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# THERAPEUTIC EFFECT OF SYNTHETIC PROSTAGLANDIN IN THE TREATMENT OF PYOMETRA IN BITCHES

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**ABSTRACT**
The current research was undertaken to study the therapeutic effect of synthetic prostaglandin in treatment of canine pyometra. Seven bitches were treated with synthetic $PGF_2\alpha$ *i.e.* Cloprostenol sodium at the dose rate of 1$\mu$g/kg body weight once daily for 7 days subcutaneously along with supportive therapy. The physiological parameters like rectal temperature and respiration rate, haematological parameters like total leucocyte count (TLC), neutrophil count and monocyte count and serum biochemical parameters like blood urea nitrogen (BUN), creatinine, aspartate transaminase (AST), alkaline phosphatase (ALP), mean total protein and globulin level which were elevated abnormally prior treatment, decreased to normal range after treatment. Other parameters such as haemoglobin, packed cell volume (PCV), total erythrocyte count (TEC), lymphocyte count and mean alanine transaminase (ALT) levels, those were at low level before treatment increased to normal range in the treatment group bitches in comparison with control group. The intensity of side effects was less severe. Two bitches came to estrus within 2 months of treatment and out of them one conceived on subsequent mating. In six bitches, there was recurrence of pyometra within 4 months of treatment. Use of cloprostenol sodium in treatment of canine pyometra in a higher dose rate for a longer duration will reduce rate of recurrence and improve the conception rate.

## INTRODUCTION

Pyometra is one of the life threatening diseases affecting the female reproductive tract in both dogs and cats (Wiebe and Howard, 2009). It is a hormonally mediated acute or chronic poly-systemic diestrual disorder that induces high mortality in bitches if not treated (Singh *et al.,* 2010). The disorder is assumed to be caused by an exaggerated response to prolonged or repeated progesterone stimulation (Nelson and Feldman, 1986). Although ovariohysterectomy is the most reliable treatment option for pyometra, in young breedable dog's pharmacological treatment using synthetic prostaglandins may be used in an attempt to preserve their breeding potential. The use of prostaglandin $F_2$ alpha ($PGF_2\alpha$) for the treatment of open pyometra has been extremely encouraging and consistent (Nelson *et al.*, 1982). The uterotonic action of cloprostenol leads to a significantly faster decrease in the diameter of the uterine lumen and its luteolytic action cause a faster drop in mean plasma progesterone concentration (Fieni, 2006). Side effects such as hypersalivation, vomiting and diarrhoea are often observed due to its action on smooth muscles (Gilbert *et al.*, 1989). However repeated administration of a low dose of cloprostenol (*i.e.* 1 $\mu$g/kg bodyweight) subcutaneously in empty stomach can eliminate the side effects (Gobello *et al.,* 2003). The current study was undertaken to know the efficacy of low dose synthetic $PGF_2\alpha$ in treating pyometra affected bitches in and around Hyderabad without hampering their breeding capabilities.

## MATERIALS AND METHODS

The present work was carried out at Department of Animal Reproduction, Gynaecology and Obstetrics, CVSc, Rajendranagar, Hyderabad. Fourteen clinical cases of different breeds in the age group of one to twelve years with known breeding history and suffering from open type of pyometra were taken for the study. Bitches were divided into two groups. Group I bitches were treated only with supportive therapies (control group). Bitches in Group II, were treated with synthetic $PGF_2\alpha$ *i.e.* cloprostenol sodium (Vetmate™, Vetcare® Divn., Thane, Maharashtra, India) at the dose rate of 1 $\mu$g/kg body weight subcutaneously once daily for 7 days with supportive therapies as reported by earlier workers (Gobello *et al.,* 2003 and Khan *et al.,* 2007). The physiological, haematological and biochemical parameters were studied before ($0^{th}$ day) and after treatment ($8^{th}$ day). All the data pertaining to post treatment return to estrus, breeding, conception and recurrence were recorded. Therapeutic efficacy was assessed in terms of return of abnormal parameters to either normal or near normal value as compared to the untreated control group, intensity of side effects and post treatment reproductive status etc. as reported by earlier workers (Thirumurugan and Rajasundaram, 2011). All bitches of control group and recurred bitches had undergone ovariohysterectomy.

## RESULTS AND DISCUSSION

### Treatment response

All the seven bitches were successfully treated by using synthetic $PGF_2\alpha$ *i.e.* cloprostenol sodium at the dose rate of 1$\mu$g/kg body weight once daily for 7 days subcutaneously along with supportive therapy. There was 100 per cent recovery rate observed in the bitches treated with cloprostenol on 8$^{th}$ day of therapy. However, Fieni (2006) and Khan *et al*. (2007) reported 84.4 and 83.33 per cent recovery rate which was lower than that of the present study.

