



Cloprostenol treatment of feline open-cervix pyometra

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Abstract

Treatment with cloprostenol, a prostaglandin synthetic analogue, was evaluated in five queens with open-cervix pyometra. Cloprostenol was administered (5 µg/kg body weight SC) on 3 consecutive days and amoxicillin (20 mg/kg body weight IM) on 7 consecutive days. Transient post-injection reactions caused by cloprostenol administration included diarrhea, vomiting and vocalizations. Reactions began as quickly as 10 mins after cloprostenol administration and lasted as long as 30 mins. All queens improved clinically after cloprostenol treatment and remained healthy until the end of the study, 1 year after treatment. All queens resumed normal estrous cycles without further treatment and two (40%) delivered a normal litter. In conclusion, use of cloprostenol is an acceptable treatment for open-cervix pyometra in queens.

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Pyometra is a uterine disorder characterized by cystic endometrial hyperplasia (CEH) caused by the action of progesterone on the endometrium. The cystic endometrial hyperplasia–pyometra complex occurs with more frequency in bitches than in queens, probably because in the cat ovulation is induced by coitus.¹ Corpora lutea and elevated serum progesterone concentrations occur only after coitus. However, ovulation induced by non-copulatory stimulation can also occur and is known as spontaneous ovulation.²

Spontaneous ovulation results in progesterone secretion by the corpora lutea, and hormonal stimulation of the endometrium could produce CEH. Consequently, CEH has also been observed in queens treated with progestins.^{3,4} Bacterial infection with opportunistic organisms from the vagina occurs secondary to CEH.¹ *Escherichia coli* is the bacterium most often isolated from fluid from the uterus of cats with pyometra.^{5,6} *Streptococcus* species, *Staphylococcus* species, *Pasteurella* species, *Klebsiella* species, *Moraxella* species and *Pseudomonas* species have also been isolated from the uteri of cats with pyometra.¹ Clinical signs include inappetence and polydipsia/polyuria, as well as vaginal discharge in cases of open-cervix pyometra.^{1,7} Recommended treatment for CEH pyometra in queens is ovariohysterectomy with antibiotic therapy and fluid replacement. However, in valuable breeding animals with open-cervix pyometra medical treatment is desirable. In

bitches, it has been reported that natural prostaglandin $F_{2\alpha}$ and cloprostenol, a prostaglandin analogue, are effective medical treatments of CEH pyometra.^{8–10} Prostaglandins increase myometrial contractility and facilitate uterine evacuation. Prostaglandins also induce luteolysis, decreasing the concentration of plasma progesterone.¹ Prostaglandin $F_{2\alpha}$ has been reported to be successful in resolving CEH pyometra in queens.^{11,12} However, there are no studies on the clinical and reproductive efficacy of cloprostenol in queens for treatment of open-cervix pyometra.

Prostaglandin is not desirable for closed-cervix pyometra. Recently, the use of progesterone-receptor antagonists have been proposed for medical treatment, but they are not available in all countries. Furthermore, the lowest effective dose of cloprostenol has not been established for treatment of open-cervix pyometra in the queen. Therefore, the aim of this study was to assess the

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clinical and reproductive efficacy of cloprostenol as medical treatment for feline open-cervix pyometra. The hypothesis was that cloprostenol could be effectively used for treatment of open-cervix pyometra in queens.

Five domestic shorthair queens, aged between 2 and 6 years, and weighing between 2 and 4 kg were referred to the Animal Reproduction Service of the Veterinary Teaching Hospital, La Plata, Buenos Aires, Argentina, with a diagnosis of pyometra. All queens showed clinical signs of open-cervix pyometra with purulent vaginal discharge, inappetence, depression, polydipsia/polyuria and vomiting. Diagnosis of pyometra was based on a complete physical examination, and ultrasonographic, hematological, biochemical and vaginal cytology studies. After a complete physical examination, samples for a vaginal cytology study were obtained. Swabs were moistened with sterile saline, introduced approximately 1.5 cm into the vagina, and quickly and gently rotated against the floor and lateral walls of the vagina. Samples were stained with Diff Quik, Biopur Diagnostics and examined at 100× and 400× magnification to evaluate vaginal cytology.¹³ Vaginal cytology samples showed between 80% and 90% intermediate cells, 10–20% superficial cells and bacteria, and between 20 and 30 degenerative neutrophils per field at 400× magnification. Subsequently, transabdominal ultrasonographic examination using an ultrasound scanner equipped with a 5–7.5–10 MHz linear transducer (Mindray; DP-600 Vet) was performed. Ultrasonographic studies of queens with pyometra may reveal a moderate-to-significant uterine enlargement with anechoic or hypoechoic fluid, and a thickened endometrium with hypoechoic areas of varying size. Lastly, samples for routine hematological and biochemical analyses were taken. The samples for hematology were analyzed with a semi-automated hematology analyzer (Sysmex F-820; Sysmex America), and a complete blood cell count was performed. The samples for biochemistry were analyzed with an auto-analyzer (Aeroset; Abbott Laboratories) utilizing a chemistry kit (Alcyon; Abbott Laboratories), and a biochemistry profile was performed. Hematological studies showed leukocytosis and neutrophilia with left shift in all queens. Two females had normocytic, normochromic anemia. Biochemical parameters showed hyperglobulinemia in three animals, and azotemia was recorded in one cat.

