Evaluation of Body Weight in Albino Rats Exposed to Chloroquine During their Intrauterine Life

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There are very few published studies assessing the safety of medications during human pregnancies . Data from animal teratogenecity studies are extremely valuable .A study was carried out to see the effect of chloroquine on body weight of albino rats which were exposed to chloroquine during their intrauterine life. In this study, 24 pregnant female albino rats were used divided in 4 groups. Total gestational period in rats ranges from 20-22 days, which in this study was divided into three trimesters, each of seven days. Using oral dose of chloroquine 700mg/kg body weight in first, second and third weeks of pregnancy, it was found that chloroquine caused statistically significant decrease in body weight of offsprings. Maximum decrease was found in those which were exposed during third week of pregnancy. In conclusion , chloroquine should be avoided during pregnancy especially during the last trimester .

Key words : chloroquine, body weight, albino rats

Chloroquine has been the mainstay of malaria chemotherapy for nearly 50 years[1]. It is the drug of choice for prophylaxis and treatment of malaria during pregnancy but it is surprising that few data have been published on its safety in pregnancy[2-5]. Chloroquine crosses the placenta to the fetus with foetal concentrations approximately same as in mother. It is excreted in human breast milk[6,7].

Exposure of 10 mg/kg of chloroquine phosphate to rats during intra-uterine and postnatal life resulted in a marked decrease in neonatal and post weaning body weight. The observed growth retardation suggested transplacental poisoning and poisoning through milk transfer[8].

Administration of chloroquine 700mg/kg body wt in pregnant rats for first 15 days of pregnancy resulted in significant reduction in the total body weights of the fetuses and of the placentae[9].

Phillips and Dawn[5] observed that in pregnant rats , low doses led to growth retardation and higher doses caused skeletal dysmorphism in their offspring .In another study on pregnant rats, 0.0214gms chloroquine was given each day between day 8 to 22 of pregnancy. Results showed significant body weight reduction of rat pups (P value<0.01)[10]. Intraperitoneal administration of chloroquine 75mg/kg body weight to chicks for 14 days resulted in reduction of their body weight. The decrease in body weight was due to reduction in muscle mass and water content[11]. Tagoe and Ofori[12] proved that chloroquine was embryotoxic in rats and produced growth retardation due to reduced yolk sac vascularity.

Materials and methods

Twenty four adult female rats and eight adult male rats of Albino Wistar strain were used in this study. Animals were kept in the Animal House of Postgraduate Medical Institute, Lahore. For acclimatization, They were kept without treatment for 15 days. They were provided with Chick feed no 3 and tap water ad libitum. Male and female rats were kept in separate cages. Care was taken regarding optimal light and temperature. For conception three female rats and one male rat were kept together in a cage for a week and then male rat was removed from the cage. Female rats were observed daily for signs of pregnancy which was confirmed by presence of vaginal plug. Presence of vaginal plug was taken as day one of pregnancy After conception male rats were separated and 24 female rats were divided into four groups A, B, C and D containing six animals each. Total gestational period in rats ranges from 20-22 days, which in this study was divided into three trimesters, each of seven days. The rats were weighed and marked. They were placed in their respective cages, which were labeled by tags. Chloroquine phosphate in powdered form was used in this study.

Group A

This was a control group containing 6 animals each which were fed on normal diet throughout pregnancy. They were allowed to complete their gestational periods without drug intake.

Group B, C and D

Each containing 6 animals, were given oral dose of chloroquine 700mg/kg body weight during first, second and third trimester of pregnancy , respectively.

After the control and experimental groups had delivered, their offspring were selected at random(about 5/adult rat).The offspring were weighed on electrical balance and observed for any gross malformations .

Statistical Analysis

Data was collected and appropriately compiled. Mean of all variables was expressed as Mean ±Standard deviation. Difference in mean values of control and experimental groups were analysed using student's t-test (two tailed) and compared for significance using two tailed probability points of the t distribution.

Results

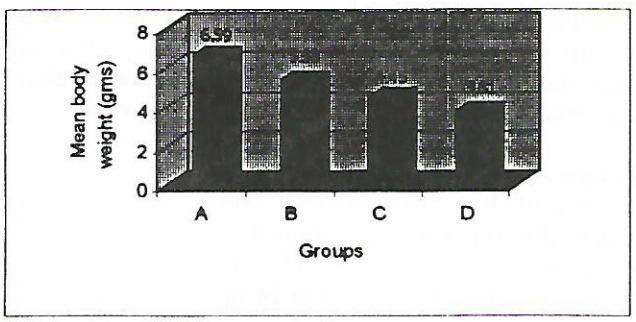
Newborn rats of group A (control) had mean body weight of 6.59gms (±1.04 SD). Mean body weight of animals of group B was 5.33gms (±.60 SD). The decrease in body weight was statistically significant (P<0.001). Animals of group C and D also showed statistically significant decrease in body weight (P<0.001). Mean body weight in animals of group C was 4.45gms (±.55 SD). Maximum decrease in body weight was found to be in animals of group D (3.81gms ±0.48 SD) in which drug was given to their mothers in 3rd week of gestation (Table 1, Fig. 1).

Table 1 Effect of chloroquine on body weight of newborn rats (n=30)

Parameters	Groups			
	A	B	C	D
Fetal weight (gms)	6.59 ±1.04	5.33 ±0.60	4.45 ±0.55	3.81 ±0.48
P value	-	P<0.001	P<0.001	P<0.001

All values are expressed as : Mean±SD

Fig. 1 Body weight in control and experimental groups



Discussion

It has become quite clear from the results of present study that chloroquine causes intrauterine growth retardation and significant decrease in body weight of offspring, when their mothers are exposed to chloroquine during the pregnancy. This study was designed to see the changes in body weight according to trimesters of pregnancy. It was found that, it is hazardous to use chloroquine during pregnancy especially the last trimester.

Chloroquine has ability to accumulate in the embryonic tissues and yolk sac. Yolk sac plays an important role in uptake and processing of nutrients. The teratogenecity of choloroquine has been hypothesized to result from its effects on lysosomal function, specifically the ability of yolk sac to capture and degrade external macromolecules. It also inhibits the proteolytic activity of yolk sac[12]. Chloroquine decreases the yolk sac vasculature and alters its nutrition[13]. The reduced vascularity of yolk sac lead to low oxygen tensions in tissues. Such low oxygen tension in tissues has been suggested to cause cell degeneration[14]. Due to improper functioning of yolk sac, growth of embryo is retarded which may be the cause of decreased body weight in this study.

Sharma and Rawat[9] also found the decrease in body weight and size of newborn rats which were exposed to chloroquine during intrauterine life. In their study, animals were exposed to chloroquine in a dose 700mg/kg body weight in first and second trimesters of gestation. Mgbodile[8]found that chloroquine administration during intrauterine and postnatal life resulted in marked decrease in neonatal and post weaning body weight. It can be concluded from this study that chloroquine should be avoided during pregnancy.

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