Int.J.Curr.Microbiol.App.Sci (2020) *9*(2): 2117-2123

International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Volume 9 Number 2 (2020)**
Journal homepage: http://www.ijcmas.com

Original Research Article https://doi.org/10.20546/ijcmas.2020.902.240

Efficacy of Antiprogesterone and $PGF_{2\alpha}$ Therapy for Treating Canine Pyometra

G. P. S. Sethi[1]*, V. K. Gandotra[1], M. Honparkhe[1], A. K. Singh[1], A. K. Arora[1] and S. P. S. Ghuman[2]

[1]Department of Veterinary Gynaecology and Obstetrics, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana, Punjab 141004, India
[2]Department of Teaching Veterinary Clinical Complex, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana, Punjab 141004, India

**Corresponding author*

Keywords

Canine, Mifepristone, PGF2α, Pyometra

Article Info

Accepted:
15 January 2020
Available Online:
10 February 2020

A B S T R A C T

The present study was aimed at evaluation of antiprogesterone and $PGF_{2\alpha}$therapy either alone or in combination for the treatment of canine pyometra. A total of twenty-three female dogs suffering from open pyometra were divided in three groups based on type of treatment viz. Group I (n = 8; $PGF_{2\alpha}$), Group II (n= 7; Mifepristone) and Group III (n = 8; $PGF_{2\alpha}$ + Mifepristone). Group I dogs were administered with $PGF_{2\alpha}$ @ 0.1 mg/kg b.wt. bid subcutaneously for 5 days. Group II dogs received Mifepristone @ 2.5 mg/kg b.wt. orally for 5 days. Group III dogs were given combination of Mifepristone @ 2.5 mg/kg bid orally upto 5 days and $PGF_{2\alpha}$subcutaneously @ 0.2 mg/kg b.wt. on alternate days i.e. days 1, 3 and 5. The animals from all the groups were administered with Enrofloxacin @ 5 mg/kg b.wt. bid intramuscularly for 5 days alongwith supportive therapy. Prior to treatment vaginal swab (for microbial assay) from all animals were taken. All the animals were subjected to hematobiochemical parameters and ultrasonography pre and post treatment. Microbial assay of vaginal swab revealed predominance of *Escherichia coli* (65.21%) followed by *Staphylococcus* sp. (21.74%), *Klebsiella* sp. (8.70%)and *Pseudomonas* sp. (4.34%). Following treatment there was significant decrease ($P<0.05$) in TLC and neutrophil percent in all the groups. Post treatment ultrasonography showed significant decrease ($P<0.05$) in uterine diameter following therapy in all the groups. The success rate in terms of cessation of discharge and disappearance of clinical signs (viz.vomition, anorexia, polydipsia, polyurea) of Group I, Group II and Group III was 87.5%, 100% and 87.5% respectively. It was concluded that antiprogesterone therapy was most effective for the treatment of canine pyometra followed by $PGF_{2\alpha}$ alone and combination of $PGF_{2\alpha}$ and antiprogesterone therapy.

Introduction

Canine pyometra is a hormonally mediated acute or chronic polysystemicdiestrual disorder. It is the most common genital disease and results in high mortality if not treated(Singh *et al*., 2010). Conventionally the treatment of choice for any older, systematically or closed cervix pyometra is ovariohysterectomy (Jutkowitz, 2005).

Drawbacks with surgery are the risk with anaesthesia and that it renders the female dog sterile. Medical treatment may be indicated for breeding females, weak or old females in whom anaesthesia would be dangerous and in cases where the owners want to keep costs at a minimum(Fieni *et al*., 2014).

Many protocols have been proposed for the treatment of pyometra such as the use of antibiotics (Threlfall, 1995) alone, use of prostaglandins ($PGF_{2\alpha}$) (Gilbert *et al*., 1989) aglepristone (Contri *et al*., 2014). Dogs treated with injectable prostaglandins frequently demonstrate adverse effects such as abdominal discomfort, vomiting, defecation, urination, tachycardia, restlessness, anxiety, fever, hyper salivation, dyspnea or panting (Feldman and Nelson, 2014).