Queens received 5 µg/kg cloprostenol subcutaneously (Ciclar PA; Zoovet) on three consecutive days and 20 mg/kg long-action amoxicillin intramuscularly (Clamoxil LA; Pfizer) on seven consecutive days. The therapy ended when queens were clinically healthy, the ultrasonography examination showed the uterine lumen as a bright echogenic central area, and hematological and biochemical parameters were normal. During treatment a physical examination was performed every day and females were monitored by ultrasonography every other day. When the treatment was

completed, vaginal cytology samples were obtained every third day until the onset of estrus. All queens were mated in the second estrous after treatment. Although it is advisable to breed queens on the first estrus after treatment, in this case the owners chose the second estrus after treatment.

Between 10 and 15 mins after cloprostenol administration, diarrhea, vomiting and vocalizations were observed in treated queens, and these moderate side effects did not last more than 30 mins post-treatment in any of the cats.

After treatment with cloprostenol the amount of vaginal discharge increased during the following 2 days, the uterus diameter decreased and queens started to eat. Fifteen days after treatment ended, no vaginal discharge was seen, and the uterus was of a normal size based on abdominal palpation in all queens. At this time, vaginal cytology reflected normal interestrus (50–60% intermediate cells and 40–50% of superficial cells).¹³ Hematological and biochemical parameters were within normal ranges at the end of treatment.^{14,15} Animals had no clinical signs of illness, and ultrasonography showed a normal uterus, without intraluminal fluid. Likewise, food and water intake were normal. All queens came into estrus between 15 and 20 days after treatment ended. All queens were mated at the second estrus after treatment. Two queens became pregnant after mating, and had a normal gestation and parturition. One queen delivered three and the other five kittens. All females remained healthy until the end of the study, 1 year after treatment.

Although CEH pyometra is less common in queens than in bitches, it is one of the most common illnesses observed in feline reproductive practice.^{1,16} Although surgery, antibiotic treatment and fluid therapy are the recommended treatment for open-cervix pyometra in queens, medical treatment of breeding animals is desirable for economic reasons. In the present study, cloprostenol was an alternative to surgical treatment in queens with CEH pyometra. After treatment all queens were clinically and ultrasonographically normal. Likewise, females remained healthy for at least 1 year after the end of the study. This study showed the efficacy of cloprostenol to evacuate the uterus and to allow recovery in queens with open-cervix pyometra. Natural and synthetic prostaglandins are used to induce luteolysis in several species in which the unique source of progesterone is the corpus luteum. In fact, while synthetic prostaglandins are administered at lower doses than natural prostaglandins, they have more side effects because they are more potent. Prostaglandins are uterotonics, and uterine contractions caused by prostaglandin administration allow expulsion of uterine fluid in queens with pyometra. However, the use of prostaglandin in cases of closed-cervix pyometra could be

associated with substantial risk of uterine rupture. While aglepristone is a good option for closed-cervix pyometra, progesterone-receptor antagonists are not available in Argentina; hence, we suggest ovariohysterectomy for these patients. Whereas in our study two animals (40%) became pregnant after treatment, in a previous study where prostaglandin F_{2α} was used, 95% of queens resumed normal estrous cycles without further treatment and 81% delivered normal litters.¹¹ These differences in pregnancy rates could be because different prostaglandin analogues were used or because a different number of study animals were used. Our results show that pregnancies can be obtained after treatment with cloprostenol in queens with open-cervix pyometra. Although some side effects were observed after drug administration, they were slight and of short duration. It has been reported that prostaglandin F_{2α} side effects are dose-dependent and are known to diminish with repetition of treatment in the bitch.¹⁶ Therefore, it is recommended to start with the lowest dosage to avoid the classic side effect of vomiting, and then to slowly increase the dosage to reach the recommended dose after 2–3 days.¹⁶ This recommendation could be extended to the use of cloprostenol in future studies to reduce the side effects seen in queens. In this study, even though we observed reduced side effects, we did not observe a slower evacuation of the uterus after cloprostenol use. All queens had an increase in the amount of vaginal discharge during the first 2 days after treatment, the uterus diameter decreased and all queens started to eat, showing a quick response to treatment.

Albeit in this study uterine discharge samples were not obtained for culture, amoxicillin proved to be a suitable choice for antibiotic treatment of pyometra in these queens.

Although amoxicillin is a good initial choice for pyometra treatment, the final choice should always be based on the culture, identification and sensitivity of the bacteria involved.

Conclusions

The results of this study show that cloprostenol is an efficient option for medical treatment of queens with open-cervix pyometra. Whether a treatment plan that includes lower and repeated daily doses of cloprostenol to reduce side effects is effective needs further investigation.

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