ORIGINAL ARTICLE Mirror of Research in Veterinary Sciences and Animals MRVSA/ Open Access DOAJ

Hematological and Histopathological Adverse Effects of kmno4 on mice

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ARTICLE INFO
Received: 28.12.2016
Revised: 28 .01. 2017
Accepted: 29.01. 2017
Publish online: 05.02.2017

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Abstract

Potassium permanganate (kmno4) is a salt of potassium that use as a general skin antiseptic and for disinfecting and cleaning wounds. However, Kmno4 can irritate mucous membrane and is poisonous if enter the body. This study designed to determine the toxicity of kmno4 in Swiss albino mice administered orally with Potassium permanganate. Thirty Swiss albino mice were divided equally into 3 groups. The first and second groups were administered kmno4 for 30 days with 0.025 mg /Kg/BW and 0.5 mg /Kg/BW respectively. The third group was administered normal saline orally and acted as a control. Blood samples were collected from treated mice for hematological investigation. Lung, kidney and liver were also collected for histopathological study. Echinocyte, Anisocytosis, Hypochromic, Poikilocytosis and Heinz bodies were the prominent hematological changes in the kmno4 treated groups. Moreover, erythrocytes seen as cue like stacks of coins with rouleaux appearance. Different histopathological changes were seen in kidney such as congested blood vessels and aggregation of mononuclear cells. In addition to the thickening of the alveolar walls and cellular infiltration. Coagulative necrosis was also appeared in the liver. In conclusion, this study approved the hematological and histological toxicity of kmno4 in the treated mice in compare to the control group. The author recommends another future studies on kmno4, since potassium permanganate is still used in daily clinical application in Iraq.

To cite this article: Ali Husein Ali. (2017). Hematological and Histopathological Adverse Effects of kmno4 on mice. MRVSA. 6 (1), 1-8.
DOI: 10.22428/mrvsa. 2307-8073.2016. 00611.x

Keywords: potassium permanganate, echinocytes, roulex, edematous materials.

Introduction

Potassium permanganate (kmno4) is an inorganic chemical compound salt consisting of two ions: a potassium ion and a permanganate ion. Kmno4 has abilities to oxidize many substances and it is very well known as a strong oxidizing agent, a substance that takes electrons from other substances. Potassium permanganate own different applications in different fields, like water treatment, organic chemistry, analytical chemistry, and even in survival situations such as dry out the wart, ruin superficial bacteria (Esin *et al* ., 2013). It use also to preserve fish from ectoparasites (Young *et al.*, 1996), however, it can

negatively affect the fish health and welfare (Kori-Siakpere *et al.,* 2009). Kmno4 composes of odorless, dark purple crystals with a metallic luster that are soluble in water revealing pink to deep purple solutions depending on the concentrations. Kmno4 has used as disinfecting agent and to cleaning the wounds and as a general skin antiseptic. However, it can irritate the mucous membrane and acts as poisonous if taken into the body (Martin, 2003). The 0.2% kmno4 thaw used in a surgical procedure aseptic incision can effectively hike the healing of incision and reduce the clinical sponsorship work. The potassium permanganate has exceedingly used in controlling external (Guang-Xia *et al.,* 2012). The substance may be poisonous to kidneys, liver, skin, central nervous system (CNS), and wide exposure can harm the target organs. Repeated exposure of the eyes to a low level of dust can produce eye irritation. Heavy skin exposure can produce dermatitis, while inhaling dust of kmno4 can produce variable degrees of respiratory damage (Duffin, 2003). Acute toxicity signs of kmno4 were observed in experimental administrated Swiss albino mice, including rapid and shallow respiration, rough hair coat, dullness, diarrhoea, bloat, gastroenteritis, congestion of liver, paleness of lungs and hypochloraemia (Saganuwan *et al.,* 2008). However, haematological and biochemical parameters did not increase significantly though there was a significant ($P<0.05$) decrease in chloride ion level in plasma. Kmno4 is adversely effecting on body biochemical due to imbalance in in Na^+ and K^+ potassium (K) concentrations that may be attributable to kidney impairment lead to elevation of serum creatinine and urea associated with vacuolar degeneration of renal tubules. As long as, potassium permanganate is still used clinically in Iraq, there is demand to evaluate the toxicity profile of the compound. Consequently, this study intends to investigate the toxicities of potassium permanganate in Swiss albino mice.

