

## **INTRAVAGINAL PROSTAGLANDIN F<sub>2α</sub> FOR THE TREATMENT OF METRITIS AND PYOMETRA IN THE BITCH**

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The purpose of this study was to determine whether intravaginal prostaglandin F<sub>2α</sub> (PGF<sub>2α</sub>) would be effective for the treatment of metritis or pyometra in the bitch. Seventeen bitches with metritis or pyometra were treated with PGF<sub>2α</sub>. Prostaglandin F<sub>2α</sub> (150 µg/kg body weight) was administered once or twice daily by infusing 0.3 ml per 10 kg body wt into the vaginal lumen. Bitches were also treated with amoxicillin (15 mg/kg body wt/48 h) and/or gentamicin (4 mg/kg body wt/day) administered as intramuscular (i.m.) injections. Fifteen bitches were treated successfully with intravaginally administered PGF<sub>2α</sub> for 3 to 12 days and with intramuscularly administered antibiotics for 4 to 12 days. Success of treatment was judged by cessation of vaginal discharge, the absence of fluid in the uterus as determined by ultrasonography, and the overall health status of the animal. As two bitches with pyometra showed clinical deterioration in spite of medical treatment, ovariohysterectomy was performed after the first and the second treatment, respectively. No side effects (salivation, vomiting, diarrhoea, hyperpnoea, ataxia, urination, anxiety, pupillary dilatation followed by contraction) were observed after PGF<sub>2α</sub> treatment. The disease did not recur during the subsequent oestrous cycles within 12 months after the initial treatment. The results demonstrate that intravaginal administration of PGF<sub>2α</sub> was effective in 13 dogs (86.6%) with metritis or pyometra, and caused no side effects. Although the study was based on a relatively small number of cases, it is concluded that prostaglandin F<sub>2α</sub> can be a useful means of treating bitches with metritis or pyometra. However, in severe cases of pyometra ovariohysterectomy is needed.

**Key words:** Metritis, pyometra, intravaginal PGF<sub>2α</sub>, bitch

Metritis usually occurs after an oestrus accompanied by mating or after parturition, and can be acute or chronic. Pyometra occurs during dioestrus (Sokolowski, 1980). The direct cause of these conditions is not known but progesterone can stimulate the development of cystic endometrial hyperplasia and

fluid accumulation within the uterus in the case of pyometra (Johnson, 1993). At the same time, ascending, haematogenic, or lymphogenic bacterial infection of the uterus may play an important role (Nelson and Feldman, 1986). Sometimes medroxyprogesterone acetate or oestradiol benzoate treatment causes cystic endometrial hyperplasia and pyometra (Burke, 1986; Johnson, 1993).

Prostaglandin  $F_{2\alpha}$  and systemic antibiotics are the most effective medical therapy for metritis and pyometra in the bitch (Sokolowski, 1980; Nelson and Feldman, 1982; Meyers-Wallen et al., 1986). However,  $PGF_{2\alpha}$  administered parenterally can cause side effects such as salivation, vomiting, diarrhoea, hyperpnoea, ataxia, urination, anxiety and pupillary dilatation followed by contraction. These side effects may last for up to 120 min after  $PGF_{2\alpha}$  administration (Sokolowski and Geng, 1977; Nelson et al., 1982).

The purpose of this study was to determine whether intravaginal  $PGF_{2\alpha}$  administration would be effective for the treatment of metritis (post-oestrus) and pyometra (dioestrus) in the bitch. Since  $PGF_{2\alpha}$  has not been approved for intravaginal use in the bitch, owners were informed that the use of  $PGF_{2\alpha}$  for treating canine metritis and pyometra was experimental, and this treatment was initiated only after we had obtained the owners' approval.

### Materials and methods

Seventeen privately owned bitches of different breeds with metritis (post-oestrus) or pyometra (dioestrus) were presented to the FeliCaVet Private Veterinary Clinic because of illness. They ranged in age from 2 to 11 years. The diagnoses were based on clinical signs (depression, lethargy, anorexia, polyuria, polydipsia, weakness, vaginal discharge if the cervix was patent), findings from abdominal palpation (uterine enlargement), vaginoscopy, and ultrasonography (Zöldág et al., 1991). Ultrasonography of the uterus was performed with a 7.5 MHz linear-array transducer (Scanner 450 VET, Pie Medical, Maastricht, The Netherlands). In some cases (closed-cervix pyometra) clinical chemistry such as white blood cell count and differential blood count were used to determine the degree of inflammatory processes. The bitches were allocated to the following three groups (Table 1) based on the clinical criteria described below:

*Group 1: post-oestrous chronic metritis (n = 6; age: 3.0 ± 1.0 years)*

The cross-sectional diameter of the fluid-filled uterine horns just before the cervix (measured by transabdominal ultrasonography) was less than 1.5 (range: 0.9–1.5) cm. Mucous, bloody, purulent, or olive-drab vaginal discharge was also present. The clinical status of the bitches was otherwise normal.

