Tikrit Journal of Pure Science
ISSN: 1813 – 1662 (Print) --- E-ISSN: 2415 – 1726 (Online)
Journal Homepage: http://tjps.tu.edu.iq/index.php/j

Histological effect of isoniazid drug in the kidney and liver tissues of albino mice *Mus Musuclus*

Muna Salah Rashid , Israa Abdoul munem
Department of Biology , College of Sciences Tikrit University , Tikrit , Iraq
https://doi.org/10.25130/tjps.v26i5.173

ARTICLE INFO.
Article history:
-Received: 28 / 6 / 2021
-Accepted: 18 / 8 / 2021
-Available online: / / 2021
Keywords: Isoniazid, Infiltration, necrosis, Kidney, Liver.
Corresponding Author:
Name: Israa Abdoul munem
E-mail:
israaabdominal@gmail.com
Tel:

ABSTRACT

The aim of this study is to investigate the histopathological changes induced by the anti-tuberculosis drug (isoniazid) in the kidney and liver tissues of white male mice *Mus Musculus*. 25 mice were distributed into five groups that included a control group, a therapeutic dose group of 0.625 mg, a group of 1.25 mg toxic group and a dose group The semi-lethal (LD50) is 80 mg, and the lethal dose LD range is 150 mg.

Oral administration of isoniazid led to pathological changes. In the kidneys, the tissue lesions were represented by the occurrence of necrosis in the cells of the urinary tubules in some areas, and the infiltration of inflammatory cells clearly, and the desquamation of some cells of the urinary tubules, and the swelling of some cells, which led to a narrowing in the lumen of the urinary tubules. The nuclei are necrotic and disintegrated. The glomerulus was some areas enlarged and some areas atrophic.

As of the liver, it was represented by the occurrence of necrosis, hemorrhage and congestion, infiltration of inflammatory cell, thickening of the plasma membrane, widening of the sinusoids some araes and narrowing them at other times.

Conclusion

The administration of isoniazid led to pathological changes in the kidneys, including necrosis, infiltration of inflammatory cell, glomerulosclerosis, nucleoli, as well as changes in the liver, including hemorrhage, rupture of the vein wall, and hemolysis of blood cells.

Introduction

At the beginning of the twentieth century, lung diseases such as tuberculosis and pneumonia were the main causes of death, and after a century the main diseases causing death were cancer, stroke and heart disease. The transformation in the basic diseases that lead to death from infectious to chronic came as a result of the discovery of many antibacterial drugs, which constituted a turning point in human history, beginning with Alexander Fleming (1881-1955) who discovered penicillin in 1928[1] Isoniazid is considered the first drug in terms of chemotherapy for tuberculosis, as it is directly absorbed when treated orally or by injection and spreads throughout the body fluids and cells. However, studies have found that isoniazid causes many side effects including rash, fever, jaundice, back pain, infection, optic atrophy, and its negative effect on the peripheral and central nerves of the[2] nervous system mentioned that recent years have witnessed the emergence of many and varied drugs used by humans to treat diseases, and although the purpose of using these drugs is for the benefit of humans, they may cause many side effects from symptoms, diseases, impairments and distortions resulting from violating the correct treatment principles. Where there is no non-toxic chemical, but the appropriate dose specific to a particular organism according to its type, age and weight is what determines the toxicity of the substance and its effect on the organism. In the therapeutic dose, the compound molecules may attack one of the affected components of the body, but in high doses, they attack different areas[3] of the body.

Materials and methods

The study was conducted in the animal house of the College of Veterinary Medicine / TikritUniversity.

Experimental animals

The study included an experiment that included 25 male albino mice *M usMusculus*, their weights ranged from (20-35) g. They were placed in cages designed specifically for breeding mice. They were plastic and with metal mesh lids, and their dimensions were (80 / 15 / 30) cm spread with sawdust, taking care to clean the cages And sterilized twice a week Throughout the experiment, the animals were placed in standard laboratory conditions in terms of ventilation and temperature, which were within (25°C ± 2) and a photoperiod (12) hours of light and (12) hours of darkness [4] and they were given the ration for feeding them. White mice in addition to sterile water continuously throughout the experiment period in special containers to avoid contamination with sawdust. The ration consists of (wheat 34% barley 20% corn 25% animal protein 10% powdered milk 10% table salt 1% [5,6].

