RESEARCH ARTICLE
Open Access

Journal of Veterinary and Animal Sciences
ISSN (Print): 0971-0701, (Online): 2582-0605
https://doi.org/10.51966/jvas.2023.54.2.428-432

Uterine haemodynamics and band neutrophils as recovery markers in medical management of canine pyometra#

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Citation: Krishnan, A. S., Harshan, M. H., Jayakumar, C., Shibu, S. and Unny, M. N. 2023. Uterine haemodynamics and band neutrophils as recovery markers in medical management of canine pyometra. *J. Vet. Anim. Sci.* **54**(2):428-432
DOI: https://doi.org/10.51966/jvas.2023.54.2.428-432

Received : 11.10.2022 *Accepted : 04.02.2023* *Published: 30.06.2023*

Abstract

Canine pyometra is a hormonally mediated life-threatening uterine disease of canines, associated with bacterial infection and inflammation. The disease is characterized by the accumulation of pus in the uterus and systemic illness. The study was undertaken to assess the relevance of band cells in circulation and Doppler ultrasonography in the prognostic evaluation of medically managed canine pyometra. A significantly higher band of neutrophils were recorded among bitches presented with pyometra, which reduced to the physiologically normal range as treatment progressed in the animals which responded to the treatment. The resistive index, which was lower than the threshold value of 0.72, increased as the treatment progressed in the responsive animals and proved to be a reliable tool as a recovery marker.

Keywords: *Pyometra, resistive index, band neutrophils*

Canine pyometra is a life-threatening disease, which commonly affects intact dioetrual bitches (Verstegen *et al.,* 2008). The development of the disease is associated with gradual cystic changes in the endometrium along with the invasion of opportunistic pathogens. Ovariohysterectomy (OHE) has been the preferred treatment of choice for pyometra, as it results in the removal of the infected uterus and prevents the recurrence of the condition. But off late, the emphasis on maintaining the breeding potential of bitches and the availability of newer drugs, has led to greater interest in medical management of pyometra. Medical management also permits the conduct of

#*Part of MVSc thesis submitted to Kerala Veterinary and Animal Sciences University, Pookode, Wayanad, Kerala*

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OHE at a later date, when the bitch would be at a lesser risk for the anaesthetic and surgical procedures. As the condition is life-threatening and failures of medical management are possible, a marker would be helpful in assessing the progress of medical management. This could help the clinician in deciding when to opt out of medical management and select OHE so that the viability of the bitch is not compromised. Elevation of band neutrophils is a common finding in canine pyometra, which is suggestive of active bacterial infection (Vidya *et al.,* 2020). Previous reports have suggested a decline in band neutrophils as the infection subsided. Elevated uterine blood flow, vasodilation and angiogenesis were commonly noticed during an inflammation (Ozbay and Deveci, 2011). Doppler ultrasonography, a non-invasive technique, could provide insights into organ perfusion and could be used to detect uterine artery blood flow and tissue perfusion (Batista *et al*., 2016). Pyometra has been documented to be distinguished by increased endometrial vascularization and uterine arterial blood flow. Recent research (Batista *et al.,* 2016; Pati *et al.,* 2021) has also suggested Doppler ultrasonography as a differentiating tool between pyometra and cystic endometrial hyperplasia (CEH). Hence, the present research was undertaken to assess the changes in band neutrophils and haemodynamics of the middle uterine artery as assessed by Doppler ultrasonography in medically managed cases of canine pyometra.

Materials and methods

The study was conducted in a total of 24 bitches presented to the Teaching Veterinary Clinical Complex, Mannuthy and University Veterinary Hospital, Kokkalai, with history and symptoms suggestive of pyometra. The study period was from December 2021 to August 2022. The presented bitches were subjected to detailed clinical, gynaecological, laboratory and ultrasonographic evaluations for confirmation of the condition.

Bitches of breedable age (18 months-8 years), in which the owners wanted to preserve the breeding potential, were included in the study (G.S.R.496-E, 2017). Additionally, bitches not in the breedable age, but in which medical management was resorted to as a means of improving the general health before conducting OHE, were included in the study. Thus, from among the bitches with gynaecological issues 24 bitches were included in the study and subjected to detailed clinical examination, including haemato-biochemical and ultrasonographic evaluation. Haematological analysis was carried out using the ORPHEE Mythic 18 Vet CBC Machine and the Total Leucocyte Count (TLC) was recorded. Peripheral blood smears were prepared after collecting blood by puncturing the ear tip and stained with Leishman's stain for assessing the band neutrophils.

