RESEARCH ARTICLE
Open Access

Journal of Veterinary and Animal Sciences
ISSN (Print): 0971-0701, (Online): 2582-0605
https://doi.org/10.51966/jvas.2024.55.2.388-393

Response to medical management in cystic endometrial hyperplasia- pyometra affected bitches graded ultrasonographically for uterine changes

S. Rahul Ram*, H. M. Harshan, C. Jayakumar, R. S. Abhilash and R. Anoopraj

Department of Animal Reproduction, Gynaecology and Obstetrics
College of Veterinary and Animal Sciences, Mannuthy, Thrissur- 680 651
Kerala Veterinary and Animal Sciences University
Kerala, India

Citation: Rahul Ram, S., Harshan, H. M., Jayakumar, C., Abhilash, R. S. and Anoopraj, R. 2024. Response to medical management in cystic endometrial hyperplasia- pyometra affected bitches graded ultrasonographically for uterine changes. *J. Vet. Anim. Sci.* **55**(2):388-393
DOI: https://doi.org/10.51966/jvas.2024.55.2.388-393

Received: 21.10.2023 *Accepted: 18.03.2024* *Published: 30.06.2024*

Abstract

Canine cystic endometrial hyperplasia- pyometra complex (CEH-P) is a hormonal and bacteria mediated reproductive disorder of intact, sexually mature bitches. Though, ovariohysterectomy (OHE) is considered as the treatment of choice in CEH-P, the advent of novel therapeutics and need for conservation of breeding potential in the affected bitch, led to the exploration of medical management as an alternative option of treatment. Ultrasonography serves as an adjunct tool to diagnose and evaluate the condition. It can also be used to grade the affected uterus on the basis of endometrial changes. The present article investigates the efficacy of medical management in different grades of CEH-P, as assessed by ultrasonography. It was observed that though bitches with severe endometrial changes recovered clinically following medical management, the endometrial changes, as could be assessed with ultrasonography, persisted. The ultrasound grading of uterus could thus be used to assess the suitability of medical management in CEH-P affected bitches.

Keywords: *CEH-P, ultrasonography, grading of uterus, medical management*

Cystic endometrial hyperplasia – pyometra is regarded as a potential life-threatening disease condition in canine practice (Melandri *et al*., 2019). The disease usually affects middle to elderly, intact bitches (Agostinho *et al.,* 2014). Bacteria played a major role in development of pyometra, while hormones played a major role in development of cystic endometrial hyperplasia, and the latter had a predisposing effect on the former (Fransson and Ragle, 2003).

1. *MVSc scholar*
2. *Associate Professor*
3. *Associate Professor and Head*
4. *Assistant Professor*
5. *Assistant Professor, Department of Veterinary Pathology, CVAS, Mannuthy*

**Corresponding author: mail2rahulram@gmail.com, Ph. 8547142451*

Ovariohysterectomy is considered as the treatment of choice for pyometra as it leads to immediate removal of diseased uterus and the uterine content, with elimination of possibility of disease recurrence. However, OHE invariably leads to loss of fertility in the affected bitch. Additionally, surgical option may not be feasible in severely affected bitches, necessitating stabilization prior to surgery. These aspects as well as discovery of novel therapeutics like mifepristone and misoprostol, led to the development of medical management as an alternative modality of treatment. Bigliardi *et al*. (2004) used B-mode ultrasonography for grading of uterus in CEH-P affected patients and suggested the possibility that bitches with severe uterine changes may not respond favourably to medical management. Similar findings were reported by (Harshan *et al*., 2022), who noted differential response to medical management in ultrasonographically graded uterus in CEH-P. The present research emphasises on the assessment of ultrasonographic changes in CEH-P affected uterus and the response to medical management in such cases.