Material and methods

Experimental Animals

This study was approved from research and animal ethical committee in college of veterinary medicine. Thirty Swiss albino mice of 7-8 weeks old, supplied from the animal house were used in this study. All mice were acclimatized for 2 weeks and housed in cages. The mice were supplied with standard food and fresh clean water was provided ad libitum. The mice were divided into 3 groups of ten mice per group and were treated as follow:

- First group (1^{st} G) was administered 0.025 ml orally KMn04 (0.025 mg /kg.BW) for thirty days in water.
- Second group (2^{nd} G) was administrated 0. 5 ml orally KMno4 (0.5mg/ kg.b.w) for thirty days in water.
- Third group (3^{rd} G) was orally administrated with 0.25 sterile normal saline for thirty days and it was served as a control group.

Blood samples were collected weekly from animals. Blood smear was done from each samples and stained with Giemsa stain for hematological investigation. At day thirty, all mice in different groups were euthanized and lung, kidney and liver were collected and kept in 10 % formalin for histopathological study. Samples were routinely processed and stained hematoxylin and eosin stain.

Results and Discussion

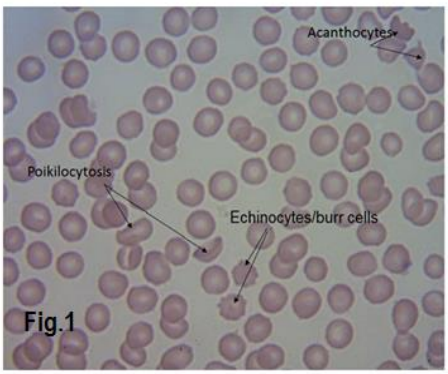
Hematological changes

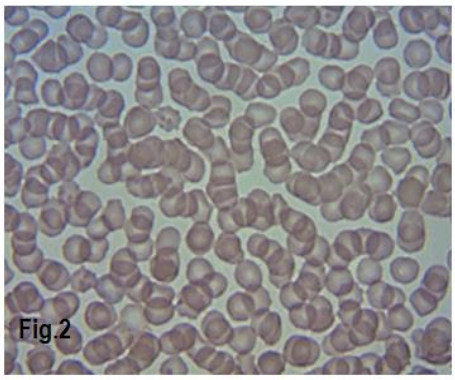
No abnormalities seen in the blood smear of the control group. Blood smears from treated mice in 1st and 2nd groups revealed different morphological changes in the shape of the red blood cells including Anisocytosis, prominent hypochromic RBCs, Poikilocytosis, acanthocytes, echinocyte (Burr Cell) and visible Heinz bodies. In addition, erythrocytes arranged in rows like stacks of coins with rouleaux appearance ((Figure. 1, 2, 3, 4). These changes seen in this study were previously observed in different pathological cases. Anisocytosis is the variation in red blood cell (RBC) diameter (or RBC volume), which has been found in association with uremia, pyruvate kinase deficiency, microangiopathic hemolytic anemia, neonates (especially premature) (Barbara, 2006). In this study, the hypochromic RBCS revealed central pallor zone accompanied with short, evenly spaced projections an echinocyte (Burr Cell) and RBCS rouleaux appearance. These results are compatible with previous study that approved the association of rouleaux RBCs in acute and chronic inflammatory disorders (Wagner *et al.*, 2013). The injuries of RBCS that happened in this studies due to orally drenching of kmno4 explain its toxicity on the RBCs that made about 45% of total blood volume in compare to 1 % of white blood cells. The blood plasma is rich in biological components such as lipids, enzymes and platelets. In the absence of significant shear flow gradients, RBCS form aggregates called rouleaux where the RBCs loosely adhere to each other like a stack of coins (Wagner *et al.*, 2013), in addition, to the presence of cell membrane fibrinogen and plasma globulin. Deal with sufficiently large shear gradients, the RBC rouleaux in a flow break-up and disperse into their constituent RBCs (Fedosov *et al*., 2011). In this study, RBCS hypochromia occurred with rouleaux appearance might be occurred due to Kmno4 irritation effects on erythrocyte and its sedimentation rate (ESR). This results is in agreement with Lai *et al.*, (2006) study that showed alter in the molecular constituents of blood due to pathological conditions and properties of the RBCs leading to enhanced rouleaux formation, which impaired perfusion and tissue oxygenation. Heinz bodies appeared in this study in mice administrated with Kmno4 might occurred due to precipitated hemoglobin that caused hemoglobinopathies and some erythrocyte enzyme deficiencies (e.g., glucose-6-phosphate). This results is compatible with study that showed abnormal increase in RBCS aggregation levels. These changes raised from any surgical procedure requiring extracorporeal circulation of blood or from any pathophysiological conditions that induce inflammation, affect circulatory or metabolic functions. Since the elevated level of RBC aggregation is an indicator of a disease or adverse effects of a clinical procedure (Anna *et al.,* 2012).

