

THE USE OF HORMONE CONTAINING CONTRACEPTIVE DRUGS AND THEIR EFFECTS ON THE REPRODUCTIVE SYSTEM OF DOGS AND CATS

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Summary. The article presents the research results as to the negative impact of the usage of progestin hormonal contraceptive drugs on the reproductive system in clinically healthy cats and dogs and in the emergence of this pathology at different methods of application.

During the research 243 cats and 134 dogs were examined, four research groups of healthy cats and dogs aged from 1.5 to 5 years were selected and formed for studies. All groups of animals were prescribed oral hormone containing contraceptive drugs with active ingredient megestrol acetate. Groups were formed according to the common animal owners asked oral hormonal contraceptive for the suppression of sexual function in cats and dogs. Medicaments were prescribed to the experimental animals within 2 years.

It was proved that the best way to use progestogenic drugs for cats and dogs is a period of about 7–15 days before the estrus. The changes that have occurred are reversible in the reproductive system.

In the appointment of contraceptives at the time of proestrus increases the probability of disease of the reproductive system in cats and dogs.

When using the direct drugs for interrupting the heat in cats and dogs, especially in a dose at 2–6 times exceeded, it could lead to irreversible damage of the reproductive system in most animals.

Keywords: cat, dog, birth control pills, megestrol acetate, uterine hyperplasia, pyometra, polycystic ovaries, estrus, reproductive system

Introduction. Demand for hormonal treatments in pets is resulted in active development and using of different hormonal contraceptives for pets. The use of contraceptive drugs often provides quick suppression of unwanted female's behavior during estrus and creates an alternative to surgical intervention for animals that are at risk during the operation (Cathey and Memon, 2010; Kutzler and Wood, 2006; Romatowski, 1989).

The main group of contraceptive drugs for pets that are used in Ukraine are hormonal contraceptives. These drugs are divided into two groups: monohormonal (one hormone is used) and bihormonal (two hormones in a fixed combination are used). Contraceptive drugs distributed in our country are sold in such dosage forms: tablets, drops for oral using, injection, sugar cubes. They are used for regulation and suppression of sexual function in females as well as males. Depending on the type and physiological characteristics of the animals, the drugs were given *per os* and subcutaneously to ensure a long-term effect. The most famous active substances and hormones on their basis is megestrol acetate ('Kontrik' pill 'Nonoestron' pill 'Pilkan-5', 'Pilkan-20' sugar cubes 'EKS-5', 'EKS-7,5' drops and pills, 'Stop-intim' pills, drops, 'Sexsinon' pills, drops, 'Sexsanet' drops), medroxyprogesterone acetate ('Medropet' pill 'Proveravet' pill 'Depogeston' injection) proligestone ('Kovinan' injection), the combination of megestrol acetate and ethinylestradiol ('Sex

Barrier', tablets and drops) (Horzheiev, Kotsiumbas and Kosenko, 2013).

However, doctors of veterinary medicine refer to this group of drugs cautiously. Based on our research there is a tendency that 9 out of every 10 veterinary clinics in Kharkiv, do not prescribe and do not use any form of hormonal contraceptive drugs. On their opinion the reason for failure are the side effects, often in the form of pyometra, polycystic ovarian and mammary tumors that in result lead to a negative reputation of clinics and doctors who have prescribed and sold 'drugs with the side effects'.

In scientific publications and some instructions from the manufacturers to the hormonal contraceptive drugs are described such side effects of the prolonged usage in animals as endometriosis, pyometra, fibrinous-cystic hyperplasia of the endometrium, mammary cancer, ovarian cysts, diabetes, liver disease, pancreas, adrenal pathology (Chatdarong et al., 2005; Romagnoli and Concannon, 2003; ACC&D, 2009; Simpson, England and Harvey, 1998; Torrance and Mooney, 1998).

Materials and methods. We have carried out research on the usage of hormonal contraceptive drugs for pets in the Kharkiv City and the Kharkiv Region, during the past three years. Most of these drugs have been used for female cats and dogs for sexual function inhibition. Data on the number of animals (cats, dogs), which obtained hormones in in the Kharkiv City and the Kharkiv Region over a period of 2014–2016, present in Table 1.

