THE SULFONAMIDE EXPOSURE AND THE HISTOPATHOLOGICAL ALTERATIONS OF DOMESTIC PIGEON

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Key words: Histopathological, sulfonamide, domestic pigeons.

ABSTRACT

A two months Toxicologicl pathology study of sulfonamide in domestic pigeons by oral intubation were done. The study was done at two dosage levels as intermediate 40mg/kg and high 80mg/kg with untreated control as third group. Clinical observation of treated birds did not show significant changes only the birds appeared to be quite after dosing for short time. Grossly, no obvious changes could be detected. Microscopically, Showed histopathological changes in pigeons represent of nephrotoxic effects characterized by degenerate and/or dilated cortical tubules in intermediate while, high dose groups appeared glomerular atrophy some with dilated Bowmans space, the severity of the changes were higher in the high dose group. In liver, peri portal and septal fibrosis in treated groups, some with parenchymal foci of inflammatory cell and vaculation of hepatocytes, while in pancreas, there was degenerate vacuolated islets of Langerhans in both treated groups, also in brain vacuolation of neurons and vacuoltion of nerve fiber in white matter of spinal cord. The severity of all above changes were higher in high dose than intermediate dose. Finally , the present study showed that domestic pigeons can tolerate varying toxic levels of sulfonamide with no mortality.

INTRODUCTION

The present study was done on toxicological pathology of sulfonamide in pigeons. The study will be interested as it appears to be the first species to be used in toxicological pathology (1). Sulfa drugs act by destroying coccidial forms which are found in the ceca, but

do not repair the tissue damage caused by the parasites (2). (3) studied the pathology of sulfonamide allergy in man, few patients with certain morphological changes that were attributed to sulfonamide therapy, among the first of these lesions were liver damage, granulocytopenia and urolithiasis , while (4) showed that the heart and other organs could be affected. in 1943, with report on kidney lesion, (5) Sulfonamides have several side effect. These have adverse reactions in elderly patient including severe skin reactions, generalized bone marrow suppression and decreased platelets (6). Moreover ,these have hematologic, hypersensitivity, renal and hepatic side effects respectively(7,8,9,10 &11).

(12) reported case report of hepatotoxicity, in this paper entitled sulfonamide hepatic injury. (13) studied the histological effects of pre-exposure prophylactic consumption of sulfa drugs on liver and kidney of albino wister rats (*rattus novergicus*). (14) reported that sulfonamide treatment of rat gave significant histopathological changes in the kidney of rats. (15) studied the systemic histopathology of rats treated with 6-sulfanilamidoindazole, a novel arthritogenic sulfonamide, the affected rats an able to moves, showed exudative synovitis and periarteritis also noted in liver, thyroid gland and lungs. (16) studied focal hepatitis ,fever and skin rash following therapy with sulfamethoxypyridazine, a long-acting sulfonamide as sensitizing agents capable of producing allergic types of drug reactions. (17) on hepatotoxicity that the liver plays a central role in transforming and clearing chemical and is susceptible to the toxicity from these agents, from the findings of the present study on toxicologic pathology of sulfonamide in pigeons,there was clear evidence of relationship of those findings to the hepatotoxicity discussed and reported by (17).The aim of the present study is to detect the toxicological pathology lesions induced by sulfonamide in pigeons.

MATERIALS AND METHODS

1- **experimental animals:**

Thirty adult domestic pigeons bought locally from market in basrah with average body weight (250gm) and kept in special cages (300 X 150 X100 cm.) in poultry unite / college of veterinary medicine/ Basrah university, all birds were acclimatized for 7 days before start the experiment. Food and water were given at lipitum.

