

The effects of experimental exposure of low doses of zearalenone (ZEN) on the histology, morphology and immunohistochemical evaluation of uterus in pre-pubertal bitches

Abstract

Mycotoxins are toxic secondary metabolites produced by fungi. Those biologically active compounds occur naturally, and they include zearalenone (ZEN), a mycotoxin that contaminates plant material, including the ingredients used in the production of commercial dog food. The influence of monotonic, low-dose and long-term exposure to zearalenone on pre-pubertal bitches has not been fully explored to date. The objective of this study was to determine the effect of long-term administration of low doses (100% and 150% NOAEL) of ZEN (subchronic mycotoxicosis) to pre-pubertal bitches on the histological, morphological and immunohistochemical (degree of apoptosis and proliferation) evaluation of the uterus. The experiment involved 30 clinically healthy prepubertal bitches aged approximately 70 days with an estimated initial body weight (BW) of 8 kg. The animals were randomly divided into two experimental groups (EI and EII) and a control group of 10 animals each. Group EI was administered 50 µg ZEN/kg BW *per os* for 42 days, group EII received 75 µg ZEN/kg BW *per os* for 42 days, and the control group was administered placebo *per os* for 42 days. The bitches were ovari hysterectomy at the end of the treatment period (at around 112 days of age), and selected sections of the uterine wall were subjected to morphometric, histological examination and immunohistochemical analyses (TUNEL and PCNA). The results of the study indicate that exposure to very low doses of ZEN (100% and 150% of the NOAEL) causes simple glandular hyperplasia of the endometrium accompanied by adenogenesis, angiogenesis and vasodilatation with the related consequences. The noted changes were more pronounced in group EI and less visible in group EII in comparison with group C, which could be indicative of a hormetic dose response. A shift towards higher apoptotic (AI) and proliferative indices (PI) was observed, in particular in group EI. Higher AI and PI values were noted in the epithelium of all uterine regions analysed and in the uterine glands in the uterine horn proximal to the body of the uterus. The above could lead to misdiagnoses of endometrial conditions, especially in animals exposed to lower doses of zearalenone.

Keywords: zearalenone, histopathology, immunohistochemistry, apoptosis, proliferation, uterus, endometrium, pre-pubertal bitches