Materials and methods

The present study was conducted at Teaching Veterinary Clinical Complex, Mannuthy and University Veterinary Hospital, Kokkalai from November 2022 to August 2023. Female dogs of breedable age (2-8 years) presented with history and symptoms suggestive of cystic endometrial hyperplasia-pyometra complex (CEH-P) were subjected to detailed clinical, gynaecological, laboratory and ultrasonographic evaluations for confirmation of the condition. A total of 14 bitches, which had serum progesterone greater than 2 ng/mL, were included in the study. The bitches included in the study were subjected to reviews on 3rd, 9th and 15th day from the initiation of treatment.

The CEH-P affected bitches were allocated to treatment groups based on the B-mode transabdominal ultrasonographic findings. Bitches with normal endometrial surface, no or few small endometrial cysts and anechoic uterine content were classified under group I, while bitches with irregular endometrial surface, many and large endometrial cysts, hypertrophic or atrophic endometrium and hyperechoic uterine content were classified under group II.

Haematological evaluation of the animals under the study was performed using the ORPHEE Mythic 18 Vet CBC Machine and the parameters, total leukocyte count (TLC, × 10^3/µL), total erythrocyte count (TEC, × 10^6/µL), Neutrophil (%) were recorded. Guarded anterior vaginal swabs were taken from all affected bitches for culture and sensitivity assessment.

B-mode trans-abdominal ultrasonographic examination was performed using a 5 to 7.5 MHz transabdominal probe (MyLab70 Vet, Esaote, Italy). The bitch was placed on lateral recumbency for the examination. Urinary bladder served as an acoustic window and the probe was fanned to locate the uterus. Region of the uterus where maximum uterine diameter present was located and uterine horn diameter (UHD, cm) was measured. 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. Resistive Index (RI) values in the middle uterine arteries of all the animals were recorded. All the parameters were repeated on subsequent days (3rd, 9th and 15th day after initiation of treatment).

Medical management was initiated with a combination of cabergoline at a dose rate of 5µg/kg b.wt. SID PO for nine days; mifepristone at a dose rate of 5 mg/kg b.wt. BID PO till complete emptying of uterus, as confirmed by ultrasound examination; misoprostol at a dose rate of 10 µg/kg b.wt. BID PO from day 3 till complete emptying of the uterus. Antibiotics and supportive treatment were given to all CEH-P affected bitches as required. Based on culture and sensitivity test

and/or responsiveness to treatment, changes in the antibiotic course were made on 3rd day after initiation of treatment. Observations were analysed using independent sample T- test.

Results and discussion

Haematological parameters (TLC and Neutrophils), B- mode ultrasonographic parameters (UHD, UWT) and Doppler haemodynamic parameters of the middle uterine artery (RI) among the animals under the study during the course of treatment were recorded and presented in Table 1.

Leukocytosis and neutrophilia with left shift were present in both groups on the day of presentation, indicative of an infection. A considerable reduction in these parameters to physiologically normal levels was observed in both the groups by day 9 of treatment. Neutrophilic leukocytosis with left shift was indicative of immature neutrophils and was typical findings of pyometra (Unnikrishnan *et al.,* 2020; Vidya *et al*., 2020; Hagman, 2023). The left shift indicated an aggressive bone marrow consequent to increased stress on the immune system (Sevelius *et al*., 1990) and response of the body to counter the active infection (Demeli and Meyer, 2023). In the present study, the reduction in TLC and neutrophil count to physiological normal values were recorded by the third review (day 9) in both the groups, indicative of recovery and improvement in condition. There was no significant difference recorded between the two groups with regards to recovery in terms of TLC and neutrophil count.

It was noted that by day 15 of medical management, even though uterine horn diameter in both the groups had undergone considerable reduction, it was significantly higher in group II when compared to bitches in group I. This finding suggested a lack of recovery in terms of endometrial changes in CEH-P affected bitches of group II.

