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Nephrotoxic and Hepatotoxic Effects of Chromium Compounds in Rats

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The nephrotoxic, hepatotoxic and cardiotoxic actions of hexava lent chromium compounds (Kaufman et al.1970; Schubert et al.1970; Evan and Dail 1974), as well as their effects on lung, blood and circulation may contribute to the fatal outcome of chromium intoxication (Langard 1978).

Although trivalent chromium have been regarded as relatively biologically inert (Baetjer et al. 1974), there are a few salts of chromium III like chromite ore roast, chromic acetate, and others that have been found to be carcinogenic when inhaled, ingested or brought in contact with the tissues (Hueper and Payne 1962; Steffee and Baetjer 1965).

Sensitive persons and industry workers have been subjects of dermatitis, respiratory tract injuries and digestive ulcers due to chromium compounds (Hagenoer, Furon 1981).

Tandon et al. (1978), studied the comparative toxicity of two forms of chromium, trivalent and hexavalent, to which chromite miners, chromate workers or consumers of the products of this industry might be exposed. They have also studied the effects of these compounds in rabbits on the morphology of liver and on the levels of certain chemicals constituents of blood,in relation to the concentration of chromium.

In this work, we have studied the effect of trivalent and hexa-valent chromium compounds on rats measuring the transaminases (GOT and GPT), urea and creatinine levels in serum of chromium poisoned animals at different times.

MATERIALS AND METHODS

80 Wistar albino rats from our laboratiry colony weighing 230 ± 12 g. and maintened on 'ad libitum' standard pellets diet (Panlab) and water 'ad lib.', were used in the investigations.

The animals were divided into two groups: Group A comprising 50

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rats and Group B comprising 30 rats. 40 animals of Group A were administered intraperitoneally with 2 mg Cr/kg as chromium chloride (E.Merck) three times a week, and 24 rats of Group B were administered i.p., three times a week also, with 2 mg Cr/kg as sodium chromate (E.Merck). These compounds were disolved in 1 ml of sodium chloride 0.9%. The pH of the injecting solution was raised to 6.5; and the dose was adjusted every week acording to the weight of the animals. 10 rats of the Group A, and 6 rats of the Group B, used as control, received an equal volume of normal saline.

10 rats treated with chromium III were sacrified after 15, 30, 45 and 60 days, whereas 6 rats treated with chromium VI were sacrified after 15 and 30 days, both 24 h following the last injection. This period was allowed to enable excretion of the unbound chromium from the body (Tandon et al. 1979).

Liver and kidneys were removed and kept for macroscopic and microscopic observations. The blood was collected from the aorta artery in centrifugate tubes to obtain serum.

Transaminases (GOT and GPT) were determined by the method of Reitman and Frankel (1957); urea was determined acording to Berthelot's equation; and creatinine was determined acording to Jaffé's reaction, in serum and by means of a Spectronic 2000 Spectrophotometer (B&L).

A part of the medial lobe of the liver, and the kidneys of both, experimental and control animals, were fixed in 10% neutral formalin. After routine histological proceding, parafin section were cut at 5 μm and stained with hematoxilin-eosin for histologi cal observations.

RESULTS AND DISCUSSION

There was no mortality among the rats treated with trivalent chromium during the experimental period (15, 30, 45 and 60 days). The animals apparently remained heatly throughout the course of the experiments.

The liver, under a gross examination, was found to be slightly congested in experimental animals after 45 and 60 days of treatment, whereas the kidneys appeared completly normal during the experimental period.

The liver and kidneys of control animals showed normal architecture. After 15 days of treatment no changes were observed in the hepatic architecture when compared to the control animals.

Enlargement of the proximal tubule of the kidney with a flatening of the epithelial lining, was observed. Fine vacuolation of the proximal tubule cells was observed at day 15.

The first alteration was observed in liver at day 30 consisting

of a slight vacuolation of the hepatocites. A progressive damage in liver was observed at day 45,with enlargement of central veins and sinusoids. Liver morphological alterations further increased when the period of metal exposure was extended to 60 days. Parenchima destruction areas were more extensive.

Table 1. GOT, GPT, creatinine and urea serum levels of control and experimental rats treated with Cr III and Cr VI.

