

Histopathological changes caused by Doxorubicin in laboratory mice (*Mus Musculus L*)

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Abstract

Objective: To investigate the histopathological changes in laboratory mice (*Mus Musculus*) being given doxorubicin.

Methods: The experimental study was conducted at the University of Basra between September 2009 and March 2011. Two groups with 5 mice each were used in this study. The experimental group was given 6mg/kg of doxorubicin intraperitoneal for 15 days. The control group was given distilled water for 15 days. On day 16, post-mortem was done. Biopsies were taken from the liver and intestine of both groups. Histopathologic slides were made for examination.

Results: Changes in hepatic tissue involved were inflammatory cell infiltration, necrosis and vacuolation. While the liver of the control group was normal in structure. The intestinal section of the experimental group showed decomposition in the intestinal villi, while the intestines of control mice was normal.

Conclusion: Doxorubicin is highly toxic to the liver and intestines of laboratory mice.

Keywords: Doxorubicin, Mice, Histopathological, Iraq (JPMA 61: 1108; 2011).

Introduction

The drug Doxorubicin is an antibiotic extracted from fungi called *Streptomyces peucetius*.¹ It is highly toxic to the cells even though it remains extracellular.²

It is absorbed rapidly in the blood and reaches a level of (700-11001 mm²) in the plasma. It has the ability to bind to blood protein at a rate of (70%).³ Then, the drug is excreted in bile at a rate of (40-50%) and in the milk at a rate of (4-5%). It has been observed that the toxic effect specially in the liver is produced 5 days after drug administration.³

This drug is used for tumour treatment, but it has a toxic effect on the mucosal epithelium of the intestines.⁴ Another study has shown that the drug has a toxic effect on the crypts of the intestines and proliferation of stem cells which are responsible for generation of living cells.⁵

Therefore, it is recommended to give doxorubicin along with other anti cancer drugs in order to reduce its toxicity.^{6,7} Good treatment response was seen in patients with stomach cancer, when both Fluorouracil and doxorubicin were given together.⁸ These drugs could lead to complications as blood poisoning and decompensation among patients with lung cancer.⁹ The aim of this study was to investigate the histopathological changes among treated laboratory mice with doxorubicin.

Material and Methods

This was an experimental study in which two

groups of mice strain (Balb / c) with 5 mice each, were used. The experimental group was given 6 mg/kg of doxorubicin. Production Company (Pharmacia & Upjohn SPA) Italy, intraperitoneal for 15 days.¹⁰ The control group was given distilled water for 15 days. On day 16, post-mortem was done. Biopsies were taken from the liver and intestines of both groups. Histopathologic slides were prepared for histopathological examination.¹¹

Results

Changes in hepatic tissue were Necrosis (Figure-1), inflammatory cell infiltration (Figure-2) and vacuolation

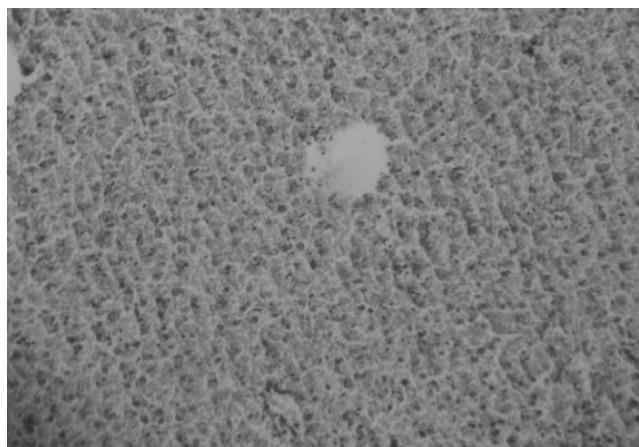


Figure-1: Section of Liver tissue from the animals administration by Doxorubicine drug shows the necrosis in the Liver (H&E).

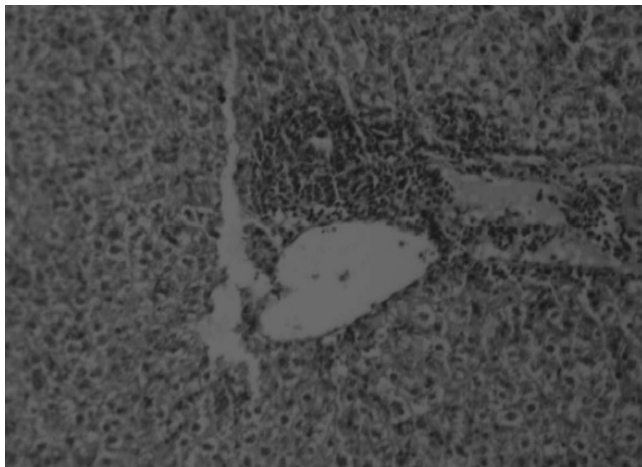


Figure-2: Section of Liver tissue from the animals administration by Doxorubicine drug shows the infiltration from inflammatory cells (H&E).