2- **Chemicals:**

Sulfonamide (Pharma triple sulpha37% water soluble powder) from pharma care manufacturing leadind Co. Ltds,Saudi Arabia. The solution was prepared and used immediately, by oral gavage using disposable syringe after removing the needle, the doses of sulfonamide were determine by testing the compound on few birds practice for treatment. The

dose for pigeons and other birds is 20 gm in 10 liters water. That means 20000mg divided by 10000 ml which will be 2mg/ml so the dose in the field was 2mg/ml as it was originally 20gm/10 liters water. As maximum toxicity study we used up to (400mg/kg)as maximum toxic dose, the only clinical signs was the bird was quite, non active, then we decided the intermediate dose will be (40mg/kg) and the high dose will be (80mg/kg). sulfa powder was dissolve in water and given orally to pigeons in 1ml water.

3- **Treatments:**

Thirty birds were randomly divided into three groups A,B&C (10 for each group); group A as intermediate dose of 40mg/kg/day sulfonamide, group B as high dose of 80mg/kg/ day sulfonamide, whereas group C was given 1 ml distilled water as control group. The experiment was done for two months, at the experiment end of all birds were killed by cervical dislocation. post mortem was done and visceral organs were taken including kidneys, liver, pancreas, brain and spinal cord.

4- **Histopathological Examinations:**

Birds were killed and organs were fixed in 10% neutral buffered formalin for further histopathological study.in formalin, then samples were cut and paraffin blocks were made, slide were cut and stained with Haematoxyline-Eosin , selected histopathological changes were photographed from treatment related histopathological changes in comparison to untreated controls, according to the method of (18).

RESULTS

- **Kidney:**

The kidney of pigeon which treated with sulfonamide showed a degeneration, dilatation of cortical tubules in group of intermediate dose (Fig. 1, 2),

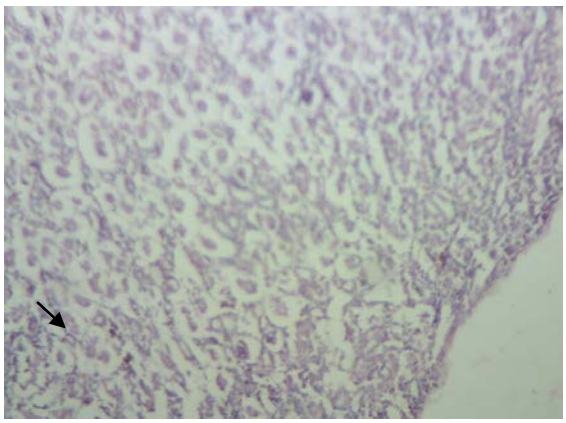

Fig. (1): Kidney of pigeon with intermediate dose with degeneration, dilatation of cortical tubules.(arrow) (H&E stain) (10x)

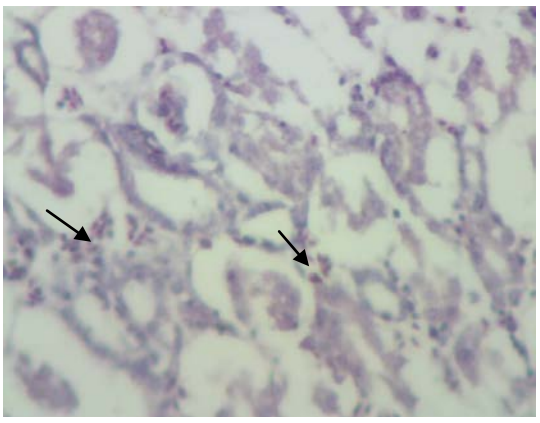

Fig. (2): Kidney of pigeon with intermediate dose with degeneration, dilatation of cortical tubules.(arrow)(high magnificent) (H&E stain) (40x)

The high dose group showed degeneration, dilatation of cortical tubules with atrophy in glomerular (Fig. 3), some with congestion and dilated cortical tubules (Fig. 4, 5). In fig. (6) a dilated bowman space of glomerular,). as compared with control group (fig7).

