Treatment of pyometra in cats, using prostaglandin $F_{2\alpha}$: 21 cases (1982–1990)

Autumn P. Davidson, DVM; Edward C. Feldman, DVM; Richard W. Nelson, DVM

Summary: *Treatment with prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) was evaluated in 21 queens with open-cervix pyometra. The $PGF_{2\alpha}$ was administered (0.1 or 0.25 mg/kg of body weight, SC, q 12 to 24 h) for 3 or 5 days. Transient postinjection reactions caused by $PGF_{2\alpha}$ administration included vocalization, panting, restlessness, grooming, tenesmus, salivation, diarrhea, kneading, mydriasis, emesis, urination, and lordosis. Reactions began as quickly as 30 seconds after $PGF_{2\alpha}$ administration and lasted as long as 60 minutes. All queens improved clinically after $PGF_{2\alpha}$ treatment. One month after completion of the initial series, 1 queen required a second series of $PGF_{2\alpha}$ injections before pyometra resolved. Of 21 queens, 20 (95%) resumed normal estrous cycles without further treatment and 17 (81%) delivered normal litter(s). Use of $PGF_{2\alpha}$ is an acceptable treatment for open-cervix pyometra in queens.*

The pathogenesis and clinicopathologic characteristics of the cystic endometrial hyperplasia-pyometra complex in cats have been reported.[1-4] Surgical treatment for pyometra includes ovariohysterectomy or hysterotomy with placement of uterine drainage tubes.[2-6] Medical management of open-cervix pyometra in queens, using prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), has been reported.[7-9] Only 1 study,[7] involving 2 queens, has been published in the United States. The objective of the study reported here was to evaluate long-term effects of $PGF_{2\alpha}$ as treatment for open-cervix pyometra in queens.

Criteria for Selection of Cases

Twenty-one queens with 1 or more episode(s) of open-cervix pyometra were treated with $PGF_{2\alpha}$[a] between July 1982 and January 1990. Open-cervix pyometra was diagnosed in each queen on the basis of mucopurulent vaginal discharge, palpably large uterus, and concurrent systemic signs of illness (fever, inappetence, lethargy). Abdominal radiography and/or ultrasonography was performed in 14 queens, and results confirmed uterine enlargement (radiographically) or fluid-filled uterine enlargement (ultrasonographically). Seventeen queens were treated by the authors at the University of California, Davis. Four queens were treated at private veterinary practices under the direction of one of the authors (ECF).

Successful short-term response was defined as resolution of pyometra at the completion of $PGF_{2\alpha}$ treatment. Successful long-term response was defined as return of queens to normal estrous cycles, and if bred, conception and carrying a litter to term.

Methods

Clinical evaluation—Queens' ages ranged from 10 to 96 months (mean, 32.4 months). Breeds included Persian (n = 6), domestic shorthair (n = 5), Himalayan (n = 4), Japanese Bobtail (n = 3), Abyssinian (n = 1), Balinese (n = 1), and Siamese (n = 1). Twelve queens had successfully delivered prior to development of open-cervix pyometra, 5 queens were nulliparous, and reproductive history was unknown for 4 queens. Eighteen queens had experienced estrus within 8 weeks of the diagnosis of open-cervix pyometra, and 14 of them were bred during that estrus.

All queens were considered ill by their owners at the time of referral. Clinical signs of disease included copious vaginal discharge (21/21, 100%), partial to complete anorexia (5/21, 24%), lethargy (5/21, 24%), weight loss (3/21, 14%), unkempt appearance (2/21, 9%), and polydipsia/polyuria (2/21, 9%). Prior antibiotic treatment had been ineffective in resolving clinical signs in 9 queens. Two queens had been treated by use of an antiseptic vaginal douche, with no improvement observed. Abnormalities detected most frequently during physical examination were mucopurulent to hemorrhagic vaginal discharge (21/21, 100%), palpable uterus (21/21, 100%), and pyrexia (5/21, 24%). Some queens did not have physical signs of disease other than vaginal discharge.

