Original Research

Quinolone Arthropathy in Broiler Chicken Administered with Enrofloxacin

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Abstract

Arthropathic potential of enrofloxacin was investigated in broiler chicken at recommended therapeutic dose. Day old broiler chicks were randomly divided into 4 groups each comprising 6 birds. Group I, control birds received non medicated water, while group II, III, IV and V were medicated with enrofloxacin at recommended therapeutic dose 10mg/Kg body weight in drinking water for 5 successive days from 43rd to 47th day of age. Juvenile cartilages were collected on 1, 3, 5 and 9 days after the last dose from respective treatment groups and subjected to histopathological examination. Degeneration of chondrocytes was noticed in day 1 post treatment group and shrunken chondrocytes with pyknotic nuclei were observed till 5th day post treatment. However, clumping of chondrocytes observed on day 5 post treatment and a few cases of degenerated chondrocytes on day 9 post treatment around the blood vessels, suggestive of reversal in chondrocyte lesions.

Key words: Arthropathy, Broiler Chicken, Enrofloxacin, Juvenile Cartilages

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Introduction

Enrofloxacin, a fluoroquinolone developed exclusively for veterinary use, is advocated in poultry in large-scale for treatment of chronic respiratory disease, colibacillosis, salmonellosis and fowl cholera (Papich and Riviere, 2009). It has been reported that fluoroquinolones are associated with a low incidence of adverse effects related to gastrointestinal, skin, hepatic, central nervous system functions, and phototoxicity (Hooper and Wolfson, 1985), significant fall in lymphocyte count (Sureshkumar *et al*., 2012), reduction in haemagglutination inhibition (HI) titre and associated histopathological changes in lymphoid organs (Sureshkumar *et al*., 2013a) and residual effects on biochemical status in time dependent manner after nine

weeks of enrofloxacin administration (Sinha *et al*., 2018). Despite several studies have explored the mechanisms of quinolone arthropathy in other species (Kato and Onodera, 1988a; Stahlmann *et al*., 1990; Cavusoglu *et al*., 2000), literature appraisal revealed that reports on quinolone arthropathy and the reversibility of lesions in broiler chicken are limited and very little is known about the toxicodynamics of these toxic effects (Gurbay *et al.*, 2001).

On the other hand, there is some evidence that free radical formation might play a role in the pathogenesis of fluoroquinolone induced cartilage defects (Thuong-Guyot *et al*., 1994). Further, Martinez-Cayuela (1998) found that enrofloxacin residues may occur in meat, milk and eggs, generate free radicals owing to its metabolism and interaction with other medicated drugs (Ershov *et al*., 2001; Carrreras *et al*., 2004; Sureshkumar *et al*., 2004). Our earlier findings revealed that there was significant decrease in glutathione S-transferase, catalase and glutathione (GSH) levels in serum, muscle and liver on 1st and 5th day post treatment with enrofloxacin (Sureshkumar *et al*., 2013b) and speculated that free radical formation might play a role in quinolone arthropathy. Hence, present study has been undertaken to explore the potential development of quinolone arthropathy after enrofloxacin administration and its reversibility if any during the withdrawal period in broiler chicken.

Materials and Methods

Day old broiler chicks (broiler strain B_1) of thirty numbers obtained from Institute of Poultry Production and Management, Madhavaram Milk Colony, Chennai-600 051 were randomly grouped into control (I) and treatment (II, III, IV and V) and maintained under standard management conditions. Treatment groups were medicated with enrofloxacin at recommended therapeutic dose 10mg/kg body weight, in drinking water for 5 successive days from 43rd to 47th day of age, while control birds received non medicated water (Knoll *et al.*, 1999). Institutional Animal Ethics Committee, Madras Veterinary College, TANUVAS has accorded permission for the biological trial. After cessation of the last dose of enrofloxacin, six birds from corresponding treatment group were sacrificed ethically at each sampling point viz. 1, 3, 5, and 9 days post treatment. Control birds were sacrificed at the end of the experiment *i.e*. on day 9 post treatment. Juvenile cartilages (articular cartilage from head of the femur) were collected in 10 percent formalin and subjected to histopathological examination (Bancroft and Gamble, 2008).

