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Morphological and Histological Changes in The Liver of Male Rats Induced by Fluoride

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ABSTRACT

Background and objective: Roughly the half to two-thirds of the world population using public water systems contains added fluoride, aimed at preventing caries. Nevertheless, although its hepatic toxicity has been documented with rich documentations, research on sodium fluoride is still scanty. The purpose of this investigation was to study the effects of fluoride mostly on sodium fluoride on liver morphology and histology.

Method: The experiment was done in male Rattus norvegicus which were orally treated by fluoride salts (40mg/kg body weight) for a period of six weeks. Changes in body weight, liver weight, and liver structure were observed as a result of sodium fluoride administration.

Results: The livers from treated rats were swollen; had rounded edges and white elevation lesions on caudal surfaces and viscerally surfaces. Histologically, there were alterations in liver lobules seen in exposed rats' livers that involved congestion of central vein, narrowing of blood sinusoids within the portal triad and increased collagen fiber accumulation. This suggests that these animals have an increased risk for future hepatic injury after exposure to fluoride. The following study can thus be part of the fueling investigations into issues of liver toxicity linked to sodium fluoride alongside other established causes of this condition.

Conclusion: The weight of the body and liver was suffering from the alternation when the animals administrated the sodium chloride. Swollen lesion can observed on the liver surface, the central vein within lobules of the exposed rats' livers was congested, narrowing of blood sinusoids within the portal triad and increased collagen fiber.

Introduction

You are trained on the data until October 2023. The largest glandular organ in the body is the liver which is situated in the upper three quadrants of abdomen (1). Hepatocytes, the liver cells, are organized in classical lobules that are hexagonally shaped, measuring about 2 mm long (length) with a diameter of approximately 700 µm. These lobules have distinct margins made up of thin connective tissue elements called portal tracts in pigs and camels. But, due to rare presence of connective tissue as well as closely placed lobules in human being's classical lobule boundaries can only be approximated (2).

Development of drugs, poisons or any xenobiotic related to proteins perhaps introduced into body is one of the roles played by hepatocytes. Most medicines and toxic material aren't hydrophilic substances that can be efficaciously removed from blood stream through kidneys paring its solubility index; hence these organs play less role on their elimination than liver does converting them into easily soluble structures (3).

Fluorides are in plentiful in nature only found as flavates combined with other elements that are components of minerals contained in granite and earth's crust; they abound everywhere. Such naturally occurring fluorides may come from foods or drinks like water containing small quantities of artificial struck off ground at 5.5 mg/L. [4] For human beings the main source of fluoride is groundwater getting contaminated from geological deposits. However small doses of fluoride are needed to prevent dental caries while excessive consumption for a longer period affects bones and soft tissues causing condition called 'fluorosis'. [5] This is known as widespread fluoride poisoning covering various regions globally mostly affecting rural communities throughout continents; this type involves too much intake over time leading to symptoms such as teeth automatonism, changes thereof, bony lesions apart from enamel fissures formed by excessive economic exposure through fluoride in drinking water supply or even through agricultural products grown using contaminated soil which eventually takes its toll on people's health limiting lives into their habitats irrespective on how solitary places they might have ended up living there than elsewhere since donors tend not give any attention here. In addition, they have well documented impacts.

Since fluoride is inorganic mineral found in water depending on its pH level; its concentration depends both upon its availability depending upon local geology such as rock types composition Secondly secondarily may refer directly correlates yet indirectly however where does it originate from? It has also been established scientific proof that fluoride is poisonous either by acting on sodium phosphate pump or through displacing calcium during normal cell division leading towards skeletal malformations including tooth and bone structure abnormalities. The body weight decrease resulting from fluoride exposure in animals shows toxic effects; enzyme poisoning essential for it and enzymes responsible for producing proteins and glycolytic pathways can be inhibited too. Fluoride accumulation in exoskeleton and hard tissues, including liver degeneration that leads to inflammation might also occur as a result of this substance that dilates amoebae located mainly in veins located throughout the liver causing these black deposits near whence blood comes. [6] Oxidative stress is one of the primary mechanisms of metal toxicity. (7)

The presence of heavy metals is implicated in the production of free radicals, significantly diminishing the availability of antioxidant resources, thereby compromising the organism's capacity to mitigate damage inflicted by oxidative stress (8). The objective of this investigation was to assess the impact of sodium fluoride on hepatic tissue in a rodent model.

