



COMPARATIVE EFFICACY OF CABERGOLINE AND AYURVEDIC MEDICINE IN CANINE CYSTIC ENDOMETRIAL HYPERPLASIA PYOMETRA COMPLEX

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ABSTRACT

The present investigation was carried out on clinical cases brought to the Teaching Veterinary Clinical Complex, College of veterinary Science and Animal husbandry, Mhow and in private clinics across Indore (M.P.). Eighteen female dogs (six in each group) of variable age brought with the history of vaginal discharge and or associated with clinical symptoms (depression, in-appetence and abdominal enlargement) with CEH-P Complex were thoroughly investigated and on confirmation of the ailment, they were randomly allocated in the following 3 treatment groups viz. 1, 2 and 3. Each group comprises of 6 female dogs. The efficacy of treatment was judged on the basis of cessation of vaginal discharge, reduction in uterine lumen diameter and drift in haemato-biochemical parameters. Based on the results obtained in the present study it could be concluded that Haemato-biochemical parameters are of prognostic value. In this study group 1 (Cabergoline + Ciprofloxacin) was considered most effective with cessation of vaginal discharge by 8th day after treatment and significant difference in Haemato-biochemical parameters before and after treatment was observed.

Key words : Ayurvedic medicine, Cabergoline, Ciprofloxacin, Depression and Uterine lumen.

Introduction

Pet ownership is increasing in India due to urbanization and rising disposable incomes among middle-class households, coupled with changing attitudes to pets. India has higher dog population in the world; ranking 7th with 10.2 million dogs (Euromonitor International, 2015). Bitches express first estrous usually at 6-14 months of age and has great variations of breed and size. They are spontaneous ovulator during estrous phase. The estrous cycle comprises of 4 consecutive phase wise anoestrus depending on the breed lasting 80-240 days, proestrus 3-16 days, estrus 4-12 days and a relatively long diestrus 60-90 days (Concannon, 2009). Reproductive anomalies play an important role in deciding the profitability of the canine breeding ventures. Uterine diseases are the most common cause of failure to conceive in dogs and 25% of the female dog population developed by 10 years of age, which is a very high incidence compared to other uterine

problems (Hagman, 2004). Canine cystic endometrial hyperplasia (CEH)-pyometra complex is the most frequently encountered endometrial disorder in bitches and its exact pathogenesis is still unknown. Canine cystic endometrial hyperplasia (CEH)-Pyometra Complex, a hormonally mediated acute or chronic polysystemic diestrual disorder, is the most common genital disease in bitches and results in high mortality if not treated (Singh *et al.*, 2010). The etiology of canine cystic endometrial - pyometra complex is still unclear, the hormonal aberration followed by bacterial infection plays an important role in the etiopathogenesis of disease. Bitches with pyometra may be either with or without vaginal discharge and with variable other clinical features. Progesterone has a role in initiating the cystic endometrial hyperplasia (CEH)-pyometra complex. Prolonged or repeated stimulation of endometrium by progesterone produces CEH-PC, if bacterial infection occurs at that time leads to pyometra.

After ovulation increased progesterone concentration (>40 ng/ml) promotes endometrial (endometrial hyperplasia) growth and glandular secretion leads to accumulation of uterine glandular secretion which provides excellent media for bacterial growth (Baithalu *et al.*, 2010). Ultrasonography helps in diagnosing CEH-pyometra complex even if vaginal discharge is minimum or absent, further haematological and serum biochemical evaluation are of prognostic values (Javeid, 2010). Canine CEH-pyometra complex has been most commonly treated by ovariohysterectomy, once the bitch has been adequately stabilized. Tewiri *et al.* (2001) reported that the clinical efficacy of polyherbal drug in the genital disorder of women. Dopamine agonist (bromocriptine or cabergoline) and PGF2 α are used to treat pyometra infection (Mandhwani *et al.*, 2018).

Materials and Methods

The study was carried out in Department of Veterinary Gynaecology and Obstetrics, Veterinary Clinical Complex (V.C.C.), College of Veterinary Science and Animal Husbandry, MHOW (M.P.) and in Private Clinics across Indore.

Experimental design

Eighteen female dogs (six in each group) of variable age brought with the history of vaginal discharge and or associated with clinical symptoms (depression, inappetance and abdominal enlargement) with CEH-P Complex were thoroughly investigated and on confirmation of the ailment, they were randomly allocated in the following 3 treatment groups.