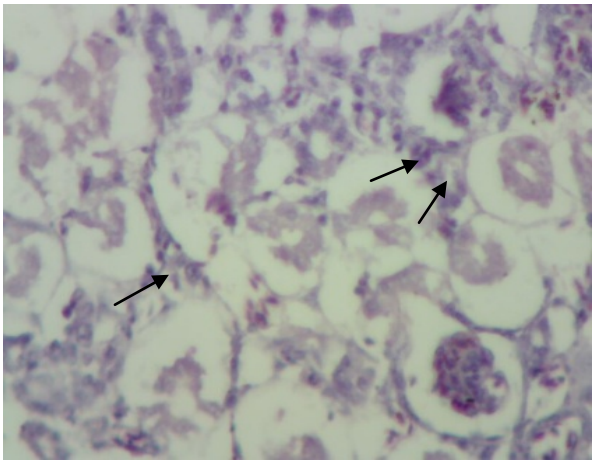

Fig. (3): Kidney of pigeon with high dose with degeneration, dilatation of cortical tubules(arrow) and atrophic glomerular.(double arrow) .(H&E stain)

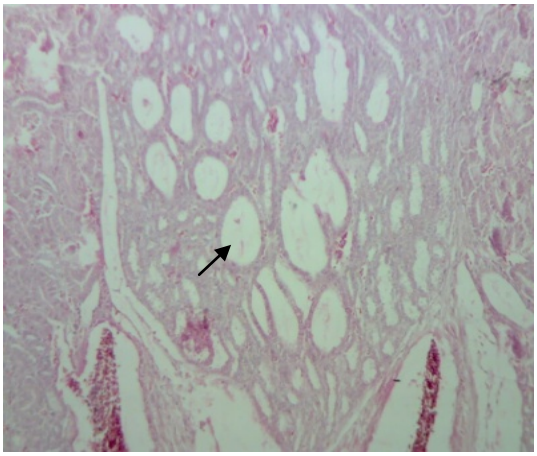

Fig. (4): Kidney of pigeon with high dose with dilated, degenerate of cortical tubules and congestion. .(H&E stain) (10x)(arrow).

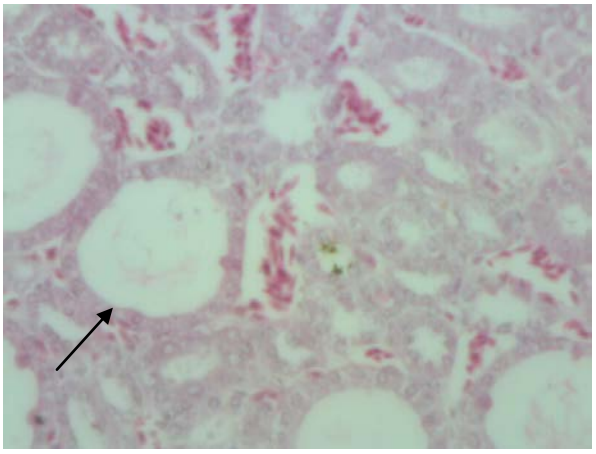

Fig. (5): Kidney of pigeon with high dose with dilated, degenerate of cortical tubules and congestion. .(H&E stain) (40x)(arrow).

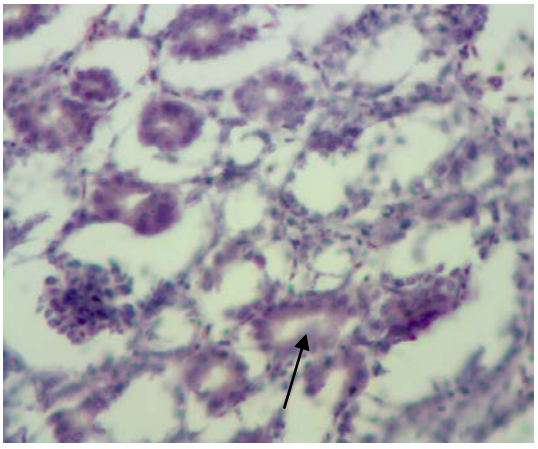

Fig. (6): Kidney of pigeon with high dose with dilated, degenerate of cortical tubules. .(H&E stain) (40x)(arrow)(high magnificent)

