RESEARCH ARTICLE

Histological Changes of Liver and Lung Induced by Bisphenol a in Pregnant Mice

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ABSTRACT

The current study was conducted to investigate the tissue lesions induced by Bisphenol (BPA) in pregnant mice. The administration of BPA (450 mg/kg) begins from the seventh to the eighteenth day of pregnancy. The results showed behavioral changes that include increased activity and movement excessive, aggressive behavior and irritability for 15 minutes after the dose, sensitivity and itching in the ear area, and sleeping for several hours with decreased activity and loss of appetite, especially on the 17th and 18th days of pregnancy, bleeding and inflammation in the vaginal area was also observed on the 16th day of pregnancy. On the other hand, the results showed that the weights of pregnant mothers increased with the increase in BPA concentration compared to the control group. Histological changes in the fetus included congestion and swelling of sinusoids, necrosis, degeneration of hepatocytes, and infiltration of mono-nucleated cells. The lung showed destruction of bronchi, and thickening of inflamed cells. Alveolar walls were showed inflammatory cell infiltration and hemorrhage.

Keywords: Bisphenol A, Histological changes, Pregnant mice.

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INTRODUCTION

Recently, some substances called endocrine disruptors have caused a change or defect in the physiology of the endocrine system, such as bisphenol-A.[1] Epoxy is used to paint water tanks.[2] Bisphenol A is used in the manufacture of medical devices such as heart devices, lungs, artificial kidneys, incubators, and safety equipment, including safety glasses, face shields, and motorcycle helmets. Exposure to bisphenol A negatively affects development and reproduction by affecting the physiology of endocrine glands, causing many birth defects and low fertility and some diseases such as obesity, diabetes, and cancers.[3] Due to the lack of local studies on the adverse effects of bisphenol A on pregnant mothers and their fetuses, the current study was designed to investigate the tissue lesions that induced by bisphenol A in organs of pregnant mice (liver, lung and kidney) and their fetuses, as well as the gross malformations of fetuses, behavioral changes and miscarriages that bisphenol A can cause in pregnant mice.

MATERIALS AND METHODS

The present study was conducted on pregnant Swiss white female mice, Mus musculus, (age: 12–9 weeks, average weight: 2 ± 23 gm), and in good health, 12 hours of light and 12 hours of darkness,[4] the females prepared for fertilization were placed with males at the rate of one male with three females in each cage, and fertilization was confirmed by observing the vaginal plug on the next morning, and the mating day was considered the zero-day of pregnancy and the next day It is the first day of it.[5] Bisphenol A used in the current study was obtained from the Japanese company Solaebio Beijing after dissolving it in corn oil. LD50 of bisphenol A was determined as 3228 mg/kg body weight.[6] 20 pregnant female rats were used and distributed into two equal groups. The control group was dosed with corn oil, and the second group administrated (orally) with Bisphenol A (450 mg/kg/single-dose/ daily) that was dissolved in the corn oil. The administration begins from the seventh day to the eighteenth day of pregnancy, as shown in Table 1.

At the end of the experimental period, mice were transferred to the animal house at the College of Veterinary Medicine, University of Mosul. The pregnant female mice were dissected on the 18th day of pregnancy, and a microscopic examination of embryos was performed. The organ specimens and embryos were fixed in formalin solution, the dehydrated, embedded by paraffin wax, and the tissues were stained with hematoxylin-eosin were done.[7] Histological sections were examined by optical compound microscope, and figures were graphed by using a compound microscope equipped with a Scmoso5000kpa digital camera.