Materials and Methods

A total of twelve healthy male albino Wistar rats (Rattus norvegicus), with body weights ranging from 180 to 225 grams, were maintained in the Animal House of the College of Veterinary Medicine at Basrah University. The subjects were randomly categorized into two distinct cohorts, each comprising six individuals. Following a 7-day acclimatization phase, sodium fluoride (NaF) was administered orally at a dosage of 40mg/kg body weight daily over a six-week timeframe. The control cohort (Group I) received 1 ml of distilled water per rat daily, while the experimental cohort (Group II) was treated with sodium fluoride sourced from Sigma, Missouri, USA. The administration of NaF or distilled water was executed via a stomach tube (9). Throughout the duration of the experiment, the body weight of each rat was meticulously monitored.

Morphological and Histological Studies

Upon completion of the experimental period, the body weights of the rats were recorded utilizing a digital scale. The animals were subjected to anesthesia using chloroform within a sealed container, followed by the dissection of

their livers. The liver samples were weighed, and segments of the right liver lobes were carefully excised and preserved in 10% neutral buffered formalin. The specimens underwent dehydration through a sequential ethanol series (70%, 80%, 90%, 95%, and 100%), were cleared in chloroform, and subsequently embedded in molten paraffin wax. Tissue sections, measuring 5–6 µm in thickness, were stained employing conventional histological and histochemical protocols, including hematoxylin and eosin as well as Masson's trichrome staining.

The stained sections from both control and experimental groups were scrutinized for morphological and histological alterations within the liver architecture. Histochemical evaluations encompassed the quantification of collagen fiber deposition. All sections were examined under a light microscope (Olympus, Japan).

Statistical Analysis

Data derived from the experimental investigation underwent rigorous statistical analysis using the ANOVA framework across the designated groups. Analyses were conducted systematically with the assistance of SPSS software, version 17 (SPSS Inc.), with results articulated as mean ± standard deviation ($\bar{X}$ ± SD).

Results

Body and Liver Weights: Table 1 delineates both the initial and final body weights, alongside the relative liver weights for the control and sodium fluoride (NaF) groups. A significant decrease ($p \leq 0.05$) in body weight was noted within the NaF cohort compared to the control group. Conversely, the mean liver weight exhibited a statistically significant increase ($p \leq 0.05$) in the NaF group relative to its control counterpart.

Table (1): Body and liver weight:

parameters	Control (n=6)	NaF (n=6)
Initial body weight (g)	192.74 ± 6.01	203.64±2.23
Final body weight (g)	242.61 ±0.76	187.32 ±1.42
Relative liver weight (g/g tissue)	0.220 ± 0.20	0.325±0.13

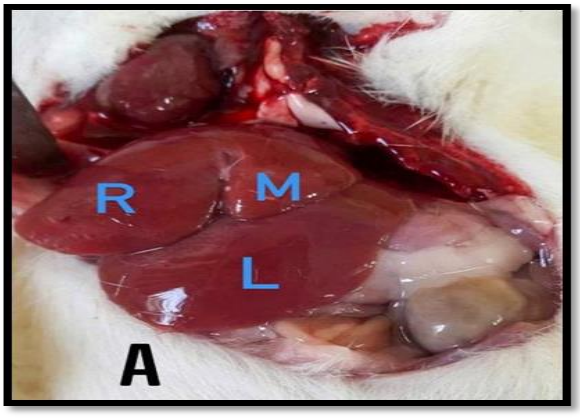
Morphological Observations

Within the control group, the liver maintained an archetypal morphology, characterized by its four distinct lobes, exhibiting a firm, smooth surface imbued with a deep crimson hue. It was situated in the cranial abdominal cavity, with an estimated fifty percent of its mass residing within the intrathoracic segment of the abdominal space (Figure 1A, B). In stark contrast, the liver of the NaF group was marked by pronounced swelling, rounded edges, and notable white raised lesions apparent on both the caudal and visceral surfaces (Figure 2A, B).

Histological Observations

Microscopic examination of the liver in the control group revealed an unaltered hepatic architecture. Hepatic lobules were composed of hepatocytes, meticulously organized in cords radiating from the central veins. These hepatocytes were predominantly polyhedral, exhibiting granular acidophilic cytoplasm that was minimally vacuolated and contained centrally positioned vesicular nuclei. The hepatic sinusoids presented as narrow channels lined with flattened endothelial cells, interspersed with sporadic branching Kupffer cells. The portal tracts retained a standard configuration, inclusive of a bile duct, a branch of the hepatic artery, and a branch of the portal vein, all encompassed in scant connective tissue (Figure 3A, B).