Several side effects have been observed after the administration of aglepristone such as anorexia, restlessness, depression, vomiting, diarrhoea, decrease in body temperature and local inflammatory reaction after injection (Fieni, 2006).

Combination of antiprogesterone and PGF2α has emerged as new therapeutic possibilities with a high success rate for the treatment of either type of pyometra (Shah *et al*., 2016). But despite greater pace of veterinary pharmacological and pathological advancement in research and innovation, suitable treatment for canine pyometra is still not formulized (Kumar and Saxena, 2018). Considering the above background, the present study was done for the evaluation of treatment response of the female dogs with pyometra to antiprogesterone and $PGF_{2\alpha}$ therapy based on the hypothesis that combination of mifepristone and prostaglandin could be more effective for the treatment of pyometra as compared to using prostaglandin or mifepristone alone.

Materials and Methods

Treatment groups

Twenty-three dogs (aged between 1 to 10 years) with the history of clinical signs of inappetence, lethargy, polyuria, polydipsia and vulvar discharge were subjected to trans-abdominal ultrasonography and blood examination. Based on therapy these dogs were randomly divided into three groups. In group I, 8 dogs were subjected to administration of natural prostaglandin (Dinoprost Tromethamine) subcutaneously @ 0.1 mg/kg b.wt. bid for 5 days. In group II, 7 dogs were subjected to administration of Mifepristone @ 2.5 mg/kg b.wt. orally bid from days 1 to 5. In group III, 8 dogs were subjected to the administration of combination of Mifepristone @ 2.5 mg/kg bid orally upto 5 days and Dinoprost Tromethamine subcutaneously @ 0.2 mg/kg b.wt. on alternate days i.e. days 1, 3 and 5.

Antibiotic

Antibiotic therapy which consisted of Enrofloxacin @ 5 mg/kg bid intramuscularly and Metronidazole @ 20 mg/kg od for 5 days intravenously was administered in all the animals. Also, a supportive therapy in form of intravenous fluids, diuretics and multi-vitamins was administered as and when required.

Laboratory estimation

Prior to treatment, vaginal swabs were collected from all the females and subjected to culture of isolation of organisms. Blood samples were collected in all the dogs before and after (5 days) the treatment. Blood samples were analyzed for Haemoglobin (Hb), total leucocyte count (TLC) and differential leucocyte count (DLC).

For estimation of Hb and TLC, fully Automatic Laser Based Hematology Analyser (ADVIA ® 2120 Hematology system, Siemens Healthcare diagnostics Inc, USA) was used. DLC was done using Giemsa stain(Jain, 1986).Blood biochemical parameters viz. Blood Urea Nitrogen (BUN), creatinine, aspartate aminotransferase (AST) and Alanine aminotransaminase (ALT) were measured to access the severity of disease and evaluation of treatment response.

Virtos DT 350 Chemistry system (Ortho Clinical Diagnostics, Johnson & Johnson Company) by using Virtos DT slides was used for estimation of blood biochemical parameters. The data with respect to hemato biochemical parameters and ultrasonography were presented as mean ± SEM. The statistical analysis was done by Student's t-test using Microsoft Excel software version 2016. P value less than 0.05 was considered as significant.

Results and Discussion

Microbial assay

Microbial examination of the vaginal swab of dogs with pyometra revealed predominance of *Escherichia coli* (65.21%) (Table 1). Other isolates identified were *Staphylococcus* sp. (21.74%), *Klebsiella* sp. (8.70%)and *Pseudomonas* sp. (4.34%).

Hematological parameters

Hematological parameters were observed before and after treatment in all the groups (Table 2). There was significant increase ($P<0.05$) in the mean Hb concentration in Group I and II and significant ($P<0.05$) decrease in TLC and neutrophil percent after completion of treatment in all the groups compared to pretreatment values.

Biochemical parameters

Biochemical parameters were estimated before and after treatment (Table 2). Four animals were found to have BUN>40 mg/dl at the time of referral. Rest all animals had BUN level in normal range.

A good response to medical treatment in the present study was obtained in all animals. A gradual decrease in elevated BUN level during treatment is indicative of positive response of the animal to the treatment and elimination of toxemia in the affected dogs.