Bigliardi *et al*. (2004) had classified CEH-P affected uterus into four categories based on endometrial integrity, uterine contents, and degree of CEH changes as observed with ultrasonography. Those under group A, lacked cysts and had normal endometrial surface with anechoic uterine fluid. Those under group B had small and sparse cysts, a normal endometrial surface, and anechoic uterine content. Group C was characterised by the presence of multiple large cysts, an uneven surface, and thickened endometrium, while those under group D had uneven, hypertrophic or atrophic endometrium, and hyperechoic uterine content with multiple large cysts. Harshan *et al*. (2022) had stated that uterus with severe changes, which came under group C and D as per Bigliardi *et al.* (2004) and which corresponded to group II of the present study, responded poorly to medical management in terms of endometrial recovery.

Table 1. Mean TLC, Neutrophil, Uterine horn diameter and Resistive index in middle uterine artery in cystic endometrial hyperplasia – pyometra affected bitches during the course of medical management

Days	Groups	Day 0	Day 3	Day 9	Day 15
TLC ($\times 10^3/\mu L$)	Group I	27.24 ± 4.33	25.87 ± 4.42	15.67 ± 1.13	13.69 ± 1.35
	Group II	47.94 ± 11.00	35.14 ± 10.82	16.93 ± 4.14	12.43 ± 1.04
Neutrophil (%)	Group I	79.42 ± 1.92	74.76 ± 2.00	69.89 ± 2.50	68.11 ± 1.28
	Group II	80.36 ± 1.17	73.16 ± 2.04	67.21 ± 1.37	66. 75 ± 2.00
UHD (cm)	Group I	2.46 ± 0.35	2.00 ± 0.24	1.42 ± 0.12	1.00^b ± 0.06
	Group II	2.78 ± 0.19	1.71 ± 0.13	1.40 ± 0.08	1.33^a ± 0.05
RI	Group I (n = 6)	0.64 ± 0.02	0.68 ± 0.02	0.75^a ± 0.01	0.82 ± 0.01
	Group II (n = 4)	0.59 ± 0.05	0.67 ± 0.04	0.69^b ± 0.03	0.79 ± 0.01

Group I: bitches suffering from pyometra with normal endometrial surface, no or few small endometrial cysts and anechoic uterine content. Group II: bitches suffering from pyometra with irregular endometrial surface, many and large endometrial cysts, hypertrophic or atrophic endometrium and hyperechoic uterine content. [n= 7 each, unless stated; means having different lowercase letter as super script differ significantly ($p<0.05$) between the groups].

Fig. 1

Fig. 2

Fig. 3

Fig. 4

Fig. 1-4. Ultrasonographic pictures of uterus in a CEH-P dog on the day of presentation. **Fig. 1.** Grade A -Uterine changes include anaechoic content, normal endometrial surface and absence of endometrial cysts. **Fig. 2.** Grade B- Uterine changes include anaechoic content, normal endometrial surface and presence of few, small sized endometrial cysts. **Fig. 3.** Grade C- Uterine changes include hyperechoic contents, hypertrophic endometrium and presence of numerus large sized endometrial cysts. **Fig. 4.** Grade D- Uterine changes include hyperechoic content, irregular or atrophied endometrium and cystic changes.

Hagman (2023) had suggested that presence of CEH may negatively affect the outcome of medical management, which could clinically be manifested as delayed reduction in UHD. In the present study it was evident that UHD in bitches of group II, where the cystic changes were more pronounced, had not recovered by day 15 of medical management.

The mean RI of both the groups were lower than the cutoff value of 0.72 suggested by Veiga *et al*. (2017) to differentiate pyometra from CEH. Krishnan *et al.* (2023) also reported that the RI value 0.72 was consistent with presence of pyometra and was useful indicator of the bitch's recovery from the disease. In the present study, the mean RI in Group I recovered beyond the cutoff value of 0.72 by 9th day of treatment, whereas in group II the change was evident on only day 15 of medical management. This corroborates with delayed recovery in bitches of group II. Rosa-Filho *et al*. (2020) too recorded lack of complete recovery from CEH changes in CEH-P affected

bitches by day 28 of medical management.

