

Effect of Routine Antenatal Daily Iron Supplementation on Fetal Weight

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Abstract

Background: To study the effect of routine antenatal daily iron supplementation on fetal weight.

Methods: In this randomized control trial thirty two adult female and ten adult male Sprague- Dawley rats (weighing 200-250 gm) were taken. They were distributed randomly into two equal study groups. Ferrous sulphate was administered orally at 0 and 10mg/kg/day starting from gestation day (GD) 1, and half of the animals were sacrificed on GD 17 and half were sacrificed on GD 20. Five millilitre of maternal blood was taken through intracardiac route for measurement of blood haemoglobin and serum ferritin level. Maternal body weight was recorded at the start and then at the end of the experiment. Fetal weight was also recorded.

Results: The results were assessed on gestational day 17 and 20. There was no significant change in the maternal weight gain and number viability of fetuses of control and experimental groups. There was an increase in the mean fetal weight, maternal haemoglobin and maternal ferritin in iron replete rats as compared to non-iron supplemented (control) rats.

Conclusion: Antenatal daily iron supplementation is effective in improving fetal weight.

Key Words: Pregnancy, ferrous sulphate supplementation, maternal body weight, fetal weight..

Introduction

The routine use of iron prophylaxis during pregnancy is a subject of considerable debate, some advocating such practice as routine, while others maintain that it should only be used when clinically indicated. When a woman becomes pregnant her iron needs increase to support her pregnancy and the growth of her baby. Iron supplements are almost universally prescribed for pregnant women at doses ranging from 30mg/day in the United States to as high as 240mg/day where prevalence of anaemia is high. The preparation commonly used is ferrous sulphate 200 mg three times daily.¹

Iron (Fe) deficiency in pregnancy has serious consequences for both the mother and the baby. In the

immediate postnatal period, these include increased risk of low birth-weight and increased morbidity. In the neonatal period, there is an increased risk of impaired motor development and coordination. In children, language development and scholastic achievement can be affected; there are significant psychological and behavioural effects and decreased physical activity. As adults, the effects persist and can result in elevated blood pressure and cardiovascular problems.^{3,4}

Iron supplementation of pregnant individuals with adequate iron status may aggravate oxidative stress, a factor which could contribute to preterm delivery. Iron supplements may raise the risks of gestational diabetes, hypertension, and metabolic syndrome in some women. During pregnancy, low Hb levels, indicative of moderate (between 70 and 90 g/L) or severe (less than 70 g/L) anaemia, are associated with increased risk of maternal and child mortality and infectious diseases. Significant correlations between maternal anaemia and low birth weight (LBW) and between severe iron deficiency anaemia and LBW have been reported. On possible approach to reduce LBW is to reduce maternal anaemia during pregnancy.^{5,6}

Material and Methods

This randomized control trial was performed in Army Medical College and National Institute of Health, from October 2010 to January 2011.

Experimental Animals: Thirty two adult female and ten adult male Sprague Dawley rats weighing 150- 300 grams were taken from the animal house of National Institute of Health (NIH), Islamabad. Pregnant rats were kept individually in clear plastic cages with heat treated wood chips as bedding and kept at standard room temperature that was maintained on 12 hour light/dark cycle. Animals were given routine laboratory diet (NIH) in the form of pellets supplemented with vitamins and water ad libitum.

Dating the Pregnancy in Rats: Female rats were given chance to mate in the ratio of 4:1 with males overnight.

The presence of the vaginal plug on the following morning indicated pregnancy and was designated as gestation day 0 (GD 0).

Experimental Design:The pregnant rats were randomly allocated into two groups of sixteen rats each. The first group remained on the control diet throughout the experiment, whilst the second group was treated with ferrous sulphate in a dose of 10 mg/Kg/day. Maternal body weight was recorded at the start and then at the end of the experiment.

Group A (Control Group) - (16 Rats):This Group was further sub-divided into two sub-groups of eight rats each.

Group A-I (Control Group) - (8 Rats):They were given 5 cc distilled water by oral gavage tube at 9 am daily for 17 days starting from GD 0 to GD 16 and then sacrificed on the next day after the last dose.

Group A-II (Control Group) - (8 Rats):They were given 5 cc distilled water by oral gavage tube at 9 am daily for 20 days starting from GD 0 to GD 19 and then sacrificed on the next day after the last dose.

Group B (Exposed to iron supplements) - (16 Rats):This group was further sub-divided into two sub-groups of eight rats each.

