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Haematological evaluation of medically treated cases of pyometra in dogs*

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Abstract

Haematological evaluation of pyometra-affected dogs, treated under different medical protocols revealed, decreased TEC (4.34±0.31 to 4.92±0.19×10^6/mm^3), leucocytosis (26.68±1.38 to 39.30±4.49×10^3/mm^3),neutrophilia(82.50±0.63to 83.38±0.46%), lymphopenia(10.25±0.41 to 11.88±0.61%), reduced VPRC (26.38±1.21 to 29.85±1.17 %) and decreased Hb (8.11±0.14to 9.04±0.45g/dL) on the day of admission. Other differentials and thrombocyte counts were within normal limits. All parameters returned to normal after medical treatment within 15 days of initiation of treatment, except TEC and Hb, which also showed improvement on different days of observation during and after treatment. Haematological changes were parallel to clinical recovery.

Key words: *Haematology, medical management, pyometra, dog*

Scientific breeding in canines has gained importance as dog rearing has become popular and is now a lucrative business. In this scenario, addressing reproductive problems indogs is inevitable in small animal practice. Pyometra is the most prevalent life threatening reproductive disorder in dogs. Even though, ovarohysterectomy is the routine treatment of choice, medical therapy is an option in young, valuable dogs meant for breeding.Haematology during different days of treatment can be used as a tool in assessing the response to treatment and its outcome in pyometra-affected dogs.Therefore the present study was designed to evaluate various haematological parameters in medically treated, pyometra-affected dogs under four different therapeutic protocols.

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Materials and methods

Female dogs presented with history and symptoms of pyometra were subjected to detailed clinico-gynaecological, laboratory and ultrasonographic evaluation for confirmation. Thirty-two clinically stable dogs below six years of age were selected and randomly allotted into four different groups (Group I to IV) of eight dogs each.

Mifepristone was administered orally @ 2.5 mg/kg body weight bid for five days in all dogs. In Group I dogs, cloprostenol @ 5µg/kg body weightwas given subcutaneously on every third day, from 48 h after commencement of mifepristone administration. In Group II dogs, cabergoline @ 5µg/kg body weight once daily orally was administered from first day of treatment. Group III dogs were treated similar to group II. In addition, cloprostenol was administered subcutaneously @ 5µg/kg body weight once daily on every third day, from 48 h after initiation of treatment. In Group IV dogs, dinoprosttromethamine was administered 48 h after the first dose of mifepristone, by incremental doses (i.e.,10 µg/kg body weight subcutaneously thrice on first day, 25µg/kg body weightthrice on second day and 50 µg/kg body weightthrice on subsequent days). In all groups, treatment was continued till complete emptying of the uterus.

Supportive therapy with intravenous fluid and antibiotics was initiated in all cases according to the clinical condition and modifications were made as per the progress of the conditionand results of culture and sensitivity studies of anterior vaginal swab collected.

Blood samples were collected on day 0, 3, 9 and 15 of treatment into EDTA vaccutainer tubes and parameters like total erythrocyte count (TEC, $\times10^6/mm^3$), total leucocyte count (TLC, $\times10^3/mm^3$), thrombocyte count ($\times10^3/mm^3$), volume of packed red cells (VPRC, %) and haemoglobin concentration (Hb, g/dL) were assessed using automatic haematology analyser (Mythic 18 Vet, Switzerland). Blood smears were prepared and differential count (DC, %) was assessed. Tabulated data were analysed statistically (Snedecor and Cochran, 1994) using one way ANOVA in SPSS version 20.

Results and discussion

Haematological parameters were evaluated on the day of admission, before initiating treatment and were again repeated on day 3, 9 and 15 of treatment.

Total erythrocyte count (TEC)

Mean TEC($\times10^6/mm^3$) of pyometra affected dogs under different medical treatment groups, on different days of observation are presented in Table 1.

The TEC was lower than normal range of 5.5 to $8.5\times10^6/mm^3$ on all the days of observation in all the treatment groups. Low values of 4.85 ± 1.47 (Patil*et al.*, 2013), 4.68+/-0.27 (Chinnu et al., 2017) and 4.99 ± 1.01 (Samantha *et al.,* 2018) inpyometra-affected dogs were reported earlier also.

Decreased erythropoiesis due to toxic suppression of the bone marrow and loss of erythrocytes into the uterine lumen in pyometra cases was attributed as the reason for reduced erythrocyte count (Hagman *et al.,* 2014; Samantha *et al.,* 2018). Short life of circulating erythrocytes due to the effect of toxins was also attributed as reason for low TEC (Hagman *et al.,* 2014; Samantha *et al.,* 2018).

