

SUCCESSFUL MANAGEMENT OF PYOMETRA IN A GOLDEN RETRIEVER BITCH WITH MIFEPRISTONE AND MISOPROSTOL

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This communication details the effective medical management of pyometra using a combination of misoprostol and the progesterone receptor blocker, mifepristone.

Keywords: Canine, Pyometra, Mifepristone, Misoprostol.

Canine pyometra is predominantly a dioestral disorder, characterized by pus accumulation in the uterus (Hardy and Osborne, 1974). The pathogenesis of pyometra includes multiple etiological factors, which include influence of hormones on uterus and the virulence of bacteria involved. High serum progesterone concentration during dioestrus leads to the development of cystic endometrial hyperplasia (CEH), which promotes bacterial adherence and growth in the endometrial epithelium. The condition favours development of pyometra with entry of bacteria (De Bosschere *et al.*, 2001). Though CEH may predispose for pyometra, the latter can also occur without CEH. The bacteria most commonly associated with pyometra is *Escherichia coli*, though several other bacteria have also been isolated. Presence of Gram-negative bacteria raises concerns, because of the possibility of exposure of the patient to endotoxins (Pancieria *et al.*, 2003).

Ovario-hysterectomy (OHE) is considered as the most effective treatment for canine pyometra, which effectively brings about an immediate removal of uterine content including endotoxins and hormonal stimulus of ovarian origin. The principal advantage of OHE is the elimination of disease recurrence. Even though OHE has these obvious benefits,

the surgical risks involved and the termination of the bitch's fertility has led to evolution of medical management of the disease as an alternative. Moreover, medical management of pyometra is expected to cause rapid elimination of uterine contents, so as to limit exposure to endotoxins. Though, PGF₂α has been used, primarily for the purpose of uterine contractions and secondarily for the corpus luteum lysis in canine pyometra, a close observation of the patient during its administration and plausible side effects of the drug are of concern. Misoprostol is a prostaglandin E₁ analogue, which has strong uterine contracting action, when administered to dogs orally at a dose rate of 10 µg/kg b.w.t. BID and was effective in evacuating uterine contents (Romagnoli, 2017). The drug is also ascribed to have cervical relaxation in dogs following intravaginal administration but these lack scientific validation (Verstegen *et al.*, 2008). The present paper presents the successful use of misoprostol along with mifepristone in the management of canine pyometra.

Case history and Observations

A 7 year old Golden retriever bitch was presented at Teaching Veterinary Clinical Complex, Mannuthy, Kerala, with a history of foul smelling haemorrhagic vaginal discharge since last

four days. The bitch had no known mating history and had inappetance since few days. Clinical examination revealed mentation to be dull and depressed. On physical examination, respiration rate, rectal temperature and heart rate was 19 per minute, 103.5°F and 101 beats per minute respectively. Mucous membranes were congested. The vulva was enlarged and sanguineous discharge was noticed.

Materials and Methods

The haematology, serum biochemistry and ultrasonographic observation on the day of presentation, 3rd, 9th and 15th day of treatment are presented in Table 1. On the first day of presentation, the leucogram, haematological findings, and serum biochemistry were suggestive of an active infection. The band cells were 6.6 per cent suggestive of immature

neutrophils as a result of aggressive bone marrow response to infection. In addition, toxic changes of neutrophils were also observed. The blood urea nitrogen (BUN), serum creatinine, and alanine transferase were within normal physiological range, while alkaline phosphatase was elevated. The serum progesterone value was 1.75 ng/dl, indicating lack of a functional corpus luteum. Trans-abdominal B-mode ultrasonography with 7.5 MHz sector transducer revealed multiple anechoic uterine sacculations with an maximum diameter of 3.6 cm. Doppler velocimetry of uterine artery was performed in longitudinal section at the lateral region of the uterine body. Pulsed wave Doppler was used to characterize the wave form and an RI of 0.60 suggestive of pyometra was recorded (Fig.-1).

Fig-1. ULTRASONOGRAM OF THE ABDOMEN OF THE PYOMETRA AFFECTED BITCH ON THE DAY OF PRESENTATION SHOWING SACCULATIONS AND HYPERPLASTIC CHANGES IN UTERINE HORN



Cytology of the vaginal discharge showed numerous degenerative neutrophils, epithelial cells and erythrocytes. Culture and sensitivity results of sterile vaginal swab taken from anterior vagina under the guidance of a sigmoidoscope to prevent contamination, revealed the presence of Gram-negative

bacilli which were sensitive to various antibiotics. Based on the case history, clinical signs and laboratory results the condition was diagnosed as open-cervix pyometra.