**Table 1**Recovery rate in bitches receiving intravaginal PGF<sub>2α</sub> and parenteral antibiotic treatment

Diagnosis (n)	Number of treatments Mean (range)	Number of days Mean (range)	Recovered N	Diameter of the uterine horn	
				Day	cm (range)
Group 1 Endometritis, metritis (n = 6)	4.2 (3–6)	4.0 (3–5)	6	D 0	1.1 (0.9–1.5)
				D 2	1.0 (0.8–1.1)
				D F	0.7 (0.6–0.8)
Group 2 Open-cervix pyometra (n = 6)	6.5 (6–7)	5.8 (5–7)	6	D 0	2.0 (1.8–2.5)
				D 4	1.3 (1.2–1.4)
				D F	0.8 (0.7–1.0)
Group 3 Closed-cervix pyometra (n = 5) <sup>a</sup>	13.3 <sup>b</sup> (10–16)	10.0 <sup>b</sup> (7–12)	3 <sup>b</sup>	D 0	2.0 (1.8–2.5)
				D 4	1.3 (1.2–1.4)
				D F	0.8 (0.7–1.0)

<sup>a</sup>Number of bitches treated in Group 3; <sup>b</sup>In two cases of closed-cervix pyometra, ovariohysterectomy was performed on the first and second day of the treatment, respectively, because of poor general health status; D 0: first ultrasound examination; D F: final ultrasound examination

*Group 2: open-cervix pyometra in dioestrus (n = 6; age: 3.5 ± 1.9 years)*

The diameter of the fluid-filled uterine horns was greater than 1.5 (range: 1.8–2.5) cm as determined by ultrasonography. There was a bloody, dark brown or purulent vaginal discharge. Health status was normal (n = 3) to suboptimal (n = 3) as judged by degree of depression, anorexia, polyuria, polydipsia, and elevation of body temperature (39.3–39.8 °C).

*Group 3: closed-cervix pyometra in dioestrus (n = 5; age: 6.4 ± 2.9 years)*

The diameter of the fluid-filled uterine horns was greater than 1.5 (range 1.8–2.5) cm; the total white blood cell count was elevated (exceeding 20,000 cells per mm<sup>3</sup>), and there was marked neutrophilia. The health status was normal (n = 1), suboptimal (n = 2) and poor (n = 2) as judged by the degree of depression, anorexia, polyuria, polydipsia, and elevation of body temperature (39.3–39.8 °C). In each case ovariohysterectomy, the traditional curative treatment for metritis and pyometra, was discussed with the owners. Although pyometra can recur within 27 months of successful medical management in >70% of bitches (Sokolowski and Geng, 1977) and the owners did not want to have most of the bitches bred again, medical treatment was requested in each reported case. All animals were treated

with broad-spectrum bactericidal antibiotics [Clamoxyl L.A. inj. (amoxicillin), SmithKline Beecham, or Vetrigent inj. A.U.V. (gentamicin), Phylaxia-Sanofi, Budapest, Hungary] intramuscularly and with PGF<sub>2α</sub> (Enzaprost F inj. A.U.V., Sanofi-Chinoin, Budapest, Hungary) intravaginally. Prostaglandin F<sub>2α</sub> therapy (150 µg/kg of body wt) was administered with the help of a sterilised plastic catheter and infusing PGF<sub>2α</sub> (0.3 ml/10 kg of body wt) once or twice daily. Immediately after PGF<sub>2α</sub> infusion the hindquarters of the animals were raised for 3 to 5 min in order to minimise retrograde loss of PGF<sub>2α</sub>. Animals with normal health status were treated with long-acting amoxicillin (15 mg/kg body wt/48 h) 2 to 5 times for 4 to 10 days. If after the second treatment there was no improvement in clinical signs (general health status, body temperature), gentamicin therapy (4 mg/kg body wt/day) was given for 8 days (n = 3). Animals with suboptimal or poor health status were treated with gentamicin daily for 10 days. Intravenous fluid therapy with balanced electrolyte solution (lactated Ringer's solution) was given to bitches with poor health status on admission (n = 2) and was repeated daily until needed. During the treatment period, a complete physical examination was performed daily to monitor actual health status and clinical response to treatment. Every second day uterine diameter was estimated by ultrasonography. Animals were considered to have recovered if no vaginal discharge was observed, there was an absence of fluid in the uterus as judged by ultrasonography, and if the animals had a normal overall health status.

