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FETAL CONTAMINATION WITH CADMIUM FOLLOWING CHRONIC EXPOSURE OF RAT DAMS DURING GESTATION

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ABSTRACT

Pregnant albino rats (n = 5) were exposed to cadmium in the form of cadmium acetate (0.14 gm/l) in both drinking water and feed *ad libitum* from day 1 to day 18 of gestation to investigate the level of maternal-fetal transfer of cadmium. Control pregnant rats (n = 5) received non-treated water and feed. Cadmium levels in maternal blood and fetal tissue in both treated and control groups were analyzed using absorption spectrophotometry and compared using the Student's t test. Mean cadmium level in the blood of treated dams (17.8 ± 0.8 µg/ml) was significantly higher ($P < 0.05$) than those of control rats (3.6 ± 0.5, $P < 0.05$). Mean cadmium levels in fetuses from treated dam (11.0 ± 3.5) was 60% of that in maternal blood and was significantly higher ($P< 0.05$) than that of control fetuses (0.9 ± 0.2). It was concluded that cadmium, contrary to previous reports, can pass through the placenta in appreciable quantity to contaminate the fetus to possibly cause fetal abnormalities in the rat.

Key words: rat, fetus, pregnant, cadmium

INTRODUCTION

Cadmium, a relatively rare element, belongs together with copper and zinc in the Periodic Table. It is commonly regarded as a pollutant of world-wide concern and has been included on the list of chemical substances considered to be potentially dangerous at the global level (IRPTC, 1987). Because of its harmful effects and ubiquitous presence in the environment, it has been a focus of numerous studies (WHO, 1992). Previous reports suggest that the transfer of cadmium through the placenta is limited. Sonawane *et al* (1975) found that less than 0.02% of the total dose of cadmium injected intravenously into dams reached the fetuses during late gestation. Cadmium given to pregnant mice and hamsters during late stages of pregnancy also indicated that very little cadmium reached the fetuses (Ahokas and Dilts, 1979). In contrast, placentas of women who smoked had higher levels than those of non-smokers (Copius-Peereborn et al. 1979). Hefny and Ahmed (2001) have also reported extensive teratogenic effects of cadmium on fetuses of albino rats, suggesting that an appreciable level of the metal must have passed through the placenta of the dams to the fetuses.

The objective of the following experiment was to determine the level of fetal contamination by cadmium following sub-lethal but chronic administration of the metal to pregnant albino rats during late pregnancy. This would also indicate the level of the metal that can pass through the rat placenta.

MATERIALS AND METHODS

Twelve weeks –old pre-parous female albino rats (n=5 for control and treated) weighing between 220 and 240g were randomly selected from the animal house of the Department of Animal and Environmental Biology, University of Port Harcourt. The animals were housed in plastic cages equipped with a feeding trough, water bottle with nozzle, and a solid bottom for collection of fecal pellets and leftover feeds. Wood shavings were used as beddings. They were fed commercially produced feed and tap water *ad libitum* and housed under laboratory conditions to acclimatize for two weeks prior to mating.

On the third week, vaginal smears were taken to determine the stage of estrus in the rats and those found to be in heat were paired with males for twenty to forty-eight hours. To take vaginal samples, an aliquot of saline was introduced into the vagina with a flame-blunted Pasteur pipette then aspirated onto a microscope slide. Successful mating was indicated by the presence of spermatozoa in vaginal smears. This was considered Day 0 of gestation and the females were then separated from the males and divided into two groups of either one or two rats per cage for a total of 5 rats per group. On Day 2 of gestation, treated group was provided ad libitum with 0.140g of cadmium acetate per liter of drinking water while the control received tap water

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only. The cadmium-contaminated water was also used to make the paste of feed for the treated group while tap water was used in the feed for the control group.,

On Day 18, 2 ml blood samples were collected from both treated and control rats via cardiac puncture. Thereafter, rats were killed and the fetuses (n=25 for both treated and control) removed, weighed and stored in capped vials. Both blood and fetal samples were stored frozen until assayed for cadmium levels using atomic absorption spectrophotometry in the Department of Biochemistry, University of Port Harcourt as described elsewhere (Friberg, 1988; Herber, 1994).