Table 1 – Using of hormonal contraceptives in cats and dogs (2014–2016)

Name of the drug	2014		2015		2016	
	Cats, n	Dogs, n	Cats, n	Dogs, n	Cats, n	Dogs, n
Depo-promone, injection	100	100	60	60	100	100
Depogeston, injection	0	0	60	60	4	4
EKS-5, drops	404	232	352	200	280	160
Kovinan, injection	80	32	160	64	320	128
Kontr Sex, pills	0	0	674	337	548	274
Kontr Sex, drops	0	0	64	64	64	64
Kontrik, pills	857	428	920	460	1960	980
Nonoestron, pills	788	491	2190	1368	582	364
Pilkan-20, bricks	5	0	5	0	0	0
Sex-barrier, pills	1920	960	2840	1420	932	467
Sex-barrier, drops	536	0	768	0	205	0
Sexanet, drops	0	0	0	0	2048	366
Stop-intim, drops	0	0	588	0	372	0
Stop-intim, pills	257	0	257	0	249	0
Total	4947	2243	8938	4033	7664	2907

The object of the study was thoroughbred and underbred cats and dogs which were treated in Kharkiv clinics with the purpose of suppression of sexual function in animals by pharmacological, hormone containing contraceptive drugs on the basis of megestrol acetate.

During the study, we have tested 243 cats and 134 dogs. From this number of animals were selected for studies healthy cats and dogs aged 1.5 to 5 years.

The total number of experimental cats and dogs of various breeds and ages were divided into four groups according to days the sexual cycle when the animals were given contraceptive drugs.

All groups of animals were prescribed oral hormonal contraceptive drugs with active ingredient megestrol acetate. Groups were formed by highest frequency of giving oral hormonal contraceptive by owners to inhibit sexual function in cats and dogs. Preparations were given to the experimental animals within 2 years. Each group of animals got the drug on the following system: the first group — about 7–15 days before the expected estrus; the second group — for 1–2 days proestrus; the third group — for 5–6 day from the beginning of estrus; the fourth group — on 1–7 day cycle (proestrus, estrus). All animals were treated medicament according to instructions for use.

Results. As a result of the clinical examination in the first and the second year it was found that after

hormonal contraceptives treatment we often disclosed such pathology of the reproductive system of cats and dogs as endometrial hyperplasia, endometritis, metritis, pyometra, hydrometra, polycystic ovaries, and observed mixed pathology (polycystic ovaries and pyometra). The results are given in Table 2.

After using hormonal contraceptive preparations based on megestrol acetate the cats most often experienced pyometra and endometrial hyperplasia (Table 2). The most frequently cases of endometrial hyperplasia and pyometra were encountered in dogs.

In the first group of cats we observed two cases of uterine pathology, hyperplasia of the uterus endometrium was revealed in two animals. In the first group of dogs there were two cases of endometrial hyperplasia and one case of endometritis. Two pathologies in the genital organs (endometrial hyperplasia) were found during the first year in the cats of the second group, over the period of the second year examinations two cases of reproductive system pathology (endometrial hyperplasia and pyometra) were revealed. Surgery was conducted in the case of pyometra. In the first year of study two pathologies of the reproductive system (endometrium and endometrial hyperplasia) were found in the second group of dogs. Over the second year five pathologies of the uterus (endometrial hyperplasia, pyometra, and hydrometra) were found in this group.

In the third group of cats over the period of the first year, the examination found three clinical cases of the pathology of reproductive system, and over the second year in five of eight animals we diagnosed such disorders as pyometra, endometrial hyperplasia, polycystic ovaries, endometritis and mixed disease (polycystic ovaries and pyometra). In dogs of the third group over the first year we diagnosed pathologies such as endometrial hyperplasia, polycystic ovarian and metritis in three of eight animals. In the second year, the examination in dogs of the third group identified six abnormalities of reproductive system

(pyometra, endometrial hyperplasia, polycystic ovarian and metritis). In the fourth group of cats over the first year of our examinations we found out six animals with disorders of the reproductive system, and two of them had endometrial hyperplasia and pyometra hydrometera. In the fourth group of dogs over the first year we have found five ill animals, over the second year the endometrial hyperplasia evolved to pyometra.

The data on all examined cats and dogs of various breeds and ages, which were divided into four groups according to the sexual cycle and to contraceptive application system, are shown in Table 3.

