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Histomorphological and histopathological study of Bisphelon effect with vitamin (c) on kidney of local breed rabbits.

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Abstract

The study included 12 adult Iraqi local mixed adults rabbits, divided into 3 groups. The first is a control group contained 4 rabbits that were treated with distilled water only: The second is the harmful material, rabbits were given 100 mg/kg of body weight of bisphenol, dissolved in olive oil, using a stomach tube. A toxicological minimum effective dose: In the third group, which serves as a control, four rabbits were given 100 mg/kg of bisphenol and vitamin C. Dosage: 20 milligrams per kilogram of body weight of ascorbic acid (vitamin C) diluted in distilled water. The experiment continued for a month and the dosage was twice a week. After the end of the experiment, the rabbits were euthanized and tissue samples were taken from the kidneys of the three groups and they underwent for routine and special tissue's processing methods. The results of histomorphological changes at the examination appeared under light microscopy.in Both routines and specials stains showed changes the most important of which were losing of epithelial cells(Podocytes) of the glomerular cells, their clear degeneration, sloughing and necrosis in the nephron, and the aggregation and infiltration of the lymphocytes cells in all layers of the kidney, the cortex and the medulla, in the group treated with Bisphenol, while the results appeared in the group treated with vitamin C. revealed clear recovery due to protective effects of Vitamin C and kidney's tissues

seen near to normal structures .Conclusion: that Bisphenol caused histomorphological changes in the rabbit's kidneys, while the protective effect of vitamin C prevented these histological changes

showed distorted glomerulus ,exudate edema with distorted glomeruli and dilated tubules degeneration of tubular cells. After three weeks of given Bisphenol a Pyknotic nuclei with degeneration of tubular cells antioxidant's like Vitamin C has protective effects against Bisphenol A.

Key words: Bisphenol + Histological effect's+ Kidneys + Rabbits

Introduction

As a beginner or inexperienced individual Bisphenol A (BPA) is a man-made substance that disrupts the endocrine system and is commonly utilized as a primary ingredient in the production of polycarbonate plastics, epoxy resins, and other polymeric materials. Human exposure to BPA is widespread, occurring through contaminated foods and settings via many pathways including as ingestion, inhalation, absorption through the skin, and injection(4,10). Therefore, this molecule has been found in various bodily fluids in the majority of individuals (>90%), regardless of the location of testing. (1,2). Bisphenol-A (BPA) is extensively utilized for its robustness, versatility, and reduced mass. The compound was initially identified by the Russian chemist Dianin in 1891 by the process of combining acetone with two phenol equivalents under the influence of a strong acid. The method was brought into commercial use in 1957(3). It serves as a monomer in the production of polycarbonate plastics and as a constituent of epoxy resins used in many consumer goods. Bisphenol A (BPA) is widely utilized in many applications including food packaging, dental restorations, medical devices, toys, electronics, plastic utensils, water containers, and papers used in fax machines, printers, and sales receipts (4). Although several investigations on reproduction and structure have documented the impacts of this chemical on experimental animals (5). impact of BPA on urinary system. Bisphenol A (BPA; 2,2-bis(4-hydroxyphenyl) propane) is a prevalent endocrine disruptor extensively utilized in the plastic industry. It has the ability to modify the regular cellular functions and the processes of synthesis, metabolism, transport, and elimination of natural hormones in the review the effect of BPA as a toxic substance on kidneys . Consequently, BPA can imitate or oppose hormonal activities within the body. Several authors employed antioxidant therapy to mitigate the toxicity of BPA (6). Recent research indicates that BPA is associated with developmental, systemic, neurological, immunological, and reproductive issues (7). As a substance that can harm reproductive health, it is associated with disruptions in the production of hormones, faulty development of embryos, dysfunction in the testes and epididymis, and incorrect functioning of accessory sex glands. Consequently, it can lead to reduced fertility or infertility. To mitigate the risk of BPA poisoning, it is advisable to reduce one's exposure to it. Nevertheless, humans are commonly exposed to this toxin by