From the Small Animal Internal Medicine Service, Veterinary Medical Teaching Hospital (Davidson), and the Departments of Reproduction (Feldman) and Medicine (Nelson), School of Veterinary Medicine, University of California, Davis, CA 95616.

[a]Lutalyse, The Upjohn Co, Kalamazoo, Mich.

Diagnostic evaluation—A CBC was performed for 14 queens, along with serum biochemical analysis for 5 queens. In each case for which CBC results were obtained, abnormalities in the leukogram existed. One queen had a low total leukocyte count, and 13 queens had high total leukocyte counts. Total leukocyte counts ranged from 4,700 to 72,000 cells/μl (mean, 34,428 cells/μl). Total neutrophil counts ranged from 840 to 54,000 cells/μl (mean, 21,339 cells/μl). Hyperglobulinemia (range, 5.1 to 5.5 g/dl; mean, 5.3 g/dl; normal 2.1 to 3.3 g/dl) was reported for 3 of 5 (60%) queens, and was the only abnormality found on the serum biochemical profile.

Vaginal cytologic examination findings were consistent with septic inflammation in the 2 queens tested. Bacteriologic culture was performed on swab specimens obtained from the cranial portion of the vagina of 5 queens; *Escherichia coli* was isolated from 4 (80%), and no bacteria were isolated from 1 (20%).

Blood for measurement of progesterone concentration was obtained from 9 queens. Plasma progesterone concentration was measured by use of a radioimmunoassay as reported.[10] Mean pretreatment plasma progesterone concentration was 4.5 ng/ml (range, 0.1 to 13.3 ng/ml; normal concentration during anestrus, < 1 ng/ml). Mean progesterone concentration on the final day of $PGF_{2\alpha}$ treatment was 0.69 ng/ml (range, 0 to 2.2 ng/ml).

Abdominal radiography revealed a large, tubular, soft tissue density compatible with uterine enlargement in 10 of 10 (100%) queens. Ultrasonography revealed large, fluid-filled uterine horns with no fetuses in 10 of 10 (100%) queens. Of the 14 queens knowingly bred prior to onset of pyometra, 8 underwent abdominal ultrasonography; viable pregnancy was ruled out. Two queens with estimated gestational duration of 14 days underwent only abdominal radiography (pregnancy was not ruled out). Four queens that did not undergo radiography or ultrasonography had estimated gestational duration of > 4 weeks; pregnancy was ruled out by results of abdominal palpation.

Patient management—Each queen was hospitalized for the duration of $PGF_{2\alpha}$ treatment. The drug, 0.1 (n = 6 queens) or 0.25 (n = 15 queens) mg/kg of body weight was administered SC every 12 to 24 hours for 3 to 5 days. Antibiotics were systemically administered concurrently to 19 of 21 (90%) queens. Trimethoprim/sulfadiazine[b] (n = 8), tetracycline (n = 7), amoxicillin trihydrate/clavulanate potassium[c] (n = 3), or cefadroxil[d] (n = 1) were used at standard dosages.

Physical reactions were observed after SC injection of $PGF_{2\alpha}$ in 16 of 21 queens (76%), and included vocalization (13/21, 62%), panting (8/21, 38%), restlessness (7/21, 33%), grooming (5/21, 24%), tenesmus (5/21, 24%), salivation (5/21, 24%), diarrhea (4/21, 19%), kneading (4/21, 19%), mydriasis (3/21, 14%), emesis (2/21, 9%), urination (2/21, 9%), and lordosis (2/21, 9%). These reactions resolved within 1 hour after $PGF_{2\alpha}$ administration. After each subsequent $PGF_{2\alpha}$ administration, reactions diminished in severity and duration in all cats. Reactions were never considered to be severe enough to warrant discontinuation of the drug.

Successful short-term response to treatment was observed in all queens. At the time of discharge from the hospital, all queens had improved appetite, normal rectal temperature, and diminished or no vaginal discharge. Initial results of reexamination scheduled within 2 weeks of $PGF_{2\alpha}$ administration indicated that all queens were clinically normal, with no vaginal discharge or palpable uterine enlargement. Abdominal radiography (n = 1) or ultrasonography (n = 5) revealed reduction in uterine size, compared with that of previous examinations.

