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Influence of Various Factors That Affect Antibiotic Excretion in Milk

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ABSTRACT: A total of one hundred and twenty milch cows reared in organized and unorganized sectors were screened for antibiotic residues in milk at Bangalore Rural, Kolar and Chickballapur districts by non probability sampling. Influence of various factors like average daily milk yield, stage of lactation, milking hygiene, history regarding treatment with antibiotics, class of antibiotic administered, route of therapy and the time of antibiotic administration on antibiotic residue excretion in milk were noted. Antibiotic commonly used was found to be Beta-lactam group and both parenteral and intramammary route is equally responsible for antibiotic residue excretion.

KEYWORDS: Screening of animals, Antibiotic residues in milk, Beta-lactams

I. INTRODUCTION

Residue is literally defined as 'that which is left over'. The contamination of otherwise usable milk by left-over antibiotic is a frequent sequel to disease treatment in milk-producing animals. Discarding contaminated milk represents a considerable economic loss in itself. Failure to discard such milk may lead to severe penalties if antibiotic is detected in the supply submitted for sale. The existence of residues in milk destined for human consumption, therefore, represents the misuse of products for which the veterinary surgeon has both ethical and statutory responsibility. The aim of this paper is to give background information on a matter of general veterinary concern. Antimicrobial residues in milk and milk products are common in many regions of the world and screening of milk for antibiotics is not a general practice in India. There are only a few published data on the occurrence and levels of antibiotic residues in Indian milk samples. This could be due to non-existence of regulatory laws on antibiotic residues in milk and the perception that this is not a major problem in processed milk sold by commercial dairies due to pooling of large quantities of uncontaminated milk resulting in undetectable amounts of antibiotic residues in bulk milk (Unnikrishnan *et al.*, 2005). In this article we discuss the various factors that were found influencing the antibiotic excretion in milk.

II. RELATED WORK

The presence of antibiotics in milk has developed concerns along three lines among public health officials. The first and possibly the most important, has to do with the development of sensitivity reactions to antibiotics, particularly Penicillins. The second matter of public health concern is that certain infectious bacteria may develop resistance to antibiotics and may become refractive to treatment. Third aspect is that it may create quality problems for the manufacturing of cultured products (Albright *et al.*, 1961).

Nisha (2008) suggested various pathological effects of antibiotic residues in food which include transfer of antibiotic resistant bacteria to humans, immunopathological effects, autoimmunity, carcinogenicity (sulphamethazine, oxytetracycline, furazolidone), mutagenicity, nephropathy (gentamicin), hepatotoxicity, reproductive disorders, bone marrow toxicity (chloramphenicol) and allergy (penicillin).

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As per Schlupe and Heim (1980), after cefacetrile administration to healthy cows, when quarters were milked out at 4 additional times within the first 10 hours after treatment no difference in excretion of cefacetrile in milk was found when compared to quarters of the same cow milked at regular milking times twice daily.

Koppinen *et al.* (2001) determined factors influencing the excretion time of penicillin in milk in a field trial including 467 cows. They observed that in addition to the product used and the number of days in lactation the total dosage applied also had a significant influence on excretion time.

Singh and Gupta (2015) conducted a study to know the level of knowledge and adoption of dairy farmers regarding clean milk production (CMP) practices. Rajasthan state was selected purposely for this study and 120 dairy farmers were selected. The results of the study revealed that 55.84 per cent of the dairy farmers had medium level of knowledge in various aspects of CMP, followed by 33 and 20 per cents of them having low and high level of knowledge, respectively. They had highest knowledge in 'Housing' [Knowledge Index (KI) =85.83], followed by 'Milking' (KI=76.66). However, they had poor knowledge in 'Cleaning of animal' (KI=50.41) and 'Cooling of milk' (KI=57.91).

Administering doses exceeding label directions were reported as one of the reasons for antibiotic positive milk samples after the end of the withholding period in cows treated with different antibiotics (Seymour *et al.*, 1988).