Although not significant, there was an increasing trend in TEC from day 0 to 15, which might be an indication of favourable response to medical treatment; review on a later date would give a better status of erythrocyte count. Patil*et al.* (2013) also reported significant increase in TEC from 4.85 ± 1.47 to 6.31 ± 0.94 before and after medical treatment. Chinnu (2016) reported increase in TEC from 4.75 ± 0.22 to 7.47 ± 0.44, by 21 days, after treatment using the same drug combination as in group IV.

Total leucocyte count (TLC)

Mean TEC ($\times10^3/mm^3$) of pyometra affected dogs on different days of observation are presented in Table 2.

Leucocytosis was noticed on day 0 in

Table 1. Mean TEC on different days of observation in different treatment groups (n= 32)

Group (n = 8)	Total erythrocyte count (×10⁶/mm³)			
	Day 0	Day 3	Day 9	Day 15
I	4.40±0.38	4.56±0.31	4.87±0.39	5.21±0.35
II	4.42±0.41	4.56±0.40	4.71±0.37	4.89±0.34
III	4.92±0.19	5.09±0.19	5.28±0.21	5.52±0.18
IV	4.34±0.31	4.49±0.30	4.69±0.25	5.00±0.28

No significant difference between groups in any of the days of observation and within group between days of observation (Tukey HSD, p>0.05)

Table 2. Mean TLC on different days of observation in different treatment groups (n= 32)

Group (n = 8)	Total leucocyte count (×10³/mm³)			
	Day 0	Day 3	Day 9	Day 15
I	28.54±1.96 ^{a,x}	21.98±0.87 ^{a,y}	18.71±0.49^{a,yz}	16.38±0.52 ^{a,z}
II	39.30±4.49^{a,x}	28.95±2.68 ^{a,xy}	20.56±1.26^{a,yz}	15.69±0.93 ^{a,z}
III	26.68±1.38 ^{a,x}	19.43±1.18 ^{a,y}	11.69±0.31^{b,z}	10.18±0.34 ^{b,z}
IV	31.43±6.75 ^{a,x}	22.56±4.94 ^{a,xy}	14.19±1.31^{b,y}	11.64±0.46 ^{b,y}

^{a,b}Different superscripts between rows indicate significant difference (Tukey HSD, p<0.05)

^{x,y}Different superscripts within row indicate significant difference (Tukey HSD, p<0.05)

Table 3. Neutrophil per cent on different days of observation in different treatment groups (n=32)

Group (n=8)	Neutrophil %			
	Day 0	Day 3	Day 9	Day 15
I	83.13±0.64^{a,x}	79.88±0.64 ^{a,x}	75.13±1.04 ^{a,y}	72.13±0.74 ^{a,z}
II	82.63±0.46 ^{a,w}	79.63±0.63^{a,x}	75.00±0.89^{a,y}	70.63±0.73^{a,z}
III	83.38±0.46^{a,x}	78.38±1.18^{a,x}	73.13±1.25^{a,y}	70.25±0.73^{a,z}
IV	82.50±0.63^{a,w}	79.50±0.60^{a,x}	75.13±0.64^{a,y}	70.75±0.59^{a,z}

^{a}Similar superscript between rows indicates no significant difference (Tukey HSD, p>0.05)

^{w,x,y,z}Different superscripts within row indicate significant difference (Tukey HSD, p<0.05)

Table 4. Lymphocyte per cent on different days of observation in different groups

Group (n=8)	Lymphocyte %			
	Day 0	Day 3	Day 9	Day 15
I	10.25±0.41 ^{a,w}	14.25±0.82 ^{a,x}	20.25±1.00 ^{a,y}	23.75±0.59 ^{a,z}
II	11.00±0.57^{a,w}	15.38±0.78^{a,x}	21.38±1.02^{a,y}	26.13±0.81^{ab,z}
III	10.38±0.56^{a,x}	15.75±1.49^{a,y}	23.88±1.30^{a,z}	27.25±0.77^{b,z}
IV	11.88±0.61^{a,w}	17.25±0.59^{a,x}	22.63±0.78^{a,y}	27.38±0.56^{b,z}

^{a,b}Different superscripts between rows indicate significant difference (p<0.05)

^{w,x,y,z}Different superscripts within row indicate significant difference (Tukey HSD, p<0.05)

all the treatment groups, indicates the existence of inflammatory process. Similar higher values of 30.45 ± 21.72 (Patil*et al.*, 2013), 29.22 ± 3.47 (Lakshmikanth*et al.,* 2016), 29.06 ± 0.87 (Shah *et al*., 2016) and 27.82 ± 11.39 (Samnatha*et al.*, 2018) have been reported in previous studies. Inflammatory leucogram with marked leucocytosis was reported in pyometra by many authors (Enginler *et al.,* 2014; Prasad*et al.,* 2017; Hagman, 2018),whichwas due to an aggressive bone marrow response to combat the infection.

