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Therapeutic efficacy of cefquinome in management of subclinical mastitis in buffaloes

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Abstract
Subclinical mastitis is an inflammatory reaction of udder tissue without apparent signs mainly caused by microorganisms characterized by high somatic cell count. The present study was conducted in 120 buffaloes affected with subclinical mastitis to assess the therapeutic efficacy of cefquinome. Buffaloes with subclinical mastitis were divided into four groups (30 animals in each group) and were subjected to 4 different treatment protocols and recovery status was assessed based on CMT score and Somatic cell count. Animals in group I and II were administered with injection Cefquinome and injection Enrofloxacin respectively. In Group III and IV herbal spray were administered along with antibiotics in group I and II. Highest recovery was recorded in group III (96.67%) and group IV (96.67%) followed by group II (93.33%), group I (90%). A significant decline in CMT score and somatic cell count was also recorded.

Keywords: Subclinical mastitis, cefquinome, somatic cell count, CMT

Introduction
Mastitis, an inflammation of mammary gland may be classified as clinical and subclinical forms. Clinical mastitis is readily observed and easily detected by abnormal milk secretions, whereas subclinical mastitis is asymptomatic and difficult to be observed and is diagnosed by the reservoir of pathogen infection in milk (Barlow, 2011) [4]. Current annual economic losses due to mastitis in India have been estimated to be Rs. 7165.51 crore that include Rs. 4151.16 crore and Rs. 3014.35 crore due to subclinical and clinical mastitis, respectively (Bansal and Gupta, 2009) [2]. Total losses due to mastitis per lactation in Purvanchal Region of Uttar Pradesh in Nondescript cows, Crossbred cow and buffalo were INR 868.34, INR 1, 314.10 and INR 1, 272.36, respectively (Singh *et al.*, 2014) [16].
Sub-clinical mastitis has more importance (5-20% in buffaloes) than clinical mastitis (1-10) because it is 15-40 times more prevalent than the clinical form**,** it drastically reduces milk yield. It usually precedes the clinical form and is usually the basis of herd problems when mastitis outbreaks occur. Early diagnosis and management of mastitis is important in large scale control programmes of diseases at farms. Selection of antibiotic for management of mastitis mainly depends upon the type of organism involved in the mastitis and ABST results which may vary with the different geographical localities (Sharma *et al.*, 2006; Zonca *et al.*, 2011) [15, 19]. Efforts have been made from years to evolve a potent therapeutic protocol.
Cefquinome is a fourth-generation cephalosporin characterized by a broad-spectrum and stable against penicilinases and beta-lactamases bacterial enzymes (Rossi *et al.*, 2019) [13], available for intramammary (IMM) and intramuscular (IM) administration for mastitis treatment. Cefquinome has been recommended for systemic treatment of mastitis, has been appealing to farmers because treating multiple infected quarters with a single course of IM treatment could be more cost-effective than using several IMM tubes although little research has demonstrated its ability to reach proper concentrations within the mammary tissue (Ehinger *et al.*, 2006) [9]. The present study deals with treatment of subclinical mastitis in buffaloes with Cefquinome.

Material and Methods
Selection of Animal: Present study was conducted in 120 buffaloes positive for subclinical mastitis on dairy farms and villages in and around Ayodhya and Sultanpur districts of Uttar Pradesh.

A thorough examination of udder was performed for the detection of any abnormality in the udder *viz*. presence of any lesion, pain, heat and swelling. Milk from each quarter were striped out for detecting the abnormality in the milk like colour and consistency. These examinations were continued until final selection of the buffaloes (Radostits *et al*., 2010) [12]. All the changes were recorded and compiled.

Screening of animals: Subclinical Mastitis (SCM) cases were defined as those without obvious clinical signs and with a high somatic cell count, as determined using the California mastitis test (CMT) and somatic cell count. So screening of buffaloes was carried out using CMT at field level having no visible changes in milk and positive for CMT were selected for therapeutic trial.

***In vitro* antibiotic susceptibility test:** Sample processing was carried out in the Laboratory of Bacteriology in the Department of Veterinary Microbiology. In-vitro Antimicrobial susceptibility of cefquinome was evaluated using the Kirby-Bauer method in milk culture as per method described by Bauer *et al*., 1966 (Fig. 1). The sub-clinically affected buffaloes were divided into four groups (30 animals in each group) according to the treatment administered and percent recovery was determined based on CMT score and Somatic cell count (Table no. 1). The groups of treatment were:

Table 1: Therapeutic regimen to treat subclinical mastitis

Group	Number of animals	Treatment
I	30	Inj. Cefquinome @1mg/Kg Single intramuscular injection for 3-5 days.
II	30	Inj. Enrofloxacin (Most effective selected on the basis of ABST) @7.5mg/Kg SID, IM for 3 to 5 days.
III	30	Group-I + herbal spray (Mastafast)
IV	30	Group-II + herbal spray (Mastafast)

Statistical analysis: Statistical analysis of data was done by using SPSS 20 software.

Results and Discussion

Table 2: Comparative efficacy of different protocols to treat sub clinical mastitis

Treatment Group	% Recovery	CMT score point		SCC (X 10^5 Cells/ml)	
		Pre	Post	Pre	Post
I	27/30 (90%)	1.9±0.52	0.88± 0.43[a]	8.7±1.96	4.63± 1.96[a]
II	28/30 (93.33%)	1.8±0.4	0.73±0.44[a]	9.53±1.92	4.3±1.53[a]
III	29/30 (96.67%)	1.63±0.48	0.63±0.48[a]	8.03±1.8	4.0±1.34a
IV	29/30 (96.67%)	1.50±0.5	0.6±0.55[a]	8.43±2.10	3.96±1.25[a]

a indicate $P<0.05$

Buffaloes with subclinical mastitis were subjected to 4 different treatment protocols and recovery status was assessed based on CMT score and Somatic cell count (Table 2). Animals in group I and II were administered with injection Cefquinome and injection Enrofloxacin respectively. In Group III and IV herbal spray were administered along with antibiotics in group I and II. Highest recovery was recorded in group III (96.67%) and group IV (96.67%) followed by group II (93.33%), group I (90%). A significant decline in CMT score and somatic cell count was also recorded. Highest recovery in group III and group IV can be attributed to the synergistic action of antibiotic Cefquinome and Enrofloxacin with herbal therapy.