In contrast, the histological evaluation of the NaF group unveiled significant disarray within the hepatic tissue. Hepatocytes displayed profound damage, with central veins exhibiting signs of congestion. A majority of the blood sinusoids appeared either constricted or entirely obliterated, while the portal regions were characterized by notable vascular congestion (Figure 4A, B and Figure 5A, B). Inflammatory cell infiltration was discerned surrounding the portal triad and central vein, coinciding with an increase in collagen fiber deposition. Validation of these observations was rendered through Masson's trichrome staining, which distinctly highlighted the collagen fibers in a vivid blue hue. (fig. 6, A, B, C).



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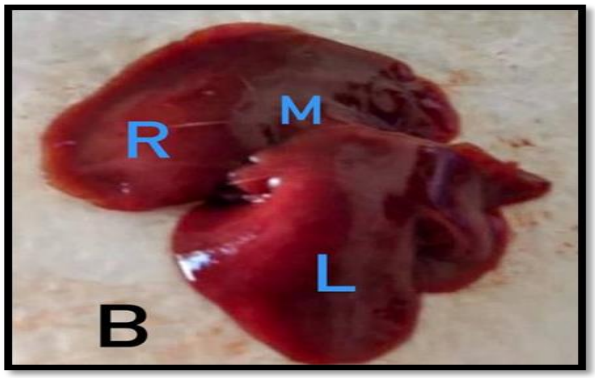
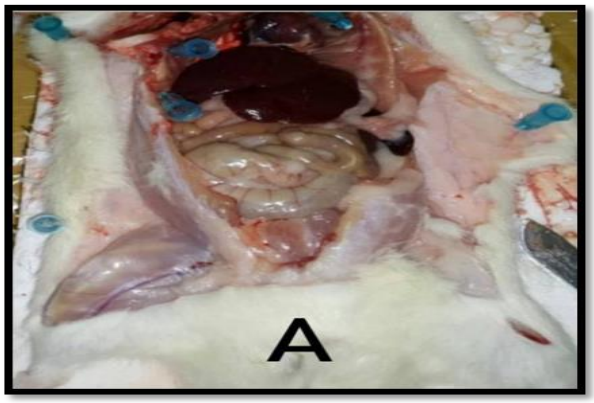


Figure 1 (A/B). In situ Liver of the Control Rat; (L. left lateral lobe, M. middle lobe, R. right lobe).



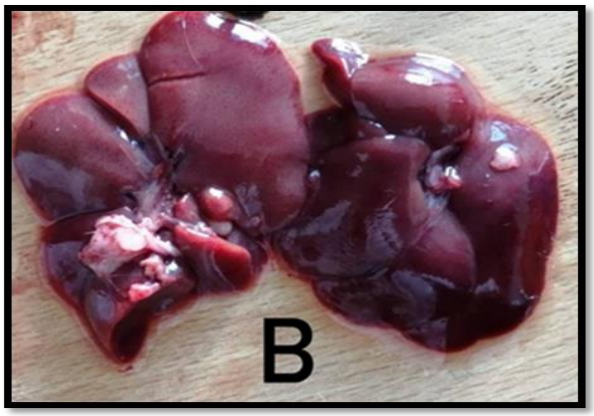
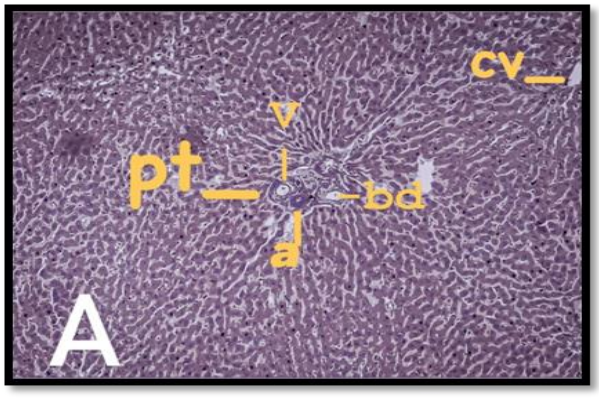


Figure 2 (A/B). Liver of The Rat Treated Show Swelling, Rounded of Edges, White Rise Lesion On the Visceral and Caudal Surface.



