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Toxicopathological effects of sodium dichromate (chromium CrVI) on small intestine of laboratory albino rats (*Rattus norvegicus*)

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(Received 24 December 2015, Accepted 10 March 2016)

Abstract

In order to determine the toxicopathological effects of sodium dichromate in the small intestine of laboratory albino rats, the present study performed on 30 albino rats (*Rattus norvegicus*) divided into five equal groups; G1 was daily administered 3 mg / 100 g. B.W of sodium dichromate orally for 30 days. G2 was daily administered 9 mg /100 g. B.W of sodium dichromate orally for 30 days. G3 was daily administered 3 mg /100 g. B.W of sodium dichromate orally for 60 days. G4 was daily administered 9 mg /100 g. B.W of sodium dichromate orally for 60 days, and G5 was served as control. The results showed mild atrophy of the intestinal villi with marked hyperplasia of goblet cells in G1, while showed moderate atrophy of intestinal villi with some areas of necrosis of enterocytes with marked infiltration of inflammatory cells in G2. G3 showed severe atrophy in the intestinal villi with infiltration of some inflammatory cells. G4 showed severe atrophy of intestinal villi with area of metaplasia of columnar epithelium to squamous epithelium (squamous metaplasia). In conclusion; the sodium dichromate had major toxic effects to the epithelium of small intestine especially in highly repeated doses.

Key words: Toxicopathology, sodium dichromate, small intestine, villi atrophy, metaplasia.

التأثيرات السمية المرضية لثنائي كرومات الصوديوم في الأمعاء الدقيقة للجرذان المختبرية البيضاء

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الخلاصة

لغرض تحديد التغييرات السمية المرضية لثنائي كرومات الصوديوم في الأمعاء الدقيقة للجرذان المختبرية البيضاء ، أجريت الدراسة الحالية على ثلاثين جرذ مختبري ابيض قسمت الى خمسة مجموعات متساوية ؛ المجموعة الأولى جرعت يوميا 3 ملغم لكل 100 غرام من وزن جسم الحيوان بماده ثنائي كرومات الصوديوم فمويا ولمده ثلاثون يوما . المجموعة الثانية جرعت يوميا 9 ملغم لكل 100 غرام من وزن جسم الحيوان بماده ثنائي كرومات الصوديوم فمويا لمدة ثلاثون يوما. جرعت المجموعة الثالثة يوميا 3 ملغم لكل 100 غرام من وزن جسم الحيوان بماده ثنائي كرومات الصوديوم فمويا لمدة 60 يوما ، أما المجموعة الرابعة فجرعت يوميا 9 ملغم لكل 100 غرام من وزن جسم الحيوان بماده ثنائي كرومات الصوديوم فمويا لمدة 60 يوما ، بينما اعتبرت المجموعة الخامسة مجموعته سيطرة حيث غذيت على العليقة النموذجية فقط دون تجريب المادة. أظهرت النتائج النسجية وجود ضمور طفيف بزغابات الأمعاء الدقيقة مع ملاحظه فرط تنسج في الخلايا المنتجة للمخاط (goblet cells) مع ارتشاح لعدد قليل من الخلايا الالتهابية في المجموعة الأولى ، بينما لوحظ ضمور متوسط الشدة لزغابات الأمعاء الدقيقة مع وجود بعض مناطق النخر في الخلايا المعوية مع ارتشاح طفيف للخلايا الالتهابية في المجموعة الثانية ، أما المجموعة الثالثة فشاهد ضمور شديد للزغابات المعوية مع ارتشاح لبعض الخلايا الالتهابية ، بينما لوحظ في المجموعة الرابعة ضمور شديد للزغابات المعوية مع وجود مناطق من الحؤول النسجي حيث تم ملاحظه تحول الظهارة العمودية للأمعاء الدقيقة إلى ظهاره حرشفية (حؤول حرشفي). نستنتج من ذلك إن لثنائي كرومات الصوديوم تأثيرات كبيرة على ظهاره الأمعاء الدقيقة وخاصة في الجرعة العالية ولفترة طويلة الأمد.

