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Effects of Cr-VI on Skeletal Muscles of Albino Mice

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ABSTRACT

Chromium plays an important role in normal carbohydrate and lipid metabolism, as it's an essential trace element in human nutrition. It was found that patients receiving long-term total parenteral nutrition (TPN) without chromium developed glucose intolerance, weight loss and peripheral neuropathy Chromium is present in a normal diet at trace (but essential) levels. Occupational exposure is related to the industrial uses of chrome compounds in production and use of steels, pigments, leather tanning and wood preservation solutions, plating chemicals, and cement. Toxicity is predominantly associated with industrial exposures. Its trivalent form is the most stable form and can't cross the cell membrane. Hexavalent chromium crosses the cell membrane and is reduced to Cr-V, Cr-IV and Cr-III. Once in trivalent form it can combine with nuclear proteins and nucleic acids causing adverse effects and derangements. Hexavalent chromium compounds appear to have severe toxicity and almost all tissues of body are affected. To evaluate the effects on skeletal muscles, present study was carried out. The mice of experimental group (2wks, 4wks, 6wks and 8wks) were injected Potassium dichromate ($K_2Cr_2O_7$) intraperitoneally according to experimental design. The drug caused slight to marked inflammation of skeletal muscle fibers and vaculations of nuclei was also observed indicating degenerative changes.

Key Words: Hexavalent Chromium, Skeletal muscle, Albino mice.

INTRODUCTION

Chromium is widely distributed on earth's crust. It is found in nature principally as chromate ore. Chromium exists in several valence states, of which the trivalent and hexavalent states are the most common. Most chromium in the food supply is in the trivalent state. Hexavalent chromium compounds are recognized as toxic and are potential carcinogens. Chromium is found in many foods[1], typically in small amounts. Good food sources of chromium include whole grains, cereals, spices (black pepper, thyme), mushrooms and brown sugar, coffee, tea, beer, wine and meat products. Brewer's yeast is also a good source of chromium. Fruits and vegetables are generally poor sources of chromium, as are most refined foods.

Chromium is an essential element required for normal carbohydrate and lipid metabolism. Chromium has been linked to maturity onset diabetes and cardiovascular diseases[2]. Human exposure to these metals occurs principally in occupational settings and environmental contamination [3]. Both acute and chronic toxicity are caused by Hexavalent chromium[4,5]. Cr (V1) is known to have hepatotoxic, nephrotoxic and teratogenic effects as well[6]. It's also known to have effect on lymphoid tissue. Population exposed to Cr (VI) for longer periods are reported to be at high risk of developing lymphomas[7].

Chromium is used in industries especially in leather tanning in Pakistan. The effluents are in general discharged in adjoining land areas. Study has been conducted on such an area in vicinity of Kasur city, containing pink colored effluent from tanneries[8]. The effects of Cr VI on skeletal muscle fibers were analyzed by observing the histological changes induced by this metal in skeletal muscles taken from the limbs of mice.

MATERIALS AND METHODS

Forty-eight male albino mice were divided in eight groups. They were kept under constant

temperature with 12 hourly light and dark cycle. Animals were acclimatized for one week.

Experimental design

A group of 24 albino mice weighing 20-40gm.were administered 0.6% aqueous solution of $K_2Cr_2O_7$ (20mgCrVI /100ml.) at a dose of 20mg/kg of body weight intraperitoneally on alternate days. Another control group of 24 mice was administered distilled water, i.p. that is on alternate days after every two weeks six mice from each group were sacrificed and portions of skeletal muscles from limbs were removed and prepared for histological studies as per routine.

RESULTS

General physical examination

All animals of control and experimental groups were found to be active and healthy at the time of sacrifice. Their feeding behavior was normal & showed no signs of ailment. No gross congenital anomaly in control and experimental animals was observed. However changes in mean weight of animal of experimental groups were observed. In 2 weeks group 13.14% increase in bodyweight and 2.5 % in 4 weeks group was seen. In 6weeks and 8weeks experimentally treated mice significant increase in weight was not appreciated.

Gross appearance of the skeletal muscles

Skeletal muscles of control group was pinkish in color whereas that of experimental mice it appeared reddish i.e. in 2 weeks & 4 weeks treated mice where as it was darker in 6 to 8 weeks treated mice.

Histological changes:

Hexavalent chromium when given on alternate days i.p. induced changes in small intestine(jejunum) of treated mice. In 2weeks group smooth muscle fibers did not show any evident change, anyhow patchy areas of inflammation could be seen. Nucleus was ovoid and appeared normal (the respective control showed normal architecture). In 4 weeks treated mice inflammatory cells in surrounding connective tissue could be seen and nuclei appeared larger than normal. At places skeletal muscle fibers appeared swollen (Fig. 1). No histological changes were seen in skeletal muscles of control animals.