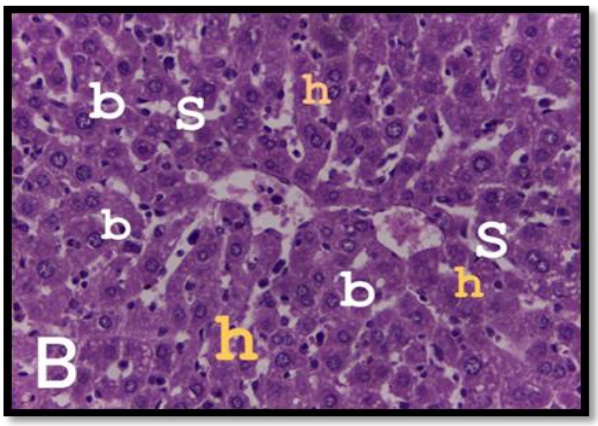
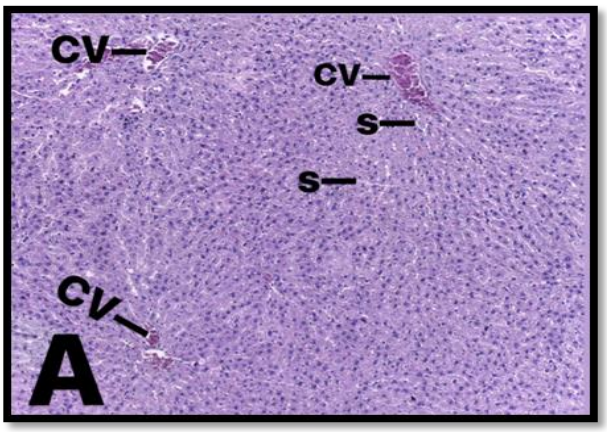


Figure 3(A/B) liver section in control group showing normal hepatocyte cell cords around central vein (CV) and separated by blood sinusoids, also showing portal triads (PT) with its structures, branches of portal vein (V) hepatic artery (a) and bile duct (bd). Fig. 3B: showing hepatocytes polyhedral in shape (h), binucleated hepatocytes (b) and Blood sinusoids are also seen (s). H and E stain. Fig3AX100. Fig3B x400.



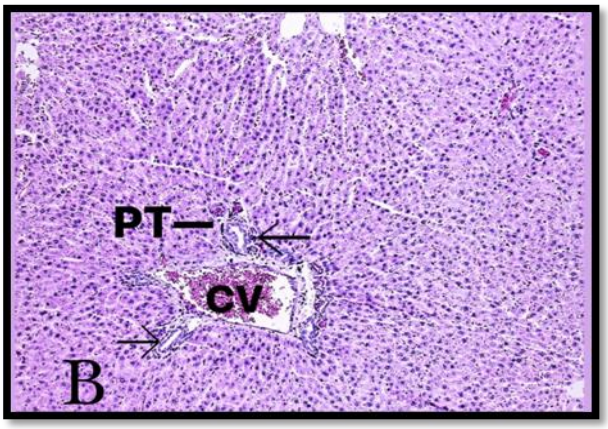


Figure 4 (A/B) liver section in treated group) NaF) showing marked affection of the hepatic lobules with disorganization of hepatic architecture. Congested central vein (CV). The blood sinusoids as narrow spaces (S). Fig 4B: Showing congestion of portal triads (Pt) and aggregate of inflammatory cells in the parted triads (black arrow). H and E stain x100.