### Results

The results of PGF<sub>2α</sub> treatments are shown in Table 1. With the exception of two bitches with pyometra, the treated animals recovered within 3 to 12 days. As two bitches (5 and 11 years old, respectively) showed clinical deterioration, ovariohysterectomy was carried out after the first and the second treatment, respectively. Both bitches recovered after ovariohysterectomy. No side effects (salivation, vomiting, diarrhoea, hyperpnoea, ataxia, urination, anxiety, and pupillary dilatation followed by contraction) were found after intravaginal PGF<sub>2α</sub> treatments. The haematological abnormalities seen in group 3 had also normalised by the end of treatment. The disease did not recur among the recovered animals during the subsequent oestrous cycles within 12 months after the initial treatment.

### Discussion

In the medical management of metritis or pyometra, PGF<sub>2α</sub> has been accepted as a medical alternative to ovariohysterectomy because it causes luteolysis, myometrial contraction, and dilatation of the cervix. In the present study intravagi-

nally administered prostaglandin therapy resulted in the dilatation of the cervix in 3 out of 5 bitches with closed-cervix pyometra. Responses to PGF<sub>2α</sub> led to the expulsion of the uterine contents and thus helped restore normal uterine anatomy and function (Lein, 1986). Different subcutaneous treatment schedules with varying dosages of PGF<sub>2α</sub> have been used for the treatment of metritis or pyometra in bitches. To minimise the side effects, the original doses (500–1000 µg/kg) of natural prostaglandin (Dinoprost) were decreased (250 µg/kg). This was very important because the LD<sub>50</sub> (5.13 mg/kg) in the bitch is low and gives a narrow therapeutic index (Sokolowski and Geng, 1977). At the same time the effectiveness of the drug did not decrease with this lower dose and the number of treatments did not have to be increased (Sokolowski, 1980). Others found satisfactory results after using a much lower dose (100 µg/kg/treatment; Nelson et al., 1982). A dose between 100 and 250 µg/kg (Meyers-Wallen et al., 1986; Nelson and Feldman, 1986; Johnson, 1992; Johnson, 1993) once or twice daily was recommended. According to Brown (1985) 200 to 250 µg/kg is more effective but side effects are still present. Arnold et al. (1988) and Nolte et al. (1993) reported that 20 µg/kg PGF<sub>2α</sub> administered two (Nolte et al., 1993) to three (Arnold et al., 1988) times daily gave the same results and there were no side effects. In a case of closed-cervix pyometra Memon and Mickelsen (1993) started the treatment with very low doses (25 µg/kg). They administered increasing doses to 250 µg/kg until the 4<sup>th</sup> day of therapy (7<sup>th</sup> treatment). The observed side effects were overcome if the animal was walking. According to Nelson (1993), a therapeutic regimen using 100 µg/kg of PGF<sub>2α</sub> initially, then gradually increasing the dosage to 250 µg/kg over 48 to 72 h may allow the clinician to assess the sensitivity of the dog to prostaglandin and allow the patient to adapt to the drug. Jackson et al. (1982) administered prostaglandin analogues (fluprostenol and cloprostenol) in a 24-h release intravaginal device for pregnancy termination. Both analogues, used in a relatively low dosage (10–25 µg/kg), showed minimal acceptable side effects as compared with the aqueous marketed form of cloprostenol administered intramuscularly. In our cases natural PGF<sub>2α</sub> (150 µg/kg) and broad-spectrum bactericidal antibiotics were used intravaginally and intramuscularly, respectively. After treatment, no side effects were observed, and the recovery rate of dogs with metritis or pyometra (86.6%) was similar to the previously published values (Sokolowski, 1980; Arnold et al., 1988). However, the number of treatments performed by us was greater than reported previously (Sokolowski, 1980). Further investigations are needed to determine the therapeutic dose to be administered intravaginally and the necessary number of treatments. Although this study was based on a relatively small number of cases (n = 17), it can be concluded that intravaginally administered prostaglandin F<sub>2α</sub> may be a useful means of treating bitches with metritis or pyometra. However, in severe cases of pyometra ovariohysterectomy is needed.

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