In 6 weeks & 8weeks treated mice marked histological changes were seen. There was infiltration of macrophages & diffuse lymphocytic infiltration. In the last group (8 weeks) hemorrhages were seen & nuclei showed vaculations (fig.2). Control mice showed normal architecture of skeletal muscles (Fig.3)

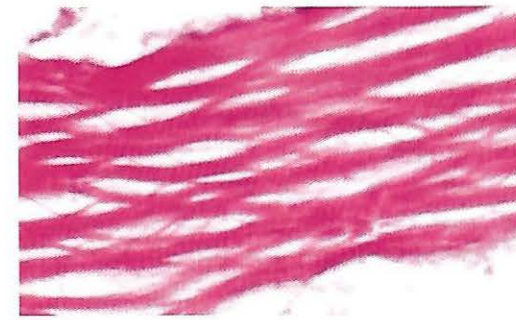

Fig. 1. Normal microscopic features of skeletal muscle.

Fig. 2. Skeletal muscle fibers appear swollen.

Fig. 3. Vacuolated nuclei and lymphocytic infiltration.

DISCUSSION

Chromium is an essential trace element having multiple valancies Cr III is required for normal metabolism but its hexavalent form is used in industry and its indiscriminate use has caused serious health concerns. In cities like Kasur and Sheikhupura where this heavy metal is being used in leather tanning industries, fetuses have been born with congenital malformations, and people drinking this water are suffering from several gastrointestinal problems. Previous studies have revealed that chromium picolinate modulates rat vascular smooth muscle cell intracellular calcium metabolism. Studies regarding microscopic changes induced by Cr VI in skeletal muscle cells have not been reported much. So keeping in mind present research was carried out to assess the effects of Cr VI on skeletal muscle cells of limbs. The microscopic changes observed in the sections showed infiltration of macrophages & also diffuse infiltration of lymphocytes. This inflammatory response was not so marked in 2 & 4 weeks treated mice where as in 6 & 8 weeks treated mice, interstitial hemorrhages were seen and muscle nuclei showed vacuolations.

Cr VI was assessed as a toxic agent affecting skeletal muscles when given intraperitoneally.Any significant increase in weight of mice was not observed except in 6 weeks treated mice. Studies conducted by Hajo & Satoni (1991), did observe a marked decrease in weight which may be due to the fact that they gave single dose of Cr VI intraperitoneally. viz, 0.6 mmol/kg of body weight, the mice must have reacted acutely to this dose. So the weight change was considered statistically insignificant.

Studies conducted by Asmatullah et.al. (1991) revealed that there was reduction in body size & organs in chick embryos when Cr-VI was injected into chick eggs before incubation. Dose dependent embryo mortality was observed and malformations observed in survivors included micropthalmia, micromelia, abnormal & twisted neck, club foot and patchy feathers. In another study Cr-VI exposure increased the incidence and types of external and skeletal malformations.[10]

CONCLUSION

The microscopic findings show us the time dependency effect of Cr VI on skeletal muscles of mice. It's prolonged use cause adverse effects pregnant females exposed to Cr-VI are prone to abort or premature delivery. The fetus born to such mothers have multiple congenital anomalies which are not compatible with life. So this can be avoided if Cr VI is not thrown away unprocessed by the industries using it. So guidelines can be formulated for the industrial use of this metal which can help mankind to live in a non-polluted environment.

REFRENCES

1. Shupack S I. The chemistry of chromium and some resulting analytical problems Environ. Hlth. Perspect. 1991, 92: 7-11
2. Anderson A R.Chromium metabolism and its role in disease processes in mass Clin.Biochem. 1986, 4(1): 31-41
3. Thomann R V, Synden C A and Squibb K S. the importance of incorporating long term storage compartment. Toxicol. Appl. Pharmacol. 1994; 128: 189-198.
4. Baruthio F. Toxic effects of Chromium and its compounds. Biol.trace Elem.Res.1992;32:145-153.
5. Katz S A and Salem H. the toxicology of Chromium with respect to its Chemical .Speciation; A review. Appl. Txicol. 1993; 13(3): 217-224
6. Mikalsen A, Alexander J, Anderson R A and Sundberg M I. Effect of in vivo chromate, acetone and combined treatment on rat liver in vitro microsomal Chromium(VI) produce activity on cytochrome P450 expression. Pharmacol. Toxicol. 1991; 68: 456-463
7. Bick R L, Girardi T V, Lack WJ, Costa M and Titelbaum D. Hodgkin's disease in association with hexavalent chromium exposure. Int.J.Heamatol. 1996; 64: 257-262.
8. Qazi J I, Sheikh S I, Haq R and Shakoori A R. Cultivation of chromium tolerant ciliate protozoan from industrial effluents of tanneries. Pakistan J. Zool. 1997; 29(4): 405-409.

9. Asmatullah, Qureshi S N, Shakoori A R, Hexavelant chromium induced congenital abnormalities in chick embryos. Appl. Toxicol. 1998: 18(3): 167-171.
10. Trivedi ii, Saxena DR, Murphy RC, Chandra SV, Embryotoxicity and fetotoxicity of orally administered hexavalent chromium in mice. Rep. Toxicol. (1989); 3(4) 275-280.

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