

Study the Histopathologic Effects of Arsenic Trioxide on Some Parenchymatous Organs of Male Rats and Under Alphalipoic Acid

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Abstract

This study was designed to evaluate the histopathological effects of arsenic trioxide (ATO) on the some organs of rats , for this reason group of rats (15) were I/P inoculated with 1.5 mg /Kg .B.wt . daily for 30 days other group(15 rat) treated with 100 mg/kg.B.wt of alphalipoic acid and ATO (1.5 mg/ kg.B.wt) for 30 .The results was revealed that the extensive pathological lesions in the liver , kidney , spleen and testes in all rats exposed to arscenci trioxide due to the pathotoxic effect of ATO and decreased lesions were in the group treated with the alpha lipoic acid .100 mg / kg .B.wt) for 30 days as ameliorative or protective effect against pathotoxicity of ATO .

Key words : *histopathogic effects of arsenic trioxide , parenchymatous organs, male rats*

Introduction

Arsenic (AS) is ubiquitous element in the environment . weathering of rocks converts Arsenic sulfide to arsenic trioxide ATO which enter the arsenic cycle as dust or by dissolution in rain , rivers , or ground water ⁽¹⁾ Arsenic is a very toxic metal and also an environmental and industrial pollutant which present in soil , water , air and food ⁽²⁾ This metal enter surface of water from the industrial and found in soil by leaching of sewage sludge through soil ⁽³⁾ .So the pollution can be affected by Arsenic through food consumption , drinking water and incidental ingestion of soil contaminated by arsenic ⁽⁴⁾ .Arsenic used in food preservative . herbicides , insecticides and rodenticides ⁽⁵⁾

The aim of study:

In Iraq , there are little researches about influence of arsenic trioxide on body organs for this reason this study was designed to find the histopathological effect of

arsenic trioxide (ATO) on body organs of rats and also to find the protective effect or ameliorate the pathotoxic effect of arsenic trioxide by alphalipoic acid .

Material and Methods

Two groups of rats (15 each group) , body weight 200- 220 gm

First group : were I/P inoculated with Arsenic trioxide 1.5 mg/ Kg .B .wt .daily for 30 days ⁽⁶⁾

Second group were also treated I/P with 1.5 mg / Kg .B.wt of arsenic trioxide for 30 days together with their I/P inoculation with alphalipoic acid 100 mg / Kg.B.wt daily for 30 days .

After 30 days all the lesions were taken from liver , kidney , spleen and testes , and kept in 10% neutral buffered formalin for fixation and processed routinely ⁽⁷⁾ for histopatholgy study under light microscope .

The Results

First group : treated with arsenic trioxide showed

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The liver :

There is dilation of sinusoids , extensive degeneration of endothelial lining central vein with loss of hepatic cord organization .There is inflammatory cellular infiltration was abundant around the central vein with suppurative necrosis and vacuolation of hepatocytes .There is desquamation of bile duct epithelia together with extensive fibrosis of the portal regions (Fig-1)