The B-mode trans-abdominal ultrasonographical examination was performed using a 5 to 7.5 MHz transabdominal probe (MyLab70 Vet, Esaote, Italy and Mindray DC-6 Vet, Shenzhen Mindray and Biomedical Electronics, China). The procedure was carried out with the animal in dorsal recumbency. The sector probe was placed on the abdomen and slowly moved anteriorly and laterally to view the urinary bladder as an acoustic window and the probe was fanned to locate the uterus and uterine horns (Fig 2). Colour Doppler ultrasonography was carried out to visualize middle uterine arteries at both sides of the uterine body in longitudinal section and pulsed-wave Doppler was performed to obtain the waveforms. The gate (sample volume) was positioned when the vessel with good colour signals could be identified. Subsequently, flow velocity waveforms were obtained with the pulsed-wave Doppler after performing angle correction, if required. Three consecutive waveforms with maximum Doppler shift were included in the study.

Medical management was initiated with a combination of mifepristone (dose 5 mg/kg BID) and misoprostol (either as 10 mg/kg BID oral or 3 mg/kg BID intravaginal, till emptying of the uterus) or mifepristone alone. The bitches were provided anti-prolactin (cabergoline, 5 µg/kg body weight OD for nine days, if the serum progesterone on the day of presentation was more than 2 ng/mL) and supportive therapy which included broad-spectrum antibiotic

(which was changed according to the initial response and results of antibiotic sensitivity test of anterior vaginal flora) and intravenous fluids. For the assessment of treatment response, the bitches were evaluated on days 3, 9 and 15 from the initiation of treatment.

In the group comprising failure of medical management, only two bitches could be included in the study as OHE in these two bitches was done post-15 days of onset of treatment, thus presenting us with an option of evaluating them for 15 days. In other bitches which did not respond to medical management, OHE was conducted immediately or within a few days of the presentation of the bitch with the disease. Hence, clinical evaluation of these bitches could be done only on the day of presentation, rendering these cases unsuitable for the study.

Results and discussion

Haematological parameters (TLC and band neutrophils) and Doppler hemodynamic changes in the middle uterine artery among the pyometra-affected bitches during the course of treatment are presented in Table 1.

Leukocytosis with marked left shift was observed on the day of presentation among all the pyometra-affected bitches (Fig 1). Leukocytosis during pyometra has been ascribed to the stimulation of bone marrow to release more immature neutrophils into the peripheral blood, resulting in marked neutrophilic leukocytosis with a shift to the left (Mojzisova *et al*., 2000; Chinnu *et al.,* 2017 and Vidya *et al.,* 2020). The increase in the number of immature neutrophils is reflected in an increase in band neutrophil proportion in the peripheral circulation (Bigliardi *et al*., 2004). The proportion of band neutrophils has been correlated with the severity of the infection (Kustritz, 2005). In the present study, it could be appreciated that by day 9 of the commencement of medical management, the band neutrophil proportion had reduced to the physiological normal values (0-3 per cent) and correspondingly, TLC values too approached the physiological normal (6-17×10^3/mm^3), suggestive of recovery from infection. The TLC attains normalcy as the infection is controlled (Unnikrishnan *et al.,* 2020). However, such a change in TLC and band neutrophils could not be appreciated in the bitches which failed to respond to medical management. Both the TLC and band neutrophils remained elevated above the physiological normal values in two bitches even after day 15 of the commencement of medical management. These two bitches were subjected to OHE at later days. Thus, a reduction of band neutrophils and their attainment of physiological values, when seen in conjunction with the lowering of TLC are suggestive of control of infection and improvement in the condition of the pyometra-affected bitches.

In the middle uterine artery haemodynamics, it could be noted that all the bitches affected with pyometra had RI values lower than 0.72 on the day of presentation (Fig. 3). Batista *et al*. (2016) had suggested that pyometra-affected bitches would have a lower RI (less than 0.72) in uterine artery than normal or CEH affected bitches. Veiga *et al*. (2012)

Table 1. Total leucocyte count (× 10^3 /mm^3), band neutrophils (per cent) and resistive index of the uterine artery in pyometra-affected bitches subjected to medical management

Days	Outcome of medical management	Day 0	Day 3	Day 9	Day 15
TLC	S (n=22)	28.97 ± 2.22	23.84 ± 3.31	14.80 ± 1.35	10.55 ± 0.75
	F (n=2)	41.41 ±21.31	28.7 ± 7.60	24.6 ± 1.90	21.7 ± 1.40
Band Neutrophils	S (n=22)	8.96 ± 1.51	6.13 ± 1.12	2.69 ± 0.43	1.16 ± 0.18
	F (n=2)	13.4 ± 5.40	8.9 ± 2.50	4.1 ± 0.10	5.025 ± 0.03
RI	S (n=15)	0.65 ± 0.01	0.70 ± 0.01	0.76 ± 0.01	0.78 ± 0.01
	F (n=2)	0.67 ± 0.02	0.67 ± 0.01	0.67 ± 0.02	0.66 ± 0.04

S: successful outcome to medical management, F: failure to respond to medical management. Physiological normal range, TLC: 6-17× 10^3 /mm^3; Band neutrophils: 0-3 per cent; RI, less than 0.72 is suggestive of pyometra.

