use of the drug Delcil, recorded a sharp decline in the yield of offspring. Conducting the analysis, it was found out that at the first mating of outbred mice 14 days after Delcide administration, the percentage of births of females was equal to zero. At the moment of the second mating, 40 days after Delcide use, the percentage of births did not exceed 30%, and the yield of offspring did not exceed 3.3 ± 0.49 heads, which indicates a high yawning of the uterus. The results of the third mating, which was carried out 64 days later, also proved unsatisfactory the average yield of the offspring was 5.5 ± 1.09 , and the percentage of births was 66%, while the average yield of outbred mice should be 7-8 heads. Fertility of the BALB/c line mice at all three mating sessions did not exceed 10%, which indicates high absurdity, with no tendency to recovery.

Literary review of domestic and foreign literature was made after the mice' high venomousness was established and after the treatment with Delcide. Having analyzed publications of domestic authors, it was found out that in Russia the influence of deltamethrin on the reproductive function of mice was not studied at all. Whereas, foreign colleagues were found to have a negative impact of deltamethrin on gametogenesis in mice.

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Introduction

Biomedical and behavioral experiments on animals have been conducted for several centuries [1]. Most modern knowledge of physiology and pathology is based on animal studies. Modern preclinical practice is impossible to imagine without using laboratory animals as a test system. Naturally, the health of laboratory animals is an extremely important factor in conducting research and preclinical practice in particular. The final result of the experiment depends on the quality of the test system.

According to *The American Anti-Vivisection Society*, mice are the most commonly used type of laboratory animal and are used in 93% of studies. According to the American Anti-Vivisection Society, laboratory mice are used in 72% of experiments in the UK.

Laboratory animal health is an object for careful control in all world kennels. For example, Charles River, examines their animals for viral, bacterial and other pathogenic agents. Unfortunately, only a few kennels in the Russian Federation conduct thorough monitoring of the health and welfare of laboratory animals. Cooperation with good kennels is complicated by difficulties with transportation and possible risks associated with it, as well as their cost and insufficient number of animals available. As a result, the need for laboratory mice to reproduce themselves is becoming more and more acute. Of course, only from a healthy breeding nucleus one can get healthy offspring. Following the high global requirements for the quality of laboratory animals, our organization monitors the health of laboratory animals. Monitoring of animal health in our organization is based on the ecology and epizootology of the region, the requirements of the Veterinary Department for the North-West region and FELASA recommendations [2]. However, there are a number of inhibiting factors that can lead to contamination of mouse populations with pathogenic agents. Therefore, it is important to take therapeutic and preventive measures. The selection of effective preventive measures affects the quality of life of the animals and their health, and therefore, the course of the experiment.

Materials & methods

In the course of the next monitoring of animal health in the cattery of "RMC "HOME OF PHARMACY"JSC, it was found out that mice were infected with arachnoentomoses, out of 16 obtained samples of biomaterial, in 9 were found parasitic arthropods.

Having assessed the existing risks of infestation spread, a decision was made to carry out additional treatment, prevention and sanitation measures. Due to a number of advantages, such as ease of processing, economic efficiency and experience of domestic researchers, the drug of choice was "Delcide".

Delcide is an insectoacaricide drug in the form of an emulsion concentrate for outdoor use, designed to combat ectoparasites of animals, disinfestation and decontamination of animal houses.

Delcide as an active ingredient contains synthetic pyrethroid deltamethrin- 4.0% and as auxiliary components twin-80, neonol and nephras.

Deltamethrin, which is part of the drug, belongs to the group of synthetic pyrethroids and has a pronounced insectoacaricidal intestinal and contact action. It is active against sarcoptoid, ixodic and chicken mites, bed bugs, feather bugs, lice, fleas, flies, gadflies, mosquitoes and other ectoparasites of animals.

The mechanism of action of deltamethrin is based on blocking neuromuscular transmission of nerve impulses at the ganglion level of peripheral nerves, which leads to paralysis and death of parasites.

Animals, males and females, were treated, bathing in accordance with the recommendations for use from the manufacturer. The number of animals is presented in (Table 1). The preparation was diluted in the amount of 1.25 ml per 1 liter of water. The treatment was carried out 2 times with a break of 10 days. After the whole complex of measures, a control study was carried out in an independent laboratory. On the basis of the protocol, out of 32 samples of arachnoentomoses biomaterial obtained by the laboratory were not found in any of them.

Reproductive functions of mice after treatment with Delcide

After receiving information about mouse infestation and for the entire duration of insectoacaricide treatment of mice, the reproduction of the herd was suspended. After receiving the laboratory's conclusion that there were no parasites, groups of males and females were formed for further breeding. In the course of reproduction, the effect of the drug Delcide on the reproductive function of mice was found.

Mice were paired 14, 40 and 64 days after Delcide administration. In all three mating sessions the same animals except for those who had given birth and departed. The ratio of males to females, when forming groups for mating outbred mice was 1:5 and mice of BALB/c 1:4 line. The design of reproduction and its efficiency are presented in (Table 1).

Table 1: Reproduction design and its effectiveness in outbred mice and mice of the BALB/c line after application of Delcide.