الكلمات المفتاحية: السمية المرضية ، ثنائي كرومات الصوديوم ، الأمعاء الدقيقة ، ضمور الزغابات ، حؤول النسجي.

Introduction

Chromium (Cr) a naturally occurring element, is abundant in the earth's crust and biologically relevant oxidation states. The CrVI compounds are more toxic compounds, has long been recognized as carcinogenic to humans inducing lung tumors also the potentially harmful health effects of CrVI following oral exposure were brought to the public's attention (1). Sodium dichromate is an inorganic chemical compound with the formula ($\text{Na}_2\text{Cr}_2\text{O}_7$); its salt, red to bright in color (2). It exists in solid form as reddish to bright orange crystals, soluble in water, available as crystal or flake powerful oxidizing agent and corrosive, cause severe burns; contact with many organic materials may cause a fire (3). Sodium dichromate is produced by roasting chromate or with soda ash and is used for the production of other chromium compounds (4). Chromium metallic is used in the metallurgical industry for the production of stainless steel and ferrous and non-ferrous alloys; the major uses of chromium in the chemical and manufacturing industries include the production of chromium pigments and in metal finishing, leather tanning, and wood preservation (5). Through food, water and air the public exposure to chromium, which the highest exposure to CrVI occurs to workers involved in chrome plating, chromate production, and stainless steel welding; the exposure in these situations is typically by inhalation or dermal contact (6). In some cases when exposing to chromium mainly by breathing for about 7.5 years; gastritis, duodenal ulcers, in addition to ulceration and perforation of the nasal septum (7). In other study reported by (8) the oral ulcers, diarrhea, indigestion, stomachache, leukocytosis and vomiting were reported among a group of Chinese villagers exposed to contaminated water containing CrVI in 1965. Other study done by (9) reported that chronic exposure to high concentrations of CrVI as sodium dichromate dihydrate in drinking water induces duodenal tumors in mice. CrVI is a contaminant of water and soil and is a human lung carcinogen, also demonstrated that CrVI is carcinogenic in rodents when administered in drinking water

caused intestine effects in rats and mice (10). Many studies demonstrated by (11) when exposure to CrVI such as different point mutations in DNA, chromosomal damage, oxidative changes in proteins and to adduct formation. The most importance of these effects of chromium and the free oxidizing radicals they may generate in the body by causing tumors and allergic sensitization. This study aimed to evaluate the toxicopathological effects of CrVI in rat's intestine for several periods of exposure onto two selected different doses.

Materials and methods

At this study thirty male and female albino rats (*Rattus norvegicus*) with ages about two months and body weight ranged between (150-200 grams) were used to perform the present study. Animals were held in the animal house of college of veterinary medicine at University of Baghdad where the research was done. The animals were kept in cages of (20X30X50 cm³) dimensions in average of three rats in each cage, the animals kept for 14 days before study for acclimatization in optimum conditions at (22±3°C) with a 14/10 hrs. Light/Dark cycle. Commercial feed pellets and drinking water were given all the time of experiment (12). The dose of experiment depend on oral LD₅₀ of male rat that reported by (13) represented 1/10 of LD₅₀ of sodium dichromate (BDH/England), we prepared 3mg / 100 g. B.W. by dissolved 30 mg of sodium dichromate in 10 ml of distilled water, the concentration was 3 mg/1ml. Animals were divided into 5 equal groups: G1 was daily administered 3 mg/100 g. B.W of sodium dichromate orally for 30 days. G2 was daily administered 9 mg / 100 g. B.W of sodium dichromate orally for 30 days. G3 was daily administered 3 mg/ 100 g. B.W of sodium dichromate orally for 60 days. G4 was daily administered 9 mg/100 g. B.W of sodium dichromate orally for 60 days while the animals of fifth group (G5) was administered daily distilled water for 60 days and served as control. The animals were sacrificed after the study performed in closed chamber saturated with chloroform (BDH/UK) to

achieve a good muscular relaxation after that the small intestine were obtained and had preserved in 10% neutral buffered formalin (Fluka chemicals/Switzerland) and sent to

laboratory of histopathology. Slides were prepared and stained with Hematoxyline (Fluka chemicals/Switzerland) and Eosin (Siga / USA) according to (14).