Treatment was initiated with progesterone receptor blocker, Mifepristone at a dose rate of 5 mg/ kg,

orally, BID to initiate cervical relaxation and continued till evacuation of uterus (day 9). PGE₁ analogue, Misoprostol was administered at a dose rate of 10 mg/kg, orally BID, with the second dose of Mifepristone, to promote cervical relaxation and induce uterine contraction for facilitating evacuation of uterus. The treatment was supplemented with parenteral administration of broad spectrum antibiotic and fluids.

Results and Discussion

Table-1. HAEMATOLOGY, SERUM BIOCHEMISTRY AND ULTRASONOGRAPHIC OBSERVATIONS IN THE PYOMETRA AFFECTED BITCH DURING THE COURSE OF MEDICAL MANAGEMENT

Parameters	Day of treatment			
	Day 0	Day 3	Day 9	Day 15
Total leucocyte count ($\times 10^3/\mu\text{L}$)	24.8	11.2	10.7	8.3
Progesterone (ng/mL)	19.25	11.11	1.75	0.93
Band cells (%)	6.66	3.6	0.94	0.73
Haematocrit (%)	28.6	28	30	34.2
Platelet ($\times 10^3/\mu\text{L}$)	71	130	448	492
Total protein (g/dl)	16.09	6.877	16.43	9.06
Albumin (g/dl)	3.586	2.072	4.124	3.12
BUN (mg/dl)	24.21	8.406	13.7	12.9
Creatinine(mg/dl)	0.943	0.748	0.99	0.76
ALT (IU/L)	38.94	-	58.58	-
ALP (IU/L)	509.4	-	200	-
Horn diameter (cm)	3.6	2.3	0.56	0.45
Lumen diameter (cm)	2.12	1.54	0.12	0
Resistive Index	0.6			0.79
Improvement in food intake	From 5 th day of treatment			
recovery of normal mentation	From 3 rd day of treatment			
Cessation of vaginal discharge	From 5 th day of treatment			

Considering the age of the bitch and the owners lack of intention for further breeding, OHE was done after two months of completion of medical treatment. Grossly, the uterus appeared as normal without any abnormal fluid accumulation. No ovarian cysts or endometrial cysts were observed.

Antiprogesterin drugs, such as mifepristone, competitively prevent progesterone from binding to its receptor.

Reviews on days 3, 9 and 15 following onset of treatment showed improvement in the condition (Table-1). Sonographic assessment revealed negligible uterine accumulation by day 9 and nil by day 15. Broad spectrum antibiotics were advised for two more weeks. Rapid improvement in the condition of the bitch was noticed with the animal regaining feed intake by day 5, normal mentation by day 3 and cessation of vaginal discharge by day 5 from onset of treatment.

This antagonism results in mimicking the effect of luteolysis and cause cervical relaxation. Mifepristone appears to be a safe and promising option for opening the cervical canal in closed-cervix pyometra in dogs as also reported by Blendinger *et al.*, 1997. Eventhough progesterone receptor antagonists have been effectively used for the medical management of pyometra, it is not recommended alone because of its inability in

inducing myometrial contractions as also mentioned by Verstegen *et al.*, 2008.

It was observed in the present case that use of misoprostol improved emptying of uterus. Gram-negative bacteria were observed in the bacterial culture of anterior vaginal swab in the current case. Thus a rapid emptying of uterus would have reduced the quantity of endotoxins absorbed by the patient, helping in early recovery. Misoprostol is effective in evacuating uterine contents because of its strong uterine contraction action as also recorded by Romagnoli, 2017. In the present study, Misoprostol was given through oral route. The option of oral dosing and fewer side effects, opens up possibilities of use of misoprostol instead of PGF₂α in the medical management of canine pyometra. Response of medical management can be assessed by serial measurement of uterine horn diameter and endometrial changes through ultrasonography. As a non-invasive technique, Doppler ultrasonography gives an idea about the organ perfusion and is used to detect uterine artery blood flow and tissue perfusion as also mentioned by Batista *et al.*, 2016. In agreement to our study many researchers opined that a resistive index value of 0.72 is considered as a threshold value used for the differential diagnosis between CEH and pyometra Carvalho *et al.*, 2021 and Pati *et al.*, 2021 have reported that it could be used as a marker to evaluate recovery from the disease.

Conclusions

The concurrent use of mifepristone and misoprostol combination could be of potential use in medical management of pyometra, especially in bitches, which might have severe side effects to PGF₂α or in which the owners find it difficult to bring the bitch regularly for administration of PGF₂α.

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