Group 1: The female dogs of group 1 (n = 6) were treated with Cabergoline @ 5 μ g/kg PO $\times$ 7 days and Ciprofloxacin @ 10 mg/kg PO, SID $\times$ 7 days, orally (tablet form). The patient was checked on 8th day and if required the treatment were continued.

Group 2: The of group 2 (n = 6) were treated with tablet containing herbal ingredients Asparagus (shatavari), *Woodfordia fruticosa* (dhatki), *Boerrhaavia diffusa* (satha), *Rauvolfia serpentina* (sarpgandha), *Astercantha longifolia* (gokhla kanta, gokshura) PO, SID $\times$ 7 days along with using ingredients *Maharasanadi qoath*, *Tinospora cordifolia* (giloy), *Rubia cardifolia* (manjistha), *Balsamodendron mukul* (guggul), *Embllica officinalis* (amla) PO, SID $\times$ 7 days, orally. The patient was checked on 8th day and if required the treatment were continued.

Group 3: The female dogs of group 3 were treated with Cabergoline @ 5 μ g/kg PO $\times$ 7 days along with tablet containing herbal ingredient Asparagus (shatavari), *Woodfordia fruticosa* (dhatki), *Boerrhaavia diffusa*

(satha), *Rauvolfia serpentina* (sarpgandha), *Astercantha longifolia* (gokhla kanta, gokshura) PO, SID $\times$ 7 days and *Maharasanadi qoath*, *Tinospora cordifolia* (giloy), *Rubia cardifolia* (manjistha), *Balsamodendron mukul* (guggul), *Embllica officinalis* (amla) PO $\times$ 7 days, orally. The patient was checked on 8th day and if required the treatment were continued.

Ultrasonography (USG) : To measure the uterine lumen diameter Ultrasonographic examination were done using ultrasound machine with the help of micro convex transducer (3.5 MHz). Coupling media were applied on the skin surface to ensure an intimate contact between the transducer and body surface. The images on the monitor were freezed and different measurements were recorded in CEH-PC affected female dogs.

Collection of blood sample : 3 ml of blood from each female dog was collected aseptically from cephalic vein on the 1st and 8th day of treatment. The sample was divided in to two parts, first part for haematological examination containing anticoagulant (EDTA @ 2 mg/ml) and second part was allowed to clot in test tube for serum separation and stored in a sterilized vial at -20 $^{\circ}$ C until biochemical analysis.

Haemato-biochemical parameters

Haematological Parameters : The following haematological parameters was estimated as per the procedure described by Jain (1986).

Haemoglobin (Hb) : Haemoglobin was determined by Sahli's acid haematin method using haemoglobinometer and values was expressed in g/dl.

Total Leukocyte Count (TLC) : The counting of white blood cells was done in a haemocytometer consisting of Neubauer's chamber. The values were expressed in thousand/cu.mm.

Differential Leukocyte Count (DLC) : The differential leucocyte count was done by preparing thin blood smears on glass slide, after staining with Leishman's stain, was examined under (100X magnification) microscope using oil immersion lens. One hundred cells were counted and values was expressed in percentage.

Biochemical Parameters : The following biochemical parameter was estimated:

BUN (mg/dl) : Serum Blood Urea Nitrogen was estimated by DAM method using Erba Manheim Diagnostics Kit as described by Marsh *et al.* (1965) and the results was expressed in mg/dl.

Serum creatinine (mg/dl) : Serum Creatinine was estimated using Erba Manheim Diagnostics Kit as

described by Bones and Taussky (1965) and the results was expressed in mg/dl.

Alkaline phosphatase (IU/L) : Serum Alkaline Phosphatase was estimated by using Erba Manheim Diagnostics Kit as described by Tietz *et al.* (1983) and the results was expressed in IU/L.

Criteria for assessment of efficacy of treatment : Amelioration of clinical symptoms including cessation of vaginal discharge, reduction in uterine lumen diameter and drift in haemato-biochemical values were criteria.