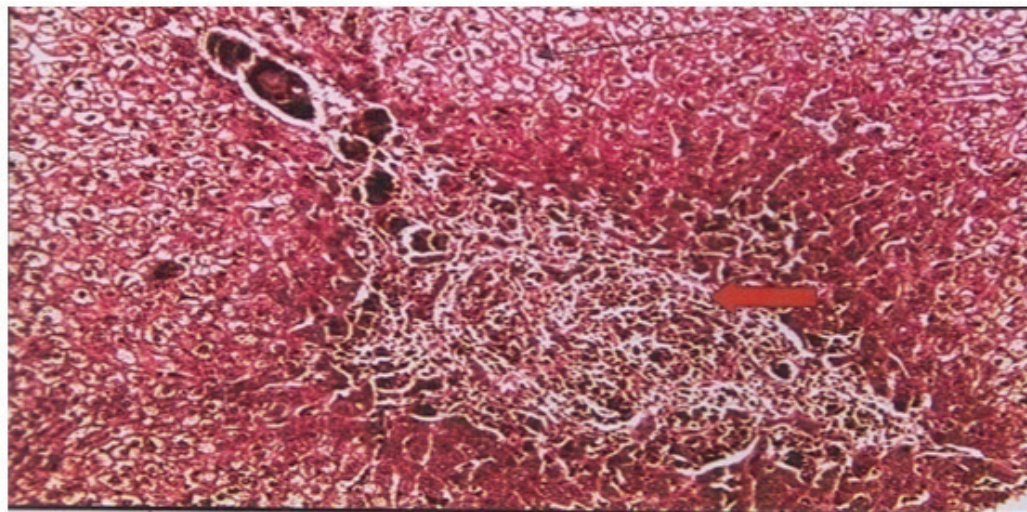


Figure (1) : liver section of rat .It received ATO (I/P 1.5 mg / kg BW) for 3 months . There is inflammatory cellular infiltration with abscess formation (red arrow) .Also there is extensive degeneration with hepatocellular necrosis (thin arrow) .10X H&E

Extravasations and congestion of all blood vessels in liver tissue with ballooning vacuolation of hepatocytes .some of hepatocytes showed extensive fatty change .

The kidney :

Showed sever degeneration and necrosis of epithelia lining proximal convoluted tubules together with disorganized and atrophied glomeruli and distorted Bowman’s capsule . there is extensive congestion of all blood vessels in the renal tissue with extensive inflammatory cellular infiltration in renal tissue (Fig-2)

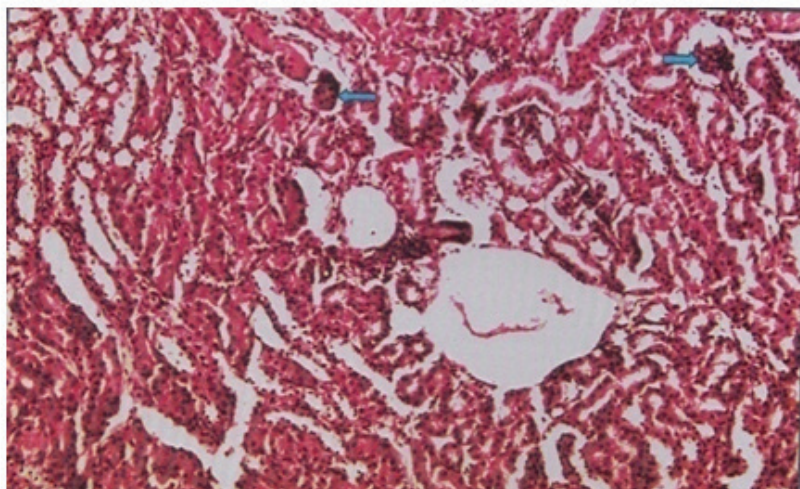


Figure (2) : renal section of rat .It received ATO (I/P 1.5mg /kg BW) for 3 months .There is severe necrosis of epithelial cells which lining of the renal convoluted tubules (green arrows) which appeared dilated with atrophied disorganized glomeruli with distorted Bowman’s capsule (yellow arrows) .10X H&E .

Testes and epididymus :

Showed loss of cellular architecture there is vacuolation of epithelia lining seminiferous tubules , suppression of spermatogenesis and pronounced reduction and devoid sperm number in the lumen of seminiferous tubules .Desquamation of epithelia lining seminiferous tubules with presence of spermatid multinucleated giant cells indicating sever degeneration , similar pathological changes were seen in the epididymus (Fig-3) .