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Table 1: Period of administration and the dose concentration

Orally administered using gavage needle from 7th -18th day.	Control (10)	10	11	Corn oil
	Trial (2)	10	11	BPA 450mg/kg

Table 2: the effect of BPA on body weights

Weights Groups	*Body weight before treatment*	*Body weight on the tenth day of pregnancy*	*Body weight before sacrifice*
Control	24.66 ± 1.16 a	26.19 ± 1.02 a	37.16± 0.60 a
450 mg/kg	24.83 ± 0.74 a	28.16 ± 16 c	39.66 ± 1.47 c

* Similar letters indicate no moral differences, and different letters indicate differences

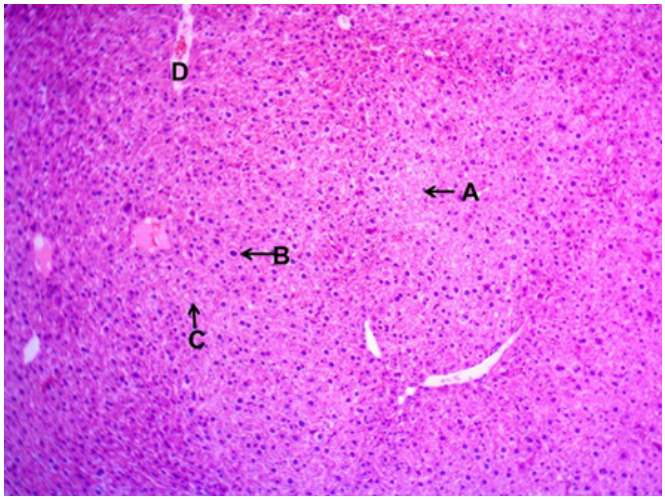

Figure 1: Histological section of Mouse liver from the 450-treated group showing thrombo necrosis (A), cell swelling of hepatocytes (B), sinusoidal stenosis (C) and central venous congestion (D). Hematoxylin and eosin stain, 00X1

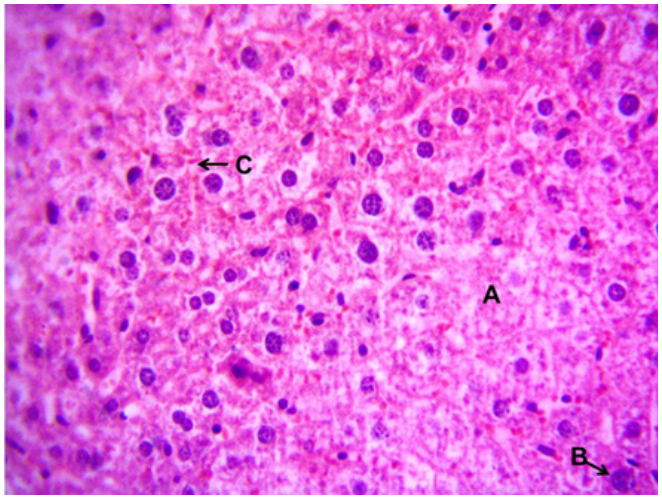

Figure 2: Histological section of the liver of a mouse from the 450-treated group showing thrombo necrosis (A), cell swelling of hepatocytes (B), and congestion and stenosis of the sinusoids (C). Hematoxylin and Eosin stain, X400

RESULTS

Behavioral Changes BPA Group

The current results showed that in the pregnant mice, after administrated with BPA, some behavioral symptoms were represented by increased activity, excessive movement, aggressive behavior and agitation for 15 minutes after the administration, and sensitivity and itching in the ear area after these behaviors, a state of calmness, lethargy and seclusion in one of the corners of the cage, and sleeping for several hours with decreased activity and loss of appetite, especially on the 17th and 18th days of pregnancy, bleeding and inflammation in the vaginal area was also observed on the 16th day of pregnancy.

The Effect of Bisphenol A on the Weight

The results of the statistical analysis showed significant differences in the weight rates of pregnant mothers during pregnancy at the probability level ($p < 0.05$) in the groups exposed to BPA. The results showed that the weights of pregnant mothers increased with the increase in BPA concentration compared to the control group, as shown in Table 2.

