

Antibiotics Residue in Milk: A Critical Review

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Abstract

India in an agriculture based nation where people mostly rely on agriculture and Livestock sector for living. The growing population creates huge demand for the agricultural goods. With modernization the demand for animal protein and the means for producing the same is increasing as well. Antibiotics are one of the few pillars which is keeping dairy sector stable as animals are prone to many new and existing infections which can only be cured with the help of antibiotics. Knowingly or unknowingly, the metabolites of antibiotics used for prevention, treatment of controlled of dairy animals may find its entry into the milk intended for human consumption and this evoke the problem of drug residue. Drug residue in milk in turn may end up with drug allergy which can even be life threatening to drug resistance a even more critical issue. Following proper expert guidelines and opting to natural therapy is the only way to counter act such issue.

Keywords: Antibiotics; Milk; Residue; Drug allergy; Drug Resistance.

Introduction

Milk is a complete food may not be always true when we look from drug residue point of view. India is an Agriculture based nation where more than 70 percent of people earn their living from farming be it agriculture or animal husbandry.¹ The growing population depends largely on animal protein to fulfil their daily body requirements. However, this comes at a cost, i.e, Drug Residue. The animal attendants or people engaged in agriculture and livestock with a view to enhance the quality or quantity yield may very frequently use drugs which are otherwise not recommended without being prescribed by an expert. The consequence of such practice in long term may

evoke drug residue and ultimately drug resistance. Drug residue mainly found in the milk from drugs used for treating and prevention common diseases of cattle and other milk producing animals. The main reasons for appearing drug residues in animal foods are Indiscriminate use of drug, improper dosing, not adhering to withdrawal period and lack of treatment record keeping. This residue if found above Maximum Residue Limit (MRL) may not only affect the people taking the milk but also hampers the health of the people consuming dairy products prepared from such milk. Maximal Residual Level (MRL) can be defined as the maximum concentration of a drug, toxicant or pesticide recommended by Codex Alimentarius Commission to be legally permitted in or on the food. Expressed in percentage, µg/kg or µg/l2.

The table below shows common antibiotics used in dairy industry and their MRL values.

Chemicals	MRLs (mg/L)
Penicillin G	0.004
Oxytetracycline	0.1
Tetracycline	0.1
Doxycycline	0.1
Cloxacillin	0.01
Dicloxacillin	0.01
Ampicillin	0.004
Amoxicillin	0.004
Sulfadiazine	0.1
Trimethoprim	0.1
Sulfamethoxazole	0.1
Enrofloxacin	0.005
Ciprofloxacin	0.005
Ceftiofur	0.1
Chloramphenicol	0.1
Gentamycin	0.2
Streptomycin	0.2

Source: Codex Alimentarius Commission (July 2015)

This review mainly discusses the drug residue in cattle milk and the harmful effect of such residue to mankind. Drug residue may find its way into the milk from various means some of the common causes of drug residue in milk is discussed here under.

Antibiotics as feed Additives

It is well known that the rate of antibiotic use is increasing globally both in medical and veterinary sector. It is also true although many new developments have been done in the manufacturing of antibiotics, prior antibiotics are getting outdated to treat infection for which they were initially developed. This is something to worry about as development of an antibiotics may takes decades incurring huge amount of money while development of resistance could be rapid. The reasons for making the otherwise effective antibiotics outdated or ineffective is mainly because of developing resistance.³ The microbes (bacteria in this case) undergo rapid mutation when exposed repeatedly under low dose and consequently becomes unresponsive to the same antibiotics in near future. In animal husbandry many organisations have been found to practice the use Monensin and Tetracycline as feed additives to enhance the food conversion ratio i.e., amount of feed consumed to gain per kg of body weight. There

is a common belief amongst those that these agents have direct or indirect role in enhancing Food Conversion Ratio (FCR).⁴ However, the beneficial effects of tetracycline are cattle feed in order to gain body weight is controversial but it is quite certain to end up with more harm than good.

Based on some literature, the diet of cattle is mostly consisting of grains and there is a positive correlation that higher the level of grains in the ration higher will be probability of liver abscess. Liver abscess overall hampers the health of the animal be it in the form of body weight gain or milk production. Tetracyclines was initially introduced in the cattle ration to control this problem apart from controlling diseases like shipping fever and foot rot. As per the reports low dose of tetracycline in feed reduces the chance of liver abscess by as much as 50 percent.⁵ This overall increases the food conversion ratio in animals and also maintains the good body score of the animal.

Although antibiotics as feed additives has been used in some countries it is to be kept in mind that antibiotic is just a helping hand for good sanitation and animal husbandry. Indiscriminate use of low dose of antibiotics in feeds would result in long term harmful effects due to development of resistant strains of organisms in host animals that might compromise animal as well as human health.⁶ Two main causes of such practice are drug resistance and drug allergy. There is a common misconception that residue in low dose does no harm. However, the fact is Low dose of residue can cause allergic reaction in the recipient ranging from mild rashes to severe anaphylaxis.⁷ Drug resistance in bacteria was observed as soon after the introduction of antibiotics. Governments around the world consider antimicrobial resistant bacteria a major threat to public health. Patients suffering from infection by such bacteria are more likely to unrecovered as the medicines used to treat them are rendered less effective.