Days	GOT *	GPT *	Creatinine*	Urea*
0**	62.3 ± 7.5***	23.1 ± 3.8	87.2 ± 4.1	21.8 ± 0.8
15	97.1 ± 9.8	26.5 ± 4.4	97.2 ± 12.0	28.7 ± 1.4
30	51.0 ± 7.3	49.2 ± 6.5	77.5 ± 3.7	32.2 ± 1.6
45	44.2 ± 6.8	13.8 ± 3.7	56.3 ± 11.5	51.7 ± 3.5
60	40.8 ± 8.6	12.3 ± 3.6	50.1 ± 3.3	67.2 ± 7.6
15	77.3 ± 9.9	61.4 ± 9.6	89.5 ± 6.2	37.4 ± 2.3
30	39.4 ± 5.7	14.2 ± 2.7	61.8 ± 8.2	63.6 ± 5.5

* GOT and GPT activities are expresed in Units/ml of serum. A Unit is defined as the amount transforming 1µmol of substrate per min at 37°C. Urea is expresed in mg/100ml, and creatinine in mol/l
** 0 days was a control. *** Values are X ± SE for 6 or more rats.

Concerning to kidney observations, the alterations produced in the proximal tubules of the rats with 15 days of treatment, were also observed after 30 and 45 days, but progressively increased after 60 days of treatment showing markedly swollen proximal tubule cells. There were no glomerule alterations during the experimental period.

Transaminases (GOT and GPT), creatinine and urea serum levels of each control and experimental animals treated with trivalent chromium (Cl_3Cr) during 15, 30, 45 and 60 days, are presented in table 1. The results show the chromium effect on the liver and kidneys as observed on the histological study.

The serum creatinine level increased slightly in animals treated with trivalent chromium at 15 days, but this level falls down progressively when the treatment time increases.

The level of urea increased in the serum of rats treated with Cr III. The increase in the urea level was more marked at 45 and 60 days than at 15 and 30 days of treatment. After 60 days the urea level was maximum and increases a 308% with respect to the control level.This is in agreement with Renkin & Robinson (1974).

The GOT serum level increased at day 15 and decreased below the control level after 30, 45 and 60 days of treatment, whereas GPT levels rise to a peak at day 30, reaching its maximum then, and

falling down steeply to levels of 12 U/ml at day 60.

In agreement with Tandon et al. (1978), the significant increase in the serum urea level in rats treated with chromium III, may be caused by kidney damage due to the metal. In addition the sharp increase in urea level from 60 days to 15 days may possible be due to more intense renal damage at prolonged period exposure.

The histological observations on kidney of rats treated with chromium III, showed a proximal tubular necrosis which is often a symptom of toxic nephropathy (Hepinstall 1966).

On the other hand,the level of serum transaminases show anomalies due probably to drastic effects of the metal on the liver of treated animals. Liver histological observations coincide with Tandon's et al. (1978) observations when similar experimental times are compared, and suggest that the hepatic dysfunction may be a definite hazard among chromium workers.

Chromium VI administered intraperitoneally (2 mg/Kg) as sodium chromate in rats, produces a transudative ascites due to intrahepatic cirrhosis, and according to Brown (1970), possibly a postsinusoidal block which causes the death of the animals. The first two animals died at day 18, and the same day the chromium treatment was stopped. Six more rats died before day 30. The remaining 10 animals died between days 32 and 47. None of them arrived to day 60.

Chromium VI produced marked morphological alterations in the liver. After 15 days of treatment, the liver capsule was fastened and the central veins were also very congested. The adjacent sinusoids of central veins were also very congested at day 30. Large areas of necrosis of the hepatocites were observed and destruction of the general architecture of the liver was found.

Concerning the kidneys, there is an evident proximal tubular necrosis at day 15 of treatment, which was more severe at 30days. Kidney alterations produced by hexavalent chromium were similar to those produced by trivalent chromium. No alterations were observed on the glomerule during the experimental period.

Transaminases (GOT and GPT), creatinine and urea serum levels of both control and experimental animals treated with hexavalent chromium during 15 and 30 days, are showed in table 1. Those results showed that the effect of Cr VI was similar to that produced by Cr III, but these effects are more severe.

It appears to be that Cr VI shows greater toxic effects than Cr III. This was previously observed by several authors (Baines 1965, Berndt 1976, Tandon et al. 1978). However, the trivalent chromium compounds ought to be considered in order to improve reduction of hazards due to chromium profesional exposition.

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