Results and Discussion

Cessation of vaginal discharge : Cessation of vaginal discharge is depicted in Table 1. All the animals at day 0 presented with vaginal discharge (purulent or sanguino-purulent) were treated and it was observed that vaginal discharge ceased after treatment by day 8 in group 1. In terms of cessation of vaginal discharge in group 1, group 2 and group 3 had 100%, 16.66% and 33% efficacy, respectively. England *et al.* (2007), Jena *et al.* (2013) and Dash *et al.* (2014) evaluated response to treatment with Cabergoline and prostaglandin in combination with antibiotics, found cessation of vaginal decrease or absent on day 6. Mandhwani (2017) also reported group wise cessation of vaginal discharge and found complete cessation of vaginal discharge by 14 day.

Reduction in Uterine lumen diameter : The values of uterine lumen diameter (mm) where study and their mean values are presented and depicted in Table 2. The Mean level of uterine lumen diameter (mm) in group 1, 2, 3 on day 1, 8 were 14.83±1.44, 16.55±1.37, 13.88±1.54; 13.55 ±1.2 15.13±1.56 13.23±1.31, respectively. Between these group on day 1 and 8 was non- significant. Uterine lumen diameter was non-significant in all groups on day 1st and on day 8th. Contrary to our observations, Mandhwani (2017) observed difference was found to be statistically highly significant ($p<0.01$) between groups on day 10. Contri *et al.* (2014) also reported significant decrease ($p <0.05$) in the sizes of the uterine horn and the uterine lumen after treatment with aglepristone in pyometra affected dogs.

Drift in Haemato-biochemical values

The mean values of Haematological parameters are presented and depicted in Table 3. The mean level of Haemoglobin (g/dl) on day 1 in group 1, 2 and 3 was 9.77±0.83, 7.98±0.25 and 7.77±0.40 and on day 8 it was 12.25±0.68, 9.10±0.34 and 8.98±0.22, respectively.

The mean Total leucocyte count (thousand/cu mm) on day 1 in groups 1, 2 and 3 was 14.28±0.21, 13.63±0.79 and 12.81±0.61 and on day 8 it was 10.5±0.20, 11.65±1.20

Table 1 : Group wise cessation of vaginal discharge after treatment.

Days	Group 1	Group 2	Group 3
Day 1	0%	0%	0%
Day 8	100%	16.66%	33.33%

Table 2 : Group wise uterine lumen diameter (mm) (Mean± SE).

Day	Group 1	Group 2	Group 3
1 day	14.83 ^{a,A} ±1.44	16.55 ^{a,A} ±1.37	13.88 ^{a,A} ±1.54
8 day	13.55 ^{a,A} ±1.2	15.13 ^{a,A} ±1.56	13.23 ^{a,A} ±1.31

Means with same lower case superscripts in a column and same upper case superscripts in a row do not differ significantly ($p<0.01$).

and 11.71±0.49, respectively.

The mean Neutrophils on day 1 in group 1, 2 and 3 were 89.17±1.49, 75.50±1.06 and 71.50±1.91 and on day 8 it was 77.83±1.92, 68.50±1.73 and 65.50±1.23, respectively. The mean Lymphocyte count on day 1 in groups 1, 2 and 3 was 16.67±1.12, 16.33±0.92 and 16.00±0.97 and on day 8 it was 14.17±1.30, 14.83±1.01 and 14.50±0.99, respectively. The mean Monocyte on day 1 in groups 1, 2 and 3 was 2.33±0.67, 3.34±0.42 and 2.00±0.58 and on day 8 it was 1.67±0.84, 3.17±0.48 and 1.67±0.76 respectively. The mean Eosinophil on day 1 in groups 1, 2 and 3 was 0.50±0.84, 1.17±0.47 and 0.83±0.40 and on day 8 it was 1.16±0.48, 1.34±0.34 and 1.34±0.42, respectively.

The mean level of BUN on day 1 in groups 1, 2 and 3 was 39.08±1.82, 36.33±0.76 and 32.93±0.76 and on day 8 it was 34.55±1.07, 28.82±0.93 and 28.23±0.77 respectively (Table 4). The mean level of Serum creatinine on day 1 in groups 1, 2 and 3 was 1.88±0.06, 1.54±0.29 and 1.13±0.06 and on day 8 it was 1.42±0.12, 1.42±0.19 and 0.93±0.04 respectively. The mean values of alkaline phosphatase on day 1 in groups 1, 2 and 3 were 94.60±5.62, 73.47±3.34 and 62.17±1.24 and on day 8 it was 83.88±3.67, 62.52±3.43 and 60.40±1.27, respectively. Significant changes were observed in Haematological parameters such as haemoglobin, total leucocyte count and neutrophils. Significant changes were observed in Biochemical parameters like blood urea nitrogen (BUN), serum creatinine and alkaline phosphatase.

