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THE DOSE-DEPENDENT EFFECTS OF DOXORUBICIN IN RAT LIVER TISSUE

Ali Tugrul AKIN*, Emin KAYMAK, Derya KARABULUT***, Zuleyha DOGANYIGIT**, Tayfun CEYLAN****, Ayse TOLUK*, Saim OZDAMAR*******

*Erciyes University, Science Faculty, Biology Department, KAYSERI

**Bozok University, Medical Faculty, Histology-Embryology Department, YOZGAT

***Erciyes University, Science Faculty, Histology-Embryology Department, KAYSERI

****Kapadokya University, Pathology Department, NEVSEHIR

*****Pamukkale University, Medical Faculty, Histology-Embryology Department, DENİZLİ

Introduction: Doxorubicin (DOX) is an anthracycline antibiotic used as an anticancer agent and is a widely used chemotherapeutic for many cancer types such as sarcoma, acute lymphoblastic leukaemia and as well as breast and liver cancers. Recently, it has been shown that DOX causes hepatic toxicity. Toxic effects of DOX are associated with increased formation of reactive oxygen species (ROS), releasing of pro-inflammatory cytokines and induction of apoptotic and necrotic changes in organs. The aim of this study is determine of dose-dependent effects of DOX on inflammation in rat liver tissue.

Methods: 30 male rats were assigned to the following groups: Group I as controls, Group II was given Chronic DOX i.p. (2 mg/kg/BW) a total of 10 times, once every three days. Groups III, Acute DOX group which received DOX (15 mg/kg BW) single dose as the intraperitoneal the 20th day of the study. On the 28th day of the experiment, under anesthesia by ether, livers of animals were obtained for histopathological and immunohistochemical evaluation. Sections of 5 µm thick were sliced with a microtome and stained with hematoxylin and eosin. TNF-alpha and IL-6 were detected immunohistochemically using a polyclonal antibody and the streptavidin-biotin-peroxidase technique.

Results: In this study, injection of both DOX Chronic (2mg/kg) and DOX Acute (15 mg/kg) triggered a significant elevation of the liver damage. Hepatic sections of the rats treated with chronic and acute DOX groups were seen intracellular cell degeneration, intracytoplasmic vacuoles, haemorrhage and picnotic cells. IL-6 immunoreactivity was significantly increased in chronic group and acute group compared to control group. TNF-alpha immunoreactivity was significantly increased in chronic group compared to control group.

Conclusion: Our results demonstrated that chronically administered doxorubicin increases liver damage. In conclusion, it may be advisable to increase studies on the use of chronic doses in combination of anti-inflammatory agents.

KeyWords: Doxorubicin, liver damage, hepatotoxicity, inflammation.