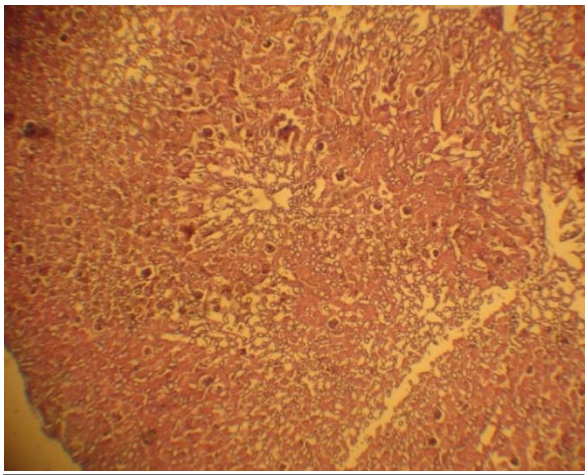

Fig. (7): Kidney in group C within normal limit.(H&E stain)(10x)

-liver:

A periportal and septal fibrosis found in groups with intermediate dose (Fig 8,9).

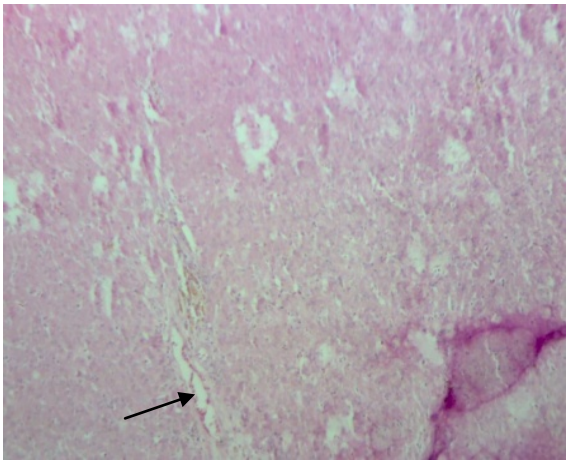

Fig. (8): Liver of pigeon with intermediate dose with peri portal fibrosis and septal fibrosis.(arrow) .(H&E stain) (10x)

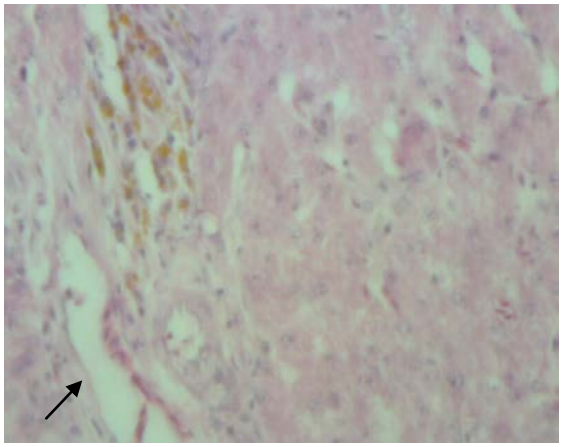

Fig. (9): Liver of pigeon with intermediate dose with peri portal fibrosis and septal fibrosis.(arrow) .(H&E stain) (10x)

The high dose showed parenchyma foci with inflammatory cells (Fig. 10), a minimal diffuse vaculation of hepatocytes (Figs. 11, 12), a periportal fibrosis with several lobules (Fig. 13). as compared with control group (fig.14).

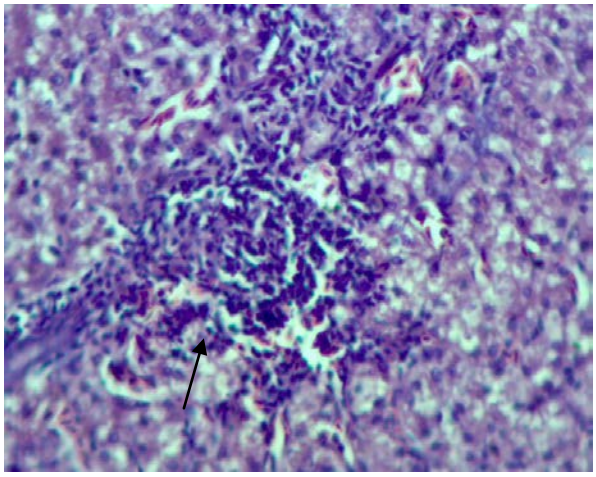

Fig. (10): Liver of pigeon with high dose with parenchyma foci of inflammatory cell.(40x)(arrow)

