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Follow-up examinations after medical treatment of pyometra in cats with the progesterone-antagonist aglepristone

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The aim of this study was to determine the therapeutic success of the medical treatment of pyometra with the antigestagen aglepristone and to document the recurrence rate in relation to the time interval after treatment with antigestagens in cats. Ten cats, 2–13 years of age and nulliparous were used in the study. The cats were treated with aglepristone at a dose of 10 mg/kg body weight subcutaneously on days 1, 2, 7 and 14 (if not cured). In addition, trimethoprim/sulphadoxine was also administered at a dose of 15 mg/kg body weight subcutaneously once a day for 7 days. Nine out of the 10 cats responded well to treatment. No recurrence was observed in a follow-up period of 2 years. No side effects were observed. The data suggest that aglepristone treatment is a promising approach for the medical treatment of pyometra in cats.

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Pyometra is a uterine inflammatory disorder characterised by cystic endometrial hyperplasia (CEH), a sequel to progesterone stimulation of the endometrium, and by ascending uterine infection with vaginal bacteria. It may involve diffuse or segmental enlargement of the uterus. Hystological lesions range from simple CEH to endometrial atrophy.[1]

Prostaglandin $F_2\alpha$ ($PGF_2\alpha$) had one major effect on the reproductive tract: contraction of the myometrium resulting in progressive expulsion of the uterine contents over a period of days. But, the ability of $PGF_2\alpha$ to dilate the cervix could not be assessed. Therefore, uterine evacuation with $PGF_2\alpha$ may be used only in open cervix pyometra. Treated cats should be hospitalised during the day for observation following prostaglandin administration. Systemic infection and peritonitis can develop. Hence, ovariohysterectomy can be needed. In addition, many side effects are usually observed after the injection of $PGF_2\alpha$.[1,2]

Antiprogestins are synthetic steroids which bind with great affinity to progesterone receptors without any of the effects of progesterone. In dogs and cats, two antiprogestins have been studied: mifepristone (RU38486) and aglepristone (RU46534). Aglepristone is the first antiprogestin registered for veterinary use with the indication 'interruption or prevention of pregnancy'; similarly, these types of compounds were successfully used for induction of parturition in the dog and cat and for medical treatment of open and closed cervix pyometra in the dog. Recently, a combination of aglepristone and prostaglandins has been used for the medical treatment of pyometra in dogs. Moreover application of antiprogestins has clearly demonstrated the role of progesterone as a major factor controlling overt pseudopregnancy in dogs. In additional, it may be used for the reduction of mammary gland hyperplasia in fibroadenomatosis of cats.[3–6] No side effects were observed in cats.[7]

In order to assess the use of antigestagens in the treatment of pyometra compared with other therapeutics procedures, it is necessary to know the healing and recurrence rate after the use of antigestagens. So far, the only information available is based only on a few cats[7] and does not allow a differentiated examination of the recurrence rate following successful treatment for up to 2 years. Therefore, the purpose of this study was to document the success of the treatment of pyometra with antigestagens in the cats as well as the recurrence rate in relation to the time interval after treatment.

Materials and methods

In this study, 10 nulliparous cats with pyometra were used. Nine of these were cross-breed cats and one was Persian.

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Firstly, anamnesis was taken and clinical examinations were performed. White blood cell counts (WBC) were determined by using an Abbott Cell-Dyn 3500 haematological analyser (Gml, Ramsey, Minnesota, USA) at first examinations and 2 weeks after the completion of treatment. Transabdominal ultrasonography was performed using a B-mode real-time ultrasound scanner 7.5 MHz linear array transducer (Dynamic Imaging Ultrasound Systems, Livingston, Scotland, UK) to confirm diagnosis, to monitor healing until 2 weeks after the completion of treatment and to determine recurrency in the first and second years. Anamnesis, clinical examination, ultrasonography and laboratory findings at first examination are shown in Table 1.

The diagnosis of pyometra was confirmed based on the presence of specific clinical (anorexia, lethargy, vomiting, abdominal distention and vulvar discharge), laboratory and ultrasonographical findings.