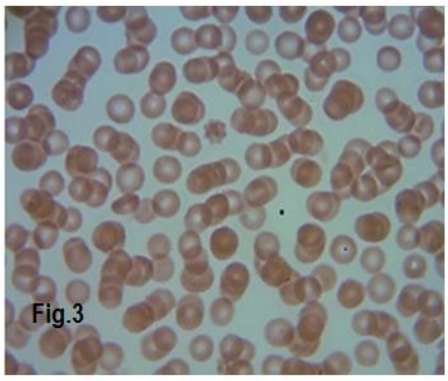
Histopathologic changes

The results of this study revealed different histopathological changes appeared in Kidney, lung and liver. Congested blood vessels and infiltration of inflammatory cells were the prominent lesions appeared in kidney (Figures 5A, B, C). At the same time all lungs revealed thickening in alveolar walls with accumulated edematous materials (Figure .6). Moreover, coagulative necrosis and infiltration of inflammatory cell were also seen in

liver (Figure. 7). In this study, the histopathological changes appeared in kidney and liver due to Kmno4 toxicity are similar to the findings reported previously in human disease processes (Elias *et al.,* 2013) that occurred due to mechanism of toxicity of heavy metals. The shallow respiration observed in treated mice accompanied with lung histpathological changes might occurred due to oxidizing effect of potassium permanganate.







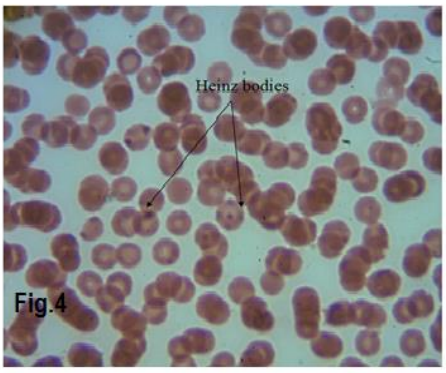


Figure.1: Shows blood smear from Kmno4 treated mice at 30 days post-treatment revealed RBCS anisocytosis (variation in red blood cell RBC diameter)(Giemsa stain 1000X).
Figure. 2: Shows blood smear from Kmno4 treated mice at 30 days post-treatment revealed rouleaux appearance of erythrocytes (Giemsa stain 1000X).
Figure. 3: Shows blood smear from Kmno4 treated mice at 30 days post-treatment revealed hypochromia (the central pallor zone of the erythrocyte)(Giemsa stain 1000X).
Figure. 4: Shows blood smear from Kmno4 treated mice at 30 days post-treatment revealed Heinz bodies (dark blue to purple due to precipitated hemoglobin)(Giemsa stain 1000X).

These results are in agreement with study that that reported the heavy metal contaminant and approved the evidence of elevated HCO3- against induced DNA damage. Damage in the DNA was used as a sensitive toxicity marker and blood cells were used as proxies for other internal tissues (Watson, 2014). Moreover, John *et al.*, (2014) revealed a massive inflammatory cell infiltration including neutrophils and macrophage inflammatory protein-2 (MIP-2) in the bronchio-alveolar lavage (BAL) due to repeated exposure to heavy metals. Induce metals-associated hepatotoxicity

reported to occur due to several potential mechanisms. One of these potential mechanisms of cadmium induced liver toxicity is the overproduction of reactive oxygen species (ROS), including hydroxyl groups, superoxide and hydrogen peroxides. These ROS cause oxidative damage to lipid membranes, unless ROS is scavenged with endogenous antioxidants. ROS could deplete antioxidants or directly act with cadmium on peroxidation reactions and iron-mediated peroxidation (Ramalingam *et al.*, 2016). Hepatic and renal damage are the most common complications occur due to ingestion of potassium permanganate. However, death occurs in severe acute potassium permanganate poisoning due to upper airway obstruction (Esin *et al.*, 2013). Histopathological changes were also seen in gills and internal organs (e.g. Kidney, liver, spleen, intestine) of fish treated with Kmno4. All gills tissue samples collected from KMnO4 treated fish showed mucous cell infiltration and hyperplasia and inflammatory cell infiltration and hyperplasia (Emily, 2006).

