



THERAPEUTIC MANAGEMENT OF CHRONIC III DEGREE ENDOMETRITIS IN CROSSBRED COWS OF ASSAM

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ABSTRACT

An investigation was carried out to find out a suitable treatment of III degree chronic endometritis in high yielding crossbred cows of Assam. A total of 70 postpartum high yielding crossbred repeat breeding cows clinically suffered from chronic endometritis (III degree) with muco-purulent discharge were selected for treatment and they were divided into seven groups each comprising ten cows. Cows of first to fifth lactation with milk yield ranging from 10-25 liters were considered for the study. The respective groups were treated with different drug combinations of Ciflox-TZ(I.U)-Ciprofloxacin750mg + Tinidazol1800mg, Ciprofloxacin240mg injection, Cloprostenol 500mcg(Vetmate), VitaA-12,00,00I.U., 4-dimethylamino-2methylphenyl-phosphinic acid 1.2gm(Tonophosphan) and Pheneramine Maleat 113.75mg(Avil) were tried to find out a suitable drug combination for treatment of chronic endometritis with muco-purulent discharge. Out of all treatments combination Ciflox-TZ(I.U)-Ciprofloxacin750mg + Tinidazol1800mg+ Ciprofloxacin240mg injection+ Cloprostenol 500mcg + VitaA-12,00,00 I.U.+ 4-dimethylamino-2methylphenyl-phosphinic acid 1.2gm + Pheneramine Maleat113.75mg and Ciflox-TZ(I.U)-Ciprofloxacin

750mg+Tinidazol 1800 mg + Ciprofloxacin 240mg injection + Cloprostenol 500mcg + Vita-A12,00,00I.U.+ 4-dimethylamino-2methylphenyl-phosphinic acid 1.2gm + Vit. E 500mg +Selenium15 mg + Pheneramine Maleat 113.75mg were found to best equally best for recovery of chronic endometris with highest conception rate with first AI. The mean serum Protein, Glucose, Cholesterol, alkaline phosphatase, progesterone and cortisol levels were estimated as highest on the day of oestrus before treatment where in contrary protein and glucose levels were lowest on the same day while all these returned to almost normal concentration on the third oestrus when A.I. was done. So, It is up to the choice of the practitioner to select either of these drug combination for treatment of the high yielding crossbred cows suffering from chronic endometritis.

Key words: biological constituents, crossbred cows, III degree endometritis, treatment

INTRODUCTION

Repeat breeding is one of major reproductive problems where postpartum uterine infections are a major cause of infertility and economic loss in dairy production systems mainly both in rural and urban dairy farmers. Endometritis of different degrees are the inflammatory conditions of uterus which is mostly prevalent in high-producing dairy cows greatly leading to early embryonic death or failure of implantation causing longer inter-calving period associating with decreased pregnancy rate per artificial insemination (AI), increased culling rate, more number of A.I. per calving, longer service period and loss of milk production. Prevailing to this problem the available literature revealed that the incidence reported to be 4.8-50% in India and abroad including Assam (Luktuke, 1977, Sharma *et al.*, 1983; Bartlett *et al.*, 1986; Bonia, 2009; Cheong *et al.*, 2011). Various treatments like intra-uterine and intra-muscular administration of immune-modulator (Anderson *et al.*, 1985; Hussain and Daneil,1991; Dhaliwal *et al.*, 2001), antibiotics alone or in combination of prostaglandins were tried for treatment of endometritis (Akhtar *et al.*, 2009; Galvão , *et al.*, 2009). However, the treatment of endometritis is still an issue of considerable controversy over therapies available for endometritis(metritis) including systemic or local antibiotics, PGF2 α so on(Arlt *et al.*, 2009; Dubuc *et al.*, 2011) and based on several arguments further studied on treatment of chronic endometritis in multi-location can not be nullified. Till understanding the fact about meaning of herd-hygiene and taking care of environment to

prevent infectious reproductive problems, treatment of suffering animals is must. Therefore, the present study was carried out to with the objective to determine the effects of observe efficacy of some drugs singly or in combinations for treatment of postpartum crossbred cows of Assam suffered from third degree endometritis.

