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Dr. Rejitha Joseph

Assistant Professor, Department
of Veterinary Physiology,
College of Veterinary and Animal
Sciences, Pookode, Kerala, India

Comparative efficacy of intrauterine oxytetracycline-metronidazole combination versus cephalixin in the treatment of repeat breeder cows

Rejitha Joseph

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Abstract

A study was conducted on twelve crossbred cattle at Thiruvambadi Grama Panchayat in Kozhikode district to evaluate the efficacy of different intrauterine antibiotic preparations in treating infertility. Six animals were treated with intrauterine cephalixin (4 g), while the remaining six received a combination of oxytetracycline (1.5 g/30 ml) and metronidazole (150 mg/30 ml). Following antibiotic therapy, one estrus cycle was discarded to allow natural uterine cleansing. Ten days after estrus, the presence of a functional corpus luteum was confirmed, after which two doses of a prostaglandin analogue were administered intramuscularly at an interval of 11 days. Artificial insemination (AI) was performed on the 3rd and 4th days following the final prostaglandin injection, and pregnancy was confirmed 90 days later by rectal palpation. None of the cephalixin-treated animals conceived, whereas four out of six animals treated with the oxytetracycline-metronidazole combination conceived. The findings suggest that the oxytetracycline-metronidazole combination is effective in improving conception rates in repeat-breeding cattle, whereas cephalixin was ineffective under field conditions in Thiruvambadi, Kozhikode.

Keywords: Cephalixin, oxytetracycline, metronidazole, prostaglandin, infertility

1. Introduction

Infertility and subfertility in dairy cattle represent significant constraints to herd productivity, extending calving intervals, increasing insemination costs, and heightening culling rates. Among these, the repeat breeding syndrome characterized by failure to conceive after three or more inseminations despite regular estrous cycles and apparently normal genital tracts is of particular economic and clinical concern^[1].

One of the frequently implicated etiologies of repeat breeding is subclinical endometritis or uterine infection, which may not present overt clinical signs but can disrupt early embryonic survival or uterine receptivity^[2, 3]. To address this, intrauterine antibiotic therapy has long been employed under field conditions, often in conjunction with hormonal synchronization protocols. However, the choice of antibiotic whether to use a broad-spectrum agent, a therapy targeting anaerobes, or a combination remains debated, especially under diverse field settings.

Previous studies have evaluated intrauterine use of oxytetracycline, gentamicin, cephalixin, and combination formulations, though results have been inconsistent. For instance, Parikh *et al.*^[4] compared multiple intrauterine drugs in repeat breeder cows (including oxytetracycline-based remedies). Kutty^[5] reported favourable conception outcomes following intrauterine gentamicin infusion in repeat breeder cross-bred cows. In a comparative trial of intrauterine infusions, Mastalone-U (a multiantibiotic combination) at higher doses resulted in poorer conception rates than lower-dose controls or other agents, cautioning against indiscriminate use^[6]. The incidence of subclinical endometritis among repeat breeders has also been documented: Kumar and colleagues^[7] reported that cows with $\geq 4\%$ polymorphonuclear cells on cytology benefited variably from intrauterine antibiotic or herbal therapies. Despite these efforts, there is still a scarcity of direct comparisons between combinations targeting both aerobic and anaerobic flora (e.g. oxytetracycline + metronidazole) versus conventional single-spectrum agents like cephalixin, especially under real-world field conditions.

Corresponding Author:

Dr. Rejitha Joseph

Assistant Professor, Department
of Veterinary Physiology,
College of Veterinary and Animal
Sciences, Pookode, Kerala, India

Moreover, the rising issue of antimicrobial resistance underscores the need for evidence-backed antibiotic choices rather than empirical therapy [8, 9].

In Kerala and much of India, where dairy farms operate under varied management conditions, there is a need for pragmatic, field-validated protocols for treating repeat breeders effectively. The present investigation was thus undertaken with the objective to compare the efficacy of intrauterine oxytetracycline-metronidazole combination versus intrauterine cephalaxin (each combined with a standard synchronization + timed AI protocol) in repeat breeder cows under field conditions in Kozhikode district, Kerala. Through this comparative approach, the study seeks to address whether broad-spectrum + anaerobe coverage provides a meaningful advantage over a conventional cephalosporin in improving pregnancy outcomes in repeat breeding cattle.