Results and Discussion

In the present study, articular cartilage collected from head of the femur of control group revealed normal chondrocytes with prominent nucleus and cytoplasm (Plate 1). Degeneration of chondrocytes was noticed as early as in day 1 post treatment group (Plate 2).

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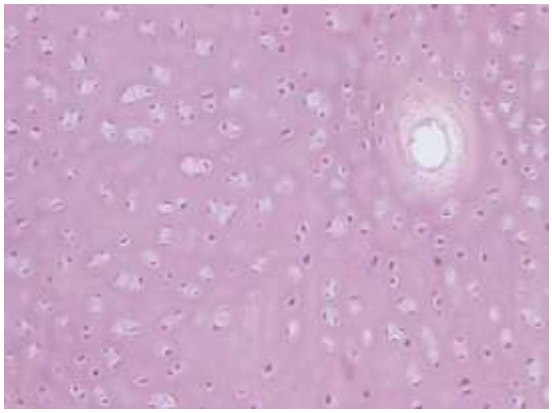

Plate 1: Articular cartilage of control group showing normal chondrocytes with prominent nucleus and cytoplasm. H&E, x100

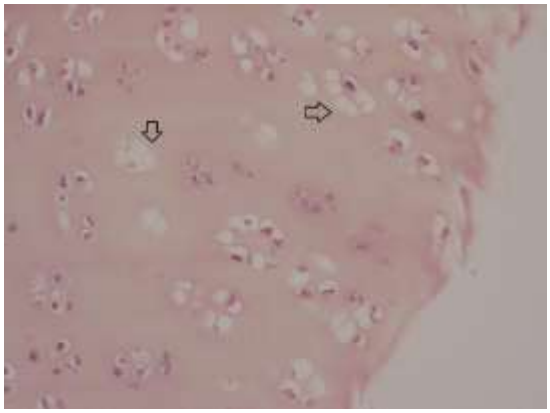

Plate 2: Articular cartilage of 1st day post treatment group showing degeneration of chondrocytes and few chondrocytes without nucleus (arrow). H&E, x200

The lesions were persisted till 5th day post treatment and chondrocytes were shrunken, degenerated with pyknotic nuclei (Plate 3) and articular cartilage revealed cavity formation with eosinophilic content (Plate 4). These observations are in line with Kato and Onodera (1988b) who studied the histogenesis of cavity formation in rats. They have shown that condensation of chondrocyte nuclei was the first finding 5 hour after a single dose (1000-3000mg/kg) of ofloxacin. In another study, Kato and Onodera (1988a) showed that the [^{3}H] thymidine binding capacity, an indicator of DNA synthesis was decreased by 80% 5 hour after a single dose of ofloxacin, when compared with control and concluded that ofloxacin is suppressing the DNA synthesis which results in the degeneration of chondrocytes.

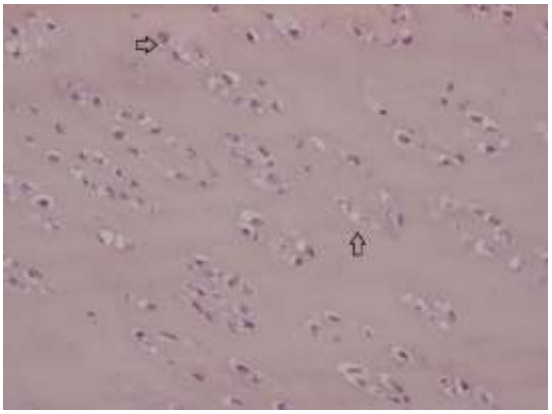

Plate 3: Sternal cartilage of 3rd day post treatment group showing pyknotic nuclei (arrow). H&E, x200