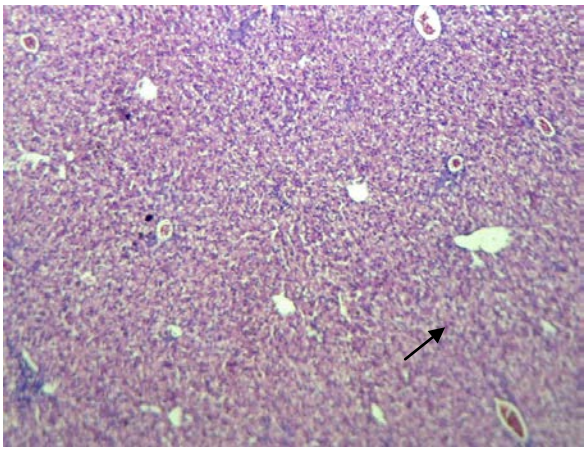

Fig. (11): Liver of pigeon with high dose with minimal diffuse vaculation of hepatocytes.(10x)(arrow)

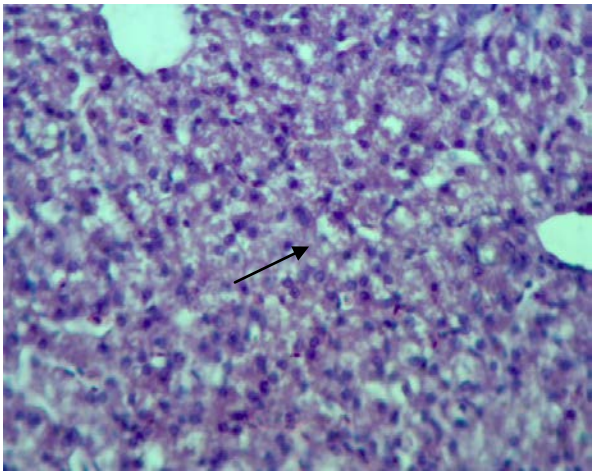

Fig. (12): Liver of pigeon with high dose with minimal diffuse vaculation of hepatocytes.(40x)(arrow)

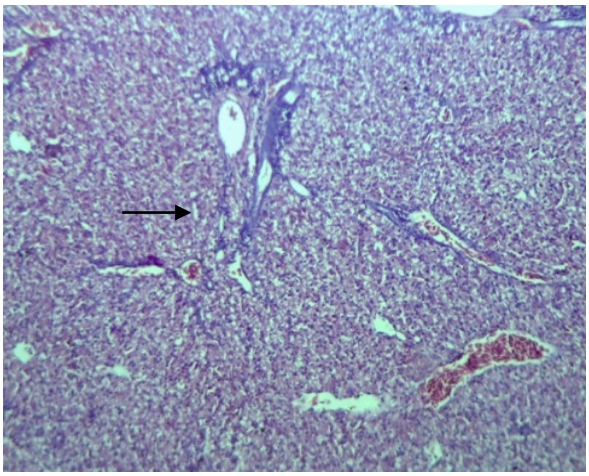

Fig. (13): Liver of pigeon with high dose with peri portal fibrosis and several lobules.(10x)(arrow)