Experimental design

Experimental animals were distributed into five groups and dosed by oral tube feeding as follows.

The control group: consisted of (5) males, they were dosed with sterile water for a month, in addition to diet.

Therapeutic group This group includes (5) males who were treated with isoniazid drug at a concentration of 0.625 mg / kg of animal weight for a month, once a day[7] Toxicological group This group includes (5) males that were treated with isoniazid drug at a concentration of 1.25 mg / kg of animal weight for a month, once a day Semi lethal LD50 group This group includes (5) males that were treated with isoniazid drug at a concentration of 80 mg/kg of animal weight orally twice a day, and the result was 50% death after 24 hours.

A lethal group that includes this group (5) males were treated with isoniazid drug at a concentration of 150 mg for 24 hours and the result was 100% death.

After the the end of the experiment period the animals were fasted for 12hours,and then the aniamls were anesthetized and dissected, and the required organs were removed.

Preparation of tissue microscopic sections

The microscopic tissue sections were prepared according to the method mentioned in [8] from fixation, washing, Dehydration, Clearing, infiltration to get wax molds they were then cut using the microtome to obtain tissue sections with a thickness of 5-7 micrometers. The slides were loaded onto clean glass slides marked with a diamond pen and left to dry. Finally, the tissue sections were stained with hematoxylin-eosin and loaded with DPX and cover glass. Then the slides were placed on a clean surface to dry.

Microscopic & Photographic Examination of Histological Section

The microscopic examination of the tissue sections prepared from the samples prepared for the study was carried out using an imaging light microscope in the Department of Biology/ College of Science, and then photographs of the sections were taken using a compound microscope equipped with a Novel type camera.

Results

Kidney results

Control group

The kidney is composed of the cortex and includes the glomerulus. It is a tuft-like network of capillaries located in the front of the renal tubular unit, and it performs the function of the first station for the process of filtering blood, which is assumed by the renal tubular unit during the urine formation process. The glomerulus is structurally supported by the mesangial (the space between blood vessels), which consists of mesangial cells within the glomerulus. Blood filters through the walls of the blood vessels through the glomerular filtration septum, which passes water and dissolved substances into a cup-like sac called "Bowman's capsule", to enter Then the glomerular filtrate the proximal renal tubule. The pulp is composed of urinary tubes(Figure 1).

Mouse kidneys therapeutic group

The results were for samples treated with the therapeutic dose and at a concentration of 0.625 mg / kg of body weight for a month, and the results were hemorrhage, rupting of tubules, absent of architure of the glomerulus, and infiltration of inflammatory cell (Figure.2).

Toxicity group

Histological examination of samples treated with the toxic dose showed a concentration of 1.25 mg / kg body weight for a month Swelling of glomeruli, hemorrhage, rupturing of the inner wall of the cytoplasm manbarn, and the thickness of the outer cytoplasmic manbarn of tubules (Figure 3).

LD50 group

The results for the samples treated with the LD50 dose at a concentration of 80 mg/kg body weight for 48 hours, and the mortality was 50%. The results were rupting of glomula, infiltration of inflammatory, and decreased the thikness of the cell of tubules (Figure.4)

Mouse kidneys are lethal group

The results were for samples treated with the lethal dose and at a concentration of 150 mg / kg of body weight for 48 hours, and the mortality was 100%. The results were hemorrhage, infiltration of inflammatory cell, swelling of the tubes, deposed of fat in cells, and the absence of space between Absent of spasce between boman and glumeula, desapear of the lumen of tuble, and cast (Figure.5)

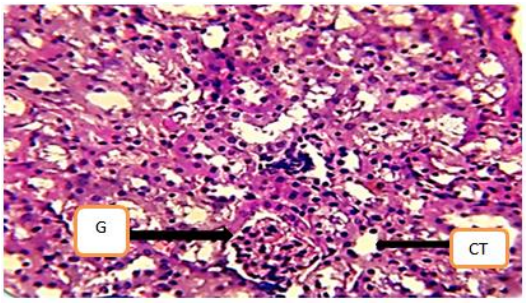

Fig. 1: ASection of mice kidneys from the control group showing Glomerulus (G) and convoluted tubule (CT) (X400,H&E)