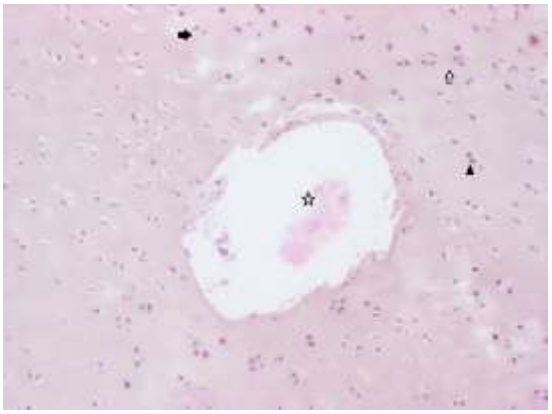

Plate 4: Articular cartilage of 5th day post treatment group showing cavity formation with eosinophilic content (☆), shrunken chondrocytes (black arrow) with pyknotic nuclei (black arrow head) and clumping of chondrocytes (blank arrow). H&E, x100

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Toxicodynamics of quinolone arthropathy remains poorly understood. Quinolones act by inhibiting microbial DNA gyrase (type II topoisomerase) responsible for coiling of circular DNA and thereby interfere with bacterial replication (Shen *et al*., 1989). Mammalian cells have type II topoisomerases and mitochondria contain circular DNA (Castora *et al*., 1983), and thus it is postulated that quinolones might be directly toxic to chondrocyte mitochondrial DNA (Stahlmann *et al*., 1990; Stahlmann, 1991). Interference with DNA synthesis is a plausible explanation for degenerative cellular changes evident in quinolone arthropathy (Kato and Onodera, 1988a). However, clumping of chondrocytes were observed on day 5 post treatment (Plate 4) and a few cases in 9 day post treatment group showed degenerated chondrocytes around the blood vessels (Plate 5).

Clumping of chondrocytes observed in the present study is indicative of cell replication and regeneration, which is a reparative process relative to healing of other tissues (Gough *et al*., 1992). Supporting our findings, Cavusoglu *et al*. (2000) demonstrated the repair response of the cartilage by intensive staining with safranin-O and toluidine blue around the chondrocyte clusters. Further, Kato and Onodera (1988a) showed that 24 hours after a single dose of ofloxacin, [^{3}H] thymidine binding capacity increased by 160% in comparison to the control group, attributed to increased proliferation of chondrocytes. The restoration of histopathological changes observed during 5th and 9th day of withdrawal period could be attributed to the depletion of the enrofloxacin residues from the body during the withdrawal period. This proposition is substantiated by San Martin *et al*. (2010) who demonstrated that based on the European Union maximum residue limits the withdrawal time was 5 days and Chattha *et al*. (2008), who observed that enrofloxacin residues were washed out in 9 days whilst its major metabolite ciprofloxacin was washed out in 8 days in chicken meat.

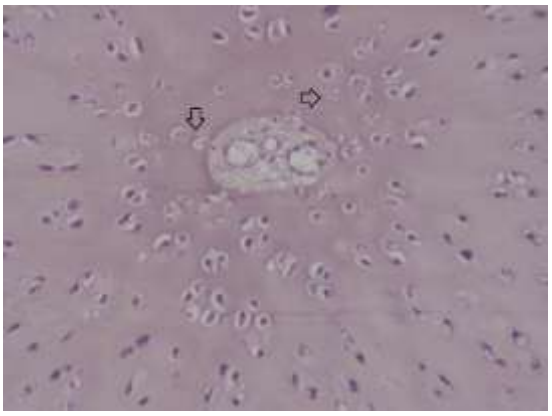

Plate 5: Articular cartilage of 9th day post treatment group showing degenerated chondrocytes around the blood vessels (arrow). H&E, x200

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Conclusion

In the present study, quinolone arthropathy was manifested in juvenile cartilages as evidenced by histopathological alteration in articular cartilages. However, the regeneration and reparative process observed in the 5th and 9th day of withdrawal period is indicative of reversal in chondrocyte lesions and suggests that enrofloxacin is safe if administered at recommended therapeutic dose and stipulated withdrawal period is adhered.

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