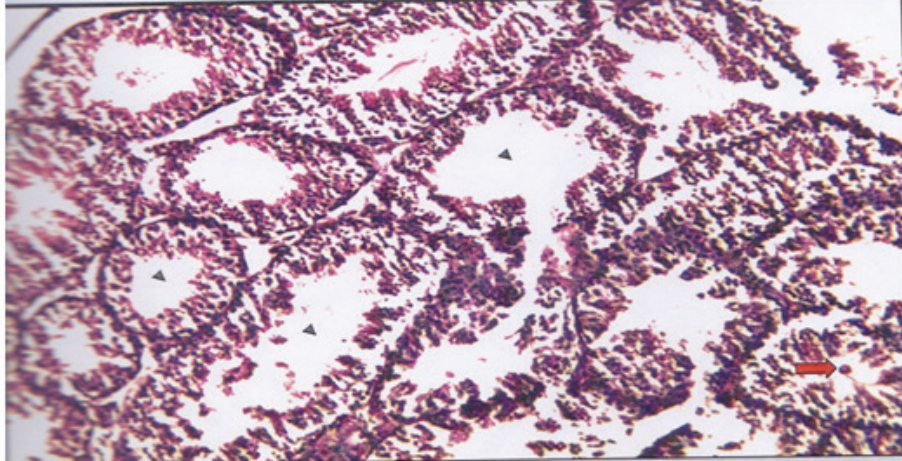


Figure (3) : Testicular section of rat.It received ATO I/P 1.5 mg/kg BW) for 3 months . Note vacuolation of spermatogonia and presence of megakaryocytes inside the seminiferous tubule .The tubules are totally devoid sperms (arrows heads) .10X H&E .

The spleen :

Showed sever depletion of white pulp with proliferation of reticuloendothelia cells lining the red pulp .Extensive necrosis and degeneration involving the whole lymphoid tissue in white pulp together with disappearance of arterioles in the white pulp (Fig-4) .

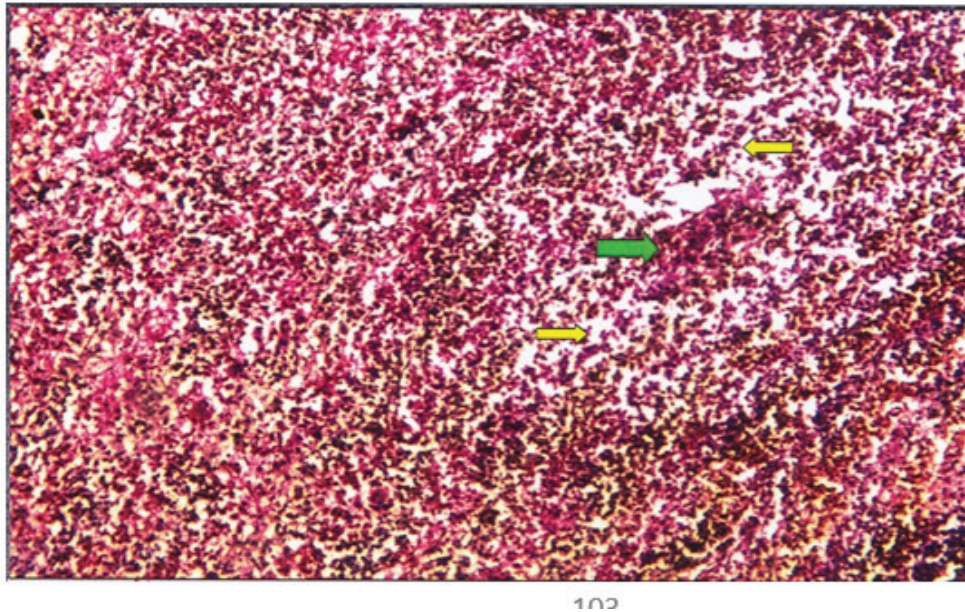


Figure (4) : Spleen of rat.It received ATO(I/P 1.5 mg/kg BW) for 3 months .Note severe depletion of white pulp with proliferation of red pulp (green arrows) . Extensive degeneration and necrosis in the splenocytes and lymphocytes of lymphoid tissue (yellow arrows) .10X H&E .