Table 2 – The emergence of the pathology of reproductive system of cats and dogs after the use of hormonal contraceptive preparations based on megestrol acetate

Day sexual cycle	Cats			Dogs		
	No.	1 season	2 season	No.	1 season	2 season
7-15 days before estrus	1	normal	normal	1	normal	endometrium hyperplasia
	2	normal	normal	2	normal	normal
	3	normal	normal	3	normal	normal
	4	normal	normal	4	normal	polycystic ovaries
	5	normal	endometrium hyperplasia	5	normal	normal
	6	normal	normal	6	normal	normal
	7	normal	normal	7	normal	endometrium hyperplasia
	8	normal	endometrium hyperplasia	8	normal	normal
1-2 day proestrus	1	endometrium hyperplasia	pyometra	1	normal	pyometra
	2	normal	normal	2	normal	normal
	3	normal	normal	3	endometrium hyperplasia	endometrium hyperplasia
	4	endometrium hyperplasia	pyometra	4	normal	normal
	5	normal	normal	5	normal	endometrium hyperplasia
	6	normal	normal	6	normal	hydrometra
	7	normal	endometrium hyperplasia	7	normal	normal
	8	normal	normal	8	endometritis	polycystic ovaries

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5-6 day at the beginning estrus	1	normal	endometrium hyperplasia	1	endometrium hyperplasia	pyometra
	2	normal	polycystic ovaries	2	normal	endometrium hyperplasia
	3	normal	normal	3	polycystic ovaries	polycystic ovaries
	4	polycystic ovaries	polycystic ovaries, pyometra	4	metritis	pyometra
	5	normal	normal	5	normal	endometrium hyperplasia
	6	endometrium hyperplasia	pyometra	6	normal	normal
	7	endometritis	endometritis	7	normal	metritis
	8	normal	normal	8	normal	normal
1-7 day of cycle (proestrus, estrus)	1	endometrium hyperplasia	pyometra	1	endometritis	pyometra
	2	endometrium hyperplasia	hydrometra	2	normal	normal
	3	endometritis	pyometra	3	metritis	endometritis
	4	normal	endometrium hyperplasia	4	normal	endometrium hyperplasia
	5	endometrium hyperplasia	pyometra	5	endometritis	pyometra
	6	metritis	metritis	6	normal	normal
	7	endometritis	metritis	7	endometrium hyperplasia	metritis
	8	normal	normal	8	polycystic ovaries	polycystic ovaries, pyometra

Table 3 – Pathology of the reproductive system of animals using drugs based on megestrol acetate in different periods of sexual cycle

Day of sexual cycle	Cats			Dogs		
	Total	Diseased	%	Total	Diseased	%
7-15 days before estrus	58	5	8.6	32	3	9.37
1-2 day proestrus	47	12	25.5*	25	8	32
5-6 day at the beginning estrus	63	42	66.6**	31	26	83.8^
1-7 day of cycle (proestrus, estrus)	75	71	94.6***	46	40	89.6^^

Note: * — $p \leq 0.05$; ** — $p \leq 0.05$; *** — $p \leq 0.05$; ^ — $p \leq 0.05$; ^^ — $p \leq 0.05$ according to 1st group of animals.

According to Table 3 contraceptives-based treatment for 7–15 days before estrus disorders of the reproductive system were accounted for 8.6% in cats and 9.37% — in dogs. When hormone containing contraceptive drugs were used at 1–2 days of proestrus, changes in the reproductive system (endometrial hyperplasia, polycystic ovarian, pyometra and metritis) were observed in 25.5% ($p \leq 0.05$) of cats and 32% dogs. When progestogen medicament was given to the animals at 5–6 day from the beginning of estrus, the pathology in the reproductive system in cats accounted in 66.6% ($p \leq 0.05$) of cases and in dogs in 83.8% accordingly. Many animals got hormone drugs for 1–7 day of the cycle (estrus, proestrus) cats with disorders of the reproductive system were recorded in 94.6% ($p \leq 0.05$) and in dogs in 89.6% ($p \leq 0.05$).

The collected data demonstrates that the use of progestogen contraceptive hormones to suppress estrus for 7–15 days before the estrus does not cause

irreversible changes in the reproductive system of dogs and cats and may be conservatively treated. At the same time, interruption of estrus and continuous use in violation of instructions leads to irreversible changes in the reproductive system of animals and can lead to surgery.

Conclusions. 1. The best period to use progestogen drugs for cats and dogs is about 7–15 days to estrus, and the changes that can occur in the reproductive system of animals are reversible.

2. Prescribing contraceptives during the estrus is increasing the likelihood of pathology of the reproductive system such as endometrium and endometrial hyperplasia, polycystic ovaries, metritis, pyometra and mixed disease (polycystic ovaries and pyometra) in cats and dogs.

3. Using of the drugs for immediate interruption of estrus in cats and dogs leads to irreversible disorders of the reproductive system of most animals.

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