III. METHODOLOGY

A total of one hundred and twenty milch cows reared in organized and unorganized sectors were screened for antibiotic residues in milk at Bangalore Rural, Kolar and Chickballapur districts by non probability sampling. A Questionnaire was prepared and details of age, parity etc. were collected from the owner of the animal. Epidemiological data with respect to average daily milk yield and stage of lactation were collected. Daily milk production of milch cattle screened was recorded in litres. Different stages of lactation of cows studied were documented and classified broadly into four categories namely 0-70 days, 70-140 days, 140-305 days and dry period.

Milking hygiene, history regarding treatment with antibiotics, class of antibiotic administered, route of therapy and the time of administration were noted. Various parameters analyzed in milking hygiene include hand wash, pre-milking udder wash, post-milking udder wash and a combination of all the above procedures. History of drug administration includes antibiotic administered cases, cases where only drugs other than antibiotics were given and cases where no drugs were given. The antibiotics commonly used in veterinary medicine belong to one of the six major groups viz., Aminoglycosides *e.g.* Gentamicin, Penicillins and Cephalosporins (β -Lactams) *e.g.* Cloxacillin, Macrolides *e.g.* Erythromycin, Quinolones *e.g.* Enrofloxacin and Tetracyclines *e.g.* Tetracycline. Route of antibiotic administration include parenteral, intramammary, intrauterine and combination of Parenteral and intramammary routes. Milk samples collected were screened for the presence of antibiotic residues by three methods namely Microbial drug residue test (MDRT), Microbiological method and ELISA.

IV. RESULTS & DISCUSSION

1. Average daily milk production in litres

Mean \pm SE average daily milk production in litres of all the cattle screened in the three districts of Chickballapur, Bangalore Rural and Kolar districts were 10.15 ± 0.78 , 11.68 ± 0.56 and 8.54 ± 0.59 , respectively. The overall Mean \pm SE average daily milk production of total cattle screened was found to be 10.12 ± 0.39 litres.

Mean \pm SE average daily milk production in litres of all cattle positive for antibiotic residues in Chickballapur, Bangalore Rural and Kolar districts were 9.33 ± 1.46 , 11.50 ± 1.32 and 7.81 ± 1.11 , respectively. The overall Mean \pm SE average daily milk production was 9.25 ± 0.76 litres. Knappstein *et al.* (2004) observed significant influence on the excretion of antibiotic residues (cefquinome) with daily milk production whereas milking frequency had no significant effect. Cannon *et al.* (1962) found that excretion of penicillin varied between individual cows after parenteral administration of antibiotics. They could not establish any correlation with milk production but frequency of milking did matter.

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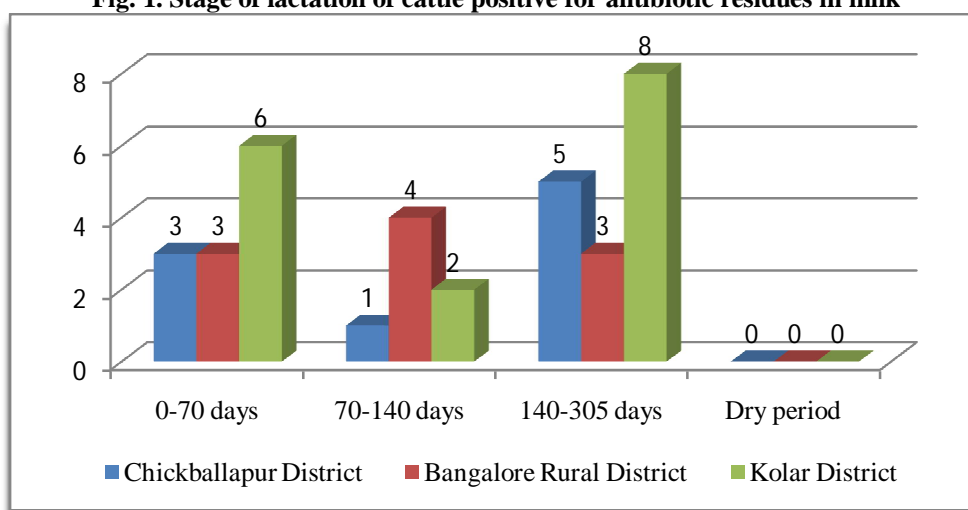
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2. Stage of lactation

Animals screened for antibiotic residues were classified into different stages of lactation namely 0-70 days, 70-140 days and 140-305 days. Out of the total 120 animals subjected for this study 32.5% of animals were in 0-70 day stage of lactation, 33.34% of animals in 70-140 day stage and 34.16% in 140-305 day stage of lactation.