Normal leucocyte count among pyometra-affected dogs was also reported (Verstegen *et al.*, 2008; Krekeler, 2010). Increase in leucocyte count was proportional to severity of disease (Prasad *et al.,* 2017); pyometra cases with Gram positive bacterial infection showed a significantly less severe left shift than the cases of Gram negative pyometra (Fransson, 2003).

Significant reduction ($p < 0.05$) in TLC was observed from day 3 onwards in group I,

Table 5. VPRC per cent on different days of observation in different groups (n=32)

Group (n=8)	VPRC(%)			
	Day 0	Day 3	Day 9	Day 15
I	26.38±1.21 ^{a,x}	31.48±1.53 ^{a,xy}	36.55±1.41^{a,yz}	38.25±1.26 ^{a,z}
II	28.08±0.81 ^{a,x}	31.33±1.06 ^{a,xy}	35.61±1.14 ^{a,yz}	39.99±1.69 ^{a,z}
III	28.69±1.19 ^{a,x}	31.73±0.92 ^{a,x}	35.54±0.97 ^{a,y}	38.44±0.33^{a,y}
IV	29.85±1.17 ^{a,x}	31.85±0.93^{a,x}	35.60±0.93^{a,y}	38.61±0.38^{a,y}

^{a,} Similar superscript between rows indicates no significant difference (Tukey HSD, p>0.05).

^{x,y,z}Different superscripts within row indicate significant difference (Tukey HSD, p<0.01)

Table 6. Mean haemoglobin concentration on different days of observation in different treatment groups (n=32)

Group (n=8)	Haemoglobin concentration(g/dL)			
	Day 0	Day 3	Day 9	Day 15
I	8.93±0.25 ^{a,x}	9.74±0.34^{a,xy}	10.64±0.48^{a,y}	11.20±0.41^{a,y}
II	8.69±0.58^{a,x}	9.43±0.65^{a,x}	10.05±0.73^{a,x}	10.90±0.57^{a,x}
III	9.04±0.45^{a,x}	9.73±0.52^{a,x}	10.60±0.47^{a,xy}	11.45±0.28^{a,y}
IV	8.11±0.14^{a,w}	9.16±0.35^{a,x}	10.35±0.23^{a,y}	11.59±0.29^{a,z}

^{a}Similar superscript between rows indicates no significant difference (Tukey HSD, p>0.05)

^{x,y}Different superscripts within row indicate significant difference (Tukey HSD, p<0.01)

III dogs; from day 9 onwards in group II and IV dogs, indicating favourable response to medical treatment. TLC came to normal range of 6 – 16 $\times 10^3/mm^3$,by day 15 in group I & II and by day 9 in group III and IV. England *et al.* (2007) reported return to normal leucogram by 10-15 days, in medically treated dogs using cloprostenol and cabergoline. Jena *et al*. (2013) reported decrease in TLC from 35.56 ± 8.36 to 11.46 ± 2.63, after cabergoline-cloprostenol combination treatment for seven days. Renukaradhya (2011) reported decrease in TLC from 38.21 ± 5.04 to 12.89 ± 2.66, by day 9, after antiprogestin-$PGF_{2\alpha}$ combination treatment. Shah *et al*. (2016) reported decrease in TLC from 20.00±1.47 to normal range (10.50 ± 0.64), by day 7, after mifepristone-dinoprost combination treatment for seven days. Chinnu (2016) reported decrease in TLC from 24.25 ± 2.80 to normal range (14.45 ± 0.82) by 14 days after combination treatment using cabergoline, mifepristone and cloprostenol. Early attainment of normal leucogram in group III may be because of the combined action of mifepristone, cabergoline and cloprostenol. Combined action of cabergoline and cloprostenol causes early luteolysis, cervical relaxation and uterine contraction, helping in better drainage of uterine contents. Once the source of stimulation of immune system is removed, return to normal leucogram occurs. In group IV dogs, frequent injections of dinoprost would have helped in better recovery due to effective luteolysis and uterine contractions.