2. Materials and Methods

The study was conducted on 12 crossbred cows with a history of repeat breeding presented at the Veterinary Dispensary, Thiruvambadi, Kozhikode district, Kerala. Animals had body score range from 2-3. Per-rectal examination revealed no palpable ovario-uterine abnormalities. Animals were randomly divided into two groups:

- **Group I (N=6):** Treated with intrauterine cephalaxin (4 g; Lixen).
- **Group II (N=6):** Treated with a combination of oxytetracycline (30 ml; 50 mg/ml Zydus) and metronidazole (30 ml; 5 mg/ml, Metrogyl).

Antibiotics were administered during estrus, and the subsequent estrus cycle was discarded to allow for natural uterine cleansing. Ten days later, per-rectal examination was performed to identify a functional corpus luteum, following which prostaglandin analogue (500 µg) was administered intramuscularly. A second prostaglandin dose was given 11 days later. Artificial insemination was carried out on the 3rd and 4th days after the final prostaglandin injection. Pregnancy diagnosis was performed by rectal palpation 90 days after AI. Two groups were compared using independent two sampled t-test and graph was plotted (Graph Pad Prism 10.5).

3. Results

In the present study, none of the six cows treated with intrauterine cephalaxin conceived, whereas 4 out of 6 animals (66.7%) treated with the oxytetracycline-metronidazole combination became pregnant and statistically significant ($P=0.025$; Figure 1). This outcome highlights the markedly superior efficacy of the oxytetracycline-metronidazole regimen in managing repeat breeding under field conditions.

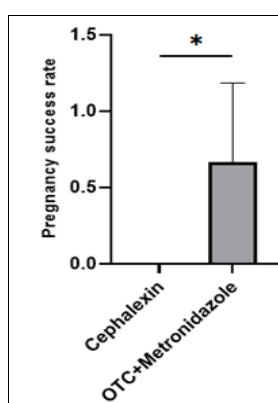


Fig 1: Comparison of pregnancy success rate of groups (* $p<0.05$)

4. Discussion

Infertility, particularly due to subclinical endometritis, is a leading contributor to reproductive inefficiency and economic losses in high-yielding dairy herds [3]. The subclinical nature of many uterine infections makes diagnosis challenging, prompting reliance on empirical intrauterine therapies aimed at improving uterine health and subsequent conception rates.

Oxytetracycline is widely recognized for its broad-spectrum antibacterial activity, particularly effective under the anaerobic conditions present within the postpartum bovine uterus [10, 11]. In field studies, its combined use with prostaglandins has yielded positive outcomes in cows diagnosed with endometritis [12].

The addition of metronidazole, which is particularly effective against obligate anaerobes and protozoa, further broadens the antimicrobial coverage and enhances therapeutic efficacy. This synergistic approach may account for the higher conception rate observed in the present study.

The use of prostaglandin analogues in both groups likely aided uterine involution and estrous synchronization, facilitating timed artificial insemination. Prostaglandins have previously been shown to improve fertility in cows with endometritis or a persistent corpus luteum [12, 13], aligning with the present protocol.

In contrast, cephalaxin, a first-generation cephalosporin primarily effective against gram-positive organisms, failed to improve conception in this cohort. Similar results have been reported by Parikh *et al.* [4], where cephalaxin showed limited efficacy in repeat breeder cows compared to other intrauterine agents such as gentamicin and oxytetracycline. The ineffectiveness of cephalaxin in this study could be due to the presence of mixed or anaerobic bacterial populations in the uterine environment, against which cephalaxin has limited action. Furthermore, the indiscriminate or prolonged use of antibiotics like cephalaxin may contribute to emerging antimicrobial resistance, as reported in cephalaxin-resistant *Campylobacter* strains isolated from livestock [9]. This underlines the importance of judicious antibiotic selection based on field efficacy and potential resistance profiles.

Taken together, these findings underscore that a combination therapy targeting both aerobic and anaerobic pathogens such as oxytetracycline with metronidazole offers superior outcomes in treating repeat breeder cows. This approach, when integrated with appropriate hormonal protocols, may substantially improve fertility in field conditions. However, larger-scale studies are warranted to validate these findings and assess potential regional variations in antimicrobial resistance and bacterial flora.

5. Conclusion

The combination of oxytetracycline and metronidazole, when used along with sexual rest, timed artificial insemination, and double administration of prostaglandin, improved the pregnancy rate in repeat-breeding cattle. In contrast, cephalaxin failed to produce positive results, suggesting that it is not a suitable intrauterine antibiotic choice under the field conditions of Thiruvambadi. The findings also raise the possibility of emerging cephalaxin resistance in reproductive tract infections. Further field-based studies with larger sample sizes are required to confirm this resistance pattern and to establish effective therapeutic strategies for managing infertility in dairy cattle.

Conflict of Interest

Not available

Financial Support

Not available

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