Results

The histopathological results displayed that the G1 which taken 3 mg / 100 g. B.W of sodium dichromate orally for 30 days had mild atrophy of the intestinal villi with marked hyperplasia of goblet cells in addition to infiltration of few inflammatory cells (fig. 1). While the G2 (9 mg / 100 g. B.W for 30 days) showed moderate atrophy of intestinal villi with areas of necrosis of enterocytes and infiltration of inflammatory cells (fig. 2).

G3 showed severe atrophy in the intestinal villi with infiltration of some inflammatory cells (fig. 3). G4 showed severe atrophy of the intestinal villi with area of metaplasia of columnar epithelium to squamous epithelium (Squamous metaplasia) and present of keratin at the surface of villi (fig. 4). The control group showed normal architecture of small intestine that showed normal villi, enterocytes and epithelium (fig. 5).

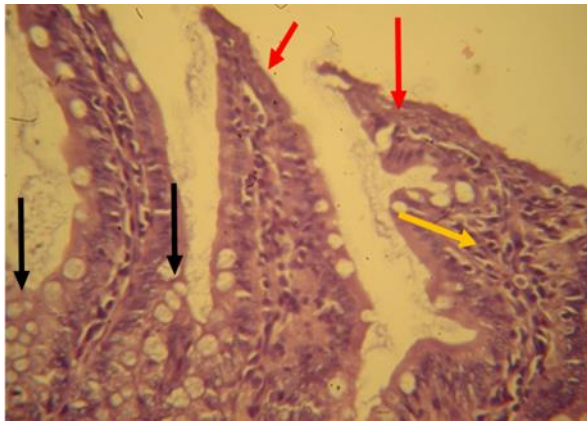


Fig. (1): Cross section of small intestine of G1 showed mild atrophy of villi (red arrow), infiltration of inflammatory cells (yellow arrow) and hyperplasia of goblet cells (black arrow) (H&E Stain X40).

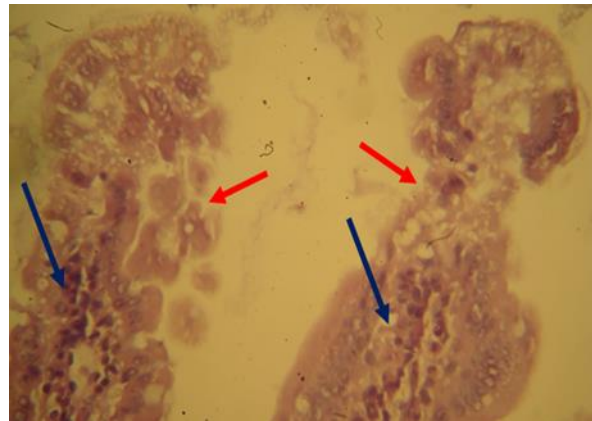


Fig.(2): Cross section of small intestine of G2 showed severe necrosis of enterocytes of villi (red arrow) with infiltration of inflammatory cells (blue arrow). (H&E Stain X40).

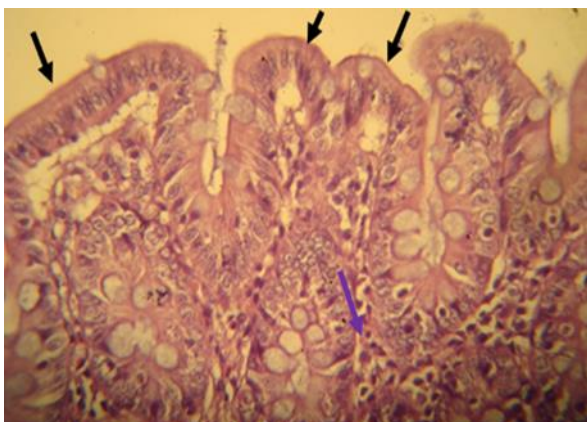


Fig. (3): Cross section of small intestine of G3 showed severe atrophy of villi (black arrow), infiltration of inflammatory cells (blue arrow). (H&E Stain. X40).

