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Research Article

EVALUATION OF DIFFERENT THERAPEUTIC PROTOCOL FOR TREATMENT OF CANINE PYOMETRA

NEHA SARASWAT*, ANUJ KUMAR, VIKAS SACHAN, JITENDRA AGRAWAL, SHANKER KUMAR SINGH and ATUL SAXENA
Department of Veterinary Gynaecology and Obstetrics,
College of Veterinary Science and Animal Husbandry, DUVASU, Mathura-281001, India

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ABSTRACT

Canine pyometra is a polysystemic diestrual disorder mainly observed in nulliparous female dogs. The present study focuses on evaluation of different therapeutic protocol for treatment of canine pyometra based on haemato-biochemical parameters. A total of 27 female dogs were clinically diagnosed for pyometra at the department of Veterinary Gynaecology and Obstetrics, DUVASU, Mathura (U.P). Pyometra cases were primarily divided into two Groups (Group II and III) and healthy females were kept in Group I as control. Female dogs of Group II and III were treated with amoxicillin-clavulanic acid @ 25 mg/kg b.wt./day via intravenous route for 5-7 days along with fluid therapy. Females of group II and III were pre-treated with atropine @ 0.025 mg/kg b.wt. and ondensetron @ 0.5 mg/kg b.wt. via intramuscular route. Females of Group II and III were treated with cloprostenol sodium @ 5 µg/kg b.wt. on day 1, 3, 5, 7 subcutaneous and intravaginal route, respectively. Tablet mifepristone @ 2.5 mg/kg b.wt. on day 2, 4, 6 orally and tablet cabergoline @ 5 µg/kg b.wt. on day 1, 2, 3, 4, 5, 6, 7 orally were provided in both the affected groups. Mean values of haemato-biochemical parameters altered significantly in canine pyometra. The therapeutic protocol in Group II and III showed success rate of 84.61and 78.58%, respectively.

Keywords: Canine pyometra, Medicinal treatment, Mifepristone, $PGF_{2\alpha}$

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Hyperplasia of the endometrium along with infection of opportunistic bacteria and infiltration of inflammatory cells resulting in the accumulation of pus in the uterine lumen, lead to pyometra. Pathogenesis involved abnormal response to the normal concentration of oestrogen and progesterone or hormonal imbalance affects the epithelial cells of the uterus lead to bacterial adherence, colonization, growth and result in canine pyometra. The progesterone stimulation during a relatively long period of time, in combination with bacterial infection or hormonal therapies lead to pyometra in young female dogs. Progesterone primed uterus interact with potential bacterial pathogen may develop to pyometra. Symptoms of pyometra include fever, lethargy, polyuria and polydipsia. Female dogs with open-cervix pyometra show a malodorous, sanguineous to mucopurulent vaginal discharge. The higher infection leads to cardiovascular, gastrointestinal effects, endotoxemic shock, myocardial failure and death. Therefore, early diagnosis and treatment is required to save life and breeding life of female dog. Present study focuses on evaluation of different therapeutic protocol for treatment of canine pyometra based on haemato-biochemical parameters.

MATERIALS AND METHODS

Total 27 female dogs with pyometra were clinically examined and diagnosed at department of Veterinary Gynaecology and Obstetrics, College of Veterinary Science and A.H., U.P. Pandit Deen Dayal Upadhyaya Pashu Chikitsa Vigyan Vishwavidyalya Evam Go Anusandhan Sansthan, Mathura (U.P). Pyometra cases under study were divided into two Groups *viz*. group II (n=13), received Cloprostenol sodium via subcutaneous route and group III (n=14), received Cloprostenol sodium via intravaginal (submucosal) route for medicinal treatment. Animals were divided into these groups based on the route of administration of prostaglandin. Group I (n=11; healthy vaccinated female dogs) kept as control, were clinically diagnosed based on history, clinical signs and ultrasonography. The blood was collected in sterile test tubes from cephalic vein with all aseptic precautions. For haematological studies, whole blood was collected in EDTA vial. Complete blood count of all blood samples was carried out by using a Nihon Kohden Celltac Alpha automated haematology analyzer. For biochemical studies, vials containing blood samples were kept in a slanted position for 15-20 min at normal room temperature, followed by being subjected to a relative centrifuge force (RCF) at 25.15g for 5 min. Supernatant serum was aspirated using a micropipette and immediately after separation serum samples were transferred into cryovials and kept at -20 °C until the use for biochemical assays. Plasma concentration of AST, ALT, ALP, BUN, Albumin, total protein (TP), C-Reactive protein and creatinine were estimated by AutoChemTM ingenious analyzer by using