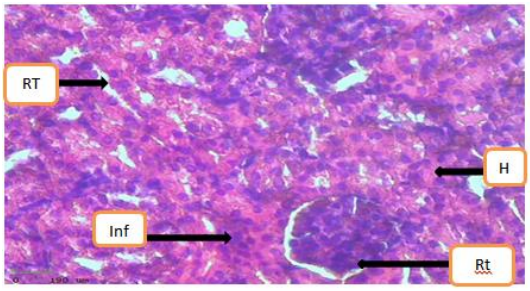

Fig. 2: A section of the kidneys of mice from a therapeutic group treated with isoniazid drug at a concentration of 0,625 mg showing the occurrence of (hemorrhage) H and rupting of tubules(RT) and absent of architure of the tubules (Rt), Inflammatory cell infiltration(Inf) (X400,H&E)

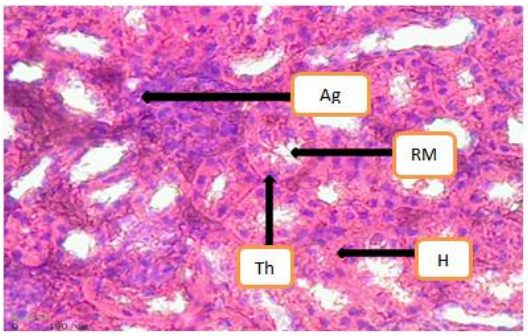

Fig. 3: A section of the kidneys of mice from toxic group treated with isoniazid at a concentration of 1.25 mg showing Absent the space between glomula and bowman capsule(Ag) and hemorrhage (H)and rupturing of inner wall cytoplasm manbarn (RM) and Thicknase of outer cytoplasmic manbarn of tubule(Th) (X400,H& E).

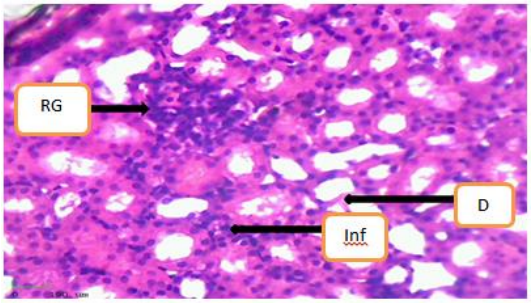

Fig. 4: A section of mice kidneys from semi-lethal group treated with isoniazid at 80 mg concentration shows the occurrence of (RG) rupting of glomula and (Inf) Infilration of inflammatory cell and decrease the thikness of the cell of tubules (D) (X400,H&E).

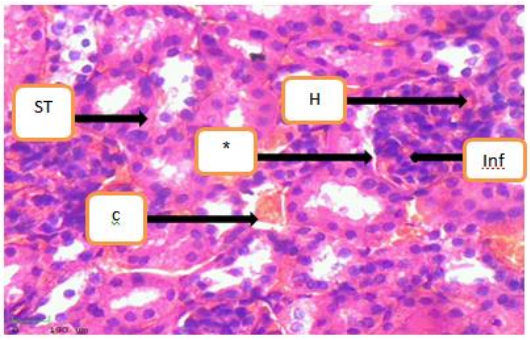

Fig. 5: in the kidneys of mice of the lethal group treated with isoniazid drug at a concentration of 150 mg showing (H) Hemorrhage and (Inf) Inflammatory cell infiltration(Inf) (Swelling of in cell tubules) (ST) and Cast(C)(X400,H&E)

Control group

The liver represents one of the appendices of the digestive system and the largest of the body glands surrounded by a capsule extending from it barriers called interlobular barriers that divide the liver into several lobules. We note the middle of each lobule central vein. These hepatic plates extend from the central vein to the periphery of the lobule. The hepatocytes are characterized by being polygonal in shape and have a central nucleus and acidic cytoplasm between the hepatic plates. We notice spaces or pockets called the sinusoids, which open into the central vein at the interlobular septa and line the sinuses with two types of cells, the first is the endothelial epithelium and the second is the Kupffer-mediated cells. There are hepatic artery, portal vein, bile duct and lymphatic vessels(Figure6).

