RESEARCH ARTICLE

Evaluating Therapeutic Efficacy of Cephalexin and $PGF_2\alpha$ in the Management of Endometritis in Crossbred Cattle

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Abstract

Twenty-four cows diagnosed with subclinical endometritis (SCE) were divided into four equal groups: Group I (Cephalexin intrauterine infusion), Group II (intramuscular $PGF_2\alpha$), Group III (combined Cephalexin and $PGF_2\alpha$), and Group IV (untreated control). Diagnostic parameters included were haemato-biochemical, enzymatic, ultrasonographic and cytological assessments before treatment and after treatment (*i.e.* next estrus). White side test (WST) with a 45.83% positivity rate and endometrial cytology with PMN cell count exceeding 5% was found. PMN cell count decreased significantly, with Group III from 13.33 ± 0.67% to 2.50 ± 0.55% post-treatment. Ultrasonography indicated reductions in intraluminal fluid and endometrial thickness in treated groups. Post-treatment haemoglobin and TLC levels were highest in Group III with values of 11.42±0.19 g/dL and 10.15±0.10 × 10^3/µL, respectively. Biochemical analyses showed significant increase in total protein and globulin levels in treated groups. Enzymatic activity of ALT and AST decreased significantly in Groups I and III, reflecting reduced uterine inflammation. Progesterone levels remained stable across all groups indicating normal luteal function. The findings highlight the efficacy of the combined Cephalexin and $PGF_2\alpha$ treatment protocol (Group III) in normalizing altered haemato-biochemical profile and managing SCE in bovine.

Key words: Cephalexin, Crossbred cattle, Endometritis, $PGF_2\alpha$.

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Introduction

Endometritis, characterized by inflammation of the endometrial lining of the uterus, is often caused by bacterial contamination following parturition. Factors such as retained fetal membranes, dystocia, or metritis exacerbate the risk of uterine infections, overwhelming the natural defense mechanisms of the reproductive tract (Sheldon and Dobson, 2004). Clinical signs, such as purulent or mucopurulent vaginal discharges, are often used to diagnose clinical endometritis (CE). However, subclinical cases, which lack overt signs, remain undetected without specialized diagnostic methods, leading to underestimated prevalence rates in the field (Chethan, 2011). Uterine cytology and the White side test (WST) are essential for identifying both clinical and subclinical endometritis. Uterine cytology using the cytobrush technique offers a precise assessment of polymorphonuclear neutrophil (PMN) infiltration, which serves as a reliable indicator of uterine inflammation. Coupled with ultrasonographic evaluation, these methods provide a comprehensive approach to diagnose and monitor uterine health (Hendricks *et al*., 2006). This study aims to diagnose endometritis affected crossbred cattle by White side test, uterine cytology and to evaluate the therapeutic efficacy of Cephalexin and $PGF_2\alpha$, individually and in combination, for managing endometritis in crossbred cows.

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Materials and Methods

Selection of Animal

This investigation was conducted on crossbred cows in estrus, presented to the Veterinary Clinical Complex, Livestock Farm Complex, CVSc & AH, OUAT, Bhubaneswar (India) as well as

on cases attended through doorstep services in and around Bhubaneswar locality. The cows in this study were owned by private farmers and managed under traditional husbandry practices. Healthy, breedable cows from the 1st to the 5th parity were selected for the experiment. Preliminary data, including each cow's age, vaccination history, breeding history, milk yield, feeding status, habitat, and behaviour, were collected from the owners. Cows with any undercurrent diseases were excluded from the study. Screening of the selected cows involved a thorough physical examination, which assessed respiration, temperature, pulse, the nature of vaginal mucus discharge, and estrus behaviour. Each animal was confirmed to be vaccinated at six-month intervals, with deworming performed before vaccination.

Gynaecological Examination and Detection of Endometritis

Gynaeco-clinical examination was conducted on each experimental cow through per-rectal examination using aseptic techniques following proper restraint of the animals (Ahmadi *et al*., 2010 and Biswal *et al.,* 2014). Rectal palpation of each cow's genital tract was performed to rule out acquired conditions, including cervicitis, salpingitis, cystic ovarian degeneration, or any adhesions to the broad ligament or pelvic cavity. A careful assessment of the vulva, vagina, cervix rigidity, uterine tone, and ovarian contour was conducted through gentle palpation. Additionally, the colour, consistency, and transparency of vaginal discharge were examined and analysed to ensure accurate diagnosis of endometritis. The cows with history of conception failure for more than three inseminations and having mucopurulent discharge or discharge with pus flakes and cloudy discharge (LeBlanc *et al.,* 2002 and Sheldon and Dobson, 2004) were subjected to White side test, uterine cytology examination and utlrasonography. Arbitrarily >5% PMN threshold was used to diagnose cows having endometritis of clinical or subclinical type as recommended by Fischer *et al*. (2010).