Data analysis: Cadmium levels in the blood of controls and treated dams and the levels in fetuses from treated and control dams were compared by a t-test.

RESULTS

The mean cadmium level in the blood of treated dams was 17.8 ± 0.8 µg/ml compared to 3.6 ± 0.5 µg/ml in control group (Table 1). Levels in fetal tissue from treated rats were 10.9 ± 3.5 µg/l (n = 25) compared to 0.9 ± 0.2 µg/l of those from control dams (Table 2, Fig. 1). The mean cadmium level in fetal sample was 60.9% of the mean recorded for treated dams. There was no significant difference between the means of fetal weights between treated and control groups.

TABLE 1: BLOOD CADMIUM LEVELS (µG/GM TISSUE WEIGHT) OF FEMALE RATS EXPOSED TO 0.14 G/L OF CADMIUM ACETATE DURING GESTATION.

S/No	Controls	Treated
1	4.0	16.0
2	3.0	19.0
3	2.0	20.0
4	5.0	16.0
5	4.0	18.0
	3.6 ± 0.5	17.8 ± 0.8

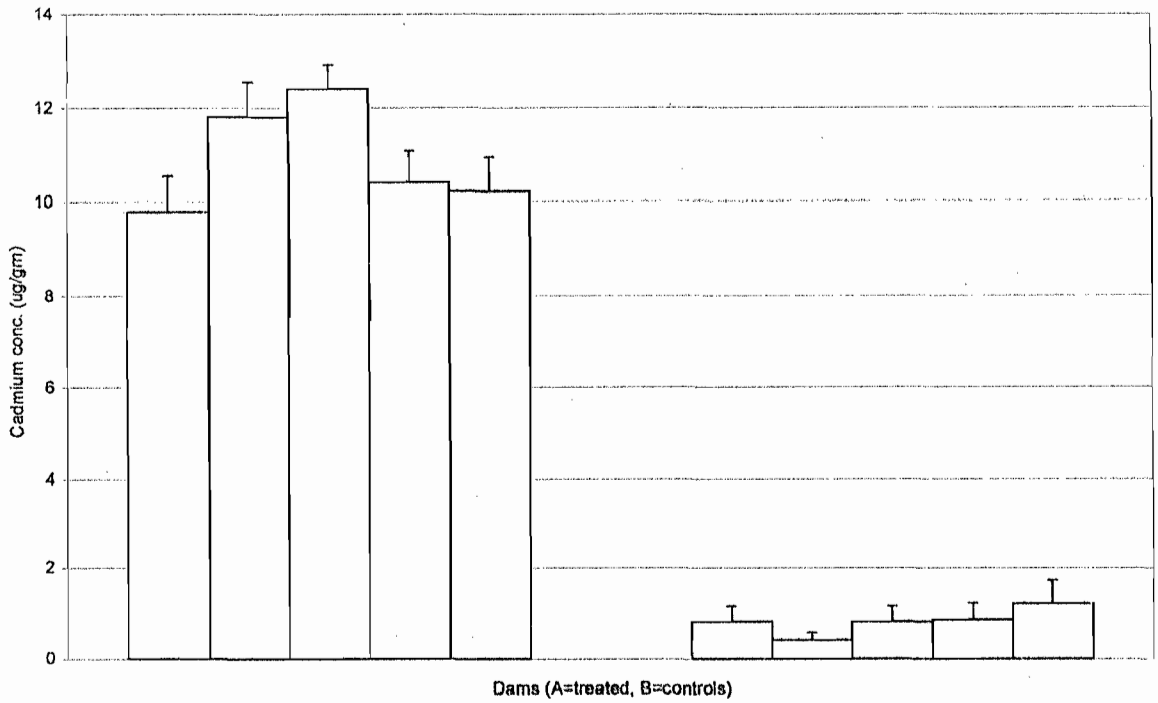

Fig. 1. Cadmium levels (± S.E.M.) in fetuses of dams exposed to 0.14 g/l of cadmium *ad libitum* during gestation and those of controls. Fetal carcasses (n = 5 per dam) harvested from control (n = 5) and treated (n = 5) dams were each analyzed for cadmium. Each bar in the chart represents data for 5 fetuses per dam.