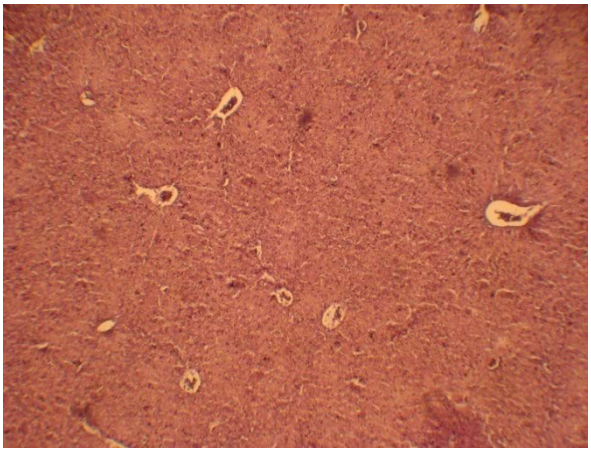

Fig. (14): Liver in group C within normal limit.(H&E stain)(125x)

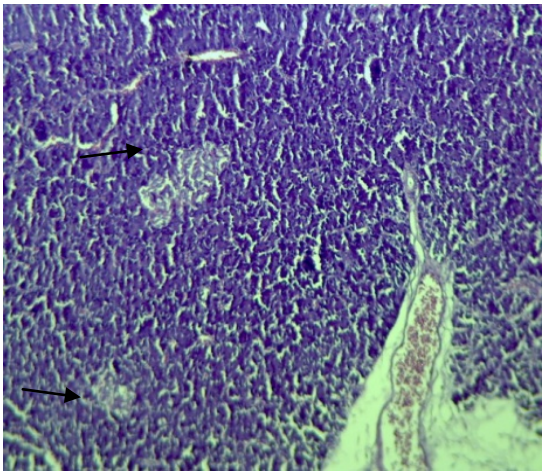

Fig. (15): Pancreas of pigeon with intermediate dose with degeneration of islets of langerhanse with vacculation.(10x).(arrow).

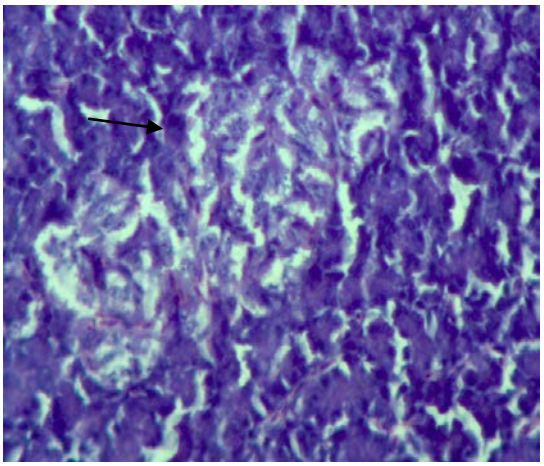

Fig. (16): Pancreas of pigeon with intermediate dose with degeneration of islets of langerhanse with vacculation.(40x).(arrow).

-Pancreas:

A degeneration of langerhanse islets with vaculation found in group with intermediate and high dose (Figs. 15, 16).

-Brain:

A minimal neuronal vacuolation were found in group high dose of sulfonamide (Figs. 17, 18),). as compared with control group (fig. 19).

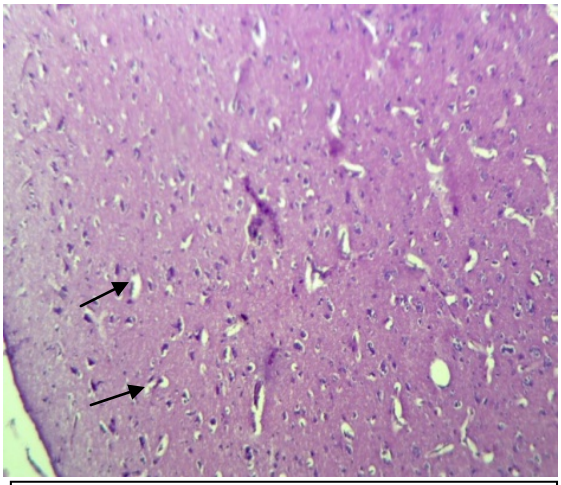

Fig. (17): Brain of pigeon with high dose with minimal neuronal vacuolation . (10x).(arrow).