MATERIAL AND METHODS

A total of 70 postpartum high yielding crossbred repeat breeding cows clinically suffered from chronic endometritis (III degree) with muco-purulent discharged (Szenci, 2010) were selected for treatment and they were divided in to seven groups each comprising ten cows. Cows of first to fifth lactation with milk yield ranging from 10-25 liters were considered for the study. These cows were maintained in private dairy farms in and around of Guwahati. The cows were investigated clinico-gynaecologically per rectum and confirmed that they were suffered from the said reproductive problem. They were treated with different treatment regimen as shown in Table 1. All selected endometritic cows were dewormed instantly followed by group wise treatment for the specified ailed cows. After completion of each treatment subsequent second cycle of the experimental cow was missed for sexual rest. On the third oestrus A.I. was done with frozen semen at right time of the treated cows and 90 days after insemination each inseminated cow was examined per-rectum for pregnancy diagnosis Jugular blood samples were collected from all experimental animals on the day of first oestrus before treatment, second oestrus of cycle of sexual rest and on the day of third oestrus before A.I. Serum samples were preserved at -20°C for estimation of hormones and biochemical constituents where progesterone and cortisol were estimated with the help of radioimmunoassay methods by using respective kits. Glucose, Cholesterol and alkaline phosphatase were determined by using quality kits when no microbial culture was made. The necessary statistical analysis was done according to the method of Snedecor and Cochran(1994) for statistical interpretation.

RESULTS AND DISCUSSION

Effect of different treatment in cows suffering from chronic endometritis: The result of the present investigation (Table 1) indicated that intra-uterine infusion of 0.20% lugol's solution (group I) had no effect in changing of the uterine condition and

mucopurulent discharge. Treatment combination given to the group II (Ciprofloxacin 750mg+Tinidazol 1800mg and pheneramine maleate + and III(Ciprofloxacin 750 mg+ Tinidazol1800 mg, Ciprofloxacin 240mg injection and Pheneramine Maleat 113.75mg) resulted only 1(10.00%) and 2(20.00%) cows conceived when 9(90%) cows conceived in group VI and VII out of all treated with treatment combinations Ciflox-TZ(I.U)-Ciprofloxacin 750mg + Tinidazol1800mg+ Ciprofloxacin 240mg injection+ Cloprostenol 500mcg + VitaA- 12,00,00 I.U.+Tonophosphan+Avil and Ciflox-TZ(I.U)-Ciprofloxacin 750mg + Tinidazol1800mg+ Ciprofloxacin 240mg injection+ Cloprostenol 500mcg + Vita-A- 12,00,00 I.U.+Tonophosphan+ Vit. E 500mg +Selenium 15mg+ Pheneramine Maleat 113.75mg follo -wed by 7(80%) and 5(50%) in group VI and V respectively. All cows of the group-II, III, IV, V, VI and VII with mucopurulent discharge treated with different combinations had shown visibly clear discharge on day 3rd after treatments with returning of uterine condition apparently to normal condition on rectal palpation during luteal and follicular stages of of all the subsequent oestrous cycles. The reason behind in difference of response of treatments to different groups cows suffered from the said reproductive problem could be interpreted as that only Lugol's infusion was not sufficient to cure the pathological condition of uterus. Ciflox-TZ-I.U. could able to cure only one cow of the group II. Both intra-uterine and intra-muscular treatment with Ciprofloxacin might have reduced both the gram-positive and gram-negative bacteria(Anonymous, 2014) and injection of PGF_{2α} improved fertility of dairy cows by elimination of bacterial infections along with leucocytic infiltration to the endometrium and early involution (Hafez and Hafez, 2000; Yasothai, 2014). On the other hand, Tonophosphan, VitaminA, selenium and VitaminE administration might have exerted combine effect considered to cause improvement of general and endometrial health conditions leading better fertility of group-VI and VII followed by group III, IVand V, respectively with different efficacy. Though, it was stated that non antibiotic substance like lugol's iodine, prostaglandin had also been proved to have better result in treating mild type of endometritis(Morrow, 1986; El-Khardrawy *et al.*2011), intra-uterine administration of 2gm of Ciprofloxacin and 25mg of PGF_{2α} injection (Al-Timimi,2011) or Ciprofloxacin and Tinidazole advocated as the effective drug for the treatment of repeat breeding in animals at field condition as compared to other intrauterine preparations (Pmane, 2010) Kumar *et al.*(2014) reported that the conception rate was recorded as 62.50% for Ciprofloxacin treated group when previously a higher conception rate(80-85%) was recorded with ciprofloxacin treatment(Purohit *et al.*, 2003 and Das, 2004).