Six patients (23%) had plasma creatinine levels more than 1.5 mg/dL at the time of presentation. After the treatment there was decrease in the creatinine value in all groups but statistically ($P<0.05$) there was decrease in group III only.

Mean serum AST concentration in animals with pyometra in different groups before initiation of treatment were higher in group II and III and after completion of treatment Group I and III had higher AST value than the normal physiological range which could be due to hepatocellular damage caused by septicemia or due to diminished hepatic circulation and cellular hypoxia in the dehydrated dog. The mean serum ALT level was in normal physiological range in all the groups before and after treatment therapy.

Ultrasonography

Uterine diameters in female dogs was found less than 1.2 cm diameter post treatment in all the animals irrespective of treatment group, except two animals, one from group I having 4.8 cm and one from group II having 3.6 cm which showed incomplete evacuation Thus, ovariohysterectomy was performed in these animals.

Treatment response

Out of 23 female dogs, 21 female dogs were responded well after the treatment. In group I and group III, 7 out of 8 (87.5%) animals responded well to the treatment. Success rate of 100% was recorded in group II.

Side effects

In group I, the observed side effects consisted of vomiting, panting and salivation. They were of moderate to mild intensity beginning 20–30 min after administration of $PGF_{2\alpha}$. In group III same side effects were observed as in Group I after $PGF_{2\alpha}$ while no side effects were observed after mifepristone administration. No side effects were observed in treatment group II where mifepristone was used.

Table.1 Percent occurrence of Bacterial isolates in swabs of female dogs suffering from pyometra.

Bacterial Isolates	Number of samples	Percent
E. coli	15	65.21
***Staphylococcus* sp.**	5	21.74
***Klebsiella* sp.**	2	8.70
***Pseudomonas* sp.**	1	4.34

Table.2 Pre and post treatment hemato-biochemical parameters and uterine diameter in pyometric female dogs

Parameters	Group I		Group II		Group III	
	Pre – T	Post – T	Pre – T	Post – T	Pre – T	Post – T
Hb (g%)	9.98±0.73	11.18±0.82*	9.3±0.91	11.01±1.17*	88.86±3.90	80.86±2.72*
TLC (mm^3)	38408.75± 11006.91	16971.25± 3636.23*	30597.14± 4551.06	15922.86± 2665.05*	42010± 6248.7	20686.25± 3966.60*
Neutrophils (%)	88.38±2.56	79.25±3.21*	88.86±3.90	80.86±2.72*	90.75±2.20	82.75±3.12*
BUN (mg/dL)	29.4±10.64	10.63±1.9	20.43±6.24	13.57±1.98	30.63±5.53	13.5±2.5
Creatinine (mg/dL)	2.1±0.69	0.95±0.08	1.39±0.41	1.04±0.15	1.23±0.22	0.8±0.05*
AST (U/L)	35.33±5.33	59±19.19	53.14±14.8	35.43±3.64	55.13±13.58	155±69.93
ALT (U/L)	27.16±3.47	46.88±7.08	39.86±7.51	35.14±8.6	30.63±5.53	43±5.76*
Uterine diameter (cm)	2.73±0.45	1.63±0.64*#	2.45±0.45	1.07±0.05*	2.67±0.36	1.35±0.39*#

*P<0.05, # = Two animals from group I and one animal from group III had non-detectable uterine diameter on ultrasonography. Hence removed from the mean, Pre – T = Pre-treatment values, Post – T = Post-treatment values, TLC, Total leucocyte count BUN = Blood urea nitrogen; AST = Aspartate aminotransferase, ALT = Alanine transaminase

Recurrence

In the present study, recurrence of pyometra was not observed in any animal after recovery. None of the animal had shown estrus activity after recovery in group I and group II. However, in group III, 4 animals had shown estrus activity after 2 months of treatment out of which one animal was mated and whelped after 2 months and had given birth to 5 pups.

Discussion

Pyometra is a frequently diagnosed bacterial infection of the uterus in intact, sexually mature bitches, leading to the accumulation of purulent material in the uterine lumen (Smith, 2006). The prevalence of *E. coli* in our study was in agreement with previous studies (Hagman, 2012; Bassessar *et al*., 2013).