ingestion, inhalation, and skin contact (4,10,11). Moreover, it is inherently difficult to restrict its utilization in daily activities. Hence, the exploration of possible treatment approaches stands as a prime choice for mitigating the harmful effects of BPA. (4,10,11). The surge in BPA research observed in the past decade has led to an upsurge in studies investigating molecular pathways and uncovering connections between BPA-induced oxidative stress and human illness. An investigation of the connection between exposure to BPA and the generation of reactive oxygen species (ROS) or oxidative stress will be carried out using the data submitted by various workers(4). In order to develop a framework for understanding how BPA-induced oxidative stress may contribute to the numerous effects that are reported following exposure, the purpose of this study is to conduct a review of the available research on BPA. (12). Chromosomes of mice has been describes first time at 1984 by authors (13) who said that bone marrow and kidneys samples can be used to identifying chromosomal aberrations in genetics diseases observed in mice. Antioxidants are substances that prevent oxidation, a chemical process that can generate free radicals, often by autoxidation. Autoxidation results in the deterioration of organic molecules, including biological organisms. Antioxidants are commonly used into industrial goods, such as polymers, fuels, and lubricants, in order to prolong their durability and usability (15). Food items are further subjected to the application of antioxidants to prevent deterioration, namely the process of oils and fats becoming rancid. Within cells, antioxidants such as glutathione, mycothiol or bacillithiol, and enzyme systems like superoxide dismutase, have the ability to protect cell against harm caused by oxidative stress (16). Vitamins A, C, and E are recognized as dietary antioxidants. However, the word "antioxidant" has also been used to describe many additional dietary substances that only exhibit antioxidant capabilities in laboratory tests, with limited evidence of antioxidant effects in living organisms. Scientific evidence does not support the claim that dietary supplements labeled as antioxidants may effectively preserve health or prevent diseases in people ("Antioxidants: In Depth" (17). Bisphenol A (BPA) has teratogenic, mutagenic, and carcinogenic properties, and can also disrupt the process of chromosomal segregation during meiosis. It has the potential to be carcinogenic and enhance vulnerability to cancer(18). The impact of BPA on tumor formation is mostly attributed to its hormone-mimicking properties. Nevertheless, an increasing amount of data suggests that the generation of reactive oxygen species (ROS) by BPA plays a crucial role in its toxicity and ability to cause cancer. Hence, the query arises as to whether antioxidants can mitigate the toxicity of BPA and, most importantly, diminish the likelihood of cancer initiation. In this work, we want to address the aforementioned topic, particularly due to the fact that several antioxidants not only enhance cellular antioxidant systems but also exhibit anti-cancer properties. (19). It is crucial to emphasize that these reference doses are established based on the oral consumption of BPA in conjunction with meals by humans(20).There were very limited study about Bisphenol toxicity on urogenital tract's mainly Kidney tissues of

Rabbits and Protective effects of Vitamins C as Antioxidants reagents.(21).

Objective of this study:-

1-Histomorphological and histopathological study of Bisphenol effect with vitamin C on kidney's rabbits.

2-Histologically Evaluation of the protective effects of Vit C as antioxidant against Bisphenol toxicity

Material and methods

1:Animals: mature mixed genders rabbits (local breeds) at the age of 4-8 months were obtained from local markets in Baghdad City. And were kept in Animals House of College of Veterinary Medicine for adaptaion at 3 weeks periods and providing on grass food and special pellets with tap water.

Chemicals and Drugs:-

1-Bisphenol : Bisphenol was administered orally via a stomach tube, dissolved in olive oil, at a dosage of 100 mg/kg of body weight. (according to 21)

2-Vitamin Cas in 025 : Ascorbic acid (also known as vitamin C) was diluted in distilled water and administered orally at a dosage of 20 mg per kilogram of body weight.(38)

3-Anesthesia : Animals were killed by Euthanization by intramuscular injection of zylazin (5 mg/kg), and ketamine (0.02 mg/kg).(39)

4-Formalin 10% :Obtained from histology departments in College of Veterinary Medicine

5-Tissue's Samples and Processing Methods : tissues samples at thickness (5 micrometer) were taken from kidneys of rabbits in each groups.(37)

Experimental Design:

A: Animal :Twelve mixed gender adults rabbits were dividing in to 3 groups as following:

1-First group 4 rabbits were orally treated with Bisphenol at dose of 100 mg/kg of body weight

2-Second group 4 rabbits were orally treated with Bisphenol at dose of 100 mg/kg of body weight mixed with vitamin C at dose of 20 mg/kg of body weight

3-Third group 4 rabbits were orally treated with distilled water as control of male and female rabbits.

B: Parameters

1.Histological and histopathological Examination under light microscopy using Route in stains Hematoxylin and Eosin

2.Histomorphological Examination under light microscopy using Special satin (Masson's Trichrome Stain).