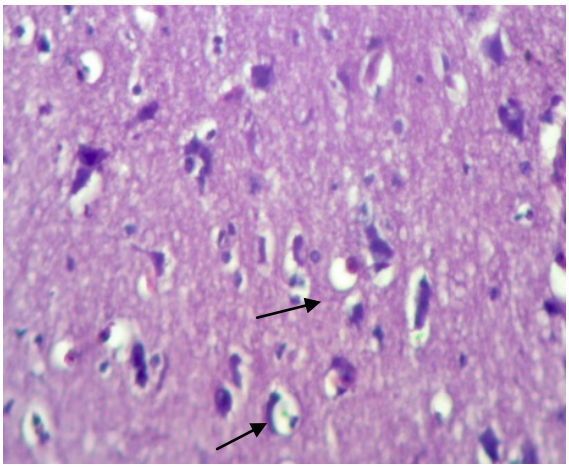

Fig. (18): Brain of pigeon with high dose with minimal neuronal vacuolation . (10x).(arrow)

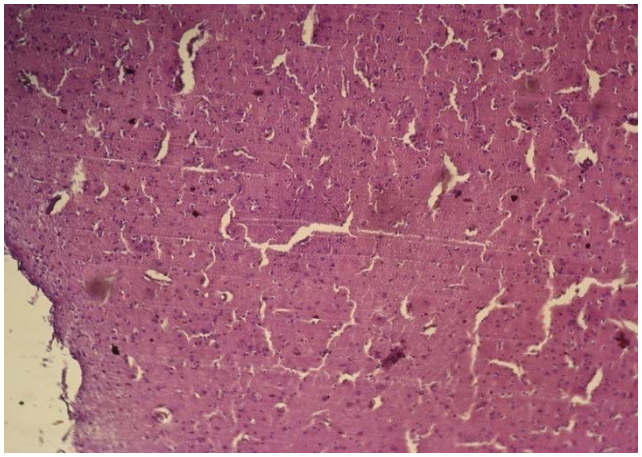

Fig. (19): Brain without any changes in group C within normal limit.(H&E stain)(125x)

-**Spinal cord:**

The high dose showed a vaculation in nerve fiber in the white matter (Figs. 20).

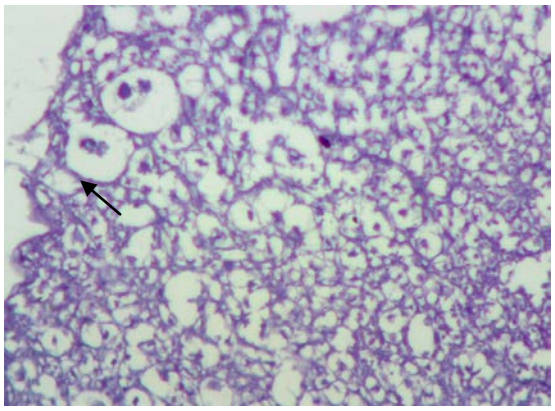

Fig. (20): Spinal cord of pigeon with high dose with vacculation nerve fiber in the white matter spinal cord (40x).(arrow).

We did study on the toxicity of the sulfonamide in pigeon because of it's important as was supported by (1) that sulfonamide are widly used in treatment of animals and human . In the present study histopathological changes in the liver and kidney. (3) reported changes in liver and kidney of people treated with sulfonamide, they explained those changes an allergic response to treatment with sulfonamide, but the present study showed that histopathological changes in liver and kidney were response response to treatment with sulfonamide.