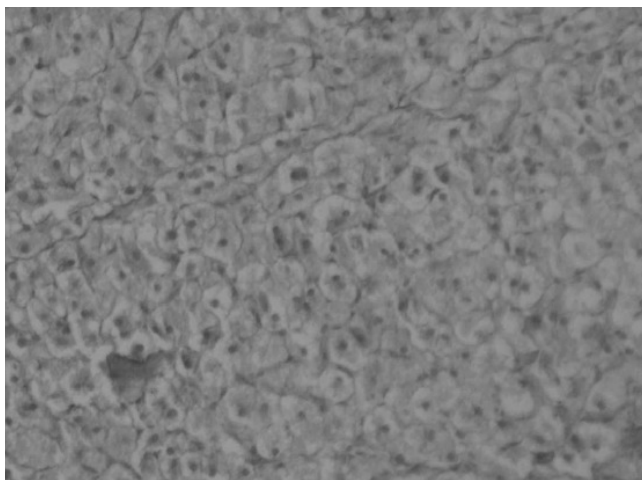


Figure-3: Section of Liver tissue from the animals administration by Doxorubicin drug shows the vacuolation in the liver cells (H&E).



Figure-4: Section of Liver tissue in animals control shows the hepatocytes and the central vein (H&E).

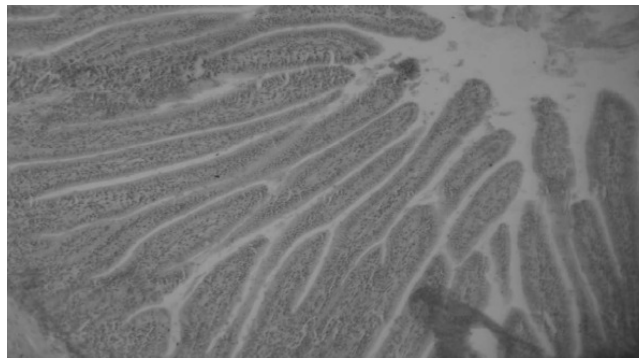


Figure-5: Section of intestine tissue from the animals control shows the intestine viilus (H&E).

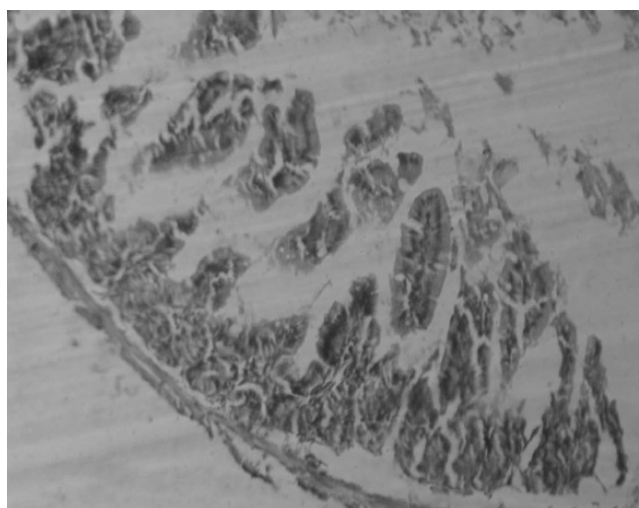


Figure-6: Section of intestine tissue from the animals administration by Doxorubicin drug shows decomposition in intestine villus (H&E).

(Figure-3). The liver of the control group was normal in structure (Figure-4).

The intestinal section of the experimental group showed decomposition in the intestinal villi (Figure-6). While the intestines of the control mice were normal (Figure-5).

Discussion

It is clear from the present work that the drug Doxorubicin has a toxic impact on organs especially liver and intestines.

The explanation for the observed vacuolation in the liver might be due to increase in the disruption of fat metabolism in addition to form of lipoproteins, which turn to triglycerides (Triglycerol), which later leads to fat infiltration in some organs.¹²

Another study has shown that the abnormal histopathological changes in the liver can be attributed to

increased apoptotic widely and inflammatory response.¹³

An indicator for liver damage was also investigated by the raised level of enzymes GOT and GPT and (Alkailineases) among treated patients.¹⁴ The hepatic tissue changes would reduce a conversion of Hb to meta Hb and that would lead to lack of carrying oxygen and eventually lead to cell death.

The toxic effect of this drug would lead to destruction of the mucous layer of the intestinal villi which in turn cause a reduction in cell proliferation, that can be explained by the inhibition of manufacturing DNA.¹⁵

The treated patients would suffer from diarrhoea due to mal absorption of nutrients from the intestinal lumen.^{16,17}

A dose of 20 mg/kg given intraperitoneal into rabbits lead to apoptosis of intestinal mucosa, after 6 hours post injection.¹⁸ While a dose of 6 mg/kg would induce severe morphological changes in the small intestinal 3 days after treatment.¹⁸ There is a relation between the dose of the drug and the toxic effect on the tissue of the body.

Conclusion

This study showed the toxic effects of doxorubicin on mice livers and intestines. These changes were identified by examining the tissue sections under the light microscope.

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