Endometrial Cytology

Endometrial samples for cytological examination were collected using a modified sterile cervical cytology brush (AGS Healthcare, GF no-659, North Street, Aathirikuppam, Tamilnadu-607805), adapted for large animals as described by Ahmadi *et al. (*2006).

White Side Test

To identify subclinical endometritis (SCE) in animals that did not show clinical sign of endometritis, a Whiteside test was conducted, following the method described by Pateria and Rawal (1990).

Ultrasonographic Evaluation

The uterus was assessed transrectally using a real-time color Doppler ultrasound system (Sonosite M-Turbo) equipped with a linear array transducer operating at 5-10 MHz. For each evaluation, the imaging parameters such as gain, brightness, and contrast were carefully adjusted to ensure optimal visualization. On day 0 of estrus, the average uterine wall thickness was measured via ultrasonography for all four groups. Additional parameters recorded included endometrial thickness, cervical diameter, and the presence of intraluminal fluid, with measurements taken in millimeters using the ultrasound scanner's integrated scale. The ultrasonographic images displayed various shades of grey, white, and black, with tissue echogenicity classified as hyperechoic, hypoechoic, or anechoic based on their capacity to reflect ultrasound waves.

Haemato-Biochemical Analyses

Five mL of blood was aseptically collected from each animal by jugular venipuncture before treatment and at next estrus. Two mL was placed in an EDTA-treated vial for haematological analysis and rest 3 mL was transferred to serum separator tubes, allowed to clot for 2 h at room temperature and then centrifuged at 1000 × g for 20 min. Serum was stored at -20°C for subsequent biochemical and hormonal analysis. Haematological parameters including haemoglobin, total leukocyte count (TLC), and differential count (DC) were assessed using standard routine techniques. Serum biochemical parameters analysed included total protein, albumin, globulin, A/G ratio, cholesterol and enzymatic markers like ALT and AST using procedures and assay kits of Coral Clinical system, Goa on the biochemistry analyser (Fujifilm India Private Limited). The concentration of serum progesterone was estimated by using the kit prepared by ELK Biotechnology. This assay uses a competitive inhibition enzyme immunoassay technique.

Treatment Protocol

Twenty-Four (24) crossbred cows in the age group of 3-7 years showing sub-clinical signs of endometritis were selected and categorized as Group-I, II, III, IV (6 cow in each Group) and were managed as under. Group-I cows were treated with 30 mL of Cephalexin as intrauterine infusion during estrus. Group-II cows were treated with 2 mL of $PGF_2\alpha$ through intramuscular route once after 11 days of estrus. Group-III cows were treated with both 2 mL $PGF_2\alpha$ through intramuscular route and 30 mL Cephalexin as intrauterine infusion. Group-IV cows included endometritic animals without any treatment and served as positive control. Treatment response was assessed through White side test, PMN cells by uterine cytobrush, USG and haemato-biochemical analyses before and after treatment.

Statistical Analysis

The data analysis was performed using the Statistical Package for the Social Sciences (SPSS) software (Version 16.0) with ANOVA.

Results and Discussion

Diagnosis of Endometritis

The selected cows in all four groups though differed significantly in their PMN cell count, all were found to have

initial PMN Cell count greater than 10%, which reduced to less than 5% in all three treatment groups, but no such change was noted in the untreated positive control group IV (Table 1). The prevalence of SCE determined using PMN Cell count measurements was calculated to be 100% initially, which could be cured with all three treatment approaches. Elevated PMN numbers in uterine cytology are a hallmark of uterine infection and a predictor of reproductive inefficiency. This correlation highlights the diagnostic value of PMN counts in identifying cows with uterine infections, even in cases where clinical signs may not be immediately apparent.

Among the 24 cows tested using the White side test (WST) with vaginal aspirates, 11 cows (45.83%) were identified as positive for subclinical endometritis (SCE). Based on the ultrasonographic findings, SCE was diagnosed in 7 cows (29.16%). A total of 9 cows (37.5%) were found to have an endometrial thickness greater than 8 mm, classifying them as cases of SCE. The prevalence of SCE determined using endometrial thickness (ET) measurements was calculated to be 37.5%. In case of uterine infections, the release of pro-inflammatory cytokines such as IL-6, TNF-α, and IL-1β triggers the migration of PMNs from the bloodstream into the uterine tissue (Kasimanickam *et al*., 2004).