(4) showed that changes in heart and other organs due to sulfonamide, while, the present study did not show changes in the heart after expose to sulfonamide. On the other hand (5) found histopathological changes of kidney related to treatment with sulfonamide, this study was agreed with the findings of the present study as well as other changes in visceral organs related to treatment with sulfonamide. (12)studied a cases of hepatotoxicity due to sulfonamide hepatic injury, the hepatotoxicity of (12) agreed with the present study as there was hepatotoxicity effects induced by the sulfonamide. (13)studied of histological changes in liver and kidney after exposure to prophylactic consumption of sulfa drugs of albino wister rats. represent by necrotic in the kidneys and liver. The present study, there were degenerative changes in the kidney as vacuolated/dilated cortical tubules and vacuolation of cell lining, fibrosis and foci of inflammatory cells in the liver, but the changes in kidney and liver not progress to necrosis as reported (13) in rats. (14) reported significant histopathological changes in the kidney of treated rats with sulfonamide, represent by of slight degenerative in the renal parenchyma, but no mention of any change in liver of treated rat, (14) agreed with the present study in respect of degenerative changes in the kidneys of treated pigeons with sulfonamide. While (15) studied the systemic histopathology of rats treated with

6-sulfanilamidoindazole a novel arthritogenic sulfonamide , the affected rats an able moves showed exudative synovitis and peri arteritis also noted in liver, thyroid gland and lungs, in the present toxicological pathology study of sulfonamide in pigeons, there were histopathological toxic changes in liver , kidney, pancreas and nervous system but no effects on joint and /or on blood vessels, as were reported by (15). (16) studied focal hepatitis fever and skin rash following therapy with sulfamethoxypyridazine along acting sulfonamide as sensitizing agent capable of producing allergic type of drug reactions in a case report, the present study only reported toxicologic pathology of sulfonamide on visceral organs such as liver, kidney, pancreas and others but no allergic responses was described by (16) the only similarity with (16) was the focal hepatitis reported in his case, could be related to the toxic hepatitis induced by sulfonamide as it was reported in the present paper. Finally (17) report on hepatotoxicity of different compound, the present report agreed with (17) as the liver play a central role in transforming and clearing chemical and is susceptible to the toxicity of these agent, in the present report there was hepatotoxic effects of sulfonamide which be one of the susceptible reactions of the liver to sulfonamide manifested by fibrosis, septal fibrosis and hepatic vacuolation.

التعرض للسلفونمايد والتغيرات المرضية النسجية في الحمام المستأنس

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الخلاصة

دراسة المرضية السمية للسلفونمايد لمدة شهرين في الحمام المستأنس بأستخدام التجريع الفموي. الدراسة شملت 3 مجاميع. جرعت المجموعتين الأولى والثانية بالجرعة المتوسطة 10 ملغم/وزن الجسم (40 ملغم/كغم) والجرعة العالية 20ملغم/وزن الجسم(80ملغم/كغم) بالأضافة الى المجموعة الثالثة كمجموعة سيطرة جرعت بالماء فقط. المشاهدات السريرية في الطيور المجرعة لم تلاحظ تغيرات واضحة،فقط ان الطيور كانت هادئة بعد التجريع لفترة وجيزة. عيانيا ،لم تلاحظ تغيرات عيانية. مجهريا،الدراسة النسجية للمرضية السمية للسلفونمايد أظهرت تغيرات سمية كلوية تتصف بوجود تنكس في نبيبات القشرة في المجموعة المجرعة المتوسطة والمجموعة المجرعة العالية ، مع ضمور في الكبيبات بالأضافة الى توسع النبيبات القشرية وتوسع في فراغ باومن للكبيبات. في الكبد لوحظ تليف ماقبل البوابي والحويجزات الليفية الناتجة في المجاميع المجرعة مع بؤر لخلايا التهابية وتجوف في خلايا الكبد. في البنكرياس وجد تنكس في جزر لانكرهانس في المجاميع المجرعة بالسلفونمايد. في الدماغ وجد تجوف في الخلايا العصبية وتجوف في الألياف العصبية في العمود الفقري. كانت شدة كل التغييرات المذكورة أعلاه أكبر في الجرعةالعالية من الجرعة المتوسطة وفي النهاية أظهرت الدراسة أن الحمام المستأنس يتحمل جرع سمية مختلفة من السلفونمايد مع عدم هلاكها .

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