TABLE 2: BLOOD CADMIUM LEVELS IN FETUSES OF DAMS EXPOSED TO 0.14 G/L OF CADMIUM *ad libitum* DURING GESTATION AND THOSE OF CONTROLS

S/No	Control	Treated
1	2.0	9.0
2	2.0	11.0
3	0.0	12.0
4	0.0	8.0
5	0.0	9.0
6	0.0	11.0
7	0.0	13.0
8	0.0	10.0
9	0.0	11.0
10	2.0	14.0
11	0.0	12.0
12	2.0	14.0
13	2.0	11.0
14	0.0	13.0
15	0.0	12.0
16	0.2	10.0
17	0.0	12.0
18	2.0	11.0
19	2.0	11.0
20	0.0	8.0
21	2.0	13.0
22	2.0	9.0
23	0.0	10.0
24	0.0	10.0
25	2.0	9.0
	0.9 ± 0.2	11.0 ± 3.5

DISCUSSION

The result of this experiment clearly demonstrated that a significant level of cadmium in maternal circulation crosses the placenta into the fetus in the rat. The mean level of cadmium in fetuses from treated dams was as high as 60% of that estimated in the maternal circulation. Since cadmium in the blood has been shown to be a good indicator of cadmium body burden (Jarup, et al, 1988) the 60% reflects a significant maternal-fetal transfer of the metal in the rat. These results contrast with earlier reports that very little cadmium reached the fetus when pregnant mice and hamsters were exposed to the metal during pregnancy (Ahokas and Dilts, 1979). Sonawane, et al, (1975) also found less than 0.02% of the total dose of cadmium injected intravenously into rat dams in the fetuses. But the reports that placentas of human female smokers had higher levels of cadmium than those of non-smokers (Copius-Peerebom, et al, 1979) and that human fetal blood levels of cadmium were about 50 to 60% of those in maternal blood (Lauwerys, et al, 1978, Roels, et al, 1978; Korpela, et al, 1986) support the results of the present experiment. Also, acute (2 mg/kg body weight) intraperitonial injection of cadmium sulphate on day 8 of gestation (Hefny and Ahmed, 2001) reportedly caused extensive teratogenic effects in the fetuses, suggesting a significant maternal-fetal transfer in the rat.

The difference between the observation in these studies may be due to a number of factors. Many factors affect the absorption of injected cadmium (Nomiyama, 1978). The animal species, type of compound, dose, frequency of administration, age of experimental animals, pregnancy and lactation, and interaction of cadmium with various nutrients (Nomiyama, 1978) all determine the extent of absorption of the metal. The method of estimation of cadmium in samples may also account for variations among various reports (WHO, 1992). Earlier reports also indicated that cadmium was rapidly sequestered by the liver, spleen and pancreas following a single oral administration (Friberg, et al, 1974; Nomiyama, 1978) or become bound to a low molecular weight protein, metallothionein, following repeated exposure in rats (Shaikh and Hirayama, 1979) and other species (Hamer, 1986; Burnam and Palmiter, 1987). All of these factors could decrease blood levels of cadmium and introduce variations in cadmium assays. Furthermore, it is not yet clear if these factors are more pronounced in some species than others.

We did not observe any significant difference in the weight of fetuses from treated and control dams as reported by others (Cvetkova, 1970; Calabrese and Kenyon, 1991; ATSDR, 1992; USDHHS, 1993). The discrepancy can be partly accounted for by the differences in dosage and frequency of administration. For example, in the study by Cvetkova, (1970), as much as 2.8 mg/m^3 of cadmium sulphate was administered through the respiratory route, 4 hours a day.

In conclusion, this experiment demonstrates that chronic administration of low-level cadmium to rats during pregnancy results in a significant contamination of the fetuses with the metal, contrary to earlier reports. This could, in our opinion, explain the various teratogenic effects attributed to this metal reported in rats. Further work need to be done to determine the influence of nutrition and other environmental factors on the transplacental transport of this metal in the rat.

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