Of 21 queens, 20 (95%) had a normal estrous cycle after $PGF_{2\alpha}$ administration. When specifically reported, estrus first was observed 0.5 to 12 months (mean, 3.9 months) after treatment. One queen had recurrence of purulent vaginal discharge 1 month after completion of $PGF_{2\alpha}$ treatment, before resumption of estrous cycles; this cat was treated successfully by administration of a second series of $PGF_{2\alpha}$. Breeding at the next estrus was recommended for each queen, but was not always accomplished. Successful breedings were reported for 20 queens from 2 weeks to 5 years after $PGF_{2\alpha}$ treatment. Eighteen queens produced live kittens. One queen had normal estrous cycles after $PGF_{2\alpha}$ treatment, but repeatedly produced only stillborn kittens and was subsequently spayed. One queen was spayed after developing pyometra 1 year after $PGF_{2\alpha}$ treatment, after resumption of normal estrous cycles and breeding. Histologic evaluation of this cat's uterus confirmed cystic endometrial hyperplasia and placental retention. One queen was never bred, although normal estrous cycles were reported. Two of 18 queens that delivered live kittens after $PGF_{2\alpha}$ treatment later developed open-cervix pyometra. Each of these queens was successfully treated again with $PGF_{2\alpha}$. Both have since carried pregnancies to term and delivered normal kittens.

Discussion

Cystic endometrial hyperplasia-pyometra complex is a progesterone-mediated uterine disorder.[1] During the luteal phase of the estrous cycle, progesterone suppresses the leukocyte response to infective stimuli in the uterus, decreases myometrial contractility, and stimulates endometrial gland development and activity.[11,12] During diestrus, the

[b]Tribrissin, Bourroughs Wellcome Co, Research Triangle Park, NC.

[c]Clavamox, Beecham Inc, Bristol, Tenn.

[d]Cefatabs, Fort Dodge Laboratories Inc, Fort Dodge, Iowa.

nongravid uterus is flaccid and contains endometrial gland secretions, which are a growth medium for bacteria.[11] Bacteria reach the uterus via ascension from the distal portion of the genitourinary tract or by hematogenous spread.[13]

Strong correlation existed between the onset of clinical signs of pyometra and recent diestrus in the queens of the study. Of the 21 queens, 18 had recently undergone estrus, and 14 were knowingly bred and, thus, were in diestrus, when plasma progesterone concentration is increased. Pretreatment plasma progesterone concentration was high (ie, > 1 ng/ml) in 7 of 9 queens, in which it was measured.

Successful treatment of pyometra by use of $PGF_{2\alpha}$ results from its effect on the uterine myometrium, cervix, and corpora lutea.[11] The drug stimulates uterine motility in dogs.[14] This myotonic effect increases intrauterine pressure. The rapid reduction in the size of the uterus in some cats of the study indicates possible similar myotonic effect in cats. In women, progressive decrease is observed in the concentration of endometrial prostaglandin receptor sites and myometrial smooth muscle toward the cervix.[15] Therefore, administration of $PGF_{2\alpha}$ should cause movement of uterine contents toward the cervix. Although prostaglandin E has a relaxant effect on the rabbit and human cervix, reports on the effect of prostaglandin F on the cervix are inconsistent.[16,17] If the same is true in cats, restricting the use of $PGF_{2\alpha}$ to treatment of open-cervix pyometra should reduce the potential for complications attributable to myometrial contraction of a fluid-filled uterus against a closed cervix. Complications related to expulsion of septic uterine contents into the peritoneal cavity did not develop in any of the cats of the study.