Based on these observations, it could be inferred that B-mode ultrasonographic grading of uterus could offer value in determining the extent of endometrial damage and the possible treatment modality. The medical management of CEH-P affected bitches with severe endometrial changes was found to result in a delayed recovery, when compared to those with minor endometrial changes.

Conclusion

B-mode transabdominal ultrasonographic grading of uterus can be applied to decide the modality of treatment for CEH-P. Uterus with severe cystic changes and damaged endometrium might elicit poor medical responsiveness and OHE might be indicated in such cases.

Acknowledgement

The authors are thankful to Kerala Veterinary and Animal Sciences University for providing all facilities for the completion of this work.

Conflict of interest

The authors declare that they have no conflict of interest.

References

Agostinho, J.M.A., de Souza, A., Schocken-Iturrino, R.P., Beraldo, L.G., Borges, C.A., Avila, F.A. and Martin, J.M. 2014. *Escherichia coli* strains isolated from the uteri horn, mouth and rectum of bitches suffering from pyometra: virulence factors, antimicrobial susceptibilities, and clonal relationships among strains. *Int. J. Microbiol*. **2014**: 1-8.

Bigliardi, E., Parmigiani, E., Cavirani, S., Luppi, A., Bonati, L. and Corradi, A. 2004. Ultrasonography and cystic hyperplasia-pyometra complex in the bitch. *Reprod. Domestic Anim*. **39**:136-140.

Demeli, A. and Meyer, J.C., 2023. The assessment of haematologic and serum chemistry parameters in canine pyometra: a systematic review and meta-analysis. *J. Small. Anim. Pract.* **64**(9):543-51.

Fransson, B.A. and Ragle, C.A. 2003. Canine pyometra: an update on pathogenesis and treatment. *Compend. Contin. Educ. Pract. Vet***. 25**: 602- 612.

Hagman, R., 2023. Pyometra in Small Animals 3.0. *Vet. Clin. N. Am.* **53**: 1223-1254.

Harshan, M.H., Krishnan, A., Jayakumar, C. and Aravind, A. 2022. Ultrasonographic grading of uterus in canine cystic endometrial hyperplasia- pyometra complex and its predictive potential in response to medical management. Compendium. National conference on canine practice and symposium on newer concepts and approaches in small animal practice and welfare, 23rd – 24th September 2022. pp 257.

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**:428-432.

Melandri, M., Barella, G. and Alonge, S., 2019. Assessment of the optimal age for a preventive ultrasonographic screening of the uterine health in bitches. *Reprod. Domest. Anim.* **54:**1182-1187.

Rosa-Filho, R.R.D., Brito, M.M., Faustino, T.G., Almeida, L.L.D., Gardés, T.P., Leite, R.F. and Vannucchi, C.I., 2020. Clinical changes and uterine hemodynamic in pyometra medically treated bitches. *Animals*.**10:** 2011.

Sevelius, E., Tidholm, A. and Thoren, T.K. 1990. Pyometra in the dog. *J. Am. Anim. Hosp. Assoc.* **26**: 33-38.

Unnikrishnan, M.P., Kurien, M.O., Jayakumar, C., Harshan, H. M, John Martin K.D. and Unny M. N. 2020. Haematological

evaluation of medically treated cases of pyometra in dogs. *J. Vet. Anim. Sci.* **51**(1): 1-7.

Veiga, G.A., Miziara, R.H., Angrimani, D.S., Papa, P.C., Cogliati, B and Vannucchi, C.I. 2017. Cystic endometrial hyperplasia-pyometra syndrome in bitches: Identification of hemodynamic, inflammatory, and cell proliferation changes. *Biol. Reprod*. **96**:58-69.

Vidya, V. K., Unnikrishnan, M. O., Jayakumar, C. and Sankar, S. 2020. Comparative analysis of closed and open-cervix canine pyometra. *J. Vet. Anim. Sci.* **51**: 153-158. ■