Bull. Environ. Contam. Toxicol. (1990) 45:430–435

Environmental Contamination and Toxicology

Fetoplacental–Maternal Uptake of Hexavalent Chromium Administered Orally in Rats and Mice

D. K. Saxena, R. C. Murthy, V. K. Jain, and S. V. Chandra

Industrial Toxicology Research Centre, Post Box No. 80, Mahatma Gandhi Marg, Lucknow 226001, India

Chromium is widely used in various industries like tanning, paints, pigments and in welding. The discharged effluents from these industries have been found to contain high concentration of this metal specially in hexavalent form (Cr^{+6}) (Perlumtter and Lieber 1970; Langard and Norseth 1986; Kumar 1987). Cheremisinoff and Habib (1972) reported chromium level ranging from 40 (leather industry) to 50,000 ppm (chrome plating) in the waste water of these industries. Chromium levels in drinking water in India are usually below 50 µg/L. However, in a few wells at Kanpur (U.P.) levels of 2 mg/L or more have been reported (Handa et al. 1985). In a similar study ground water in Faridabad showed 31 mg/L chromium. River water in Kanpur has also been reported to contain less than 50 µg/L and rarely 104-380 µg/L in areas receiving factory discharges (ITRC 1986). An Indian standard for Cr has not been formulated so far and WHO guidelines for drinking water (0.05 ppm) is taken as permissible limit. Chromium is toxic to skin, lungs and gastrointestinal tract (WHO 1988). Though the hexavalent chromium compounds are reduced to the trivalent form in the biological system, the former compound shows greater organ toxicity than the latter form. It is also reported that Cr^{+6} is taken up and retained by the placenta and foetus of mice treated intravenously during early and late gestational days (Danielsson et al. 1982).

Numerous experiments have shown a time distribution pattern of trivalent and hexavalent chromium between maternal and fetal tissue as influenced by state of gestation (Dencker et al. 1983). Most of this knowledge of the hexavalent chromium transfer from dam to foetus comes from the direct effect of this metal administered intravenously to rodents. Therefore, the present study was designed to obtain quantitative measurement of chromium transfer by the rat and mice

Send reprint requests to: Dr S.V. Chandra at the above address.

placenta during the entire period of gestational exposure with Cr^{+6} salt given through drinking water and to observe any relationship between transfer and placental and fetal uptake that might exist and also species differences.

MATERIALS AND METHODS

Industrial Toxicology Research Centre bred healthy female albino rats (170±20 g body weight, Druckrey strain) and mice (25±5 g body weight, Swiss albino strain) of proven fertility were mated with normal males. Their zero day of pregnancy was confirmed by the presence of sperms in the vagina of rats and by vaginal plug in mice. The pregnant females were randomly grouped and kept individually in plastic cages in air-conditioned room with regular 12 hr cycles of light and darkness. They were provided with pellet diet (Hind Lever Ltd., India) ad libitum (metal content of animal feed (ppm dry weight) Cu 10.0, Mn 55.0, Co 5.0, Fe 70.0, Zn 45.0). The pregnant rats were assigned to various treatment schedules as shown in Table 1, from zero day of pregnancy till one day before delivery. Chromium dosage was selected on the basis of earlier report (Gross and Heller 1946) which was maximal non-toxic concentration. Daily water intake and body weight was recorded throughout the experiment.

Table 1. Treatment schedule for control and experimental groups

Groups (Numbers)	Species (treatment)*
I (10)	Rat (drinking water only)
II (12)	Rat (Cr^{+6}**, 500 ppm as $K_2Cr_2O_7$ through drinking water)
III (10)	Mouse (drinking water only)
IV (13)	Mouse (Cr^{+6}**, 500 ppm as above)

*The treatment continued from 0 day of pregnancy till one day before delivery.
**Daily Cr^{+6} intake as calculated by the water intake was 11.9±0.36 and 3.6±0.65 mg/day/animal for rat and mice, respectively.