Among the animals positive for antibiotics in milk 34.3% were in 0-70 day stage of lactation, 20% of animals in 70-140 day of lactation and 45.7% in 140-305 day stage of lactation (Fig. 1).

Fig. 1. Stage of lactation of cattle positive for antibiotic residues in milk



Karzis *et al.* (2007) suggested that there was a moderate negative correlation between stage of lactation and withdrawal period of antibiotics. No significant difference in withdrawal period between infected and non-infected udder halves was reported by Petzer *et al.* (2008), but a weak positive correlation was observed between withdrawal period and stage of lactation.

3. Milking hygiene

Out of the total 120 cattle farmers, 103 (85.83%) had followed all clean milking practices like hand wash, pre-milking udder wash and post-milking teat dips. In animals positive for antibiotic residues in milk 91.4% of dairy farmers had followed all clean milking practices. Bochantin and Bewley (2016) evaluated the management of the environment and cleanliness of the parlor in the reduction of mastitis in dairy farms. In-parlor milking procedures, which include pre- and post-teat dip with proper germicides, existing bacteria from the udder was removed and the risk of mastitis was decreased. Singh and Gupta (2015) conducted a study to know the level of knowledge and adoption of dairy farmers regarding clean milk production (CMP) practices. The results of the study revealed that 55.84 per cent of the dairy farmers had medium level of knowledge in various aspects of CMP, followed by 33 and 20 per cent of them having low and high level of knowledge, respectively.

4. History of drug administration

Among the total animals screened for the presence of antibiotic residues in milk antibiotic was administered in 39.2% of cases, an anti-inflammatory drug in one case (0.8%) and no antibiotic was administered in 60% of cases.

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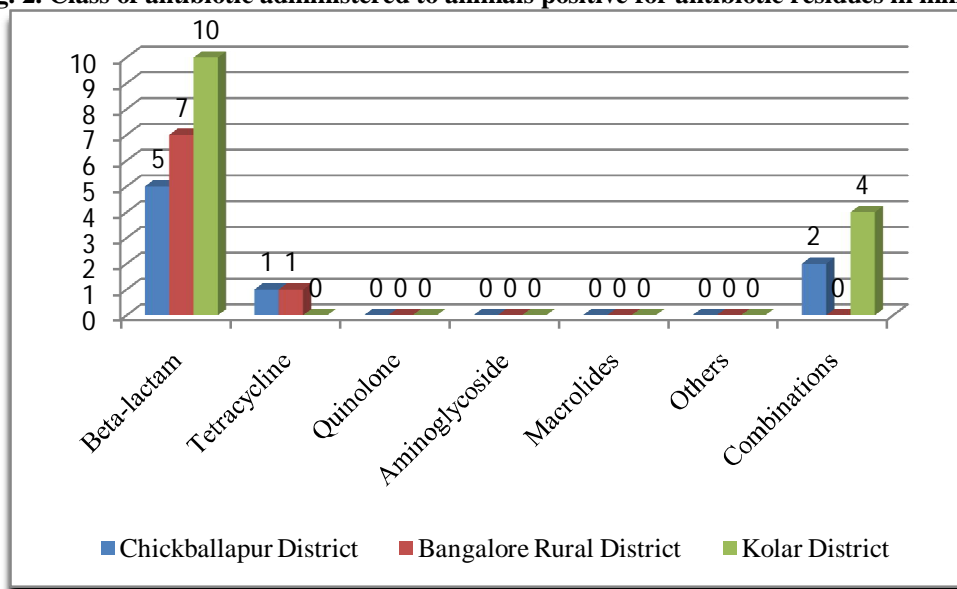
Among the animals found positive for the presence of antibiotic residues in milk by any one of the tests employed, 85.7% of cases had a history of antibiotic administration and 14.3% of cases had no history of antibiotic administration. One case in Chickballapur district and two each in Bangalore Rural and Kolar districts were positive for antibiotic residues by any one of the three tests employed even without the history of antibiotic administration. Allison (1985) cited various reasons that could be attributed to the failure of antibiotic residue testing in milk samples like presence of natural bacterial inhibitors, contamination of milk with teat dips, dairy disinfectants and other similar substances.