Results and Discussion

Commonly employed in the plastics industry, Bisphelon is a hazardous substance that can change normal biological functions such as synthesis, metabolism, and transport. It seems that the cellular toxicity of Bisphenol is caused by conjugates and bound forms. As a result, the method of exposure to this substance determines the degree of kidney injury generally. The symptoms, which differed from those caused by chronic poisoning in earlier trials, were seen in male and female rabbits given varying dosages of Bisphenol over a 30-day period. This variation can be the consequence of the material's

compositional shape as well as its hazardous content and concentration.

After two weeks of treatment with Bisphenol, the kidney damage in the treated groups was the same for both male and female kidneys. This pathological disease is characterized by irregular or widespread loss of the outer layer of cells in the renal tubules, known as the brush border, as well as the flattening of the renal tubular cells due to the widening of the tubules (fig B).

After three weeks, however, intratubular casts and various kinds of sloughing cells which are in charge of granular cast formation were seen in the treated groups. Even though the denuded epithelium and cellular debris made the intra-tubular blockage obvious, the rearrangement of intercellular adhesion molecules caused the denuded tubular epithelial cells to cluster together. Next, dilated tubules and reduced and deformed glomeruli appeared. Additionally, a localized degeneration and varying degrees of renal tubular necrosis/apoptosis were seen. (Fig. A, B, C).

In contrast, during the last week following a 30-day period, the Bisphenol-treated groups showed cellular infiltration of inflammatory cells that were evident in the central interstitial tissue. The majority of these cells were lymphocytes and plasma cells, and they also showed signs of inflammation, edema, and interstitial fibrosis with varying degrees of tubule atrophy. Furthermore, there were noticeable inflammatory foci in both focal and diffuse glomerulonephritis, as well as a variety of necrotic masses with varying sizes and forms. In addition, there were more deformed glomeruli and atrophy, as well as tubule dilatation.

Additionally, the majority of treated groups showed varying degrees of renal tubular necrosis/apoptosis along with multifocal regions of lymphocytic cell infiltrates in interstitial space and a localized degeneration of proximal tubules. A more severe intratubular cast was seen, along with a distinct kind of sloughing cell that causes granular casts to develop. The intra-tubular blockage was especially noticeable because of the denuded epithelium and cellular debris (Fig. A, B, C).

We examined Bisphenol effects on male and female rabbits. Glomerular degradation, which is filtered through the glomerular layer and absorbed by renal cylindrical cells, was visible under a microscope (22, 23). Additionally seen was the dilation of the Bowman capsule and the degeneration of spherical cells with Pyknotic centers. These substances cause damage to the kidney overall, particularly to the cortical region, and eventually go to the proximal tubule, where they progressively impair the organ's function (24, 25., 26). Moreover, the accumulation of free radicals in the renal tissues due to Bisphenol-induced enhanced lipid peroxidation may be the cause cell injury represented in these changs these changes. Cadmium are environmental pollutants that are implicated in potential reproductive effect including damage to the prostate gland . buildup in the kidney causes glomerular filtration to be compromised in rats under cadmium management (27,28) An increase in intracellular water brought on by Bisphenol and abnormalities in fluid balance might be the cause of vacuolar degeneration in the renal tissue. (29,30). The impact of these compounds during their elimination by renal tissue can be linked to additional renal lesions, even though the degeneration and necrosis of the kidney may be caused by an increased defensive mechanism against foreign particles, intoxication, hemodynamic abnormalities, or changes in inflammation and apoptosis-

related genes(5). Further research is required to determine the exact reason, according to (31,32)Vitamin C treatments against Bisphenol in our study showed marked protective effects seen very well in microscopically examination appears as near to normal kidneys structures mainly Podocytes(epithelial cells) of glomeruli that's indicated very clear recovering effects of vitamin C on histological structures of kidneys , that's in agree with author's results(33). As well as agree with other's study about protective effects of Vitamin C against different Oxidative stress producing agents as Bisphenol and as supplements to aid in kidney injury healings and endothelia's cells integrity(34).Bisphenol caused Impairments of kidney function due to deterioration's effects on renal tubules. As well as stopping facilitation of excretions and secretion and so no drain of wasting product's that attributed to severe defects in nephron function mainly infiltration of glomeruli and tubular function main histological and histopathological findings observed were damaging in Podocytes cells which are responsible for glomeruli function(filtration and excretion) and were very clear seen in light microscopyas in figure (B) and that what we are founds in our microscopic examinations with small foci of necrosis associated with degenerative changes in cortex and medulla and fibrosis in interstitial space, the presence of Bisphenol A (BPA) as a widespread environmental contaminant is a contributing factor to its accumulation in chronic kidney disease (CKD). Our observations align with the findings of several authors. (35,36,37).