Mouse liver therapeutic group

The results obtained from histological examination of samples treated with therapeutic dose at a concentration of 0.625 mg/kg of body weight for a month, rupture in the center vein wall, hemorrhage, the presence of kupffer cells, hepatocyte necrosis and karyolysis (Figure No.7).

Mouse liver toxicity group

The results of the samples treated with toxic dose for a month and at a concentration of 1.25 mg / kg of body weight were rupture in the center vein wall, hemorrhage, the presence of kupffer cell and hepatocyte necrosis (Figure No.8)

LD50group

The results were for the samples treated with a semi-lethal dose at a concentration of 80 mg/kg body weight for 48 hours, and the death was 50%. The results were hemorrhage, desquamation of the vein wall, fatty deposed in the cell, necrosis of hepatocytes, and the presence of kupffer cells (Figure No 9).

Mouse liver lethal group

The results were for samples treated with the lethal dose and at a concentration of 150 mg / kg of body weight for 48 hours and the mortality was 100%. The results were hemorrhage, fat deposition in the cell, necrosis, Inflammatory cell infiltration and rupture in

the centeral vein wall in The central vein wall (Figure No.10).

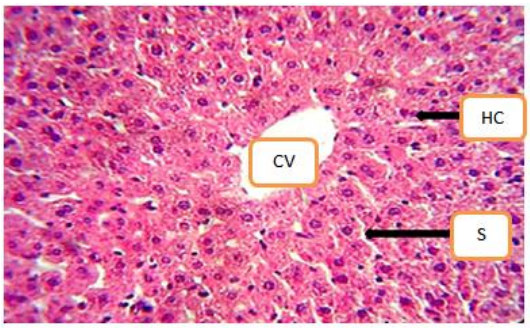

Fig. 6: a section of the liver of a mouse from the control group showing (CV) central vein and Sinusoid(S) and (Hepatic cell (HC)(X400, H&E)

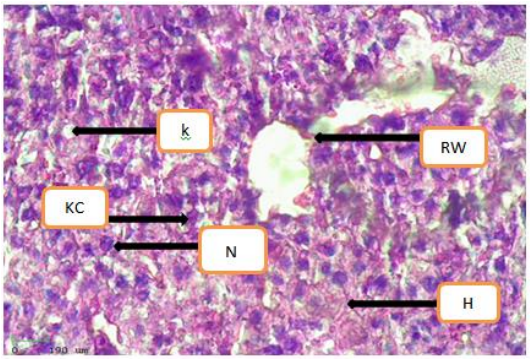

Fig. 7: a section of the liver of a mouse treated with the therapeutic dose of isoniazid at a concentration of 0.625 mg showing the occurrence of rupture in center vein wall (RW), hemorrhage(H), kupffer cell(KC), necrosis(N) and karyolysis(K) (X400, H&E)

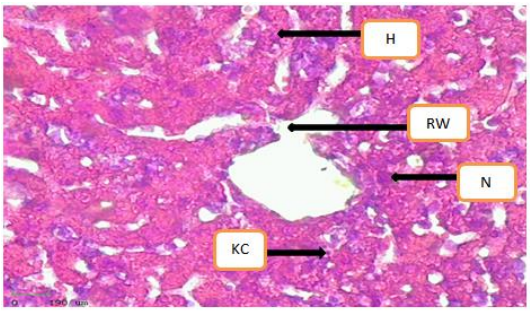

Fig. 8: a section of the liver of a mouse treated with the toxic dose of isoniazid at a concentration of 1.25 mg showing the occurrence of rupture in center vein wall (RW) and hemorrhage(H) and the presence of kupffer cell(KC) and necrosis(N) (X400, H&E)

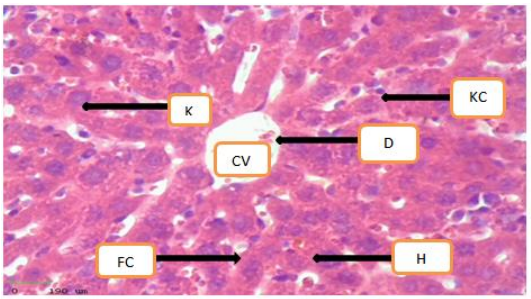

Fig. 9: section of the liver of mice from a semi-lethal group treated with isoniazid drug at a concentration of 80 mg showing the occurrence of hemorrhage(H), desquamation(D), (Fatty deposed (FC) in the cell, necrosis(N), and kupffer cell(KC) (X400,H&E).