The second group treated with arsenic trioxide and alphalipoic acid :

The liver :

Showed the severity of lesions were mostly decreased , there is preserved cytoarchitecture of hepatic lobules , mild congestion of blood vessels and mild inflammatory cellular reaction , some hepatocytes showed more activation (Fig-5)

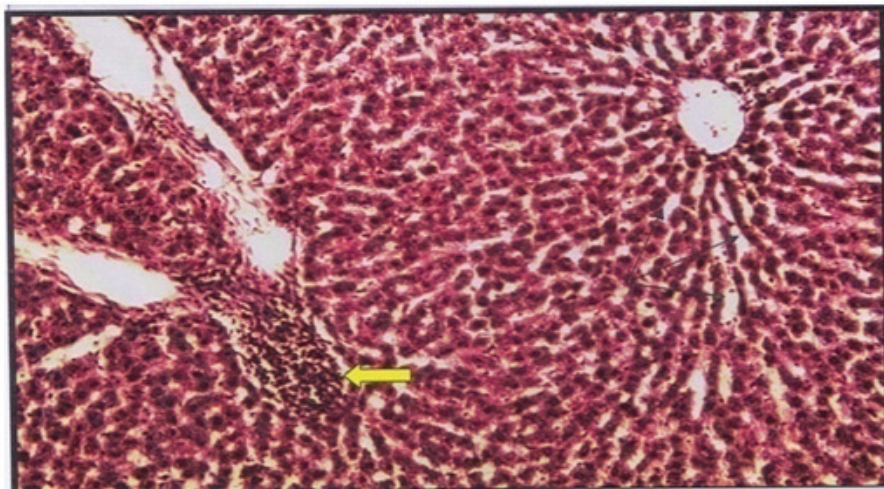


Figure (5) : liver section of rat. It received ATO (I/P 15mg /kgBW) and supplemented with (ALA) (I/P 100 mg /kg BW). There is presence of cytoarchitecture of hepatic lobules consisting of central veins and radially arranged hepatocytes . Few infiltration of inflammatory cells with (yellow arrows) mild dilation of sinusoids (thins arrows) .10X H&E .

The Kidney :

Showed also decreased in the severity of lesions comparable to arsenic trioxide treated group , it revealed normal organized glomeruli , with mild dilation of proximal convoluted tubules , there is tubular regeneration of their epithelial lining . There is no inflammatory cellular reaction and there is no hemorrhage and congestion in the renal tissue (Fig-6)

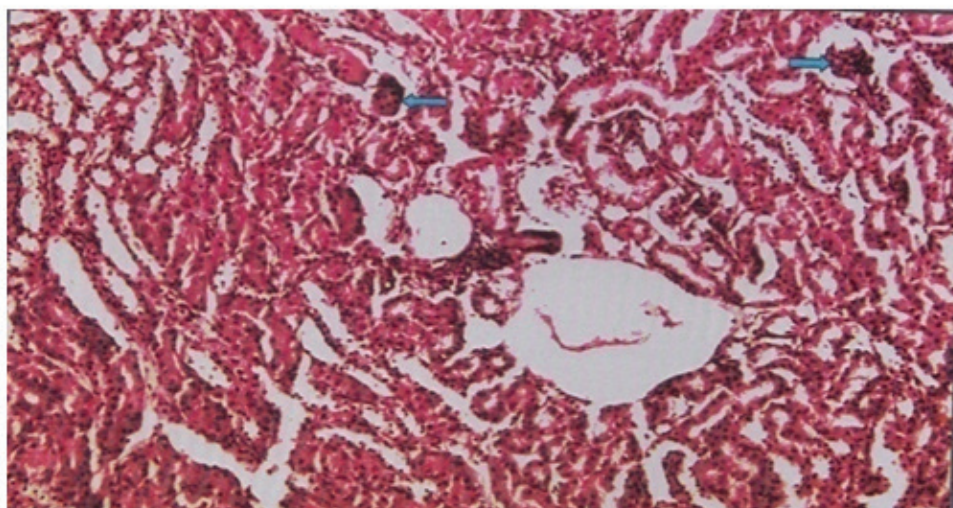


Figure (6) : renal section of rat . It received ATO (I/P 1.5 mg/kg BW) and treated with ALA (100mg/ kg B.W) for 3 months . Note mild dilation or renal convoluted tubules , normal organized glomeruli (blue arrows) and tubular basophilia were seen .10X H&E