Differential leucocyte count

Mean neutrophil per cent among pyometra-affected dogs under different medical treatment groups, on different days of observation are presented in Table 3.

Neutrophiliawas noticed in all the treatment groups on day 0. Similar values of 82.4 ± 4.47 (Patil*et al.*, 2013), 82.67 ± 1.94 (Chinnu, 2016) and 84.6 ± 5.33 (Samnatha*et al.*, 2018) were reported earlier. It was reported that leucocytosis in pyometra cases was always due to an increase in neutrophils (Jitpean*et al*., 2014). The purulent exudate present in the uterus exerts a chemotactic effect so that increased granulopoesis occurred and this resulted in neutrophilia (Singh *et al*., 2006).

Significant decrease ($p < 0.05$) in neutrophil per cent to normal range of 60-77 per cent was noticed from day 9 onwards in group I and III. In group II and IV, such decrease was noticed from day 3 onwards, reaching normal range by day 9. The values reached normal range by day 9 in all groups. Decreasing

trend in neutrophil per cent indicates the reduction of inflammation in response to medical treatment. Jena *et al*. (2013) reported decrease in neutrophil per cent from 78.28 ± 2.37 to 65.71 ± 0.81, after cabergoline-cloprostenol combination treatment for seven days. Shah *et al*. (2016) reported decrease in neutrophil per cent from 78.00 ± 0.71 to 68.75 ± 0.85, by day 7, after mifepristone-dinoprost combination treatment for seven days. Chinnu (2016) reported decrease in neutrophil per cent from 87 ± 0.97 to 71.67 ± 0.56, by 21 days after combination treatment using cabergoline, mifepristone and cloprostenol.

Mean lymphocyte per cent among pyometra-affected dogs under different medical treatment groups, on different days of observation are presented in Table 4.

Lymphocyte per cent on day 0 (ranging from 10.25 ± 0.41 to 11.88 ± 0.61) was below the normal range of 12-30 per cent. Similar values of 11.00 ± 1.43 (Jena *et al*., 2013) 10.5 ± 0.67 (Chinnu, 2016) and 10.5 ± 4.74 (Samnatha*et al.*, 2018) were reported earlier. Lymphopenia was either due to suppression of immune system, caused by endotoxaemia or due to an absolute neutrophilia (Singh *et al.,* 2006).Decrease in lymphocyte count was directly proportional to severity of disease (Prasad *et al.,* 2017).

Significant increase in lymphocyte count to normal range by day 3 was noticed, which might be due to the control of infection by the medical treatment adopted. Jena *et al*. (2013) reported increase in lymphocyte per cent from 11.00 ± 1.43 to 26.14 ± 0.86, after cabergoline-cloprostenol combination treatment for seven days. Renukaradhya (2011) reported increase in lymphocyte per cent from 8.42 ± 2.35 to 15.00 ± 1.673, by day 4, after antiprogestin-$PGF_{2\alpha}$ combination treatment. Chinnu (2016) reported increase in lymphocyte per cent from 10.5 ± 0.6 to 15.17 ± 1.08 by seven days after combination treatment using cabergoline, mifepristone and cloprostenol.

Per cent of monocytes on the days of observation was within normal limits of 3 to 10 per cent.Similar values among pyometra-affected dogs, was reported by Patil*et al.* (2013), Lakshmikanth*et al*. (2016) and Samantha *et al*. (2018).Monocytosis was reported in pyometra by many authors (Verstegen*et al,* 2008;Hagman, 2018), which was attributed tothe chronic nature of the suppurative process (Singh *et al*., 2006). Per cent of eosinophils on the days of observation was within normal limits of 2 – 10 per cent.Similar values among pyometra-affected dogs, ranging from 1.60 ± 0.45 to 2.05 ± 0.76 per cent were reported by Gupta *et al*. (2013) and Lakshmikanth*et al*. (2016). Per cent of basophils on the days of observation was within normal limits. Similar values among pyometra-affected-dogs were reported by Patil*et al.* (2013) and Lakshmikanth*et al*. (2016).

Thrombocyte count

Thrombocyte count was within normal limits of 200 – 500 $\times 10^3/mm^3$ on all the days of observation in all the groups. Almost similar values were reported by Patil*et al*. (2013)and Shah *et al*. (2016).