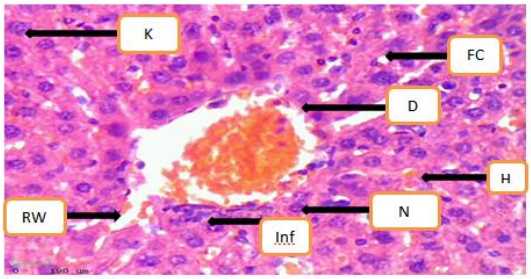

Fig. 10: section of the liver of mice from a lethal group treated with isoniazid drug at a concentration of 150 mg showing the occurrence of Hemorrhage(H), Fatty deposed in the cell (FC), necrosis(N), (Inflammatory cell infiltration (Inf) and Rupting in wall central vein(RW) (X400,H&E)

Discussion

The results from the use of isoniazid drug in combination with other antibiotics used in the treatment of tuberculosis. Reports indicated an increase in the level of urea and creatine in patients to a very high level, causing acute kidney failure and serious tissue damage.[9] In the current study, it was found that many tissue damages have occurred, the severity of which increases with increasing the dose and the duration of the dose. These damages were generally represented by damage to the tubules. It was also noted that nuclei necrosis and lysis and inflammatory cell infiltration. The glomerulus was some areas enlarged and some areas It was atrophic and lost its cellular arrangement, which was dominated by congestion. It was also observed that fibrosis in the kidney tissue increased with increasing dose. It was also observed that hemorrhage and congestion spread in the stroma of tissue and their intensity was directly proportional to the dose. These results agree with the findings of [10], where the researcher noticed the same damage to the kidneys when mice were dosed with diclofenac sodium. As for the damage to the tubules, it is caused by stimulating the immune system in response to the toxicity resulting from the drug, so large amounts of antibodies accumulate in blood vessels and tissues. The interstitium of the kidney causes an increase in the thickness of the endothelial tissue of the glomerulus, which results in damage to the tubules..

Also, the accumulation of antibodies in the blood stimulates an increase in renin secretion, which leads to constriction of the glomerular arterioles and thus a decrease in blood flow to the renal tubules, which results in damage to these [11]tubules.

The results showed that renal tubules are necrotic due to toxicity, where the tubular epithelial cells die as a result of not getting enough oxygen, as their metabolic activity depends on oxygen. Which is supplied by the blood vessels, and that any damage that occurs to the blood vessels from necrosis and narrowing of the renal artery leads to slow blood flow and then a lack of oxygen supply to cells [12].

The occurrence of bleeding and congestion in the treated kidney tissues is attributed to the direct destruction of the epithelium lining the blood vessels, which caused the leakage of red blood cells into the renal tissue [13].

Studies have shown that isoniazid has a toxic effect on the liver. It has been observed that it causes hepatotoxicity due to the secretion of toxic components, especially hydrazine, which is covalently linked with cellular molecules, causing a decrease in the concentration of glutathione .For the liver, its severity varies according to the concentration of the dose. These damages were generally represented by necrosis, hemorrhage, infiltration of inflammatory cell, thickening of the plasma membrane, lysis of red blood corpuscle, onset of fibrosis, enlargement of Cover cells, nucleolysis, degeneration and proliferation of vacuoles. This is consistent with[14] when they tried to use rifampicin to treat itching caused by cholestasis, where they noticed many tissue damages to the liver, represented by fatty degeneration, Inflammatory infiltration and necrosis to a large extent. Liver of rats when treated with paracetamol. The reason for bleeding in the tissues is due to the increase in pressure inside the blood vessels, which leads to a breakdown in the wall of the blood vessels and the expulsion of red blood cells. As for the reason for the breakdown of red blood cells, the interactions between toxic compounds and glutathione form compounds that lead to the dissolution of blood cells [15,16]. has pointed out indicated that the cause of the decomposition of red blood cells is mediated by macrophages due to local hemorrhage, and this decomposition leads to the formation of globin and heme, as globin is reduced by dissolving it in body fluids and heme cleaves to give hematodin and hemosedrin. At the site of bleeding, it is oily or yellowish-red, while hemosiderin is deposited in macrophages.