Discussion

The results of arsenic trioxide toxicity in organs of rat were varied including degeneration, necrosis, inflammatory cellular reaction together with hemorrhage and congestion in the all organs, these pathological changes were due to toxicity of ATO lead to liberation of reactive oxygen species and induce oxidative stress⁽⁸⁾ which induce tissue damage and necrosis due to effects of superoxide, Hydrogen peroxide, hydroxyl and nitric oxid both of these reactive species were released under the effect of ATO in the tissue and its effects were decreased or suppressed due to treatment with alphalipoic acid (ALA) which was evident in all the organs⁽⁹⁾ whom considered that the opposite effect of alphalipoic acid against reactive oxygen species induced by effect of ATO in tissues, other workers reported that the ATO increased infiltration of inflammatory cells like neutrophils and enhance its migration under the effect of inflammatory mediators, protease⁽¹⁰⁾ alphalipoic acid produce its effect as antiinflammatory activity and reduced or inhibited inflammatory reaction which is more evident in this study and agreed with⁽¹¹⁾. The results in this study indicated that the ATO increased its effect in tissues by oxidative stress mechanism and supplementation with alpha lipoic acid exhibit an opposing action, so protect tissue against ATO toxicity.

Liver : is the main target site of ATO toxicity inducing hepatocyte damage, necrosis, vacuolation and fatty change, these finding were consistent with other studies⁽¹²⁾; all these lesions were reduced or inhibited when animals treated with alphalipoic acid indicating the protective effect of alpha lipoic acid against ATO toxicity, these results also agreed with⁽¹³⁾

The Kidney : also showed extensive pathological lesions characterized by damage, necrosis of renal tubular epithelia, hemorrhage, congestion and inflammatory cellular reaction, all these lesions were occurred as a result of ATO toxicity under effect of reactive oxygen species⁽¹⁴⁾ and the supplementation of alpha lipoic acid inhibit the pathological lesions, these findings agreed with⁽¹⁵⁾ who found that large dose of alpha lipoic acid protect rat against cisplatin induced renal damage.

The testes and epididymus : showed histopathological lesion like distortion of seminiferous tubules, suppression of spermatogenesis and vacuolation

of germinal cells, these lesions were occurred as a result of ATO toxicity with liberation of oxidative stress and the reactive oxygen species cause damage⁽¹⁶⁾ and inhibited or depressed spermatogenesis together with dilation of seminiferous tubules and epididymus resulted from direct effect of ATO on testicular tissue. Also these changes may occurred after inoculation of ATO which effect on sex hormone like testosterone, lentinizing hormone and follicular stimulating hormone which important for spermatogenesis⁽¹⁷⁾ who considered that the ATO as endocrine disruptor. on the contrary the supplementation with alpha lipoic acid ameliorate all these testicular changes, since alpha lipoic acid plays an important protective role against reproductive toxicity of ATO which was more evident in this study, a similar finding reported by Momeni et. al. 2012⁽¹⁸⁾

Other organs spleen : Is the main lymphoid tissue showed sever pathological lesions occurred as a result of ATO toxicity and under the effect of reactive oxygen species, similar findings agreed with⁽¹⁹⁾ whom reported that the ATO toxicity cause splenic tissue necrosis and depletion of lymphoid tissue in white pulp and these lesions were depressed or inhibited when use alphalipoic acid which cause white pulp hyperplasia and inhibited necrosis, so the ameliorative effect of alpha lipoic acid against Immunotoxicity of ATO on spleen tissue, and decreased the reactive oxygen species induced by ATO, so the spleen retain normal tissue architecture under the supplementation of alphalipoic acid which cause regulation of immune lymphoid tissue in spleen⁽²⁰⁾

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHSER in Iraq

Conflict of Interest: Non

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