One day before delivery, pregnant females were anaesthetized by ether, the uterine horns were removed by

caesarian section, and the foetuses along with their respective placentae were taken out. These were washed in normal saline, weighed and kept for metal estimation. One foetus with its placenta was taken from each dam for metal analysis. Simultaneously, the blood was collected directly from the heart in heparinised vials and processed for metal estimation. Blood, placentae and the foetuses of six animals from each group were digested in a mixture of HNO_3:$HClO_4$ (6:1) on a mantle heater. The residue was dissolved with 0.1 N HCl. Total chromium content in these samples was measured using DC Plasma Emission Spectrophotometer (Beckman Spectraspan V). Spiked and blanks samples were also processed and analysed simultaneously.

Differences between various parameters of control and treated animals were evaluated by using Student's 't' test. The 5% level of significance was chosen for all the studies.

RESULTS AND DISCUSSION

The administration of hexavalent chromium (500 ppm) through drinking water during gestation period significantly reduced the body weight gain of rats compared to their respective controls. Similar treatment in mice also showed reduced weight gain but it was statistically insignificant compared to their controls. There was, however, no significant change in placental or fetal weight in rats or mice between experimental groups and controls.

In rats, chromium level increased significantly in the blood, placenta and foetuses of treated mothers compared to their respective controls. In Cr^{+6} treated mice also, similar pattern was evident in the blood and placenta but fetuses registered greater accumulation (1230 per cent) compared to their respective controls (Table 2).

The concentration ratio of placental and foetal chromium to blood chromium and of fetal chromium to placental chromium did not show any significant difference in treated rats compared to controls but in Cr^{+6} treated mice, all these ratios attained significance as compared with their respective controls (Table 3).

The results of the present investigation in pregnant rats and mice demonstrate (i) Cr^{+6} at a 500 ppm dose given in the drinking water can reach the fetoplacental unit of both rats and mice, and (ii) species difference exists in the distribution pattern of Cr^{+6} in the feto-placental unit of rat and mice.

Table 2. Chromium contents (μg/g fw) in blood, placenta and foetuses of control and hexavalent chromium (500 ppm through drinking water) treated rats and mice

Tissues	Rat		Mice	
	Control	Treated	Control	Treated
Blood	0.021± 0.002	0.067± 0.080* (219)	0.026± 0.001	0.064± 0.003* (146)
Placenta	0.072± 0.004	0.219± 0.030* (304)	0.096± 0.015	0.304± 0.036* (233)
Foetuses	0.046± 0.008	0.142± 0.009* (308)	0.038± 0.003	0.366± 0.012* (1230)

Values represent the mean ± S.E. of 6 animals.
Statistical significance evaluated by Student's 't' test.
Values in parentheses represent per cent change vs. controls.
f.w. = fresh weight; *$P < 0.001$.

Table 3. Chromium concentration ratio in blood, placenta and foetuses of rats and mice exposed to hexavalent (500 ppm through drinking water) during gestation

	Placental/ blood chromium conc.	Fetal/blood chromium conc.	Fetal/placental chromium conc.
Rats			
Control	3.35±0.321	2.06±0.216	0.625±0.053
Treated	3.07±0.295	2.08±0.105	0.640±0.068
	NS	NS	NS
Mice			
Control	3.54±0.308	1.37±0.098	0.382±0.027
Treated	4.63±0.315	5.54±0.430	1.152±0.095
	$p < 0.05$	$p < 0.001$	$p < 0.001$

Values represent the mean ± S.E. of 6 animals.
Statistical significance evaluated by Student's 't' test.
NS - Not significant.

Earlier reports have shown the transfer of Cr^{+6} to the placenta and foetuses of mice and hamsters. Danielsson

et al. (1982) reported the Cr^{+6} transfer to the embryos and foetuses of mice treated at different gestational days. The transfer and embryonic retention of Cr^{+6} was presumed to produce resorptions in mice (Iijima et al. 1975). Comparative mobilization studies between Cr^{+3} and Cr^{+6} in the mice showed the transfer of Cr^{+6} to the foetuses whereas Cr^{+3} was reported not to pass from the placenta to the foetuses (Danielsson et al. 1982).