Histological Changes

The results of the microscopic examination of the livers of mothers treated with BPA indicated hepatic histological changes

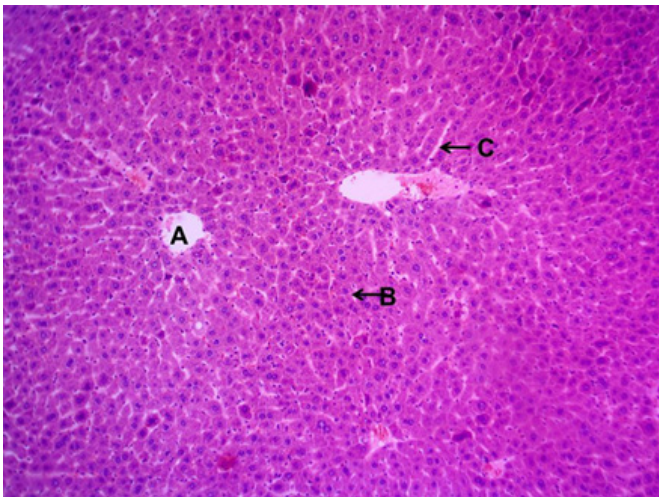

Figure 3: Histological section of the liver of a rat from the control group showing the normal shape of the central vein (A), the arrangement of hepatocytes around it and their regularity in the form of bars (B), sinusoids (C), and Kupffer cells (K). Hematoxylin and Eosin stain X400

such as the presence of thrombotic necrosis, cellular swelling of hepatocytes, stenosis of the sinusoids, and congestion of the central vein (Figures 1 and 2), compared with the control group (Figure 3). Otherwise, peribronchiolar, congestion of blood vessels, hemorrhage, pulmonary emphysema of the

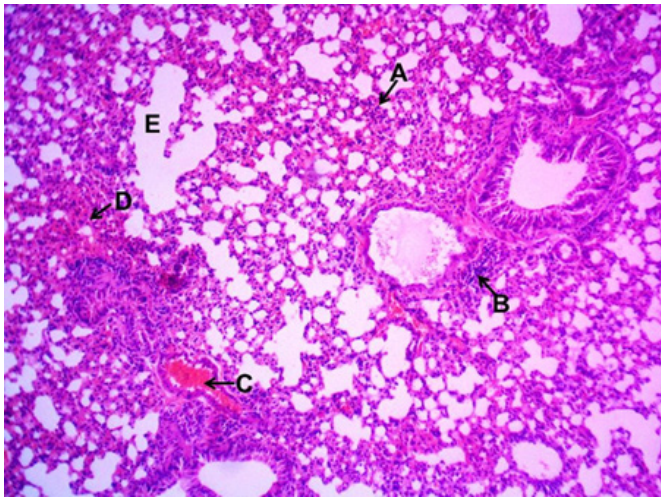

Figure 4: Histological section of the lung of a mouse from the group treated with a dose of 450 shows the presence of lung inflammation represented by a thick infiltration of inflammatory cells in the lung alveoli (A), peribronchioles (B), vascular congestion (C), hemorrhage (D), and emphysema of the alveoli (E). Hematoxylin and eosin stains. X100

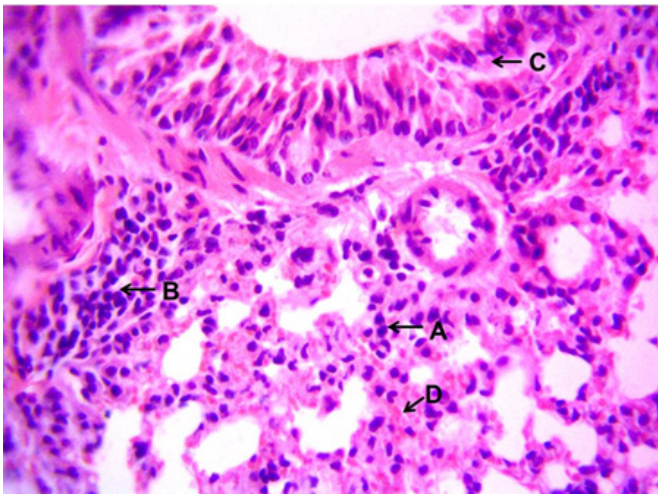

Figure 5: Histological section of the lung of a mouse of the 450-dose group showing the presence of lung inflammation represented by a thick infiltration of polymorphic inflammatory cells in the pulmonary alveoli (A) and peribronchioles (B), hyperplasia of epithelial cells lining the bronchioles (C) and interalveolar hemorrhage (D). . Hematoxylin and eosin stains. X400

alveoli, hyperplasia of epithelial cells lining the bronchioles, interalveolar hemorrhage, and emphysema with thickenings in the walls of the alveoli (Figures 4 and 5) compared with the control group (Figure 6).