A decline in thrombocyte count among pyometric dogs has been reported previously (Fransson, 2003; Chinnu, 2016; Samantha *et al.,* 2018). Endotoxic effects on bone marrow could interfere with the synthesis of thrombocytes, leading to thrombocytopenia.In the present study, thrombocytes count were within normal range, probably because seriously affected dogs, having chances of severe affection, were removed from the study. Thrombocyte count has been shown to significantly differ between dogs with and without sepsis (Hauptman *et al.,* 1997).

Volume of packed red cells (VPRC)

Mean per cent of VPRC among pyometra-affected dogs under different medical treatment groups, on different days of observation are presented in Table 5.

The VPRCon day 0 (ranging from 26.38±1.21 to 29.85 ± 1.17 %) was found to be lower than the normal range (37 – 55 %). Similar lower VPRC per cent of 35.14 ± 2.10, 29.73 ± 8.48 and 30.19 ± 6.20 was reported earlier (Gupta *et al.,* 2013 andSamantha *et al*., 2018). The VPRC value less than 35 per cent were considered as anaemic (Fransson, 2003;

Verstegen*et al.,* 2008) and 36 – 40 per cent was considered to reflect borderline anaemia, which was masked by dehydration (Hagman*et al*., 2006). The VPRC values below 35 – 38 per cent were noticed in 60 per cent of pyometra cases (Fransson, 2003; Enginler*et al.,* 2014). Low VPRC in the present study might be a reflection of reduced TEC, caused by toxic suppression of the bone marrow and consequent reduction in erythropoiesis.

Significant increase ($p < 0.05$) in VPRC was observed from day 9 onwards in all the groups, which came to normal range by day 15. Increase in VPRC might be due to the increase in TEC. Jena *et al*. (2013) reported increase in VPRC from 34.03 ± 0.89 to 40.83 ± 1.09 per cent, after cabergoline-cloprostenol combination treatment for seven days. Chinnu (2016) reported increase in VPRC from 33.0 ± 2.49 to 38.68 ± 1.69 per cent by 14 days after combination treatment using cabergoline, mifepristone and cloprostenol.

Haemoglobin concentration

Mean haemoglobin concentration (g/dL) among pyometra-affected dogs on different days of observation are presented in Table 6.

Haemoglobin on all the days of observation (ranging from 8.11 ± 0.14to 11.59 ± 0.29) was found to be lower than normal range of 12-18 g/dL.Lower values of 5.62 ± 0.32 (Shah *et al*., 2016) and 10.2 ± 2.24 g/dL (Samantha *et al.,* 2018)have been reported previously. Hagman (2004) recorded higher Hb of 13.6g/dL in pyometric dogs. In pyometra-affected dogs, iron deficiency could occur due to iron sequestration in the bone marrow as a result of acute phase protein- mediated reactions associated with inflammation. Lactoferrin and other acute phase reactants mediate an iron sequestration within the myeloid cells in the bone marrow, withdrawing iron from the normal erythropoiesis.

Haemoglobinconcentration was found to gradually increase on subsequent days of observation, indicating positive response to treatment, caused by control of inflammation. Highly significant increase ($p<0.01$) in Hb from day 3 onwards in group IV dogs indicates an improved erythropoisis in this group. Jena *et al*. (2013) reported increase in Hb from 11.10 ± 0.28 to 13.38 ± 0.33 g/dL, after cabergoline-cloprostenol combination treatment for seven days. Chinnu (2016) reported increase in Hb from 12.13 ± 0.62 to 14.38 ± 0.73 g/dLby seven days after combination treatment using cabergoline, mifepristone and cloprostenol.

The TEC, VPRC and Hb values in the present study indicated existence of anaemia among pyometra-affected dogs. Non-regenerative, normocytic, normochromic anaemia as well as microcytic hypochromic anaemia was reported by many researchers, among pyometra-affected dogs (Jitpean *et al.,* 2014;Lakshmikanth *et al*., 2016; Hagman, 2018). Loss of erythrocytes into uterine lumen (Hagman *et al.,* 2009), short life of circulating erythrocytes, concomitant iron deficiency (Hagman *et al.,* 2009) were contributing to anaemia. Dehydration often complicates evaluation of anaemia (Samantha *et al.,* 2018).

Considering the low TEC, VPRC and Hbon the day of initiation of treatment and also considering the absence of severe dehydration among the dogs selected for study, it was concluded that pyometra-affected dogs were suffering from anaemia. Hagman (2018) also reported anaemia in 55 per cent of pyometra cases.

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