Haematological findings showed that haemoglobin concentration, TLC, neutrophils and lymphocyte counts were statistically similar initially, but differed significantly among four groups at day 21 post-treatment, with the highest values of all, except lymphocytes, in all groups. Further, the values of TLC and neutrophils count increased significantly, while lymphocyte, monocytes and eosinophil counts decreased ($p<0.05$) at subsequebnt estrus following all three treatments, but no such change was noticed in positive control group. The Hb level improved significantly and basophils decreased non-significantly at 21 days post-treatment in groups I to III (Table 1). Sarma *et al*. (2012) documented a notable increase in haemoglobin levels ($p<0.01$) following treatment in their experimental groups. Reddy *et al*. (2012) and Sahoo *et al*. (2014 observed no significant changes in total leukocyte count before and after treatment. Heidarpour *et al*. (2014) observed a notable reduction ($p<0.01$) in lymphocyte and neutrophil counts post-treatment in cows with clinical and subclinical endometritis, however the decrease in eosinophil counts was non-significant (Heidarpour *et al*., 2014; Sahoo *et al*., 2014). Kim *et al*. (2005) observed elevated monocyte levels in postpartum cows with endometritis, attributing this to the immune system's attempt to resolve localized infections. Basophil counts remained largely within the physiological range, consistent with Ahmad *et al*. (2003) and Pathan *et al*. (2011), who found no significant variations in basophil levels across different reproductive states. While basophils are not the primary cells implicated in reproductive pathophysiology, their role in early immune activation cannot be overlooked.

The mean values of all the serum biochemical constituents studied initially were statistically similar between groups, however at post-treatment stage day 21, the total protein, globulin, A:G ratio and cholesterol concentrations increased, while the ALT and AST concentrations decreased in all 3 treatment groups as compared to their pre-treatment values and even control Group IV (Table 1). Reddy (2012) reported significantly reduced total protein values (6.28±0.17 to 6.93±0.19 g/dl) prior to the initiation of therapy in SCE cows, which increased significantly post-treatment (7.35±0.19 to 7.62±0.17 g/dL), indicating notable variation within the group. Decrease in albumin levels post-treatment suggests a possible redistribution of protein, likely as part of the inflammatory response or altered metabolic processes during recovery from reproductive disorders. Magnus and Lali (2009) and Biswal *et al*. (2014) have documented an increase in globulin during recovery phases, suggesting a common physiological mechanism aimed at combating infection and supporting reproductive recovery. Decrease in the A:G ratio observed could be that the treatment led to an immune response, resulting in increased globulin levels as part of the recovery process. Serum cholesterol is a precursor for reproductive hormones, and since endometritis is both an inflammatory and infectious reproductive disorder, it is presumed to cause alterations in the hormonal balance of the body. Das *et al*. (2012) and Amle *et al*. (2014) also recorded significantly lower cholesterol values in repeat breeder cows compared to normal cyclic animals. The ALT and AST activities observed in this study fall within the normal physiological range, as outlined by Radostits *et al*. (2007). Post-treatment, both ALT and AST levels decreased significantly in this study, indicating recovery from uterine infection and a return to normal metabolic function. The elevation of these enzymes could be linked to the inflammatory condition of the endometrium, which likely caused tissue damage (Heidarpour *et al*. 2014).

The serum progesterone levels in all 4 groups before and after treatment were statistically similar (Table 1). Suresh *et al*. (2021) observed comparable progesterone levels between normal cyclic cows and repeat breeder cows (2.41±0.12 and 2.19±0.29 ng/mL). Progesterone, a hormone produced by the corpus luteum following ovulation, decreases as the corpus luteum regresses in non-pregnant animals. This decline typically begins around days 18-19, leading to the onset of estrus by days 20-22 (Ahammed *et al*., 2018).

Conclusion

The study found that subclinical endoetritis causes significant alteration in the haemato-biochemical profile of animal, and these could be normalized at subsequent estrus following various therapies. The combined Cephalexin (i/ut) and $PGF_2\alpha$ (i/m) therapy emerged as the better strategy in place of Cephalexin or PGF2α alone in normalizing blood profile as well as endometrial PMN cell counts and managing endometritis in crossbred dairy cows.