DISCUSSION

The results of the current study indicated that rats administrated with BPA suffering from many behavioral symptoms represented by increased activity, excessive movement, aggressive behavior, sensitivity, and itching in the ear area. Muscular system activation and nervous excitability and these results are similar to what I observed[8] when mice were fed ketamine, or perhaps these behaviors were due to the effect

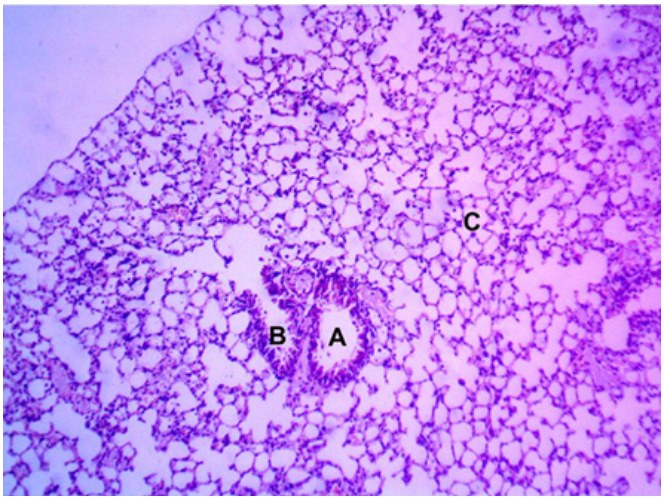

Figure 6: Histological section of a mouse lung from the control group showing the normal histological features of the lung tissue represented by the bronchioles (A), respiratory bronchioles (B), and the alveoli (C). Hematoxylin and eosin stains. X100

of BPA on the central nervous system and the cardiovascular system,[9] or maybe to effect of BPA on the immune system and enhanced sensitivity as indicated by [10] finding BPA concentrations in urine samples of 411 pregnant women in China with allergies compared to healthy women, and these results are also consistent with what was stated[11] that BPA causes behavioral problems such as anxiety, hyperactivity, inattention and aggression when they were studied on children who Their mothers were exposed to the effect of this substance during pregnancy, as well as children who were exposed to BPA from birth until the age of twelve, and bleeding and inflammation in the vaginal area was also observed on the 16th day of pregnancy with. The continuation of the pregnancy and the non-abortion of all fetuses, and this is similar to what was mentioned by [12] that exposure to BPA leads to a change in various vital functions such as reproduction, behavior, metabolism and immunity, and may be due to the effects of high blood pressure.[13] High weights of pregnant mothers, and these results are similar to study carried out by [14] referred that the use of BPA during pregnancy lead to increase the fat tissue mass, an increase in the size of adipocytes and an increase in the expression of adipocytes, as studies conducted on rats and laboratory mice that were treated with chemicals and some Exogenous drugs cause weight gain due to increased body fat accumulation due to disruption of multiple metabolic signaling pathways in the organism and BPA-induced metabolic syndrome which can lead to permanent changes in adult physiology.[15] It was also noted that the incidence of fetal abortions increased by 40% compared to the control group. The presence of BPA in urine has been shown to be a major cause of miscarriage. In addition to gross abnormalities in the mothers' organs, in the liver, abnormalities were very visible, represented by changes in the parameters of the liver, atrophy in the liver lobes, erosion in its tissues, and congestion in blood vessels with hemorrhage in the liver lobes. These results are similar to what was found

by 16, and are consistent with a study stated[17] that high doses of BPA caused changes in liver enzymes. In the lung, an accumulation of purulent substances was observed on the right lobe of the lung with severe congestion and its appearance as a dark black balloon in the left lobe and damage to the lung tissue.

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