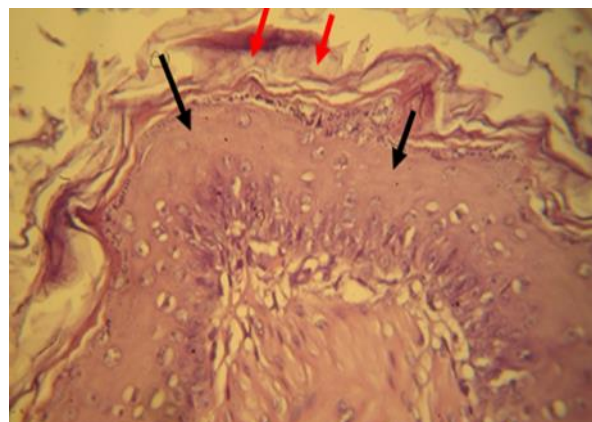


Fig. (4): Cross section of small intestine of G4 showed squamous metaplasia of villi epithelium (black arrow), presence of keratin in the surface of villi (red arrow) (H&E Stain. X40).



Fig. (5): Cross section of small intestine of G5 showed normal architecture of intestinal villi (arrow). (H&E Stain. X40).

Discussion

The results of histopathological study of 30 days of exposure to the sodium dichromate records a mild to moderate changes in the epithelium of small intestine in 3mg/100 g. B.W. and 9 mg / 100 g. B.W. respectively that may due to the proportional concentration of the toxic materials with the time, which that agreed with the results mentioned by (15) who found that in both males and females, there was a clear exposure concentration response relationship when the pathological changes combined at all sites of the small intestine (duodenum, jejunum, or ileum), these increments were noticed significant at the highest exposure concentrations in each sex. In addition, the incidence in 57.3 mg/L females exceeded the historical control ranges for drinking water studies and for all routes of administration. The current results showed moderate atrophy in the villi of small intestine (duodenum) that may due to duration of the exposure to the toxic compound caused an adaptive response to the villi in order to overcome the toxicity, these idea may agree with (15) who reported that the duodenal villi of exposed mice to sodium dichromate were short, broad, and blunt and there were increased numbers and disorganization of the mucosal epithelial cells that was particularly prominent in the

epithelium lining the villi. Also our study didn't record any proliferation of the epithelium lining of the small intestine either in the 30 days or 60 days of exposure to the sodium dichromate, these facts may disagreed with the (16) who mentioned that the epithelial hyperplasia was observed in male and female mice at any exposure concentrations in the chronic studies. Our results in the toxicopathological effects of sodium dichromate for 60 days of exposure revealed area of necrosis of villi of the small intestine that may due to the toxic compound caused death of the cells after a long periods adaptation (atrophy) especially when the sodium dichromate lead to over initiation of free radicals that may cause death to the enterocytes of the villi, these suggestion may agree with the ideas mentioned by (16) who illustrated that significant decreases in the ratio of reduced / oxidized glutathione (Redox reaction) were reported in the oral mucosa and jejunum of the rats and the duodenum and jejunum of the mice, suggesting up regulation of a response to sodium dichromate that induced oxidative stress in these cells. Our results revealed a metaplasia in the epithelium lining of the intestine that may due to the chromium caused very irritant state to the intestine epithelium with long time of exposure, these squamous metaplasia also reported by (17) who mentioned that the sodium dichromate toxicity for 3 month that caused primary non neoplastic lesions were observed in the glandular stomach of rats exposed to 1000 mg/L and included focal ulceration, regenerative epithelial hyperplasia, and squamous epithelial metaplasia ; in addition, there was no concentration-related increases in neoplasms or non-neoplastic lesions were observed in the fore stomach or glandular stomach of rats or mice in the 2 year study (18), we concluded that the sodium dichromate was highly toxic substances to the small intestine especially in high doses and in chronic duration.

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