The luteolytic effect of $PGF_{2\alpha}$ observed in several domestic species has not been definitively documented in cats.[10] Administration of $PGF_{2\alpha}$ to queens during early diestrus does not induce luteolysis.[18] Decrease in plasma progesterone concentration after $PGF_{2\alpha}$ administration to late-gestational queens is transient and believed attributable to depletion of intracellular free cholesterol used for progesterone synthesis.[10,19] Administration of $PGF_{2\alpha}$ causes abortion in queens after the 40th gestational day, presumably because of myometrial contraction and expulsion of uterine contents (ie, fetuses).[19] The $PGF_{2\alpha}$-induced decrease in luteal function should not induce abortion during late gestation because of concurrent placental production of progesterone.[10,20]

Plasma progesterone concentration decreased from pretreatment concentration in 7 of 9 queens during $PGF_{2\alpha}$ administration. These findings were compatible with $PGF_{2\alpha}$-induced partial luteolysis or decreased steroidogenesis. One queen successfully treated with $PGF_{2\alpha}$ had plasma progesterone concentration < 1 ng/ml before and during treatment, indicating that increased progesterone concentration may not be a requirement for persistence of pyometra. The success of $PGF_{2\alpha}$ treatment in this queen was presumably attributable solely to its myometrial effect. Thus, successful treatment of open-cervix pyometra in cats, using $PGF_{2\alpha}$, is attributable to direct uterine effects, perhaps facilitated by transient, partial luteolysis.[10,16,21] The presence of live fetuses should be ruled out by use of ultrasonography prior to $PGF_{2\alpha}$ administration because of the drug's abortifacient potential.[18]

The onset of estrous cycles after $PGF_{2\alpha}$ treatment varied from 0.5 to 12 months, indicating possible influence of day length on this seasonally polyestrous species. The overall successful conception rate was high: following a single course of $PGF_{2\alpha}$ treatment, 85% (17 of 20 queens) produced live kittens. One queen successfully delivered after 2 initial $PGF_{2\alpha}$ treatments. The overall recurrence rate of pyometra was 14% (3 of 21). Treatment of 2 of these queens was attempted and resulted in successful pregnancies, indicating that sequential treatment of queens with recurrent pyometra can be successful and could be considered if the queen's condition permits.

Adverse reactions observed after $PGF_{2\alpha}$ administration reflect the physiologic effects of endogenous prostaglandins. Endogenous prostaglandins are derived from arachidonic acid by the action of cyclooxygenase, and mediate many normal physiologic processes, including vasodilation, hemostasis, pulmonary vasoconstriction and bronchodilation, gastrointestinal tract secretion, renal blood flow and glomerular filtration rate, inflammation, hyperalgesia, and fever.[22] Prostaglandins regulate intracellular synthesis of cyclic AMP to induce alterations in cellular protein kinases and ultimately cell function. The contractile effect of $PGF_{2\alpha}$ on the myometrial, gastrointestinal tract, tracheobronchial, and bladder smooth musculature accounts for the clinical responses observed.[22]

Candidates for $PGF_{2\alpha}$ treatment should be young and otherwise healthy queens, with evidence of a patent cervix (ie, vaginal discharge). Potential contraindications to the use of prostaglandins include planned pregnancy, sepsis, peritonitis, significant organic disease, and presence of mummified fetal remains.[11] During $PGF_{2\alpha}$ treatment, queens may need to be hospitalized as warranted by their clinical condition, to enable administration of adjunct supportive care, such as IV administration of fluids and antibiotics, and to permit monitoring of adverse effects and outcome of treatment. Some queens could be treated on an outpatient basis. Concurrent administration of a broad-spectrum bactericidal antimicrobial is advised.[11]

Difference between the 0.1- and 0.25-mg/kg dosages associated with adverse reactions was not detected. Both cats with long-term therapeutic failure resulting in ovariohysterectomy were treated with 0.25 mg/kg, suggesting that response to treat-

ment depends on the degree of underlying uterine lesions rather than dosage of $PGF_{2\alpha}$. The lower dosage (0.1 mg/kg, q 24 h) is recommended, although the minimal effective dose of $PGF_{2\alpha}$ has not been established. This dosage should only be used for natural $PGF_{2\alpha}$. Synthetic $PGF_{2\alpha}$ is more potent in its actions than is natural $PGF_{2\alpha}$.[20] Use of synthetic $PGF_{2\alpha}$ at the dosage recommended for natural $PGF_{2\alpha}$ may result in a fatal outcome. A safe and effective dosage of synthetic $PGF_{2\alpha}$ has not yet been established for cats. Because prostaglandins are not approved for use in domestic cats, informed consent should be obtained prior to their use.

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