Animal line and mating order	The total number of females, goal	The total number of males, goal	Number of females who gave birth, goal	% of females who gave birth	Number of births of puppies	The average number of heads in a litter, M ± SD (n)	
Outbred	1 pairing	30	6	0	0	0	
	2 mating	28	5	7	25	23	3,3 ± 0,49
	3 mating	21	4	14	66	77	5,5 ± 1,09
BALB/c	1 pairing	200	50	8	4	15	1,9 ± 0,83
	2 mating	190	47	9	4,7	24	2,7 ± 0,87
	3 mating	178	44	11	6,1	39	3,5 ± 0,82

The mating outbred mouse population was selected from our kennel based on physiological parameters suitable for reproduction of these animals. BALB/c mice were brought as breeding nucleus from a third-party cattery, their physiological parameters were evaluated during the selection and formation of mating groups.

Results & discussion

In assessing fertility, we took into account the percentage of births shown in (Figure 1). It was found out that at the first mating of outbred mice 14 days after Delcide administration, the percentage of giving birth to females was equal to 0, and at the third mating, which was carried out 64 days after Delcide administration, the fertility of outbred mice increased to 66%, i.e. in dynamics the fertility of outbred mice was restored. Fertility of the BALB/c line mice at all three mating sessions did not exceed 10%, which indicates high absurdity, with no tendency to recovery.

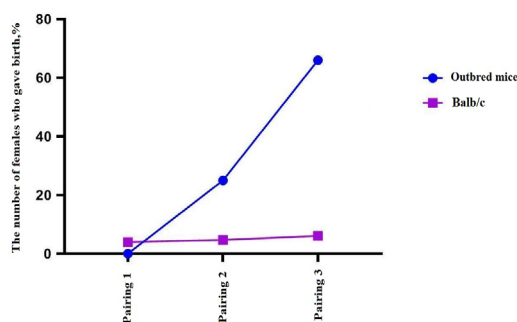


Figure 1: Fertility dynamics of outbred mice and mice of the BALB/s lineage against the background of Delcide application.

It is interesting that before Delcide administration in January and February 2020 the average yield per female of outbred mice was from 7 to 8 heads, which corresponds to the standards of outbred mice [8-10]. In the March, there was an interruption in the production of offspring after the application of Dolcide at the end of February 2020. And in April and May there was an obviously progressive tendency of average number of offspring per female, which indicates the restoration of reproductive potential of outbred mice (Figure 2).

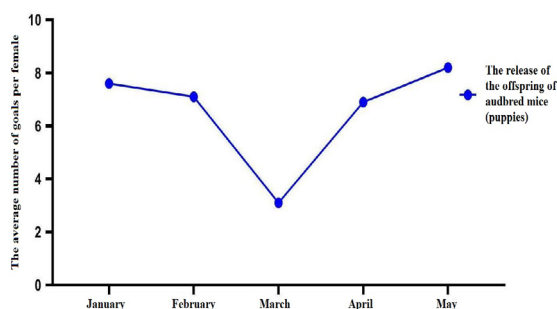


Figure 2: Average yield of offspring on 1 female from January to May 2020.

Based on the results of the revealed changes, a review of the literature on the use of deltamethrin and its influence on reproductive functions of mice was conducted.

The influence of deltamethrin on mice has not been studied in the domestic literature, in the work of Tokarev A.N. and Yengashev S.V. (2011), the effect of the preparation of deltamethrin was studied on three generations of outbred rats, which were fed 0.15; 1 and 3.75 mg/kg of the active substance. According to the results of the study the difference between experimental and control animals in fecundity, duration of pregnancy period and safety of the obtained offspring was not determined [3].

We also studied the literature of foreign authors on the influence of deltamethrin on reproductive functions of mice.

In 2015 R. Ketaki, N. Moid and co-authors, evaluated the impact of deltamethrin on reproductive performance of male outbred mice. The drug was administered in different doses intragastrically within 45 days. The results obtained showed that the use of deltamethrin resulted in a significant decrease in the body weight of laboratory mice, and a decrease in the number of spermatozoa of their viability and mobility was also observed [4].

Jia Z. Z., Zhang J. W. and co-authors [5] conducted a study in 2019 to evaluate the oxidative stress caused by deltamethrin and its effects on meiosis, apoptosis and autophagy of mouse oocytes. The results showed that the rate of oocyte maturation decreased significantly, as well as the quality of oocytes decreased, causing abnormal distribution of mitochondria in them.

Thus, these results showed that deltamethrin can inhibit oocyte maturation in mice and have a negative impact on oocyte survival.

Slima A. B., Abdallah F. L., Keskes-Ammar L. and co-authors [6] in 2011 studied the effect of dimethoate and deltamethrin in different doses and their mixtures on the reproductive qualities of male mice. The medications were administered orally for 21 days. At the end of the experiment, the weight of testicles and semen parameters were determined. The obtained data showed that the number of sperm cells was significantly reduced in all experimental groups, and the percentage of morphologically abnormal sperm cells was significantly increased in comparison with the control group.

In 2017, VIMA A. B., Chtourou Y. and Barkallah M. [7] studied the effect of deltamethrin on male mice and their offspring. The males received intragastric deltamethrin in a dose of 5 mg/kg daily for 35 days. Then males were mated with females who did not receive the drug in order to obtain offspring.

The study showed that the impact of deltamethrin significantly affected the reproductive functions of males, namely:

- Variation of seed tubules
- Germ cell detachment
- Sperm Cell Destruction
- Reduced total sperm density
- Reduced sperm motility

Conclusion

Thus, our data on the negative impact of delcide on reproductive function in mice are fully consistent with the literature.

The use of this insectoacaricide drug for mice planned for reproduction is highly undesirable.

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