5. Class of antibiotic administered

Beta-lactam class of antibiotic was the most commonly used drug (21.7%) in animals screened for antibiotic residues in milk.

Beta-lactam class of antibiotic was also the most common drug administered to animals positive for antibiotic residues in milk (62.9%) (Fig. 2). This finding is in complete agreement with the observations of Podal *et al.* (2015) who reported that β -lactam antibiotics, including the penicillins, cephalosporins, carbapenems and others, make up the largest share of antibiotics used in most countries and penicillins are the most commonly used antibiotic for the treatment of bovine mastitis. The study conducted by Edima *et al.* (2012) confirmed the contamination of 27.08% of milk samples collected in Ngaoundere region with antibiotic residues. Antibiotics of the beta-lactam and/or tetracycline group (penicillin, oxytetracycline) may be the source of contamination of 53.85% of positive milk samples.

Fig. 2. Class of antibiotic administered to animals positive for antibiotic residues in milk



6. Route of antibiotic administered

Parenteral route of administration was the most common route of drug administration (17.5%) in case of animals screened for the presence of antibiotic residues from the 3 districts of Karnataka. Other routes of antibiotic administration were also recorded.

In case of animals positive for antibiotic residues in milk a combination of parenteral and intramammary route was the most common route (42.9%) of antibiotic administration. Podal *et al.* (2015) suggested various routes by which antibacterials can be administered to animals and the most common routes were parenteral, topical, oral (sometimes

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through water and feed), intra-mammary and intra-uterine. All of these routes may result in antibiotic residues in milk either as parent drug or as its metabolites.

The observations in the present study were in agreement with those of Fejzic *et al.* (2014) who opined that parenterally injected antibiotics were excreted much faster through milk, while residues were found for the longest period and in higher concentrations with intramammary application.

Significantly higher concentration of cefoperazone was found in milk from quarters with subclinical mastitis than from quarters with clinical mastitis at 16 to 24 hours after intramammary administration (Zurich *et al.*, 1993).

The transfer from treated quarters to non-treated quarters has been described for a number of antibiotics. Transfer of penicillin to untreated quarters was confirmed by later investigations in cows with or without clinical symptoms of mastitis (Rollins *et al.*, 1970, Aureli *et al.*, 1990).

7. Time interval between milk sample collection and antibiotic administration

Time interval between milk sample collection and antibiotic administration for animals positive for antibiotic residues in milk in this study was between 0-24 hours in 80% of cases.

Schluep and Heim (1980) found slightly different concentrations of cefacetrile or penicillin in milk of healthy cows in dependence of interval between treatment and milking, but this did not influence the duration of excretion in milk. When quarters were milked out at 4 additional times within the first 10 hours after treatment no difference in excretion of cefacetrile in milk was found compared to quarters of the same cow milked at regular milking times twice per day.

In contrast, Hamann and Heeschen (1995) reported lower concentrations of cefoperazone in milk of cows milked at intervals of 4 hours after intramammary treatment compared to cows milked after 12 hours.

Elimination of erythromycin in milk following intramammary therapy of specific mastitis in cows was studied by Bansal and Bajwa (2011). Considerable variations occurred in the excretion of drug; levels for treated quarters being 8.25 to 37.61 µg/ml at first milking that declined rapidly at 24 hours and no drug activity was observed beyond 36 hours post treatment.

The study reports of the above researchers were in agreement with the present study in which the majority of the antibiotics were excreted within 24 hours of administration.

V. SUMMARY

Antibiotics are extensively used in dairy farms for the treatment of mastitis which in turn may be a potential cause for the contamination of milk with antibiotic residues. The objective of this study was to screen cattle milk for the presence of antibiotic residues and to evaluate different methods to detect them. A total of one hundred and twenty milch cows reared in organized and unorganized sector were screened for antibiotic residues in milk at Chickballapur, Bangalore Rural, and Kolar districts by non probability sampling. Antibiotic commonly used was found to be Beta-lactam group and both parenteral and intramammary route is equally responsible for antibiotic residue excretion. Majority of the antibiotics were excreted within 24 hours of administration.

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