C-REACTIVE PROTEIN EVALUATION OF MEDICALLY TREATED CASES OF PYOMETRA IN DOGS

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Abstract

The potential of biomarkers as diagnostic or prognostic tool in canine pyometra is under investigation. The CRP evaluation of pyometra-affected dogs revealed very high levels (128.51 ± 4.07 to 136.64 ± 6.77 µg/mL) on the day of admission. The levels returned to normal after medical treatment (10.00 ± 0.28 to 12.01 ± 2.49 µg/mL) in all the treatment groups by day 15 after initiation of treatment, which was in parallel to clinical recovery. The present study revealed that CRP can be considered as effective end point marker to evaluate efficacy of the treatment.

Key words : *CRP, medical management, pyometra, dog.*

Pyometra is recognised as the most prevalent and life threatening reproductive disorder among canines. The disease is associated with endotoxemia, sepsis, systemic inflammatory response syndrome (SIRS) and eventually death, if not diagnosed and treated promptly. Even though ovariohysterectomy (OHE) is the historical treatment for pyometra, medical management is an option in young, valuable dogs meant for breeding. The breeding life of bitch can be restored if the condition is diagnosed early. Significant prognostic changes in biochemical profile of pyomeric dogs are widely reported. The C-reactive protein (CRP), an acute phase protein is found to be elevated in pyometra affected dogs and its sequential measurements are used to assess post-operative recovery after OHE. Role of CRP in monitoring the progress of medical therapy needs to be critically evaluated. Therefore the present study was designed to evaluate the CRP levels in medically treated, pyometra-affected dogs under four different therapeutic protocols.

Materials and methods

Female dogs presented with history and symptoms suggestive of pyometra were subjected to detailed clinical, gynaecological, laboratory and ultrasonographic evaluation

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for confirmation of the condition. Thirty- two clinically stable dogs below the age of six years were included in the present study and randomly allotted into four different treatment groups (Group I to IV) of eight dogs each.

Mifepristone was administered orally @ 2.5 mg/kg body weight twice daily for five days in all dogs. In Group I dogs, mifepristone was followed by cloprostenol @ 5 µg/kg body weight subcutaneously on every third day, from 48 h after commencement of mifepristone administration. In Group II dogs, cabergoline @ 5 µg/kg body weight once daily orally was administered from first day of treatment onwards. 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 mifepristone administration. In Group IV dogs, mifepristone was followed by dinoprosttromethamine, 48 h after the first dose of mifepristone, by incremental doses (i.e.,10 µg/kg body weight subcutaneously thrice on first day, 25 µg/kg body weight thrice on second day and 50 µg/kg body weight thrice on subsequent days). In all groups, treatment was continued till complete emptying of the uterus, as confirmed by ultrasound examination.

Supportive therapy with intravenous fluid and antibiotics was initiated in all the cases according to the clinical condition of each case and necessary modifications were made as per the progress of the condition of the patient and results of culture and sensitivity studies of anterior vaginal swab collected. A volume of 5 mL peripheral blood samples were collected on day 0, 3, 9 and 15 of treatment from the cephalic vein into vaccutainers with clot activator. Sera samples were separated centrifuged and a minimum of 1.5 mL sera samples were aliquotted and stored at -20°C, for CRP analysis.

Results and discussion

Mean serum CRP concentration (µg/ml) among pyometra-affected dogs under different medical treatment groups, on different days of observation are presented in Table.

The CRP concentration was highly elevated on day 0 (ranging from 128.51 ± 4.07 to 136.64 ± 6.77 µg/mL), which decreased on subsequent days of observation, reaching normal levels by day 15. The concentration on day 0 was well above the previously reported normal range of 5 µg/mL (Caspi *et al.,* 1984), 13.2µg/mL (Yamamoto *et al*., 1994) and 5.20 ± 0.60 µg/mL (Lakshmikanth, 2016), clearly indicating the existence of inflammatory process. Mean CRP concentration of 61.4 µg/mL, 212.9 ± 17.3 µg / mL, 114.6 µg /mL and 81.00 ± 6.90 to 127.00 ± 11.00 µg/mL respectively, were reported by Yamamoto *et al.* (1993), Jitpean*et al*. (2014), Dąbrowski*et al.* (2015) and Lakshmikanth (2016) in pyometra dogs. Infection triggers both local and systemic immunological responses. These responses lead to the increased production of pro-inflammatory cytokines by activated macrophages and neutrophils, as the main signal for the induction of transcription factors for acute-phase proteins (APPs). The APP levels during the course of inflammation reflect the state of immune system activation (Dabrowski *et al.,* 2013).

In response to treatment, there was highly significant reduction ($p<0.01$)in CRP

Table 1. Serum CRP concentration (Mean ± SE) on different days of observation in different treatment groups (n=32)

Group (n=8)	Serum CRP concentration (µg/mL)			
	Day 0	Day 3	Day 9	Day 15
I	129.13±6.57 ^{a,w}	90.44±5.85 ^{a,x}	41.25±4.34 ^{a,y}	11.91±1.23 ^{a,z}
II	136.64±6.77^{a,w}	79.73±5.37^{a,x}	34.35±4.21^{a,y}	12.01±2.49^{a,z}
III	128.51±4.07^{a,w}	75.04±2.63^{a,x}	36.74±3.84^{a,y}	10.00±0.28^{a,z}
IV	131.95±3.42^{a,w}	77.63±3.54^{a,x}	42.94±4.74^{a,y}	11.21±0.59^{a,z}

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

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

concentration on all the days of observation from day 0 to 15, to a mean value ranging from 10.00 ± 0.28to 12.01 ± 2.49 µg/mL. A marked decrease in CRP concentration from 72.5 mg/L to 17.9 mg/L and from 86 mg/L to 33.2 mg/L was reported in two pyometra cases after treatment (Galezowski*et al*.,2010). Dąbrowski*et al.*(2015) reported a decrease to23.3 µg/mL, once inflammation was resolved. Lakshmikanth (2016) reported decrease in CRP concentration from 81.00 ± 6.90 to 30.00 ± 2.30 µg/mL in open-cervix pyometra and from 127.00 ± 11.00 to 39.00 ± 2.00 µg/mL, in closed-cervix pyometra, 10 days after surgical treatment.The CRP concentration was found to vary according to the intensity of inflammatory activity (Dabrowski*et al*., 2013; Enginler*et al.,* 2014) and hence CRP could be used as an end-point marker of treatment efficiency (Hagman, 2014). The kinetic properties of canine CRP during an acute phase response are characterized by a low concentration at normal homeostasis (Yamamoto *et al.,* 1994; Otabe*et al.,* 1998), a short lag-phase after the inflammatory stimulus of around four hours (Higgins *et al.,* 2003), reaching a peak in concentration after approximately 24 h and a quick normalization after the end of inflammatory stimulus (Yamamoto *et al.,* 1992). The findings of the present study revealed that estimation of serum CRP concentration could be utilised as an effective tool in the evaluation of treatment progress of canine pyometra.

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