Sengupta and Nandi(2013) that indicated that the parenteral and intra-uterine antibiotics had synergistic effect with estradiol, vitamin A, E and Se treatment in recovery from endometritis where a minimum time interval was required for complete recovery of the endometrium for best conception rate- it was possible due to synergistic effect of both parental and intrauterine infusion of antibiotics along with prostaglandin caused increasing blood flow and leucocytic infiltration into the uterus(Lewis, 2003, Weens *et al.*, 2006) as well as anti-oxidant effects with improved oxygen uptake helped by vitamin E (Spears, and Weiss, 2008; Kaewtamun *et al.*,

2011) substantiating with increasing uterine defense mechanism rendered by selenium(Thatcher *et al.*, 2011). Injection of oestrogen depressed the appetite of rats(Clifton and Meyer, 1956)and a decrease in blood glucose in women receiving oestrogen therapy (Wynn and Doar, 1969) There was increase of milk yield just after treatment started with antibiotic with other combinations of drugs than that of before treatment in all experimental cows of group III, IV, V, VI and VII which might be due to gradual recovery of the ailment.

Serum biological constituents of cows treated different drug: The result of the serum concentration of glucose, protein, cholesterol, alkaline phosphatase, progesterone and cortisol shown in Table 2. The present findings indicated that the mean concentration of serum glucose was found to be lowest during oestrus of metritic cows before treatment which was again found to be higher on the second oestrus of sexual rest period and reaches highest on day of the third oestrus when A.I. was done. Variation of might be due to stress of chronic endometritis where reversed variation of serum cholesterol level was seen. Ahmad *et al.*(2004) reported significantly ($P<0.05$) higher values of glucose (58.08 ± 2.59) and cholesterol (290.72 ± 15.95) in endometritic cows as compared to cyclic (50.72 ± 1.12 and 199.12 ± 9.38) and non-cyclic cows (50.56 ± 1.12 and 202.96 ± 14.84) when total protein level reported to be differed significantly ($P<0.05$) among cows of all the three groups, being highest in endometritic (19.16 ± 1.00), followed by non cyclic (15.23 ± 0.89) and lowest in cyclic (9.19 ± 0.45) cows while similar serum cholesterol concentration on the day of induced oestrus of responded cows (Ahlwat and Derashri 2009). Bonia (2015) reported that the mean serum level of cholesterol and alkaline phosphatase were varied significantly ($P< 0.01$) at different days of both normal and sub-ostrous cycles crossbred cows. The serum glucose was found to be 22.3 ± 2.18 mg/dl and total protein 6.1 ± 0.51 g/dl in metritic cows and on comparison of this result with normal values it was found that glucose level was found to be

below the normal levels 5.7-8.1 mg/dl and 45-75 g/dl respectively (Radostitis *et al.*, 2000). The present higher mean serum alkaline phosphatase values on the day of oestrus of the metritic cows and subsequent cycles of treated cows were might be indicative of cellular damage and normal cyclic changes in female genitalia during the oestrus period (McDonald 1980) like that of Singh and Dutt (1974) while Mehta *et al.* (1989) reported non significant levels. Schultz *et al.* (1971) opined that levels of this serum enzyme varied according to stages of oestrous cycle. The highest level of this serum enzyme on the day of oestrus might be the indication of more cellular changes in genitalia during oestrus period where higher activity with dropping of serum glucose level might also been related to the physiological changes during different reproductive stages and the possibility could be role out relationship between alkaline phosphatase and steroid hormones.