*Corresponding author: saraswatnehhaa@gmail.com

Arkray kits. The medicinal treatment protocol included antibiosis (Non-nephrotoxic agents)-amoxicillin-clavulanic acid, @ 25 mg/kg b.wt./day via intravenous and intrauterine route for 5-7 days along with fluid therapy (60 ml/kg b.wt. + % dehydration × body weight /100) intravenously. Pre-treatment with atropine @ 0.025 mg/kg b.wt. and Ondensetron @ 0.5 mg/kg b.wt. via intramuscular route. Inj Cloprostenol sodium @ 5 µg/kg b.wt. (Group II via subcutaneous route and Group III via intravaginal route) on day 1, 3, 5, 7 tab mifepristone, 2.5 mg/kg b.wt. on day 2, 4, 6 orally and tab cabergoline, 5 µg/kg b.wt. on day 1, 2, 3, 4, 5, 6, 7 orally provided in both groups. All data were expressed as mean±S.E. Statistical analysis was conducted to determine the difference between the groups. The comparison between the groups was analyzed by the unpaired student's t-test. The statistical difference between the pre and post-therapy data was analyzed by paired student's t-test. P values less than 0.05 were considered significant.

RESULTS AND DISCUSSION

The uterus was examined to evaluate pus pockets, nature of the content, irregularity of endometrium and thickness of the endometrium (Figs. 1 and 2). Considerable alterations in haemato-biochemical parameters were recorded in pyometra cases as compared to healthy female dogs (Table 1 and 2). Moreover, the significant alterations were recorded in leucogram between healthy and pyometra cases. The mean values of total leucocyte count (TLC) and neutrophil percent was significantly ($P<0.001$) higher, and lymphocyte percent was significant ($P<0.001$) lower in pyometra affected animals as compared to the healthy control group. This alteration might be due to the leucocytosis with relatively increased neutrophils and decreased lymphocytes as observed due to diffuse suppurative inflammation of the uterus to combat infection, bone marrow inflammatory response and endotoxemia induced impaired immune response that may lead to a suppressive effect on lymphocyte activity (Lakshmikanth *et al.*, 2016; Samantha *et al.*, 2018). On comparing haemogram, the mean values of haemoglobin (10.33±0.52 vs 15.25±0.55; $P<0.001$), TEC (4.81±0.23 vs 6.22±0.18; $P<0.05$) and HCT (31.86±1.76 vs 45.77±1.65; $P<0.001$), were significantly lower in pyometra group as compared to healthy control group. This might be due to the fact that female dogs with pyometra have anaemia due to erythrocytes diapedesis into the uterine lumen, reduced life span of circulating erythrocytes and suppression of erythropoiesis in the bone marrow associated with toxaemia. Loss of blood through the vaginal discharge in the open cervix pyometra might induce normocytic normochromic anaemia (Yu, 2012). Furthermore, platelet count in the present study was significantly ($P<0.001$) lower in pyometra affected females as compared to healthy control group. Thrombocytopenia may be attributed to the adverse effect of endotoxins on the bone marrow interfering in the synthesis of platelets. The monocyte, eosinophil, MCV and MCH values did not differ significantly between pyometra affected and healthy bitches.

The various serum biochemical parameters are presented in table 2. The significant alterations were recorded in kidney function test. The mean values of blood urea nitrogen (BUN) were significantly ($P<0.05$) higher in pyometra affected bitches, however no significant difference was observed in creatinine level between pyometra and healthy control group. This might be due to bacterial invasion stimulated the immune system to form immune complex at the basement membrane of the glomeruli causing an immune complex associated glomerulonephritis along with tubulo-interstitial inflammation led to renal dysfunction in pyometra affected bitches (Shah *et al.*, 2017; Samantha *et al.*, 2018). On comparing liver enzymes, the mean values of SGOT and ALP were significantly higher at $P<0.001$ and $P<0.005$ level respectively, as compared to healthy control group.