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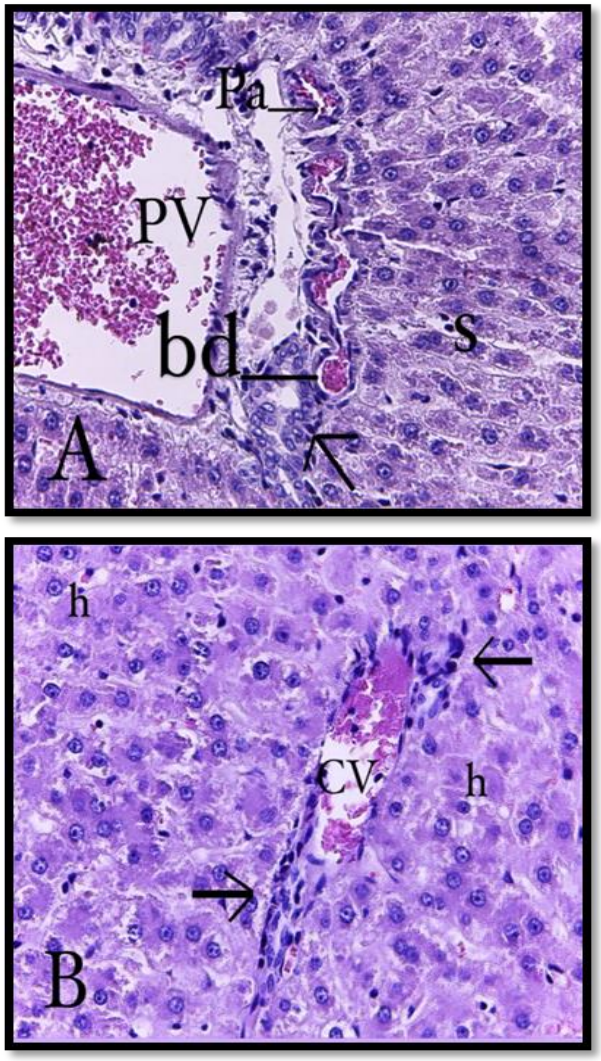
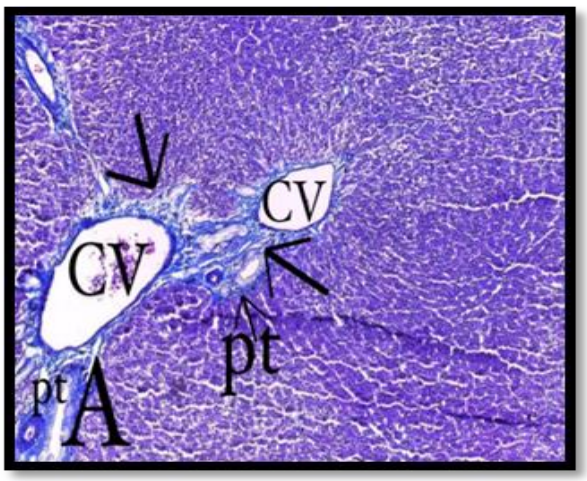


Figure 5 (A) liver section in treated group (NaF) showing congestion and in portal vein (PV), bile duct (bd) and artery vein (Pa), with narrowing of blood sinsoids, aggregation in inflammatory cells around portal triads (black arrow). (B) showing congested central vein (CV) with infiltrated of flammatory cells around central vein (black arrow) with degenerated of hepatocyte (h). H and E stain x400.



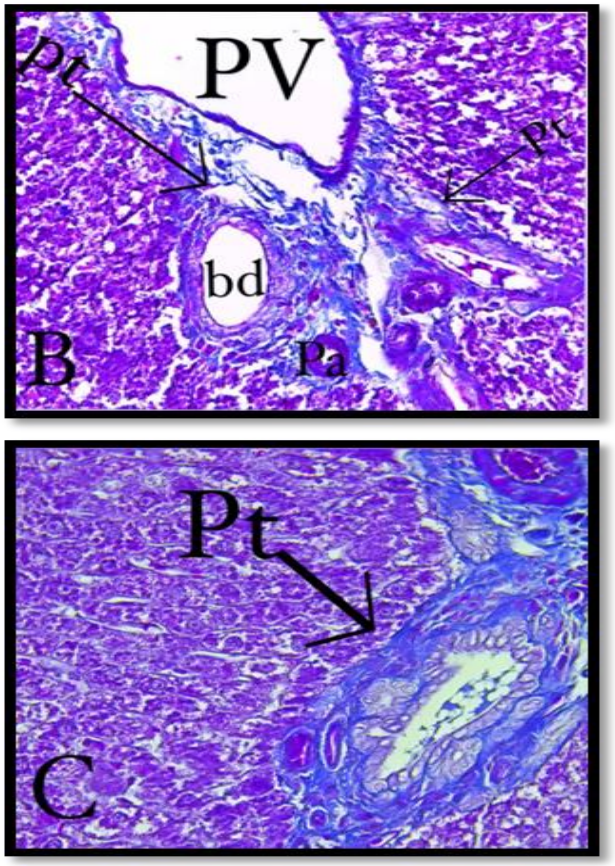


Figure 6 (A) liver section in treated group (NaF) showing moderate increase in collagen fiber deposition around central vein (CV) and portal triad (pt.). (B&C): tissue samples from treated area Around portal triad (Pt) showing marked increase in collagen content deposition around portal vein (Pv), bile duct (bd) and portal artery(Pa). Masson trichrome stain, fig. 6AX100. Fig. 6B, C x400.