To judge the efficacy of any treatment for pyometra hematological parameters viz. Hb, TLC and neutrophil percent are considered as one of the best indicators (Shah *et al*., 2017). In our study there was increase in Hb and significant decrease in TLC and neutrophil percent. These findings are in consonance with the observations of Jena *et al*., 2013, who observed increase in Hb, and decrease in the TLC and neutrophil percent after treatment with $PGF_{2\alpha}$. Following antiprogesterone treatment, the decrease in TLC and neutrophil percent was also observed by other workers (Contri *et al*., 2014; Shah *et al*., 2016).

In pyometric dogs' biochemical profile (BUN, Creatinine) is often compromised (Shah *et al*., 2017). Effective treatment show results in normal range of these profiles (England *et al*., 2007). In our study BUN and creatinine were in normal range after treatment therapy. ALT values were in normal physiological range while AST values were higher in group I and III after treatment. These findings were in accordance with Jena *et al*., 2013 in which they treated seven dogs were with natural $PGF_2\alpha$ i.e. dinoprost tromethamine and the biochemical parameters i.e. BUN, creatinine and AST dogs returned to normal range at the end of treatment. Shah *et al*., 2016 conducted similar study in which they treated 11 out of 12 animals suffering from pyometra in which 6 animals were treated with dinoprost tromethamine while 6 animals were treated with combination of mifepristone and dinoprost tromethamine.

All the biochemical parameters i.e. BUN, creatinine, AST and ALP were in normal range after the treatment therapy. Jurka *et al*., 2010successfully treated pyometra affected dogs with use of aglepristone. The concentration of aspartate transaminase and creatinine were higher in pyometra affected dogs which returned to normal physiological range after the treatment.

The findings of ultrasonography were in accordance with findings of Haji *et al*., 2017who reported normal ultrasonographic report of the uterus and marked improvement in dog's condition at the end of treatment with $PGF_{2\alpha}$. Significant decrease ($p \leq 0.05$) in the sizes of the uterine horn and the uterine lumen after treatment with aglepristone in pyometra affected dogs was reported by Contri *et al*., 2014.

Similar side effects like vomition, panting, restlessness and hyperpnoea were observed within few minutes after $PGF_{2\alpha}$ administration in the previous studies (Jena *et al*., 2013; Pande, 2001).

In our study four out of 7 female dogs had shown estrus signs in group III (combination of mifepristone and $PGF_{2\alpha}$). In previous studies (Contri *et al*., 2014) 83.56% of dogs affected with pyometra showed signs of estrus

at the 12-month examination after being treated with aglepristone. Our findings contrast with findings of Pande, 2001in which 7 out of 9 successfully treated dogs affected with pyometra with prostaglandin had experienced estrus after treatment while in our study none of dog treated with prostaglandin showed signs of estrus. Kumar and Azad, 2018 successfully treated a female dog affected with pyometra with the use of prostaglandin @ 100µg/kg body weight twice daily subcutaneously for five days and the estrus activity was shown by the dog after treatment and the dog conceived when mated in successive cycles.

In conclusion antiprogesterone therapy was most effective for the treatment of canine pyometra followed by $PGF_{2\alpha}$ alone and combination of $PGF_{2\alpha}$ and antiprogesterone therapy as it resulted in evacuation of pus from the uterine lumen and all hemato-biochemical parameters were in normal range in all the animals after the treatment. *E. Coli* was the most common bacteria causing pyometra in dogs.

References

Bassessar, V., Verma, Y. and Swamy, M. 2013. Antibiogram of bacterial species isolated from canine pyometra. Veterinary World.6(8): 546-549.

Contri, A., Gloria, A., Carluccio, A., Pantaleo, S. and Robbe, D. 2014. Effectiveness of a modified administration protocol for the medical treatment of canine pyometra. Veterinary research communications.39: 1-5.

England, G. C. W., Freeman, S. L. and Russo, M. 2007. Treatment of spontaneous pyometra in 22 female doges with a combination of cabergoline and cloprostenol. Veterinary Record. 160; 293–296.