Elevated SGOT might be coupled to some destruction in other tissues (Lakshmikanth *et al.*, 2016) and elevated ALP indicated that toxaemia originating from pyometra may inhibit the synthesis of liver enzymes and damage the hepatic membrane. The mean value of CRP was significantly ($P<0.001$) higher in pyometra group as compared to healthy control group. This might be due to pro-inflammatory cytokines induced biosynthesis of C-reactive protein (CRP) in hepatocytes which binds to the phosphocholine on micro-organisms to assist in complement binding and enhances phagocytosis by macrophages. In addition, elevated CRP levels in dogs with Systemic inflammatory response syndrome (SIRS) and sepsis have been linked with increased mortality. The mean value of total protein and albumin was significantly lower at ($P<0.001$) and ($P<0.05$) level, respectively in canine pyometra as compared to healthy control group. Hyperproteinaemia with a marked increase in globulin over albumin fraction is present in canine pyometra (Shah *et al.*, 2017). This increased total plasma protein value might be due to loss of albumin through the damaged kidneys and increased production of γ-globulin as a result of stimulation of defence mechanism against infection. However, Percent eosinophil, percent monocyte, MCV, MCH values, SGPT and bilirubin concentrations were found within the normal physiological

Table 1. Hematological parameters (mean±SE) in healthy control and pyometra group on day 0 (start of treatment)

S. No.	Parameters	Healthy group (n=11)	Pyometra group (n=27)
1.	Leucocyte (10^3/µL)	11.20±0.57	47.59±3.39**
2.	Neutrophil (%)	74.54±2.11	88.54 ±1.30**
3.	Lymphocyte (%)	15.51±1.02	6.97± 0.30**
4.	Monocyte (%)	1.93±0.78	2.02±0.23
5.	Eosinophil (%)	2.07±0.73	1.46±0.24
6.	Hb (g/dL)	15.25±0.55	10.33±0.52**
7.	TEC (10^6/µL)	6.22±0.18	4.81±0.23*
8.	HCT (%)	45.77±1.65	31.86± 1.76**
9.	MCV (fL)	73.45±1.06	64.01±1.82
10.	MCH (pg)	24.3±0.40	21.79± 0.79
11.	Platelet (10^3/µL)	351.18±10.74	197.31±21.16**

Mean within a row differ significantly (p**<0.001, p*<0.05)

Table 2. Serum biochemical parameters (Mean±SE) in healthy control and pyometra group on day 0 (start of treatment)

S. No.	Parameters	Healthy animals (n=11)	Pyometra (n=27)
1	Blood urea (mg/dL)	19.06± 1.53	83.93± 13.05*
2	Creatinine (mg/dL)	1.03±0.068	2.33±0.37
3	SGOT (µ/L)	14.18±0.18	52.64±6.14*
4	SGPT (µ/L)	44.64±7.29	64.65±8.13
5	ALP (µ/L)	67.67±9.96	238.29±22.96**
6	Bilirubin (mg/dL)	0.4±.01	0.6±0.3
7	CRP (mg/dL)	2.56±1.34	69.7±3.52**
8	Total protein (g/dL)	8.15±0.27	6.12±0.11**
9	Albumin (g/dL)	2.75 ±0.07	2.19±0.12*

Mean within a row differ significantly (p**<0.001, p*<0.05)

range in pyometra group.

The mean values of different haematological parameters were recorded at day 0 and day 7 and depicted in table 3. Total leucocyte count and % neutrophil were significantly (P<0.01) decrease from day 0 to day 7 in Group II and III. Percent lymphocyte was significantly (P<0.01) increase from day 0 to 7 in both the treatment group. This could be due to the evacuation of pus from the uterus by the effect of prostaglandin and antibiosis. The present finding was supported by (Shah *et al.*, 2017; Vijay *et al.*, 2021). Haemoglobin content and platelet count were significantly (P<0.05) increase from day 0 to 7 in both treatment groups. This might be due to the fact that reduction in septicemia/toxaemia led to a bring down suppressive effect on erythropoiesis in the bone marrow along with other factors which are involved in anaemia.