Cats were treated with subcutaneous injections of 10 mg/kg body weight aglepristone (Alizine, Virbac, Carros, France) on days 1, 2, 7 and 14 (if not cured) after first clinical examination. In addition, trimethoprim/sulphadoxine was administered at a dose of 15 mg/kg body weight subcutaneously once a day for 7 days. The examination plan was furthermore applied on day 2 and 7 following the first presentation. Another consultation took place on days 14 and 21 after the first treatment. The short-term success of the treatment was defined up to day 21 after the start of the treatment, the medium-term success up to 1 year and long-term success up to 2 years after the first application. Animals were observed for possible side effects during the treatments. The response to treatment was monitored by clinical signs, laboratory and ultrasonographic findings 2 weeks after completed treatment. Pyometra was still present in one cat and ovariohysterectomy was performed.

Results

The mean (± SEM) age of the cats was 8.20 ± 1.06 years (range 2−13 years). During clinical examinations of cats with pyometra, clinical signs including the presence of anorexia, lethargy, vomiting, abdominal distention and vulvar discharge were recorded. The duration of the signs was between 4 days and 3 weeks. In two cats the heat was regularly suppressed by progestins.

Clinically, a distinctive increase of vulvar discharge could be detected in all cats within the first 24 h after application of aglepristone. Except for one cat, all were diagnosed as completely recovered according to clinic and ultrasonographic findings at 14 days. In all cases, general condition and feed consumption improved rapidly and were normal within 7 days. Vulvar discharge totally ceased, except in cat 4, on day 14.

During the first ultrasonographic examination of the cats with pyometra, distended and fluid-filled uteri were identified cranial and dorsal to the bladder. Uteri with pyometra appeared as enlarged with convoluted, tubular horns filled with anechoic to hypoechoic fluid. The maximum lumens diameter of the filled uterine horns were between 0.7 and 5.7 cm at first examination. Then, they gradually decreased after first aglepristone administration. Uteri could not be imaged on 14−21 days in all cats, except cat 4.

At first examination, the WBC count of six cats (cats 1, 4, 5, 6, 8, 10) showed leukocytosis (leukocytes $\geq$19.500/mm^3) while four animals (cats 2, 3, 7, 9) had a normal leukocyte count (between 5500 and 19.5000/mm^3) (Table 1). The number of blood leukocytes was within the normal range on day 21 in all cats, except cat 4 (24,000/mm^3).

Nine cats completely recovered according to clinic, laboratory and ultrasonography results on day 21. This corresponds to a short-term success rate of 90%. The general and reproduction health of nine cats could be followed for 2 years. No recurrences were observed. No side effects were observed related to treatment.

Pyometra was still present on day 21 after the first treatment in cat 4. This cat underwent ovariohysterectomy and had an uneventful recovery.

Discussion

The CEH/pyometra complex can be diagnosed at any age. The disorder has been described as being prevalent in cats over 5 years of age that have never had kittens, as well as being most common in cats that have had one or more litters.[1,2] In our study, the average age was 8.42 years. Typical clinical signs are depression, dehydration, lethargy, pyrexia, anorexia or inappetence, vomiting, diarrhoea, listlessness, abdominal distention, polyuria and polidipsia and weight loss. Only the cats with open cervix pyometra have an obvious watery or thick and viscous vulvar discharge. The discharge is often creamy and light tan-pink to dark brown in colour.[1,2,8] The same results were obtained in this series of cats. Increased total WBC are identified in cats with pyometra, even if normal or decreased WBC may be detected.[2,9] In this study increased WBC and normal WBC were recorded.

