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Effect of Beryllium Nitrate on Early and Late Pregnancy in Rats

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Beryllium is widely used in fatigue-resistant alloys, nuclear reactors, space devices, missiles parts, electronics and other specialized purposes (Galley 1972). Workers both in industries and mines are constantly exposed through inhalation or direct skin contact. A number of investigations have been made in different laboratories in relation to its toxicological effects in laboratory animals and humans (Aub et al. 1949; Groth et al. 1980; Lisco and White 1954; Davies and Harding 1950). The lethal dose (LD_{50}) of beryllium nitrate through intravenous route in rats has been reported from our laboratory to be 3.16 mg/kg body weight (Mathur et al. 1985) but not much is known about its effects on reproductive physiology. The present communication deals with the effect of beryllium nitrate on early and late pregnancy in the albino rats.

MATERIALS AND METHODS

Adult female albino rats (150±10 gm), (Sprague Dawley strain) were selected from the animal colony of the department. They were maintained under uniform husbandry conditions of light and temperature and were given Hindustan Lever pellet diet and water *ad libitum*.

The female rats were left overnight with males (in the ratio of 2:1). Next morning the vaginal smear was examined for spermatozoa to confirm the mating (Prakash and Mathur 1976). The day on which the spermatozoa were found in the smear was considered as first day of pregnancy (day 1 *post coitum*).

Beryllium nitrate was dissolved in sterilized pyrogen free distilled water and was injected intravenously to each rat at a dose of 0.316 mg/kg body weight (1/10th of LD_{50}, Mathur et al. 1985). To prepare this dose 0.316 mg of beryllium nitrate was dissolved exactly in 1.00 ml of sterile water and was injected

intravenously to each experimental rat as per its body weight (0.1 ml/100 g body wt.). The female pregnant rats were selected at day 1 p.c. and divided into different groups. The animals of first group were injected with $Be(NO_3)_2$ intravenously at day 1 p.c. once only and were laparotomized on day 10 p.c. The number of implantation sites were recorded and the wound was sutured. The animals were again laparotomized on day 20 p.c. and the number of foetuses were recorded. The animals were then left in cages to deliver the pups. The animals of second group served as control which received an equal volume of sterile distilled water through intravenous route at day 1 p.c. and were laparotomized on day 20 p.c. This group served as control for group 1.

The animals of 3rd group were first laparotomized on day 10 p.c. to confirm the implantation and were divided into different groups (Table 1). The animals of these groups were exposed to beryllium nitrate intravenously once only at 11, 12, 13, 15 and 17th day p.c. respectively and separately. The animals were laparotomized on day 20 p.c. and the foetuses were counted. The animals were left in the cages to deliver the pups. Five different sets of control rats were maintained for group 3 which were first laparotomized on day 10 p.c. and then after suturing the wound, an equal volume of sterile water was injected (i.v.) at day 11, 12, 13, 15 and 17 p.c. separately. These groups served as controls against their respective experimental group (Table 1). The data were analysed statistically using student's 't' test and the effect at the 0.05 level or less was considered to be statistically significant.

RESULTS AND DISCUSSION

Table 1 shows the effect of beryllium nitrate on early and late pregnancy in the albino rats. It also shows that in the control group, no resorption of the embryos was observed at the early and late pregnancy. The pregnant animals delivered the normal pups which survived. When the beryllium nitrate was administered at day 1 p.c., it did not induce significant effect on early and late pregnancy, but the pups died within 2-3 days of the delivery. Furthermore, when the animals were exposed to beryllium nitrate on day 11 p.c., all the foetuses were resorbed. Whereas, when it was administered on 12th, 13th, 15th and 17th day p.c. there was no resorption of foetuses at late pregnancy. However all the pups died after 2-3 days of the delivery.

Table 1. Effect of beryllium nitrate on early and late pregnancy in albino rats.

	Group of pregnant rats were selected at day 1 p.c.											
	1	2	3AE	3AC	3BE	3BC	3CE	3CC	3DE	3DC	3EE	3EC
Beryllium exposure Ist stage (Day p.c.)	1	-	-	-	-	-	-	-	-	-	-	-
No.of rats used.	6	8	5	5	6	5	5	5	6	5	6	5
No.of rats with sites (Day 10 p.c.)	6	8	5	5	6	5	5	5	6	5	6	5
Mean normal sites (Day 10 p.c.)	6.2	6.2	7.2	6.2	5.7	5.9	6.2	6.5	5.3	6.0	5.3	6.2
Mean resorbed sites (Day 10 p.c.)	0	0	0	0	0	0	0	0	0	0	0	0
Beryllium exposure 2nd stage (Day p.c.)	-	-	11	-	12	-	13	-	15	-	17	-
No.of rats with foetuses	6	8	1	6	6	5	5	5	6	5	6	5
Mean foetuses day 20 p.c.												
1. Live/ Normal	5.7	6.2	0.8	6.2	5.0	5.9	6.2	6.5	5.3	6.0	5.3	6.2
2. Dead/ Resorbed.	0.5	0	6.4	0	0.7	0	0	0	0	0	0	0
Pups delivered(Mean)	5.7*	6.2	0.8*	6.2	5.0*	5.9	6.2*	6.5	5.3	6.0	5.3*	6.2

* Foetuses were died within 2-4 days of delivery
E = Experimental; C = Control.

Our results clearly reveal that the administration of beryllium nitrate at day 1 p.c. does not affect the implantation and the late pregnancy, however, when it is administered at day 11 p.c. all the foetuses were resorbed.

The present finding reports that when the rats are exposed to beryllium on day 1 of pregnancy, it does not seem to interfere with the normal gestation until the 5th day, the blastocysts float freely in the uterine lumen and survive only on uterine secretions. There is no rich vascular connection between uterine endometrium and the blastocysts and thus the implantation occurs normally. It is expected that after the 5th day to the beryllium exposure, the level of beryllium in the blood is reduced and only the traces of beryllium may enter into the developing foetus through maternal circulation which does not affect the normal gestation but produces same toxic effect. The treated females delivered normal appearing pups which die within 2-3 days after the delivery.

When rats are exposed to beryllium on day 11th p.c.it may immediately enter into the foetal circulation through maternal blood and produce toxic effect which are sufficient for the resorption of foetuses. When the rats are exposed on day 12th or 13th, 15th and 17th, the foetuses do not resorb. These findings reveal that the exposure of beryllium after the formation of placenta (after 12th day p.c.) prevents resorption. There appears to be a functional intergrity of placenta. It may be expected that the development of foetal endpoints generally modify the placenta for the support of embryos. Therefore, the placental modification in the term of biochemical constituents like placental protein and glycogen may prevent the foetal resorption. However, this fact is still to be elucidated. As the pups delivered from beryllium exposed pregnant females died after 2-3 days, it indicates that beryllium may enter into the foetus through maternal circulation at any stage of pregnancy and causes toxic effects. Its exact mode of action is yet to be worked out.

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