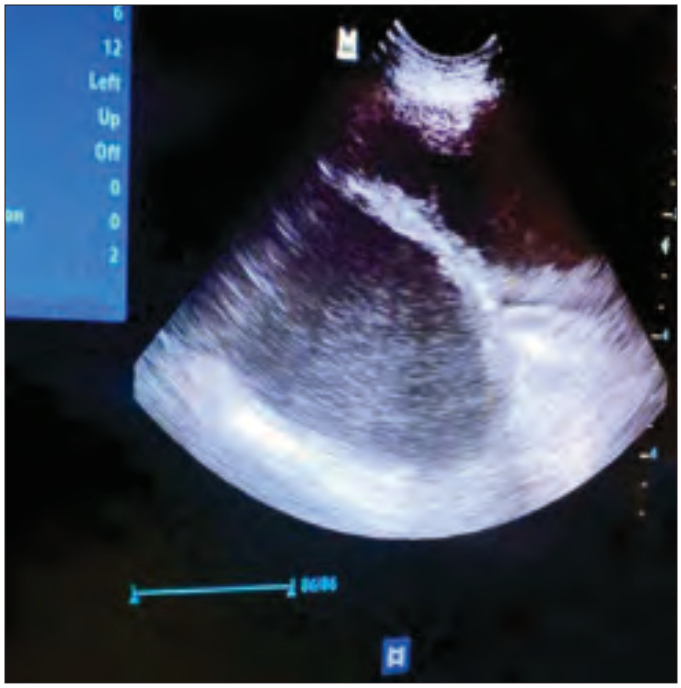

Fig. 1. Ultrasonography image showing severe distension of uterus with hyperechoic content

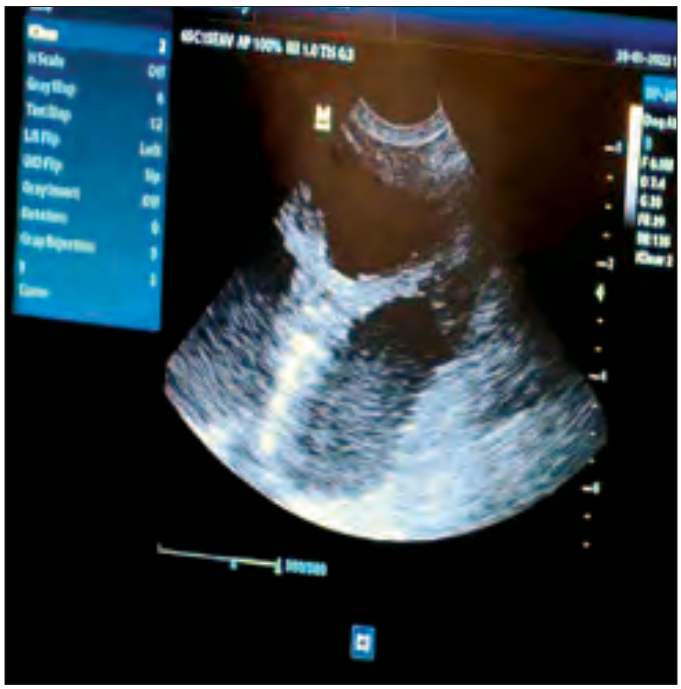

Fig. 2. Ultrasonography image showing hyperechoic content in uterus along with irregular endometrial surface

This observation was commensurate with the previous reports by (Shah *et al.*, 2017; Vijay *et al.*, 2021). This may be due to the reversal of toxaemia had reduced adverse effects on thrombocytes. This study was supported by (Shah *et al.*, 2017; Vijay *et al.*, 2021). However no significant difference was observed in TEC and HCT% from day 0 to 7.

The mean values of different biochemical parameters were recorded at day 0 and day 7 and depicted in table 4.

Table 3. Hematological parameters (Mean±SE) in different pyometra groups on day 0 (start of treatment) and day 7 (after the end of treatment)

Parameters	Days	Group Il (n=13)	Group Ill (n=14)
WBC (10^3/µL)	Day 0	50.43±7.26	42.14±5.72
	Day 7	14.70±0.63**	20.49±0.92*
Neutrophils (%)	Day 0	89.92±0.01	87.78±0.02
	Day 7	79.38±0.05**	86.03±0.01
Lymphocyte (%)	Day 0	6.47±0.03	9.45±0.02
	Day 7	17.5±0.01**	12.87±0.01**
Monocyte (%)	Day 0	2.17±0.21	1.74±0.31
	Day 7	2.01±0.01	1.518±0.01
Eosinophils (%)	Day 0	1.44±0.03	1.04±0.2
	Day 7	1.11±0.01	0.8±0.02
Hb (g/dL)	Day 0	11.95±0.72	10.35±1.19
	Day 7	13.6±0.61*	12.34±0.80*
TEC (10^6/µL)	Day 0	5.5±0.28	4.91±0.58
	Day 7	6.3±0.33	5.37±0.43
HCT (%)	Day 0	38.51±3.13	33.65±3.71
	Day 7	40.51±1.89	36.30±2.42
MCV (fL)	Day 0	65.06±1.43	65.07±2.21
	Day 7	61.95±2.29	67.20±3.14
MCH (pg)	Day 0	21.46±0.91	22.66±0.99
	Day 7	21.59±0.41	23.63±0.91
Platelet (10^3/µL)	Day 0	202.44±45.24	191.54±48.27
	Day 7	311.50±57.03*	260.09±39.56*