The above studies were done by administering Cr^{+6} intravenously. In the present study, however, the Cr^{+6} administration through the oral route of exposure, which is natural due to the environmental pollution, has been shown for the first time, to pass to the fetoplacental unit.

The present study revealed species variation in the sense that though an increase was evident in chromium concentration in the blood and placenta of both rats and mice, the fetal uptake was significantly greater in the treated mice. These results indicate a significant difference in the role of the fetoplacental barrier between these two species, with mouse fetoplacental unit allowing a greater inflow of Cr^{+6} from maternal blood to the foetuses, whereas in rats, the fetoplacental barrier restricts the inflow of orally administered hexavalent chromium.

This type of species variation between rats and mice is well documented for the metal distribution with other metals. Kraintz and Talmage (1952) observed an apparent species variation between rats and rabbits in distribution of Cr^{51} buffered with acetate. Even the nature and severity of specific embryopathic and teratogenic lesions for a given metal vary from species to species (Mottet and Ferm 1983).

It is concluded that Cr^{+6}, when given orally, passes the fetoplacental unit, however, the distribution pattern in rats and mice was different indicating the species variation.

Acknowledgement. The authors are grateful to the Director, Industrial Toxicology Research Centre, Lucknow, India, for his keen interest and encouragement. The secretarial assistance of Mr G.M. Nair is gratefully acknowledged.

REFERENCES

Cheremisinoff PN and Habib YH (1972) Cadmium, chromium, lead, mercury: A plenary account for water pollution. Part I. Occurrence, toxicity and detection. Water Sewage Works, 119: 73

Danielsson BRG, Hassoun E, Dencker L (1982) Embryotoxicity of chromium: distribution in pregnant mice and effects on embryonic cells in vitro. Arch Toxicol 51: 233-245

Dencker L, Danielson B, Khayat A, Lingren A (1983) Disposition of metals in the embryo and fetus. In: Reproductive and Developmental Toxicity of Metals, Ed. Clarkson TW, Nordberg GF and Sagar PR, Plenum Press, New York and Lond, pp 607-631

Gross WG, Heller VG (1946) Chromates in animal nutrition. J Ind Hyg Toxicol 28: 52-56

Handa BK, Kumar A, Goel DK, Sondhi TN (1985) Pollution of ground water by chromium in Uttar Pradesh (India). Health Effect of Environmental Pollutants, 14(6):AB-49

Iijima S, Matsumoto N, Lu CC, Katsunuma H (1975) Placental transfer of $CrCl_3$ and its effects on fetal growth and development in mice. Teratology 12: 198-205

ITRC (1986) Status report on safe drinking water, Bhattacherjee JW and Ray PK, ITRC, Lucknow

Kraintz L and Talmage RV (1952) Distribution of radioactivity following intravenous administration of trivalent chromium in the rat and rabbit. Proc Soc Exp Biol Med 81: 490-492

Kumar YR (1987) Environmental Pollution and Health Hazards in India, Ashish Publishing House, New Delhi

Langar S, Norseth T (1986) Chromium, In: Friberg L, Nordberg GF, Vouk VB (Ed) Handbook on the Toxicology of Metals, Vol II. Elsevier Amsterdam-New York-Oxford, p 185

Mottet NK, Ferm VH (1983) The congenital Teratogenicity and Perinatal Toxicity of Metals, In: Clarkson TW, Nordberg GF and Sagar PR (ed) Reproductive and Developmental Toxicity of Metals. Plenum-New York and London, p 107-125

Perlumtter NM, Lieber M (1970) Dispersal of plating wastes and sewage contaminants in ground water and surface water. In Geological Survey Water Supply Paper 1879-G, Washington, DC, US Governmental Printing Office, p 67

WHO (1988) Environmental Health Criteria 61, "Chromium" World Health Organization, Geneva

Received November 30, 1989; accepted February 7, 1990.