The mean progesterone concentration was found to be lower during before treatment which was found to be higher after treatment on the day of subsequent heat after sexual rest and highest on the day 3rd oesterus on which artificial insemination was done as similar to report of Bonia and Goswami (2011) respectively when they recorded the mean serum concentration of cortisol levels as 26.20 ± 2.58 , 20.80 ± 1.63 , 21.30 ± 1.69 , 21.30 ± 1.23 and 28.60 ± 4.63 nM/lit on day 0, 5, 10 and 20 respectively in normal cyclic cows. The respective values were 26.40 ± 2.59 , 21.60 ± 0.97 , 23.29 ± 1.55 , 22.50 ± 1.11 and 26.95 ± 1.95 nM/lit respectively in sub-oestrous cows on day 0, 5, 15, 0 (day of oestrus of next cycle). The mean concentration of cortisol level in serum of endometritic cows before treatment were found to be highest and after treatment and the levels were drop down gradually to the lowest concentration on the day of AI though the pattern of changes of cortisol levels during the both types of oestrous cycle was in agreement findings of findings of Bonia and Goswami (2011). Reversely higher values were reported at or around oestrus in crossbred cows (Rao and Pandey, 2008) and in buffalo (Rao and Pandey, 1981; Singh *et al.*, 2008). The higher levels of serum cortisol in metritic cows of the present study indicated pathological stress condition while the variation of levels of cortisol at normal oestrus might be due to biological stress factors like restlessness with wide range of body activities (McDonald, 1980; Bonia and Goswami, 2011). In this connection Tanaka *et al.* (2008) observed that there was relationship between milk production and oxidative stress markers concentration in plasma with some concomitant variations of oestrogen, progesterone and cortisol during the time of onset of oestrus (Walker *et al.* 2008). Report revealed that there was no elevated concentration of glucose or cortisol in metritic cows without mentioning degree but in a

another study both were found to be elevated in cows stressed by recumbence which could not be accepted for chronic endometritis with mucopurulent discharge of different quantity in postpartum cows (Forslund *et al.*; 2010). Almost similar result of serum concentration of protein, glucose, cholesterol and progesterone during oestrus of the experimental crossbred cows. Anyhow, meager information on biological constituents in regards to III degree endometritis is available.

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Table 1. Response and conception rate of endometritic cows after administration of different treatments