Mean within group differ significantly (p**<0.001, p*<0.05)

Blood Urea Nitrogen and creatinine values were significantly (P<0.05) decrease from day 0 to 7 in both treatment groups. This finding was supported by (Shah *et al.*, 2016; Vijay *et al.*, 2021). SGOT and ALP concentration were significantly (P<0.05) decrease from day 0 to 7 in Group II and III. However, no significant difference was observed in SGPT value from day 0 to 7. CRP concentration was significantly (P<0.01) decrease from day 0 to 7 in both treatment groups. Total protein and albumin was also significantly (P<0.05) decrease before and after the end of treatment in both treatment groups. This could be due to the reversal of toxaemia/sepsis. This finding was also supported by (Shah *et al.*, 2017; Vijay *et al.*, 2021).

Group III showed less improvement in comparison to Group II as confirmed by haematology, vaginal discharge in artificial insemination sheath and ultrasonography. Further treatment was extended in this group for 12-14 days and the biochemical parameters were reached to almost normal physiological range. The success of

Table 4. Serum biochemical parameters (Mean±SE) in different pyometra groups on day 0 (start of treatment) and day 14

Parameters	Days	Group Il (n=13)	Group Ill (n=14)
BUN (mg/dL)	Day 0	64.82±26.60	58.38±9.56
	Day 7	24.58±0.73	21.44±9.56*
Creatinine (mg/dL)	Day 0	1.37±0.1	1.36±0.17
	Day 7	0.70±0.09*	0.77±0.05*
SGOT (u/L)	Day 0	62.04±16.91	40.22±5.42
	Day 7	13.45±0.42*	15.82±0.87*
SGPT (u/L)	Day 0	61.44±22.38	28.48±2.48
	Day 7	36.60±10.76	33.61±5.92
ALP (u/L)	Day 0	196.02±29.50	192.41±37.71
	Day 7	84.08±6.29*	124.05±13.89*
Bilirubin (mg/dL)	Day 0	0.6±0.05	0.5±0.01
	Day 7	0.5±0.03	0.4±0.02
CRP (mg/dL)	Day 0	67.45±3.1	69.45±2.7
	Day 7	8.45±1.5**	10.34±1.4**
Total protein (g/dL)	Day 0	7.93±0.63	8.34±0.71
	Day 7	6.18±0.20*	7.01±0.26*
Albumin (g/dL)	Day 0	2.98±0.21	2.08±0.21
	Day 7	2.09±0.09*	2.39±0.17*

Mean within group differ significantly (p**<0.001, p*<0.05)

treatment was evaluated with improved activity and appetite, a change in the nature of discharge from haemorrhagic pus like to serous along with ultrasonography. Prolong treatment of 12-14 days was also supported by (Gabor *et al.*,1999).

CONCLUSION

Group II & III showed success rate of 84.61 and 78.58%, respectively. In pyometra affected cases haematology reveals leucocytosis along with neutrophilia count and lymphocytopenia. Anaemia was evident by decreased TEC, haemoglobin concentration. Increased values of BUN and creatinine indicate the decreased efficiency of kidneys to remove nitrogenous wastes from circulation. Acute phase reactions indicated by elevated CRP and decreased albumin. Group II having $PGF_{2\alpha}$S/c, prolactin inhibitor and anti-progesterone agents showing maximum beneficial effect and recovery of pyometra as revealed by USG and haematology after the end of treatment. Group III having $PGF_{2\alpha}$ via intravaginal route showed minimal/no side effect but duration of treatment was prolonged. Complete clinical recovery was not seen in dogs suffering with CEH-Pyometra complex, so they were shifted to ovariohysterectomy.

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