As for the infiltration of inflammatory cells, it calls to say that there are degenerative changes in the tissue that stimulate the secretion of chemical attractions, and then the infiltration of the area with lymphocytes, as the cells affected by the action of toxic substances secrete chemical attracting factors that attract white cells such as neutrophil cells and monocytes for defense About the body [17], where both [18] indicated the role of damaged cells in secreting attracting factors to attract inflammatory cells to areas of damage for the purpose of defending the body, and removing dead cells and debris [19] The enlargement of Cover cells is due to their defensive role in the body against foreign bodies and by virtue of their phagocytic function, which leads to their enlargement [20].

The results of the histological examination showed that some hepatocytes suffer from hypertrophy, which leads to the narrowing of some of the sinusoids, and this phenomenon occurs as a result of the adaptation that occurs when any physiological defect occurs, as the cells prepare to divide to compensate for the damaged cells, and on the contrary, an expansion of the sinusoids resulting from degeneration was observed in other areas. hepatocytes; This is consistent with the study conducted by [21], where he observed when giving rabbits a dose of alcoholic extract of fenugreek seeds that hepatocytes necrosis occurred on one occasion and the disappearance of the radial arrangement of the liver and swelling of the hepatocytes on another time While attributed the cause of hepatocyte swelling to a defect in the permeability of its plasma membrane due to the toxicity resulting from the drug, which leads to the entry or exit of substances severely, leading to cell swelling or contraction according to the direction of the imbalance between the existing elements and their salts, and this affects the cellular structures The internal cells, including the mitochondria, cause the cell to go through stages of programmed death or degeneration. Hence, the swelling of hepatocytes in turn led to the narrowing of the sinusoids. On the one hand, the expansion of the sinusoids is due to the shrinkage and degeneration of hepatocytes [22]. The degeneration of hepatocytes results from a disturbance in the metabolic processes of the hepatocytes, and the exposure of the nuclei of the cells to lysis indicates that the hepatocytes are vulnerable to harm, because they are the first cells to receive substances through the hepatic portal cycle [15].

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التأثير النسيجي لعقار أيزونيازيد في أنسجة الكلى والكبد لدى الفئران البيضاء

منى صلاح رشيد ، اسراء عبد المنعم محمد

قسم علوم الحياة ، كلية العلوم ، جامعة تكريت ، تكريت ، العراق

الملخص

الهدف من هذه الدراسة هو فحص التغيرات النسيجية المرضية التي يسببها العقار المضاد لمرض السل (أيزونيازيد) في أنسجة الكلى والكبد لدى ذكور الفئران البيضاء. تم توزيع 25 فأرًا على خمس مجموعات تضمنت مجموعة سيطرة ، ومجموعة جرعة علاجية 0.625 ملغم، ومجموعة سامة 1.25 ملغم ومجموعة جرعة. 150 ملغم قاتلة

أدى تناول أيزونيازيد عن طريق الفم إلى تغيرات مرضية. في الكلى ، تمثلت الآفات النسيجية في حدوث نخر في خلايا الأنابيب البولية في بعض المناطق، وتسلل الخلايا الالتهابية بشكل واضح، وتقشر بعض خلايا الأنابيب البولية ، وانتفاخ بعض الخلايا. مما أدى إلى تضيق تجويف الأنابيب البولية. .. كانت الكبيبة متضخمة في بعض المناطق وضامرة في بعض المناطق

في الكبد ، تم تمثلت بحدوث نخر ، نزيف واحتقان ، ارتشاح الخلية الالتهابية ، سماكة غشاء البلازما ، اتساع الجيبانيات وتضييقها في أوقات أخرى