In Group I, the somatic cell count and CMT score point decreased significantly from 8.7±1.96 (X 10^5cells/ml) to 4.63± 1.96 (x 10^5 cells/ml) and from 1.9±0.52 to 0.88± 0.43 respectively. The decrease of somatic cell count in Group II was also statistically significant (9.53±1.92 to 4.3±1.53 x 10^5cells/ml) whereas CMT score point decreased significantly from 1.8±0.4 to 0.73±0.44. In Group III the SCC declined to 4.0±1.34 (x 10^5 cells/ml) from 8.03±1.8 (x 10^5 cells/ml) whereas CMT score point decreased significantly from 1.63±0.48 to 0.63±0.48. In Group IV the somatic cell count decreased significantly from 8.43±2.10 (X 10^5cells/ml) to 3.96± 1.25 (x 10^5 cells/ml) and CMT score point declined to 0.66±0.55 from 1.50±0.5. The health of mammary gland is assessed by the quantity and quality of milk produced (Bansal *et al.*, 2007). Healthy udder produces milk with low Somatic Cell Count (SCC) and no abnormal appearance such as clots. The somatic cells are the milk-secreting epithelial cells that have been shed from the lining of the mammary glands, while leukocytes are due to injury or infection in mammary glands. The usual changes observed in mastitic milk are the consequences of the secretions of these cells (Hovinen and Pyorala, 2011) [10].

The most common bacteria involved are *S. aureus, S. agalactiae, S. pyogenes, Trueperella pyogenes (T. pyogenes), E. coli, K. pneumoniae, K. oxytoca, Enterobacter aerogenes, Pasteurella* spp. (Abdalhamed *et al.*, 2018; Zhang *et al.*, 2018) [1, 18] but *Staphylococcus aureus* and *E. coli* where the major pathogens in mastitis Staphylococcus aureus is a normal inhabitant of udder whereas *E. coli* is an environmental pathogen. Therefore, when these organisms get the opportunity due to trauma or injury to udder, improper milking technique and unhygienic condition, they enter the teat canal and mastitis develops.

Cefquinome (CFQ), a fourth-generation cephalosporin. Cefquinome is approved only for veterinary use and it is highly stable to β-lactamases. Because of its broad spectrum, it has

highly, moderate, and good activity against *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and staphylococci species, respectively. In lactating, it is used IMM for the treatment of clinical coliform and other bacterial mastitis (*Streptococcus uberis*, *Streptococcus dysgalactiae*, *Staphylococcus aureus* (CVMP, 2003; Prescott, 2006) [7, 11] as indicated. Cefquinome, fourth-generation cephalosporins, possesses improved antibacterial activity compared with second- and third-generation cephalosporins and is highly effective against gram-negative bacteria. Cefquinome is

resistant to b-lactamases that are produced by the majority of clinically important bacteria. Chemically, cefquinome is a new cephem; its zwitterionic structure can facilitate rapid penetration across biological membranes, including the porins of the bacterial cell wall. The *in vitro* activity of cefquinome against *Escherichia coli* is comparable with, or better than, third generation cephalosporins; the MIC at 90% and MIC at 50% are 0.13 mg/ml; the resistance rate is 0.4% (Schmid *et al*., 1994; Zonca *et al*., 2011) [14, 19].

Ehinger *et al*., 2006 [9] reported that Minimum inhibitory concentrations (MIC) of cefquinome against common mastitis-causing bacteria such as *E. coli.*, *Streptococcus* spp., *Staphylococcus aureus and Klebsiella* spp. are 0.06 to o.13 (µg/mL), 0.25 to 0.5 (µg/mL), 0.5 to 1 (µg/mL) and 0.13 (µg/mL) respectively.

These pharmacological and antibacterial properties suggest that cefquinome can be of value in the treatment of coliform mastitis. therapeutic efficacy has been observed given once dosage than dosing fractionation following intra-mammary administration of cefquinome, a fourth generation cephalosporin that is developed solely for veterinary use (Yu *et al.*, 2016a) [17].

In the present study, the advantage of one antimicrobial therapy over the other was clearly indicated. This difference was indicated in terms of return to milk production, disappearance of clinical signs of acute mastitis, and return to normal of various hematological and biochemical parameters. This study clearly supported the efficacy of cefquinome in the treatment of bovine mastitis and indicated that cefquinome therapy can improve recovery and survival of mastitic buffaloes and reduce the loss of milk production. (Rossi *et al.*, 2019) [13] reported that percentage points increase in cure rate would justify the use of a fourth-generation cephalosporin (Cefquinome), as opposed to a traditional IMM drugs (cloxacillin and ampicillin) to treat *S. agalactiae* subclinical mastitis.

Conclusion

Subclinical mastitis remains an economically important condition for dairy industry. Subclinical mastitis is characterized by high cell count without visible abnormalities in milk and udder. Cefquinome can be used for treatment of subclinical mastitis. Both CMT and Somatic cell count are reflections of subclinical mastitis status and their decline is indicative of improvement in udder health.

Fig 1: Antibiogram of Cefquinome against Milk culture

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