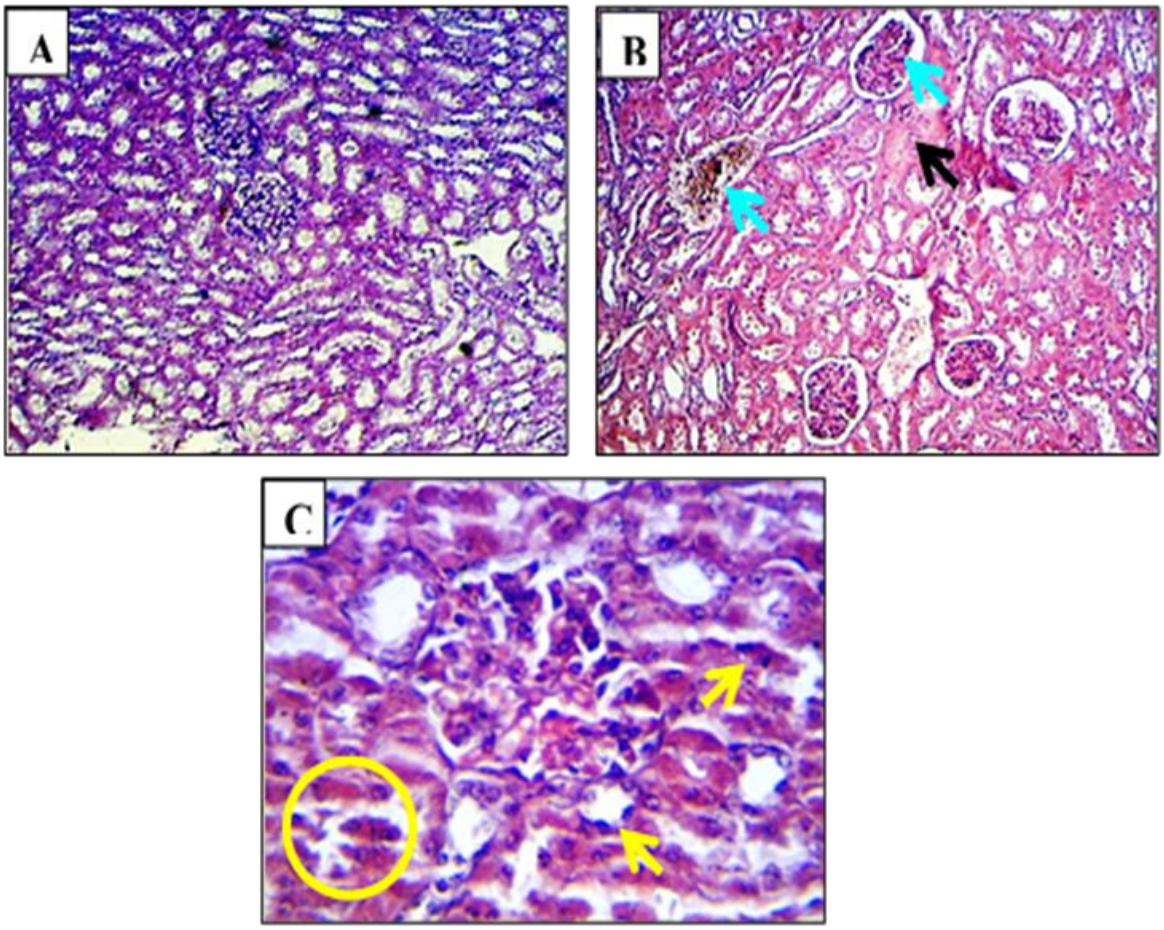

Figure 1. Photomicrography of rabbits kodney demonstrated with Bisphenol. (A) Vitamin C treatments group Masson Trichrome stain 100X .(B) After two weeks which gave Bisphenol showed distorted glomerulus (blue arrows), exudate edema (yellow arrows) with distorted glomeruli and dilated tubules degeneration of tubular cells H & E.X200. (C) After three weeks of given Bisphenol a Pyknotic nuclei (blue arrows) with degeneration of tubular cells (yellow circle) Masson Trichrome stain 400x.

Conclusion

In summary, this study demonstrated the impact of Bisphenol on the kidney, the current study sought to incorporate newer, potentially groundbreaking findings. It was observed Bisphenol interacted with cell tissue proteins through histopathological alterations, indicating that these materials may have adverse effects on the kidney. To investigate the mechanisms by which the bisphelon cause these negative effects at these tissues, more long-term research is nevertheless required.

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