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Therapeutic management of canine pyometra by using mifepristone and misoprostol

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Abstract

Pyometra is characterized by the accumulation of purulent material within the uterus, which manifests in both local and systemic symptoms. It is typically a post-estrus syndrome in adult female dogs associated with a variety of clinical and pathological manifestations of the genital system and multisystemic disease. The management of canine pyometra using mifepristone along with misoprostol was studied in five female dogs with ultrasonographic and haemato-biochemical profile analysis. All the female dogs recovered at the end of treatment. Endometrium thickness and uterine lumen diameter were significantly decreased in all the animals at the end of treatment. In Hemato-biochemical analysis, TLC value decreased significantly in all the dogs after completion of treatment while AST, ALT and BUN values decreased non-significantly.

Keywords: Pyometra, female dog, mifepristone, misoprostol

1. Introduction

Pyometra is the most commonly documented reproductive disorder in intact female dogs, often associated with cystic endometrial hyperplasia (CEH), posing not only a threat to future fertility but also a risk to life. It is a common reproductive syndrome of intact, sexually mature female dogs during the dioestrus stage with various clinical as well as pathological signs specific to the reproductive system along with systemic signs (Fransson, 2003) [2]. It is also characterized by endometrial inflammation, accumulation of purulent exudate within the lumen and bacterial infection (Santana and Santos, 2020) [6]. It is postulated that intrauterine bacteria, which ascend from the vagina during pro-estrus and estrus, induce the disease during dioestrus by acting on the progesterone-primed endometrium directly via toxin production or indirectly by the release of inflammatory mediators. Parity and age are significant risk factors in the development of pyometra.

The pathogenesis of pyometra in female dogs is complex and it is affected by several factors including bacterial infection, neutrophilic activity, uterine motility, and concentration of immunoglobulins (Schlafer and Foster, 2016) [7]. Pathogenesis of pyometra is multifactorial and progesterone seems to be a key factor, however, cystic endometrial hyperplasia has been described as a predisposing condition for canine pyometra.

During the period of progesterone dominance, endometrial gland secretions increase along with pronounced endometrial proliferation and reduced myometrial contractility, causing accumulation of the secretions within the uterine lumen which will act as a media for bacterial growth and finally leads to development of pyometra. These effects are cumulative after repeated estrus cycles, explaining the increased incidence in middle-aged to older female dogs. Young female dogs with open cervix pyometra, normal organ functions and predictable breeding values are the candidature for medical therapies. On the other hand, mid to old aged dogs with systemic inflammatory responses with compromised organ functions often unfit for ovario-hysterectomy.

2. Materials and Methods

This study was carried out in the Veterinary Clinical Complex, College of Veterinary Science and A.H., NDVSU, Jabalpur from April to June 2022. For this total of 12 female dogs affected with pyometra were selected based on history, body condition, clinical signs and ultrasonographic examination.

2.1 Case History

Early diagnosis and subsequent therapeutic intervention improve the chances of recovery and restore fertility and prevent progression to life-threatening complications. All the female dogs exhibit some or all of the typical signs of pyometra characterized by depression, anorexia, polydipsia, polyuria, pyrexia, vomition and mucopurulent/ purulent vaginal discharge. After recording history and clinical signs all the animals were further examined by trans-abdominal ultrasonography and were classified as pyometra (open and closed cervix pyometra).

2.2 Case Diagnosis

The confirmatory diagnosis was done by ultrasonography. Ultrasonography examination reveals the presence of multiple anechoic fluid-filled pockets of various sizes in the uterus. Hematological and biochemical parameters like Haemoglobin (Hb), RBC, WBC, lymphocytes, neutrophils and biochemical parameters like BUN, creatinine, ALT and AST were estimated.

2.3 Treatment Protocol

The selected female dogs were treated with tab. mifepristone @ 2.5 mg/kg body wt. orally on days 1, 2 and 7 of treatment along with intravaginal insertion of tab. misoprostol on day 3, 4, 5 and 6 of treatment. The animals were supported with fluid therapy, antibiotics, anti-inflammatory and anti-histaminic for 5 days. The efficacy of the treatment protocol was assessed by the reduction in the uterine diameters by ultrasonography, hematology and serum biochemistry on days 0 and 7.

3. Results

There was a significant clinical recovery in terms of physiological, hematological and biochemical parameters in all the female dogs. All the animals recovered after 7-10 days with complete evacuation of pus. Endometrium thickness and uterine lumen diameter were significantly decreased from day 7 to day 10 (Table 1). In some dogs, normocytic normochromic anaemia was also reported on day 0 which was treated with haematinic therapy along with nutritional management and exhibited normal hemoglobin at the end of treatment. Leucocytosis with neutrophilia was reported on day 0. The TLC value and neutrophil count decreased from day 0 to day 10 in all the animals whereas AST, ALT and BUN values also decreased at the end of treatment (Table 2).

Day 0 mean total uterine diameter (mm) on ultrasonography examination was 6.55 ± 0.53 which started decreasing after the onset of treatment and showed within range at day 10 *i.e.*, 2.58 ± 0.49 . Between day 0 to day 7 and day 10, there was a statistically significant decrease in the mean values of total uterine diameter across all the animals. As indicated in Table 1, the mean endometrial thickness of the uterus in pyometra

dogs was assessed by ultrasonography on days 0 through day 10 and before the commencement of therapy (day 0), the mean values of an endometrial thickness (mm) were 4.96 ± 0.34 afterward, it progressively dropped in all treated dogs over the therapy from days 7 (3.45 ± 0.29) to day 10 (1.01 ± 0.52).