Babu *et al.* (2016) also reported variation in Haemato-biochemical parameters. They found that There was significant decrease ($P>0.05$) in the, TEC, PCV, Hb and TLC in pyometra affected female dogs as compared to healthy group. In the present study although, neutrophilia with regenerative shift to left, and

Table 3 : Drift in Hematological values.

Parameters	Group 1		Group 2		Group 3	
	Day 1	Day 8	Day 1	Day 8	Day 1	Day 8
Hb	9.77±0.83	12.25±0.68	7.98±0.25	9.10±0.34	7.77±0.40	8.98±0.22
TLC	14.28±0.21	10.57±0.20	13.63±0.79	11.65±1.2	12.81±0.61	11.71±0.49
Neutrophils	89.17±1.49	77.83±1.92	75.50±1.06	68.50±1.73	71.50±1.91	65.50±1.23
Lymphocyte	16.67±1.12	14.17±1.30	16.33±0.92	14.83±1.01	16.00±0.97	14.50±0.99
Monocyte	2.33±0.67	1.67±0.84	3.34±0.42	3.17±0.48	2.00±0.58	1.67±0.76
Eosinophil	0.50±0.84	1.16±0.48	1.17±0.47	1.34±0.34	0.83±0.40	1.34±0.42

Table 4 : Drift in biochemical values.

Parameters	Group 1		Group 2		Group 3	
	Day 1	Day 8	Day 1	Day 8	Day 1	Day 8
BUN	39.08±1.82	34.55±1.07	36.33±0.76	28.82±0.93	32.93±0.76	28.23±0.77
Serum creatinine	1.88±0.06	1.42±0.12	1.54±0.29	1.42±0.19	1.13±0.06	0.93±0.04
Alkaline phosphatase	94.60±5.62	83.88±3.67	73.47±3.34	62.52±3.43	62.17±1.24	60.40±1.27

lymphocytopenia was noticed in pyometra affected dogs, however, the difference was not significant. The mean percentages of neutrophils, lymphocytes, monocytes and eosinophils in pyometric dogs were 80.81 ± 1.99 , 15.00 ± 1.90 , 3.50 ± 0.40 and 0.34 ± 0.23 , respectively. The corresponding values in normal healthy dogs were 71.54 ± 6.23 , 24.00 ± 6.0 , 4.10 ± 0.40 and 0.78 ± 0.57 , respectively. The mean serum creatinine (mg/dl) was increased in pyometra affected dogs as compared to healthy dogs (1.37 ± 0.26 vs 0.74 ± 0.05).

Variation in Haemato-biochemical parameters were also observed by Mandhwani *et al.* (2017). She reported that the difference in mean haemoglobin (g/dl) level between these groups was non-significant. However, the mean total DLC on day 0, 6 and 14 in groups 1,2,3,4 and 5 was found highly significant between time interval with in groups. Leukocytosis and neutrophilia were characteristically present in CEH-PC affected bitches. all the biochemical parameters estimated in affected animals were significantly higher in nearly all the animals. The different in creatinine, alkaline phosphatase and BUN levels between groups and time interval with on groups was highly significant ($p < 0.01$).

Drift in all of the above Haemato-biochemical parameters are in agreement with Shah *et al.* (2018). cases revealed leukocytosis, neutrophilia, lymphocytopenia and anemia. Marked leucocytosis (104.8 ± 4.0) was observed in all the pyometra cases. The leucocytosis was more marked in closed cases of pyometra complex in comparison to open cases. In present study there was marked neutrophilia (94.25 ± 0.73) with shift to left and these changes were more pronounced in

closed cases of CEHPC. Lymphocyte count (5.25 ± 0.41) was decreased in all the cases. Lymphocytopenia was more marked in the closed cases of Pyometra than open cases. All the eight cases were anemic based on Hb (5.62 ± 0.32), PCV (18.55 ± 1.18) and TEC (3.24 ± 0.59).

Sharma *et al.* (2020) found that treatment with methylergometrine along with antibiotic course had been associated with significant improvement in physiological, Hematological, Biochemical and Ultrasonographical parameters of the she dogs suffering from open pyometra, without any side effects.

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