All the characteristic clinical signs of pyometra like vaginal discharge, polydipsia, polyuria, lethargy and anorexia disappeared by 8$^{th}$ day of therapy indicating complete clinical recovery. Abdominal palpation revealed no palpable uterus revealing reduced diameter of uterus which was further confirmed by radiography or ultrasonography. All physiological parameters like rectal temperature and respiration rate; haematological parameters like total leukocyte count (TLC), neutrophil count and monocyte count; serum biochemical parameters like blood urea nitrogen (BUN), creatinine, aspartate transaminase (AST), alkaline phosphatase (ALP), mean total protein and globulin level which were elevated prior treatment decreased to normal range in the cloprostenol treated group as compared to control group. Haematological parameters such as haemoglobin, packed cell volume (PCV), total erythrocyte count (TEC) and lymphocyte count; biochemical parameter like alanine transaminase (ALT) those were at low level before treatment increased to normal range in the treatment group bitches in comparison with control group. This resulted in return of normal blood haematological profile and serum biochemistry in all the treated bitches on 8$^{th}$ day of observation that is represented in Table 1. These findings were in accordance with the observations of Maity *et al*. (2009) who preferred carboprost tromethamine (a synthetic $PGF_2\alpha$ analogue) in treatment of pyometra. Prostaglandin causes localized contractions in the smooth muscles in the ovary resulting in painful cramps in women (Sharma and Mehta, 2012). When used in medical treatment of canine pyometra, it causes cervical dialatation, myometrial contraction resulting in expulsion of exudates from uterus and removes progesterone influence on uterus by its luteolytic effect (Lein, 1986 and Cain, 1998). Synthetic $PGF_2\alpha$ analogues such as cloprostenol are more potent in causing luteolysis and maintaining uterotonic action and therefore required less frequent administration (Corrada *et al*., 2006 and Verstegen *et al.,* 2008).

### Side effects

After administration of cloprostenol side effects like vomition, panting, restlessness and hyperpnoea were observed within 15 minutes and all side effects disappeared within 1 to 1.5 hours. However the intensity and severity of side effects were lower due to low dose of synthetic $PGF_2\alpha$ analogue used for treatment. These findings were in agreement with the findings of Fieni (2006) and Maity *et al*. (2009). Side effects were observed might be due to poor general condition of the bitches as reported by Fieni (2006) or might due to parasympathetic action of synthetic prostaglandin derivative resulting in contraction of smooth muscle of gastrointestinal tract and tracheo-bronchial tract as reported by Maity *et al*. (2009). However, Gobello *et al*. (2003) reported no adverse side effects were observed after administration of low dose of cloprostenol. Though according to previous reports, salivation was the most common side effect observed after $PGF_2\alpha$ therapy, in the