Group	Number of Cows treated	Treatment combination	Drug volume and route of administration	Number of Cows conceived (%)
Group-I	10	Lugol's 0.20%	30 ml, intra-uterine	0(0)
		Pheneramine Maleat inj. 113.75mg (Avil, Intervet)	5ml, intra-muscularly	
Group-II	10	Ciprofloxacin 750 mg+ Tinidazol 1800 mg (Ciflox-TZ(I.U), Intervet)	30 ml, intra-uterine for three days daily	1(10)
		Pheneramine Maleat 113.75mg (Avil, Intervet)	5ml, intra-muscularly	
Group-III	10	Ciprofloxacin 750 mg+ Tinidazol 1800 mg (Ciflox-TZ(I.U), Intervet)	30 ml, intra-uterine for three days daily	2(20)
		Ciprofloxacin 240 mg injection (Intervet)	6 ml, intra-muscular for five days daily	
		Pheneramine Maleat inj. 113.75mg (Avil, Intervet)	5ml, intra-muscularly	
Group-IV	10	Ciprofloxacin 750 mg + Tinidazol 1800 mg (Ciflox-TZ(I.U), Intervet)	30ml, for three days daily	5(50)
		Ciprofloxacin 240 mg injection (Intervet)	6 ml, intra-muscular for five days daily	
		Cloprostenol 500mcg (Vetcare)	2 ml intra-muscular	
		Avil- Pheneramine Maleat 113.75mg (Intervet)	5ml, intra-muscularly	
Group-V	10	Ciprofloxacin 750 mg+ Tinidazol 1800 mg (Ciflox-TZ(I.U), Intervet)	30 ml, intra-uterine for three days daily	7(70)
		Ciprofloxacin 240 mg injection (Intervet)	6 ml, intra-muscular for five days daily	
		Cloprostenol 500mcg (Vetcare)	2 ml intra-muscular	
		Vita-A- 12,00,000 I.U. (Veta-A, TTK)	4 ml deep intra-muscular at alternate days for five occasions	
		Pheneramine Maleat 113.75mg (Avil, Intervet)	5ml, intra-muscularly	
Group-VI	10	Ciprofloxacin 750mg + Tinidazol 1800 mg (Ciflox-TZ(I.U), Intervet)	30ml, intra-uterine for three days daily	9(90)
		Ciprofloxacin 240mg injection (Intervet)	6 ml, intra-muscular for five days daily	
		Cloprostenol 500mcg (Vetcare)	2 ml, intra-muscular	
		VitaA- 12,00,00 I.U. (Veta-A, TTK)	4 ml deep intra-muscular at alternate	

			days for five occasions	
		Tonophosphan(Intervet)	6ml, intra-muscularly at alternate days for five occasions	
		Pheneramine Maleat 113.75mg (Avil, Intervet)	5ml, intra-muscularly	
Group-VII	10	Ciprofloxacin 750mg + Tinidazol 1800 mg(Ciflox-TZ(I.U),Intervet)	30ml, intra-uterine for three days daily	9(90.00)
		Ciprofloxacin 240mg injection(Intervet)	6 ml, intra-muscular for five days daily	
		Cloprostenol 500mcg(Vetcare)	2 ml, intra-muscular	
		VitaA- 12,00,00 I.U.(Veta-A, TTK)	4 ml deep intra-muscular at alternate days for five occasions	
		Tonophosphan(Intervet)	6ml, intra-muscularly at alternate days for five occasions	
		Vit. E -500mg +Selenium -15 mg(eCareSE, Vetcare)	10ml, intra-muscular for 3 days	
		Pheneramine Maleat 113.75mg (Avil, Intervet)	5ml, intra-muscularly	

Table 2. Mean levels of different biochemical constituents of blood before and after treatment of chronic endometritis

Experimenta l Groups	Biological constituents	Day of oestrus (Before Treatment)	2 nd Oestrus(Sexual rest)	3 rd Day of Oestrus/AI
Group-I	Glucose (mg/dl)	53.43±4.38(10)	61.45±3.87(10)	62.88±5.23(10)
	Protein g/dl	9.23 ±0.35(10)	9.49±0.34(10)	9.48±0.46(10)
	Cholesterol(mg/dl)	125.35±1.65(10)	107.51±3.21(10)	106.78±2.78(10)
	alkaline phosphatase (IU/ml)	467.52±45.89(10)	338.59±51.06(10)	339.21±65.34(10)
	Progesterone(ng/ml)	0.35±0.05(10)	0.58±0.02(10)	0.59±0.05(10)
	Cortisol (nM/L)	57.37±0.26(10)	40.58±0.15(10)	38.17±0.83(10)
Group-II	Glucose (mg/dl)	55.12±4.12(10)	56.58±4.10(10)	68.42(1)
	Protein g/dl	9.89±0.36(10)	10.38±0.52(10)	10.45(1)
	Cholesterol(mg/dl)	124.87±3.02(10)	105.76±2.89(10)	106.31(1)