Group B-I (Exposed to iron supplements) - (8 Rats):They were given 5 cc distilled water by oral gavage tube containing ferrous sulphate 10 mg/kg of body weight/day (same as the normal human dose) at 9 am daily for 17 days starting from GD 0 to GD 16 and then sacrificed on the next day after the last dose.

Group B-II (Exposed to iron supplements) - (8 Rats):They were given 5 cc distilled water by oral gavage tube containing ferrous sulphate 10 mg/kg of body weight/day (same as the normal human dose) at 9 am daily for 20 days starting from GD 0 to GD 19 and then sacrificed on the next day after the last dose.

Preparation of dosage of drug:Iron (crystalline ferrous sulphate FeSO₄.7H₂O) was finely ground by mortar and pestle. Dose was adjusted on the basis of human dose which is 10 mg/Kg body weight/ day and weighed by means of electric balance and mixed in 5ml of drinking water.

Euthanasia of Animals:Before the animals were euthanized their final weights were taken. The animals were sacrificed by an overdose of ether anaesthesia. Cotton soaked in ether was placed into the jar. The animal to be sacrificed was lifted by tail and dropped into the jar.

Collection of Blood Samples for Biochemical Assessments:When the animal became unconscious, it was taken out of the jar and placed on the dissecting

board. Five millilitre of maternal blood was taken through intracardiac route. Two millilitre was collected into labelled heparinized capillary tubes for haemoglobin measurement. The remaining maternal blood was collected in labelled nonheparinized tubes and centrifuged at 5000rpm for 5 minutes to separate serum. Maternal haemoglobin was measured using Sysmex Kx-21 and the results were obtained within 55 seconds. Serum ferritin was measured using Beckman Coulter Access-2 and the results were obtained within 45 minutes.

Results

All rats showed no abnormal clinical signs during the experimental period. The results showed no significant change in maternal weight gain and number viability of fetuses ($p > 0.05$) of control and experimental groups on GD 17 and GD 20. There was an increase in the mean fetal weight of the iron supplemented rats than that of control rats at GD 17 and GD 20. In the two groups of rats, the mean maternal blood hemoglobin and serum ferritin value was significantly greater in the experimental than the control rats at GD 17 and GD 20. (Table 1)

Table 1: Effect of antenatal iron : Comparison between control and experimental group (Number of animals in each group=16)

	Control Gorup Mean ± SE		Experimental Gorup Mean ± SE		P- value
	Day 17	Day 20	Day 17	Day 20	
NO* of fetuses	7.0±0.42	7.13± 0.4	7.13±0.52	7.25±0.37	>0.05 **
Fetal weight(gms)	0.547±0.012	4.262±0.13	0.748±0.012	5.613 ±0.15	<0.001***
Maternal Hb(g/dl)	9.35±0.131	9.47±0.144	11.463± 0.307	11.55 ± 0.234	<0.001**
Ferritin (ng/ml)	8.17 ± 0.269	11.01± 0.262	8.80 ± 0.382	11.44 ± 0.266	<0.001***

*NO=Number; ** Not significant ; *** Highly significant

Discussion

Birth weight is arguably one of the strongest predictors of infant survival. In our study, we observed that antenatal daily iron supplementation led to a significantly increase in fetal weight. This is in accordance with a number of animal and human studies. Although it is difficult to project directly from rats to humans, given the differences in timing of development of milestones, the data supports results published in human studies. It is possible that iron supplements may be preferentially transferred to the placenta and fetus thus contributing to higher birth weight. One another mechanism to support the

increase in fetal weight is that iron supplementation may improve the appetite of the mother, thus resulting in increased intrauterine growth.⁷

The amount of iron that can be absorbed from diet alone is sufficient to cover women's increased iron requirements during pregnancy except when women can draw enough iron from pre-pregnancy iron reserves. The data presented in this study showed that the daily use of iron supplementation during pregnancy raises maternal haemoglobin and serum ferritin level compared to the group receiving no supplementation. In most species, maternal blood volume increases and haematocrit and hemoglobin concentration fall during pregnancy. Iron supplementation with or without folic acid during pregnancy results in a substantial reduction in women's risk of having Hb level less than 10mg/ dl in late pregnancy, at delivery and six week postpartum. Pregnant women who received iron supplementation had differences in indicators of iron nutritional status during pregnancy in comparison with those who did not i.e. their Hb, iron, transferrin saturation and ferritin levels declined less.^{8,9}

Conclusion

Research is needed on the safe and effective amounts of iron and on schemes to provide in preventive supplementation programs on functional outcomes.

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