**Table 1: Physiological, Haematological and Biochemical parameters**

| Parameters | | Before treatment (0th day) | | After treatment (8$^{th}$ day) | |
|---|---|---|---|---|---|
| | | Group I | Group II | Group I | Group II |
| Physiological | Rectal temperature (ºF) | 102.83 ± 0.28 | 103.5 ± 0.36 | 103.34 ± 0.18 | 102.31 ± 0.27 |
| Parameters | Heart rate (per minute) | 112.00 ± 4.00 | 107.28 ± 4.00 | 109.86 ± 2.23 | 105.71 ± 2.34 |
| | Respiration rate (per minute) | 29.57 ± 1.15 | 29.86 ± 1.75 | 32.00 ± 0.90 | 24.57 ± 0.92 |
| Haematological | Haemoglobin (gram %) | 11.0 ± 0.32 | 11.08 ± 0.42 | 10.70 ± 0.29 | 12.37 ± 0.28 |
| parameters | PCV (%) | 33.83 ± 0.92 | 34.24 ± 1.18 | 33.30 ± 0.90 | 37.98 ± 0.97 |
| | TEC ($\times 10^6/\mu$L) | 5.48 ± 0.17 | 5.51 ± 0.21 | 5.33 ± 0.14 | 6.18 ± 0.14 |
| | MCV (fl) | 66.88 ± 0.52 | 66.44 ± 0.77 | 66.77 ± 0.51 | 67.96 ± 0.51 |
| | MCH (pg) | 21.44 ± 0.32 | 21.41 ± 0.28 | 21.14 ± 0.31 | 21.60 ± 0.28 |
| | MCHC (%) | 31.48 ± 0.27 | 31.30 ± 0.28 | 31.28 ± 0.27 | 31.46 ± 0.27 |
| | TLC ($\times 10^3/\mu$L) | 33.27 ± 7.74 | 36.63 ± 9.58 | 34.14 ± 7.76 | 14.31 ± 2.16 |
| | Neutrophil (%) | 76.86 ± 1.06 | 79.57 ± 1.02 | 78.00 ± 0.97 | 69.86 ± 0.63 |
| | Lymphocyte (%) | 11.14 ± 0.94 | 8.86 ± 0.74 | 10.00 ± 0.92 | 20.28 ± 0.42 |
| | Monocyte (%) | 9.86 ± 0.51 | 9.00 ± 0.31 | 10.28 ± 0.52 | 7.43 ± 0.20 |
| | Eosinophil (%) | 2.14 ± 0.40 | 2.57 ± 0.29 | 1.71 ± 0.28 | 2.43 ± 0.20 |
| Biochemical | BUN (mg/dL) | 26.28 ± 1.47 | 24.28 ± 1.67 | 29.85 ± 1.18 | 19.28 ± 0.36 |
| parameters | Creatinine (mg/dL) | 2.10 ± 0.08 | 2.06 ± 0.09 | 2.18 ± 0.06 | 1.80 ± 0.05 |
| | AST (U/L) | 49.14 ± 1.24 | 48.71 ± 1.34 | 50.86 ± 1.20 | 42.28 ± 0.81 |
| | ALT (U/L) | 28.28 ± 2.09 | 25.00 ± 1.92 | 24.28 ± 1.49 | 31.00 ± 1.72 |
| | ALP (U/L) | 153.43 ± 5.83 | 154.71 ± 5.77 | 158.71 ± 5.33 | 137.57 ± 5.21 |
| | TP (g/dL) | 7.94 ± 0.27 | 8.10 ± 0.39 | 8.13 ± 0.24 | 7.13 ± 0.16 |
| | Albumin (g/dL) | 2.91 ± 0.09 | 2.93 ± 0.13 | 2.93 ± 0.11 | 3.17 ± 0.04 |
| | Globulin (g/dL) | 5.03 ± 0.27 | 5.17 ± 0.29 | 5.20 ± 0.27 | 3.95 ± 0.17 |
| | Total Bilirubin (mg/dL) | 0.46 ± 0.06 | 0.43 ± 0.07 | 0.48 ± 0.07 | 0.40 ± 0.05 |

N.B. Group I: Untreated control group (n = 7) Group II: Treatment group (n = 7)

present study it was not observed might be due to the administration of Atropine sulphate 10-15 minutes prior to administration of $PGF_2\alpha$ as reported by Lein *et al*. (1989). Withholding food and water supply to the bitches 4-6 hours prior to administration of $PGF_2\alpha$, use of Atropine sulphate and providing mild walk to bitches after $PGF_2\alpha$ injection were practised as recommended by Reddy *et al*. (2010) who used cloprostenol for terminating pregnancy. All these minimized the side effects by facilitating early metabolism and excretion of $PGF_2\alpha$ end product.

**Recurrence**

Though complete clinical recovery was observed in all the bitches on 8th day of treatment, in six bitches there was recurrence of pyometra within 4 months of treatment. There was recurrence of pyometra in one bitch within one week of end of therapy; another two bitches recurred within two weeks of therapy and other three showed recurrence of pyometra within 2 months of end of therapy. Recurrence rate was found to be 85.72 per cent in the cloprostenol treated group. All health parameters shifted towards abnormal range with externally visible clinical signs of pyometra in the recurred bitches. However, Renton *et al*. (1993) reported that the range of recurrence for bitches treated only with $PGF_2\alpha$ was from 10 to 77 per cent. Higher incidence of recurrence in the present study might be due to the fact that the uterotonic effect of $PGF_2\alpha$ did not reverse the disease permanently and many dogs may had a decrease in clinical signs towards subclinical levels which then became undetectable as reported by Gobello *et al*. (2003). All the recurred bitches had undergone ovariohysterectomy.

**Post treatment reproductive status**

In the cloprostenol treated group, two bitches came to estrus within 2 months of treatment which were subsequently mated. Ultrasonographically, one bitch was confirmed to be pregnant. Conception rate was found to be 14.28 per cent in this group. This finding was lower than that of the reports of Maity *et al*. (2009) who reported 50 per cent conception rate after using carboprost tromethamine for treatment of pyometra which might be due to lower dose of cloprostenol used.