	alkaline phosphatase (IU/ml)	450.74±54.39(10)	401.34±53.61(10)	398.67(1)
	Progesterone(ng/ml)	0.43±0.04(10)	0.57±0.07(10)	0.63(1)
	Cortisol (nM/L)	56.62±1.23(10)	38.59±0.98(10)	36.41(1)
Group-III	Glucose (mg/dl)	55.45±3.94(10)	57.56±4.76(10)	67.98(2)
	Protein g/dl	9.88±0.67(10)	10.78±0.75(10)	10.89(2)
	Cholesterol(mg/dl)	124.58±3.76(10)	104.57±4.52(10)	104.34(2)
	alkaline phosphatase (IU/ml)	471.33±61.23(10)	367.13±47.57(10)	362.07(2)
	Progesterone (ng/ml)	0.44±0.02(10)	0.59±0.05(10)	0.75(2)
	Cortisol (nM/L)	61.03±1.71(10)	43.29±0.75(10)	34.92(2)
Group-IV	Glucose (mg/dl)	54.43±3.54(10)	57.58±4.76(10)	66.68(5)
	Protein g/dl	9.88±0.67(10)	10.78±0.75(10)	10.89(5)
	Cholesterol(mg/dl)	124.22±4.04(10)	105.77±2.32(10)	105.56±0.1.66(5)
	alkaline phosphatase (IU/ml)	453.58±55.33(10)	390.07±36.17(10)	389.41±51.42(5)
	Progesterone(ng/ml)	0.38±0.05(10)	0.53±0.04(10)	0.58±0.03(5)
	Cortisol (nM/L)	56.87±1.02(10)	40.51±0.67(10)	39.75±0.77(5)
Group-V	Glucose (mg/dl)	55.45±3.59(10)	57.32±3.76(10)	65.74±5.97(9)
	Protein g/dl	9.88±0.43(10)	10.04±0.39(10)	10.75±0.41(9)
	Cholesterol(mg/dl)	124.78±2.71(10)	107.43±2.69(10)	106.67±3.36(9)
	alkaline phosphatase (IU/ml)	455.06±55.39(10)	391.21±45.33(10)	392.46±39.87(9)
	Progesterone(ng/ml)	0.36±0.04(10)	0.51±0.05(10)	0.53±0.03(9)

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	Cortisol (nM/L)	53.83±0.83(10)	43.26±0.65(10)	39.89±0.83(9)
Group-VI	Glucose (mg/dl)	54.72±3.89(10)	57.45±4.01(10)	65.74±5.29(9)
	Protein g/dl	8.99±0.49(10)	9.96±0.71(10)	10.52±0.43(9)
	Cholesterol(mg/dl)	124.78±2.71(10)	107.43±2.69(10)	106.67±3.36(9)
	alkaline phosphatase (IU/ml)	455.06±555.39(10)	391.21±45.33(10)	392.46±39.87(9)
	Progesterone(ng/ml)	0.36±0.04(10)	0.51±0.05(10)	0.53±0.03(9)
	Cortisol (nM/L)	53.83±0.83(10)	43.26±0.65(10)	39.89±0.83(9)
Group-VII	Glucose (mg/dl)	53.34±3.63(10)	60.78±4.54(10)	64.56±2.97(9)
	Protein g/dl	9.64±0.33(10)	10.41±0.33(10)	10.38±0.54(9)
	Cholesterol(mg/dl)	124.78±2.71(10)	107.43±2.69(10)	106.67±3.36(9)
	alkaline phosphatase (IU/ml)	455.06±55.39(10)	391.21±45.33(10)	392.46±39.87(9)
	Progesterone (ng/ml)	0.36±0.04(10)	0.51±0.05(10)	0.53±0.03(9)
	Cortisol (nM/L)	53.83±0.83(10)	43.26±0.65(10)	39.89±0.83(9)

Within parentheses indicated number of observations