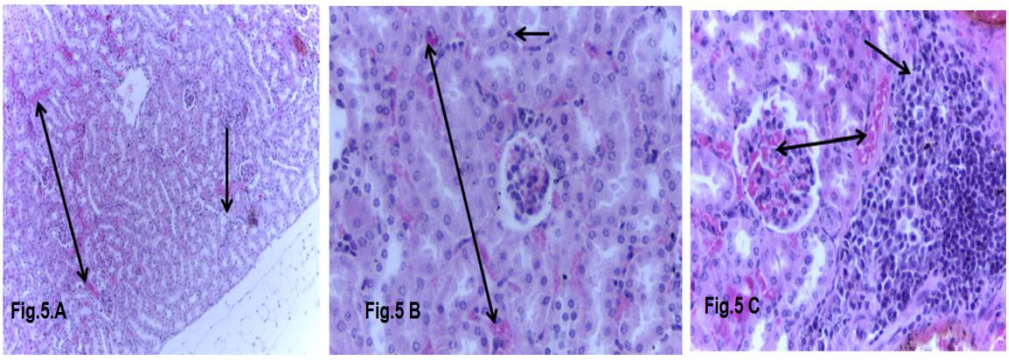


Figure. 5: Shows congested blood vessels (double head arrow) and infiltration of inflammatory cells (single head arrow) in the kidney at 30 day post treatment with Kmno4. (H&E A.100X; B. 200X; C.400X)

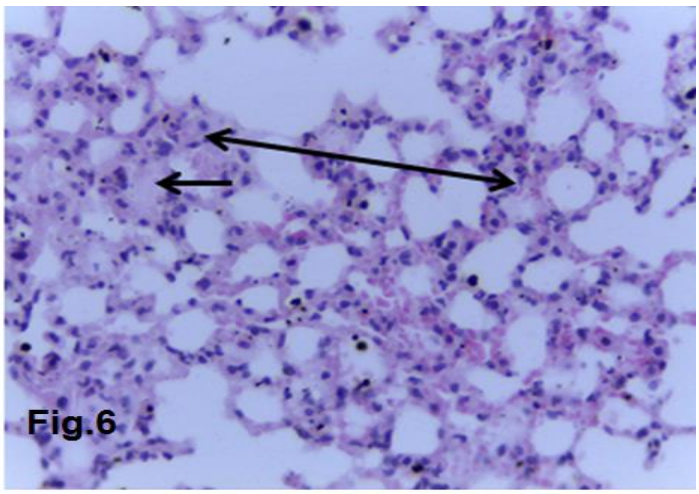


Figure. 6: Shows thickening in alveolar walls with edematous materials) double head arrow), and odematous materials (single head arrow) in the lung at 30 day post treatment with Kmno4. (H&E A. 200X).

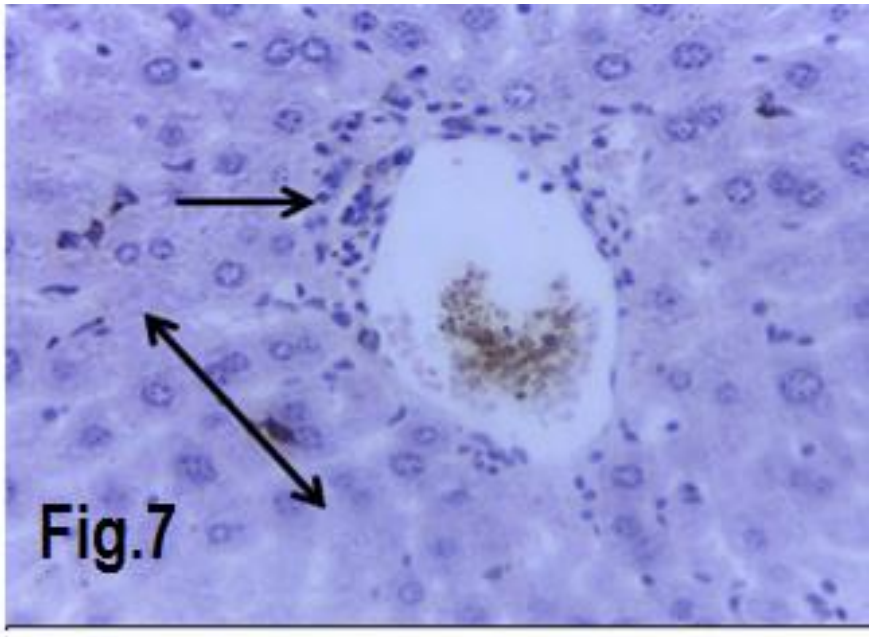


Figure. 7: Shows coagulative necrosis (double head arrow), and inflammatory cells (single head arrow) in the liver at 30 day post treatment with Kmno4. (H&E A. 200X)

In conclusion, this study approved the prominent hematological changes in the RBCS of kmno4 treated mice in compare to the control group. Moreover, histopathological changes were appeared in lung, liver and kidney due to kmno4 toxicity. The author recommends another future hematological and histological studies on animals treated with kmno4, since potassium permanganate is still used in daily clinical applications in Iraq.

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