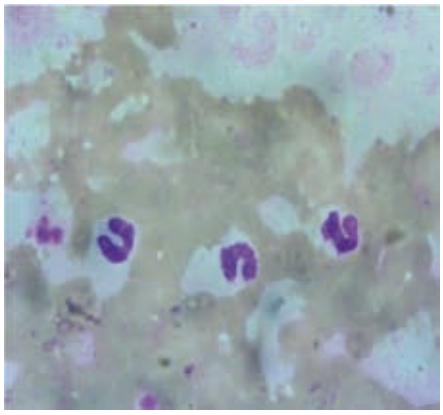

Fig 1. Microphotograph of peripheral blood smear from pyometra-affected bitches showing marked left shift (Leishman stain, ×1000)

reported an RI of 0.62 in pyometra-affected bitches. The RI of the uterine artery in anoestrus bitches was reported as 1.13 (Alvarez-Clau and Liste, 2005) and in dioestrus bitches as 0.99 (Veiga *et al*., 2012).

In the bitches responding to medical management, the RI values increased and reached the threshold value of 0.72 by day 9 of treatment and remained high (Fig. 3), which corresponded to the time of improvement as reflected by TLC and band neutrophil proportion. However, in the two bitches, which failed to show improvement to medical management, the RI remained low throughout the course of treatment.

Though RI was found to reflect the recovery of the bitch from pyometra, certain limitations were encountered for the recording of RI. Out of the 22 animals, which responded to the treatment, the haemodynamics could be assessed only in 15 of the bitches on all four days of observation (days 0, 3, 9 and 15). In the other seven bitches, haemodynamics could not be assessed on all four days of observation, due to animal movement, lowering of organ perfusion and other disturbances faced in a clinical setting.

Thus, it could be inferred that uterine artery haemodynamics offer adjunct diagnostic and prognostic possibilities in the therapeutic management of canine pyometra. The proportion of band neutrophils can also provide insights into the recovery in medically managed cases of pyometra.

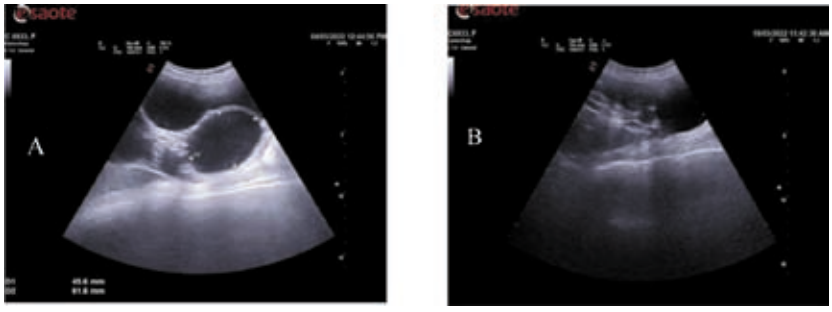

Fig. 2 B-mode ultrasound image of the uterus in a pyometra-affected bitch subjected to medical management (A- day of presentation, showing hypoechoic sacculations.; B – day 15 of commencement of medical management, showing complete evacuation of luminal contents)

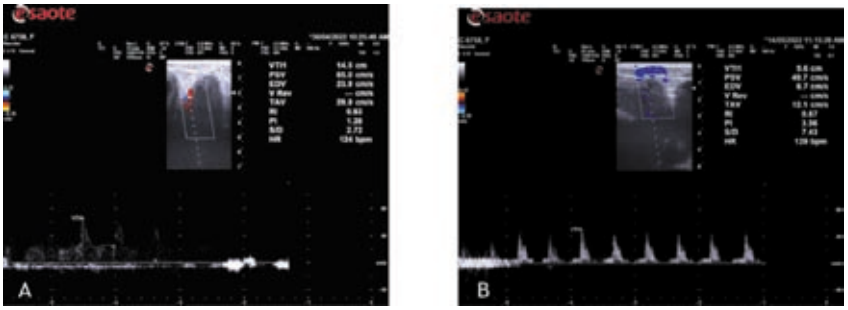

Fig. 3. Pulse wave Doppler graph of the middle uterine artery blood flow in a pyometra-affected bitch subjected to medical management (A- day of presentation, lower RI; B – day 15 of commencement of medical management, higher RI)

Conclusion

Evaluation of band neutrophils and Doppler haemodynamics indices of uterine artery during the course of treatment in pyometra-affected bitches can provide an assessment of clinical improvement and response to medical management. The option of OHE may be considered in those bitches, which fail to show an improvement in these indices following medical management.

Conflict of Interest

The authors declare that they have no conflict of interest.

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