## CONCLUSION

All the seven bitches recovered from pyometra temporarily by the use of synthetic $PGF_2$á *i*.e. cloprostenol sodium at the dose rate of 1$\mu$g/kg body weight once daily for 7 days subcutaneously along with supportive therapy. The intensity of side effects was less severe due to low dose used. Though all physiological, haematological and biochemical parameters in the seven treated bitches returned to normal range at the end of treatment, again all the parameters shifted towards abnormality immediately after stopping the treatment in the recurred bitches. Two bitches came to estrus within 2 months of treatment and out of them one conceived on subsequent mating. In six bitches there was recurrence of pyometra within 4 months of treatment. It is recommended to use cloprostenol sodium in treatment of canine pyometra in a higher dose rate for a longer duration which will reduce rate of recurrence and improve the conception rate.

## REFERENCES


**Cain, J. L. 1998.** Drugs used to treat reproductive disorders. *Vet. Clin. North. Am.* **28:** 395-396.

**Corrada, Y., Arias, D., Rodrýguez, R., Tortora, M. and Gobello, C. 2006.** Combination dopamine agonist and prostaglandin agonist treatment of cystic endometrial hyperplasia-pyometra complex in the bitch. *Theriogenology*. **66**: 1557-1559.

**Fieni, F. 2006.** Clinical evaluation of the use of aglepristone, with or without cloprostenol, to treat cystic endometrial hyperplasia-pyometra complex in bitches. *Theriogenology*. **66:** 1550-1556.

**Gilbert, R. O., Nothling, J. O. and Oettle, E. E. 1989.** A retrospective study of 40 cases of canine pyometra-metritis treated with prostaglandin $F_2\alpha$ and broad-spectrum antibacterial drugs. *J. Rep. Fer. S*. **39:** 225-229.

**Gobello, C., Castex, G., Klima, L., Rodryguez, R. and Corrada, Y. 2003.** A study of two protocols combining aglepristone and cloprostenol to treat open cervix pyometra in the bitch. *Theriogenology*. **60:** 901-908.

**Khan, L. A., Raghuwanshi, D. S., Vhora, S. C. and Utage, S. G. 2007.** Efficacy of certain therapeutic regimens in canine pyometra. *Indian J. Anim. Rep.* **28:** 49-52.

**Lein, O. H. 1986.** Prostaglandin therapy in small animal reproduction. In: Kirk Current Veterinary therapy IX. *Philadelphia,WB Saunders Company*, pp. 1233-1235.

**Lein, D. H., Concannon, P. W., Hornbuckle, W. E., Gilbert, R. A., Glendening, J. R. and Dunlap, H. L. 1989.** Termination of pregnancy in bitches by administration of Prostaglandin $F_2\alpha$. *J. Rep. Fer. S*. **39:** 231-240.

**Maity, S., Sarkar, S. and Saha, T. 2009.** Efficacy of Carboprost Tromethamine therapy in canine pyometra. *Indian. Vet. J.* **86:** 730-731.

**Nelson, R. W., Feldman, E. C. and Stabenfeldt, G. H. 1982.** Treatment of canine pyometra and endometritis with prostaglandin $F_2\alpha$. *J. American Veterinary Medical Association*. **181**: 889-903.

**Nelson, R. W. and Feldman, E. C. 1986.** Pyometra. *Veterinary Clinics of North America: Small Animal Practice* **16:** 561-576.

**Reddy, K. R. C., Rao, K. S., Raju, K. G. S., Raghavender, K. B. P. and Reddy, A. G. 2010.** Therapeutic efficacy of Mifepristone, cabergoline and cloprostenol for termination of pregnanacy in bitches. *Indian J. Anim. Rep.* **31:** 19-22.

**Renton, J. P., Boyd, J. S. and Harvey, M. J. A. 1993.** Observations on the treatment and diagnosis of open pyometra in the bitch (Canis familiaris). *J. Rep. Fer. S*. **47:** 465-469.

**Sharma, S. and Mehta, P. 2012.** Negative impact of fenoterol, a myometrial relaxant on the histo-architecture of the mice ovary. *The Ecoscan*. **1:** 179 -184.

**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 bitches. *Intas Polivet*. **11:** 86-87.

**Thirumurugan, K. and Rajasundaram, R. C. 2011.** Efficacy of antiprogestin (aglepristone) and prostaglandin f (cloprostenol) in treatment of 2 open cervix pyometra in bitches *J. Indian Veterinary Association*. **9:** 38-40.

**Verstegen, J., Dhaliwal, G. and Onclin, K. V. 2008.** Mucometra, cystic endometrial hyperplasia, and pyometra in the bitch: Advances in treatment and assessment of future reproductive success. *Theriogenology*. **70**: 364-374.

**Wiebe, V. J. and Howard, P. 2009.** Pharmacologic advances in canine and feline reproduction. *Topic in companion animal medicine*. **24:** 71-99.