Surgical treatment for CEH/pyometra in the cat is ovariohysterectomy, fluid and antibiotic therapy. Surgery permanently eliminates the site of infection.[1,2] If the cat is young and the owners are keen to breed from her, or if she is old and a poor surgical risk, medical treatment may be attempted. $PGF_2\alpha$, a smooth muscle contracting drug should be restricted to cases of open cervix pyometra and used in conjuction with antibiotic therapy.[1,2,10] Either trimethoprim/sulphadiazine or amoxycillin trihydrate/clavulanate potassium is the initial antibiotic of choice.[2,11] Many side effects have been observed after injection of $PGF_2\alpha$. Within 30−120 s, the cat may begin vocalising and

Table 1. Anamnesis, clinical examination, ultrasonography and laboratory findings at first examination

	Cat 1	Cat 2	Cat 3	Cat 4	Cat 5	Cat 6	Cat 7	Cat 8	Cat 9	Cat 10
Age at the onset of treatment (years)	10	13	12	2	8	10	8	4	7	8
Duration of clinical signs	3 weeks	1 week	4 days	1 week	2 days	2 weeks	1 week	3 days	4 days	1 week
Clinical sign/s	Anorexia Vomiting Abdominal distention Vulvar discharge	Anorexia Lethargy Abdominal distention Vulvar discharge	Lethargy Vulvar discharge	Anorexia Lethargy Abdominal distention Vulvar discharge	Anorexia Lethargy Vulvar discharge	Anorexia Vomiting Vulvar discharge	Lethargy Abdominal distention Vulvar discharge	Anorexia Lethargy Vulvar discharge	Lethargy Vulvar discharge	Anorexia Vulvar discharge
Presence of vulvar discharge	Open cervix	Open cervix	Open cervix	Open cervix	Open cervix	Open cervix	Open cervix	Open cervix	Open cervix	Open cervix
Ultrasonographic findings	An enlarged uterus with convoluted, tubular horns filled with anechoic to hypoechoic fluid	An enlarged uterus with convoluted, tubular horns filled with anechoic to hypoechoic fluid	An enlarged uterus with convoluted, tubular horns filled with anechoic to hypoechoic fluid	An enlarged uterus with convoluted, tubular horns filled with anechoic to hypoechoic fluid	An enlarged uterus with convoluted, tubular horns filled with anechoic to hypoechoic fluid	An enlarged uterus with convoluted, tubular horns filled with anechoic to hypoechoic fluid	An enlarged uterus with convoluted, tubular horns filled with anechoic to hypoechoic fluid	An enlarged uterus with convoluted, tubular horns filled with anechoic to hypoechoic fluid	An enlarged uterus with convoluted, tubular horns filled with anechoic to hypoechoic fluid	An enlarged uterus with convoluted, tubular horns filled with anechoic to hypoechoic fluid
Laboratory findings (WBC/mm^3)	24,900	16,800	15,800	36,700	23,200	46,000	12,200	47,800	15,800	26,800

panting; become restless; knead; exhibit intense grooming behaviour; have tenesmus, salivation, diarrhoea and mydriasis; and vomit, urinate, defecate, and exhibit a lordosis posture. The grooming is directed at the flanks and vulva. Additional side effects have included tail flagging and tearing at newspapers in the cage.[1,2,12,13]

Antiprogestins are synthetic steroids that bind with great affinity to progesterone (P_4) receptors, preventing P_4 from exerting its biological effects. The antiprogestin aglepristone acts as a true P_4 antagonist at the uterine level, without initially decreasing serum P_4 concentrations.[5] Aglepristone competitively bind progesterone receptors and decrease intrauterine progesterone concentrations potentially allowing increased myometrial contractility and cervical relaxation.[14] Hecker et al[7] described the possibility of aglepristone therapy in four cats with pyometra. The cats were treated twice with subcutaneous injections of 10 mg/kg body weight aglepristone with an interval of 24 h and on the seventh day after first clinical examination. Two months after the end of treatment the cats were controlled again. No clinical signs were observed. No side effects were observed. In our study, 9/10 cats completely recovered by day 21 after the start of the treatment (healing rate of 90%). No recurrence was observed in a follow-up period of 2 years (recurrence rate of 0.0%). Two of the cats (cats 8 and 9) have been bred following aglepristone theraphy for pyometra and delivered live kittens. Unhealed cat 4 underwent ovariohysterectomy. The other cats owners did not want to mate their cats because of the advanced age. No side effects were observed during treatment.

The results of our study indicate that the progesterone receptor blocker aglepristone is an efficient and safe option for medical treatment of cats with pyometra in the short and long term. Whether aglepristone used for the treatment of pyometra has a role on the reproductive capacity of the animal needs to be further investigated.

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