The mean TLC values ($10^3/\mu\text{l}$) recorded before the initiation of treatment (day 0) was $17.33^A \pm 1.80$. These values were highly elevated as compared to the normal physiological range ($6-17 \times 10^3/\mu\text{l}$). However, a significant decrease in the mean TLC values after the completion of the treatment at day 10 *i.e.*, 12.35 ± 1.01 . In the present study, BUN ($33.13 \pm 2.42 \text{mg/dl}$) was in affected dogs at day 0 that significantly reduced in treated animals on day 10 ($17.88 \pm 1.83 \text{mg/dl}$) and showed within range. However, AST (U/L) was also elevated in pyometra dogs at day 0 which decreased significantly from day 0 (44.26 ± 2.41) to day 7 (32.66 ± 1.71) and further decreased day 10 (31.85 ± 1.73) non-significantly.

4. Discussion

After medical treatment, all hematological parameters that had been increased before to treatment such as total leukocyte count, neutrophil count, BUN, creatinine, alanine aminotransferase (ALT) and alkaline phosphatase (ALP) dropped to normal range in all fully recovered animals. Even when it is not possible to differentiate the kind of fluid, ultrasonography may still be very helpful in detecting minor fluid accumulation. The ultrasonographic feature of a pathologically altered uterus varies, although luminal fluid is frequently detected (Pollard and Hecht, 2015) ^[5]. The haemato-biochemical characteristics of animals show the systemic consequences of pyometra. A notable shift in the leukogram of affected dogs is observed when the overall leucocyte count rises significantly (Bigliardi *et al.*, 2004) ^[1]. Sevelius *et al.* (1990) ^[8] proposed that the disseminated suppurative inflammation of the uterus in response to the infection and the bone marrow inflammatory response account for the significant leucocytosis seen in cases with pyometra.

According to Wheaton *et al.* (1989) ^[11], pre-renal uremia was often the cause of the increased blood urea nitrogen level that was seen in some of the individuals in their investigation. Pre-renal variables are those that cause the glomerular filtration rate to drop and affect the kidney's ability to function efficiently. A satisfactory response from the animal to the treatment and removal of the toxemia in the afflicted female dogs is shown by a progressive decrease in the increased blood urea nitrogen level throughout the treatment. This toxemia reversal was in line with earlier research (Verstegen *et al.*, 2008) ^[10].

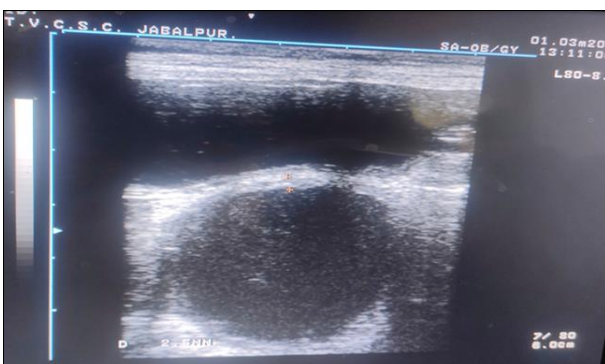
Patil *et al.* (2013) ^[4] reported a comparable range of AST levels following ovariohysterectomy in dogs. In line with the results of this study, Lopate (2017) ^[3] also reported that mild to moderate increases in serum aspartate aminotransferase concentrations in animals that are occasionally encountered may be caused by septicemia-induced hepatocellular damage, as well as by diminished hepatic circulation and cellular hypoxia in the dehydrated female dogs. According to Sodikoff (1995) ^[9], cholestatic liver disorders are the main causes of elevated serum AST activity in dogs.

Table 1: Effect of treatment regimens on uterine parameters in dogs affected with canine pyometra.

S. No.	Parameters	Day 0	Day 7	Day 10
1.	Total Uterine Diameter (mm)	6.55 ^A ±0.53	3.70 ^B ±0.65	2.58 ^C ±0.49
2.	Endometrial thickness (mm)	4.96 ^A ±0.36	3.45 ^B ±0.29	1.01 ^C ±0.52

Table 2: Effect of treatment regimens on hematology & hematobiochemical parameters of dogs affected with pyometra

S. No.	Parameters	Day 0	Day 7	Day 10
1.	TLC (10 ³ /µl)	17.33 ^A ±1.80	13.61 ^B ±1.06	12.35 ^B ±1.01
2.	Neutrophil (%)	73.68 ^A ±2.72	65.33 ^B ±1.19	50.26 ^C ±1.00
3.	BUN (mg/dl)	33.13 ^A ±2.42	20.05 ^A ±2.40	17.88 ^B ±1.83
4.	AST (U/L)	44.26 ^A ±2.41	32.66 ^B ±1.71	31.85 ^B ±1.73

**Fig 1:** A dog showing purulent pus discharge (Red arrow) from vagina**Fig 2:** Intravaginal insertion of tab. Misoprostol in a pyometra dog.**Fig 3:** Ultrasound investigation after high temperature myocardial lesion

revealed that a combination of misoprostol and mifepristone treatment protocol along with antibiotics and supportive fluid therapy can be a better alternative to young female dogs to preserve the reproductive capability and also in geriatric dogs which are unfit for traditional ovariohysterectomy. It is a very good combination specially for treating close cervix pyometra because Misoprostol (prostaglandin E1) helps to relax the cervix.

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5. Conclusion

As an alternative to conventional prostaglandin and other treatment protocols with lots of side effects, our investigation