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Hepatic toxicity of artemisinin in turkeys

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Abstract

Development of resistance to anticoccidials/antiparasitic drugs, removal of licensed antihistomonal formulations and a shift towards organic production has put the focus on natural occurring compounds for controlling poultry protozoa. Artemisinin originates from *Artemisia annua* and is known to be an efficient antimalarial drug in humans. Inhibitory activity against coccidia of birds was also reported (Allen et al., 1997). However, in chickens toxic side effects were described following application of the compound (Arab et al., 2009; Shahbazfar et al., 2011).

In a previous study investigating the effect of artemisinin against histomonosis, artemisinin (100 and 2600 mg/kg feed) was administered to day-old turkey chickens (Thofner et al., 2012). As a result, sudden deaths occurred on day 5 and 6 in the group receiving 2600 mg artemisinin per kg feed, the remaining birds in the group were then euthanized. In the present study a panel of formalin fixed and paraffin embedded organs sampled during necropsy of the dead/euthanized birds was stained with haematoxylin and eosin for histological examination. Immunohistochemical detection of cytokeratin was performed on liver sections to distinguish the bile duct epithelium from hepatocytes and blood vessel endothelium.

Post mortem findings in the medicated birds showed distended gallbladders (15/15), fatty appearing pale liver (8/15), enlarged kidneys with increased tubular appearance (15/15), urate deposits in ureters (15/15), empty intestines (9/15), soft long bones (9/15) and beaks (6/15). Proliferated and convoluted bile ducts with no lumen, varying degrees of renal degeneration, but no signs of inflammation were observed. No histopathological findings were noticed in any other organs taken from the treated birds.

Proliferation of bile ducts was previously described as a response to injury, e.g., toxic or obstructive (Stalker and Hayes, 2007). The present findings may suggest that metabolism or excretion of artemisinin in birds may take place in the liver; however, no analysis on bile or faecal matter was performed.

Previous studies demonstrated artemisinin causing unspecified degeneration of the brain, kidney and liver. This study suggests that also the bile ducts proliferate as a response to toxic injury caused by artemisinin.

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