Monensin (Ionophore) produced by *Streptomyces cinnamomensis* is a polyether antibiotic commonly used against control of coccidiosis. The history of Monensin use is quite fascinating. Initially the sodium salt of Monensin was released into the market for use against lactating and pregnant cows to counter ketosis. The beneficial role of monensin in ruminants is based on its ability to shift ruminal fermentation yielding higher propionate in expense of acetate and butyrate volatile fatty acid thereby reducing blood ketone and augment blood glucose levels. The practice was scrapped off from market in 2006.⁸ Currently monensin is used in some

countries for growing calves for fattening purpose within regulatory limits. Therefore, the literature stating the residual effect on monensin from milk is very limited. Since monensin are not used in humans so it can be said that monensin resistance in cattle has no role in imparting resistance to humans. However, few reports have been published in this context stating even it is not used for human treatment it does somehow shows cross resistance to vancomycin in some case. Further, thorough investigation needs to be implemented for this purpose.⁹

Antibiotic for Dry Cow Therapy

It is one of the routine tasks in a dairy farm to infuse an antibiotic preparation into the udder of cow while leaving cow for drying off (rest for 45-60 days during the last trimester of pregnancy). Drying off of a cow is done with mainly three objectives. Firstly, to treat existing bacterial infection in the udder, if any. Second, to prevent the growth of bacteria in the udder when the milk is left in the udder. Lastly, to let the mother and the developing foetus get sufficient nutrition as no energy is waste for milk production during this stage.¹⁰ Generally, a long-acting broad spectrum antibiotic is selected for this purpose. Bacteria invades into the udder mainly through the manure when the teat spincture of cow is still open right after milking. For this purpose, cows are not allowed to sit immediately after milking. One of the major reasons for developing resistance in Veterinary sector is the antibiotic treated milk since it is unfit for human consumption (under withdrawal period) the calves are allowed to suckle the milk which leads to the development of antibiotic resistant intestinal bacteria in the calves. The same may happen in case of humans if proper withdrawal period is not followed.¹¹

Calving prior to expected period and culling of cows during dry period are two main reason for antibiotic residues in milk and meat respectively. For this purpose, the minimal dry period and antibiotic withdrawal period must be followed irrespective of the purpose.

The probability of getting new intramammary infection and rapid amplification of the existing infection is a common phenomenon in dairy farms. The aim of dry cow therapy is the elimination of the existing infections and prevention of newer infection as during dry period cows are not milk and milk is the good source of media for microbial growth.¹²

Antibiotics in the Treatment of Mastitis

Mastitis is one of the most devastating disease in a dairy farm causing huge economic loss. The recovered animal may not be able to produce the same quantity of milk which she was producing in that particular lactation. In severe case it may even led to culling of otherwise healthy animals. Mastitis can be defined as inflammation of the mammary gland.¹³ Based on clinical symptoms mastitis can be broadly classified into two types; Clinical and Subclinical form. In clinical mastitis udder becomes hot, painful, swollen and sometimes the parenchymal tissue turned firm. Milk flakes are apparent while milking hence it is easy to diagnose. However, milk characteristics does not change much in subclinical mastitis apart from reduced milk yield hence most of the times it goes unnoticed until advanced into clinical form. Subclinical mastitis is more important due to the fact that it is 15 to 40 times more prevalent than the clinical form and 70% of total losses on account of mastitis is due to subclinical mastitis.¹⁴ Since the loss is high so the dairy farmers are very much concerned with the treatment of mastitis. Mastitis itself is as very difficult to control due to multiple aetiology and rapid progression of disease. Many a times, Intramammary antibiotic tubes alone is used. Routine practice of mastitis as observed involves intramammary antibiotics, parenteral antibiotics, parenteral anti-inflammatory and local massage. Intra-mammary infusion of antibiotics for mastitis therapy was cited as a major reason for milk contamination and frequent use of antibiotic therapy leads to antibiotic resistance.¹⁵ Since mastitis is very common in farm condition farmers many a times indulge in self-treatment of the same. Most commonly used antibiotics in mastitis across the globe are β -lactams, tetracycline, quinolones, sulphonamides, streptomycin and chloramphenicol.¹⁶ While doing so they are actually inviting two major havoc. First, the dose and duration of therapy is not calculated based on individual animals which makes the bacteria unresponsive and progression of disease to chronic form. Sometimes, mastitis may even progress to toxic form in both the case the ultimate result is culling of animal. Second, bacteria which were exposed to low dose of antibiotics may become resistant to the same agent and that resistant bacteria may find its entry into consumer creating resistance in humans too. The molecular mechanism involve in such type of resistance may vary viz, reduce uptake of antibiotic by bacterial cell from the media, altered binding protein structure such as penicillin binding

protein and rapid destruction of the antibiotics by enzymes.¹⁷

Conclusion

Antibiotic residue in milk is an alarming concern as the ultimate victims are the consumers. Antibiotics in dairy sectors apart from using in routine treatment protocols, are also used as feed additives to enhance feed conversion ratio, dry cow therapy and to treat existing udder infection. As losses due to mastitis is huge, antibiotics in dairy farms are routinely used. It is always advisable to prevent a disease as far as possible then to look for treatment once disease has occurred. Keeping the animal udder in the healthy environment and detecting mastitis as early as in subclinical form is the only way to prevent the physical and economic losses due to mastitis. In order to overcome the raising issue of antibiotic residue in milk and milk products first and foremost rule to be followed or implement is selling of veterinary drugs only with prescription by a registered vet. This to a major extent prevent indiscriminate use of antibiotics on dairy animals. Rules should be implemented from farm levels itself by testing milk from cows undergoing or recently treated antibiotics. Milk samples from dairy plants should also be taken into radar for routine antibiotic residue testing before dispatching milk to markets or further processing into milk products. Where applicable rather than opting for antibiotics some of the natural agents which are proved to be highly effective in controlling mastitis such as *Cedrus deodara*, *Curcuma longa* and *Eucalyptus globules* which are having anti-inflammatory and infective properties should be used in order to cut short the treatment cost and also to minimize the chances of drug residue in milk.

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