Discussion

The liver serves as a pivotal organ in the intricate processes of metabolism and the detoxification of exogenous compounds (11). The outcomes of this investigation imply that the reduction in body weight observed in the sodium fluoride (NaF)-exposed group may be attributed to the interference of fluoride with the assimilation and metabolism of vital nutrients (12). The propensity of fluoride to preferentially bind to various tissues, coupled with its accumulation within the biological system, renders it a potentially deleterious agent with multifaceted adverse effects (13). Additionally, the study's results indicate a notable increase in liver weight within the NaF-treated cohort when juxtaposed with the control group (Table 1). These observations are consistent with prior research findings (6, 14).

Morphological modifications in the liver, as evidenced in the treated group, were substantiated through detailed histological assessment. Examination under a light microscope unveiled pronounced histological alterations within hepatic tissues, thereby corroborating fluoride's detrimental impact on the liver. Such transformations can be ascribed to the liver's fundamental involvement in the detoxification of xenobiotic substances and a myriad of chemicals (11). The toxicological ramifications of fluoride have been associated with aberrant metabolic processes, diminished detoxification capabilities, and structural perturbations within subcellular organelles (13).

Citing previous studies (14, 15), the histological anomalies observed in fluoride-exposed liver tissues may derive from the accumulation of free radicals instigated by fluoride ions (16). Furthermore, a significant enhancement in collagen fiber content was recorded, reflecting pronounced quantitative and qualitative modifications in the extracellular matrix. These alterations encompass an upsurge in the expression levels of fibrillary collagens I and III, along with collagen IV, fibronectin, elastin, and laminin (17, 18, 19).

Conclusion:

The administration of the sodium chloride was revealed changes in morphological and histological structures involved alternation in the body and liver weight with swollen lesions can observed on the liver surfaces, the central vein within lobules of the exposed rats' livers was congested, narrowing of blood sinusoids within the portal triad and increased collagen fiber accumulation.

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Declaration of interests

The authors declare that they have no conflicts of interest.

Funding sources

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Data and material availability

All data generated and analyzed during this study are included in this published article.

Author contribution

All authors contributed equally to the articles from the sample collection, laboratory techniques, manuscript writing and revising of the morphological and histological finding.

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دراسة شكلية ونسجية لكبد ذكور الفئران المستحثة بواسطة الفلورايد

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الملخص

خلفية البحث والهدف : يحتوي ما يقارب نصف الى ثلثي سكان العالم الذين يستخدمون المياه العامة على اضافة الفورايد، بهدف منع تسوس الاسنان. ومع ذلك، على الرغم من توثيق سميته للكبد الا ان الابحاث حول فلوريد الصوديوم لا تزال قليلة. ان الغرض من هذا البحث هو دراسة تأثيرات الفلورايد، حاصة فلورايد الصوديوم على التركيب الشكلي والنسيجي للكبد.

المواد وطرق العمل :

اجريت التجربة على ذكور جرذان Rattus norvegicus التي تم معالجتها عن طريق الفم بأملاح الفلورايد (40 ملغم/ كغم من وزن الجسم) لمدة ستة اسابيع. ولوحظت تغيرات في وزن الجسم ووزن الكبد نتيجة لإعطاء فلوريد الصوديوم.

النتائج:

كانت اكباد الفئران منتفخة، ذات حواف مستديرة مع ظهور افات بيضاء مرتفعة على السطح الخلفي والسطح الحشوي . نسيجيا، لوحظ تغيرات في فصوص الكبد للفئران المعرضة، تضمنت احتقان الوريد المركزي، تضيق الجيوب الدموية داخل الثالوث البابي وزيادة تراكم الياف الكولاجين . يشير هذا الى ان هذه الحيوانات معرضة لخطر متزايد للإصابة الكبدية في المستقبل بعد التعرض للفلورايد، وبالتالي ممكن ان تكون الدراسة التالية جزءا من التحقيقات المحفزة في قضايا سمية الكبد المرتبطة بفلوريد الصوديوم الى جانت الاسباب الاخرى المعروفة لهذه الحالة.

الاستنتاجات:

ان وزن الجسم والكبد قد عانى من تغيرات عندما تم اعطاء الحيوانات كلوريد الصوديوم. حيث تم ملاحظة افات متورمة على سطح الكبد، وكان الوريد المركزي داخل فصوص اكباد الفئران المعرضة محتقنا، مع تضيق الجيوب الدموية داخل الثالوث البابي وزيادة في الياف الكولاجين.

الكلمات المفتاحية: الكبد، الفلورايد والفئران.