Table 1: PMN cell count, haemato-biochemical parameters, and progesterone assay before and after treatment in SCE affected cattle

Attributes	Day	Treatment Group (n=6 each)			
		I Cephalaxin	II $PGF_2\alpha$	III Both C+P	IV Control
PMN Cell	0	10.17^{aB}±0.48	11.50^{bB}±0.43	13.33^{cB}±0.67	11.83^{b}±0.48
	21	3.33^{abA}±0.82	4.50^{bA}±0.55	2.50^{aA}±0.55	12.17^{c}±1.17
Haemoglobin (g/dL)	0	9.90±0.82	10.03±0.58	9.67±0.26	9.87±0.23
	21	11.20^{b}±0.58	10.95^{b}±0.38	11.42^{b}±0.19	9.78^{a}±0.30
TLC (10^3/µL)	0	6.85^{A}±0.09	7.22^{A}±0.06	6.98^{A}±0.18	7.28±0.16
	21	7.90^{B}±0.07	9.17^{B}±0.08	10.15^{B}±0.10	7.18±0.22
Neutrophil (%)	0	30.03^{A}±0.27	30.63^{A}±0.55	30.55^{A}±0.43	29.62±0.28
	21	37.67^{bB} ±0.15	41.20^{cB}±0.21	42.55^{cB} ±0.19	30.15^{a}±0.28
Lymphocytes (%)	0	59.37^{B}±0.45	60.43^{B}±0.34	59.53^{B}±0.42	60.53±0.36
	21	56.25^{bA}±0.50	51.78^{aA}±0.48	50.37^{aA}±0.48	60.07^{c}±0.35
Monocytes (%)	0	5.24^{B}±031	5.12^{B}±0.15	4.97^{B}±0.16	4.82±0.16
	21	3.34^{A}±0.71	3.41^{A}±0.18	3.23^{A}±0.29	4.71±0.17
Eosinophils (%)	0	4.90^{B}±0.14	4.85^{B}±0.16	5.10^{B}±0.16	4.70±0.12
	21	3.15^{A}±0.18	3.07^{A}±0.19	3.02^{A}±0.21	4.62±0.14
Basophils (%)	0	1.23^{a} ±0.13	1.75^{b}±0.08	1.43^{a}±0.08	1.50^{a}±0.14
	21	1.43±0.14	1.63±0.11	1.55±0.12	1.55±0.09
Total protein (g/dL)	0	7.17±0.12	7.13±0.10	7.15±0.11	7.08±0.10
	21	7.67^{b}±0.08	7.42^{b}±0.12	7.40^{b}±0.09	6.98^{a}± 0.14
Albumin (g/dL)	0	3.87±0.07	3.88±0.17	3.85±0.15	3.87±0.17
	21	3.63±0.11	3.58±0.13	3.33±0.10	3.78±0.13
Globulin (g/dL)	0	3.30^{A}±0.23	3.25^{A}±0.18	3.30^{A}±0.20	3.22±0.19
	21	4.03^{bB}±0.11	3.83^{bB}±0.21	4.07^{bB}±0.12	3.20^{a}±0.23
A:G ratio	0	1.22^{B}±0.14	1.23^{B}±0.11	1.21^{B}±0.12	1.24±0.14
	21	0.91^{bA}±0.05	0.96^{bA}±0.09	0.82^{aA}±0.05	1.23^{c}±0.13
ALT (U/L)	0	35.28^{B}±0.72	35.10^{B} ±0.73	35.28^{B}±0.68	35.63±0.81
	21	25.23^{aA}±0.31	30.43^{bA}±0.59	24.92^{aA}±0.44	35.43^{c}±0.64
AST (U/L)	0	125.72^{B}±0.29	128.07^{B}±0.76	123.62^{B}±0.64	124.87±0.97
	21	84.77^{aA}±0.66	91.58^{bA}±1.09	83.77^{aA}±0.73	124.18^{c}±1.09
Total cholesterol (mg/dL)	0	165.72^{A}±0.89	171.27^{A}±0.89	166.13^{A}±1.44	164.75±1.15
	21	198.07^{bB}±0.63	198.22^{bB}±1.11	200.90^{bB}±0.68	164.38^{a}±1.32
Progesterone (ng/dL)	0	0.75±0.08	0.81±0.05	0.71±0.07	0.68±0.08
	21	0.64±0.07	0.72±0.05	0.76±0.06	0.71±0.07

Values bearing different superscripts (abc) in a row and (AB) in a column for a parameter differ significantly ($p<0.05$).

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