Feldman, E. C. and Nelson, R. W. 2014. Cystic endometrial hyperplasia/pyometra complex. In: Canine and feline endocrinology and reproduction. 3rd ed. St. Louis, Mo: Saunders; 852-867.

Fieni, F. 2006. Clinical evaluation of the use of aglepristone, with or without cloprostenol, to treat cystic endometrial hyperplasia-pyometra complex in female doges. Theriogenology. 66:1550–56.

Fieni, F., Topie, E. and Gogny, A. 2014. Medical treatment for pyometra in dogs. Reproduction in domestic animals. 49: 28-32.

Gilbert, R.O., Nothling, J.O. and Oettle, E.E. 1989. A retrospective study of 40 cases of canine pyometra-metritis treated with prostaglandin F2α and broad-spectrum antibacterial drugs. Journal of Reproduction and Fertility Supplement.39:225–29.

Hagman, R. 2012. Clinical and molecular characteristics of pyometra in female dogs. Reproduction in Domestic Animals.47:323-25.

Haji, M., Borpujari, D., Talukdar, D., Ahmed, F., Lalrintluanga, K. and Sarma, K. 2017. Cystic Endometrial Hyperplasia-Open Pyometra Complex in A Female Pug. The Indian Journal of Animal Reproduction.39:42-48.

Jain, W. C. 1986. Schalm's Veterinary Haematology 4thedn. Lea &Febiger. Philadelphia, London.

Jena, B., Sadasiva, Rao. K., Reddy, K. C. S. and Raghavan, K. B. P. 2013. Physiological and haematological parameters of female doges affected with pyometra. Veterinary World. 6:409-12.

Jurka, P., Max, A., Hawryńska, K. andSnochowski, M. 2010. Age-related pregnancy results and further

examination of female doges after aglepristone treatment of pyometra. Reproduction in Domestic Animals.45(3): 525-29.

Jutkowitz, L. A. 2005. Reproductive Emergencies. Veterinary Clinics of North America: Small Animal Practice.35(2): 397-20.

Kumar, A. and Azad, C. S. 2018. Therapeutic management of pyometra in a female dog. The Pharma Innovation Journal. 7(11): 565-66.

Kumar, A. and Saxena, A. 2018. Canine Pyometra: Current Perspectives on Causes and Management – A Review. The Indian Journal of Veterinary Sciences & Biotechnology.14(1): 52-56.

Pande, N. 2001. 'Studies on diagnosis and treatment of pyometra in female doges.'M.V.Sc. Thesis, Punjab Agricultural University, Ludhiana.

Shah, M. A., Pande, N., Shah, I. A., Agrawal, R., Sharma, U. and Ghuman, S. P. S. 2016.Treatment of pyometra in female dogs using prostaglandin PGF2α ± Antiprogestin (Mifepristone). Indian Journal of Animal Reproduction. 37 (1): 23-26.

Shah, S. A., Sood, N. K., Wani, B. N., Rather, M. A., Beigh, A. B. and Amin, U. 2017. Haemato-biochemical studies in canine pyometra. Journal of Pharmacognosy and Phytochemistry.**6**(4): 14-17.

Singh, K. P., Singh, B., Singh, J. P., Singh, S. V., Singh, P. and Singh, H. N. 2010. Diagnostic and therapeutic management of pyometra in female doges. IntasPolivet.11: 86-87.

Smith, F. O. 2006. Canine pyometra. Theriogenology. 66: 610–12.

Threlfall, W. R. 1995. Diagnosis and medical management of pyometra. Seminars in veterinary medicine and surgery (small animal) (USA). 10(1): 21-29.

How to cite this article:

Sethi. G. P. S., V. K. Gandotra, M. Honparkhe, A. K. Singh, A. K. Arora and Ghuman. S. P. S. 2020. Efficacy of Antiprogesterone and $PGF_{2\alpha}$ Therapy for Treating Canine Pyometra. *Int.J.Curr.Microbiol.App.Sci.* 9(02): 2117-2123. doi: https://doi.org/10.20546/ijcmas.2020.902.240