Invest Clín 16(2): 51-59, 1975

NUTRITIONAL ANEMIA DURING PREGNANCY. A STUDY IN A MIDDLE CLASS POPULATION TREATED WITH PLACEBO

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ABSTRACT

The hematological effect of the lack of supplementary iron during pregnancy, was studied in thirty eight, middle class, well nourished women, treated with placebo. A high frequency of anemia and iron and folate deficiency was found at the end of pregnancy. Six weeks after delivery, in spite of the fact that hemoglobin was normal, iron and folate were still low. The frequency of anemia and nutrient deficiency in cord blood was not significantly different from other groups who received prenatal iron salts. It is suggested that iron and folate stores, in well nourished pregnant women, are insufficient to maintain their hematological status, but the newborn will not be in much disadvantage in relation with those whose mothers received iron during gestation.

INTRODUCTION

Nutritional anemia during pregnancy is a well established problem especially among women of low socio-economic condition. The increased nutritional requirements of pregnancy, coupled with a deficiency in diet and a high incidence of parasitism, have been shown responsible for anemia among poor pregnant women, especially in the developing countries of the tropics.

However, a high incedence of folate deficiency has been found in middle class, apparently healthy and well nourished, pregnant women, not receiving folic acid supplementation, and whom despite iron therapy throughout pregnancy showed iron deficiency in the last trimester in 5% of the cases (10). These results promted us to determine what the

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developments in a well nourished middle class population are which is subjected to placebo from the beginning of pregnancy until the sixth week after delivery.

MATERIAL AND METHODS

Sixty middle class women were chosen at random from the entire population attending a private prenatal clinic from the first trimester of gestation. Medical and socio-economic records were maintained in order to ascertain that the subjects were generally healthy and consuming a fairly balanced diet (meat and vegetables every day), were from a well established home and possessed a stable source of income. Serial studies of blood, feces and urine were made for each patient, in order to rule out metabolic or infectious diseases.

Blood samples, for the purpose of this study, were taken in the first, second trimester, and at the time of labor, after overnight fasting. Additional samples were withdrawn from the cord, immediately after delivery, and from the mother, six weeks post-partum. At each visit to the obstetrician, the patients were provided with placebo capsulas (made of corn starch) labelled "antianemic I"* and instructed to take one twice a day, between meals. Those patients who showed hemoglobin or iron deficiency during the second trimester, were removed from the study and treated with ferrous salts.

Each blood sample was analyzed for hemoglobin(2), serum iron and transferrin saturation index(1), serum folate(6) and red cell folate(7).

In 8 patients a bone-marrow aspiration was performed 6 weeks after delivery, and morphologic studies and Dry's technique(5) for hemosiderine demonstration were made.

As in previous work(4) the minimal normal values of the parameters studied in maternal and cord blood, were considered to be:

Haemoglobin: 11 g/100 ml; 13.7 g/100 ml. Serum Iron: 50 ug/100 ml; 90 ug/100 ml. Transferrin Saturation Index: 15 %; 40 %. Serum Folate: 3 ng/ml; 12 ng/ml. Red Cell Folate: 160 ng/ml; 380 ng/ml.

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* Kindly supplied by Meyer-Productos Terapéuticos. Caracas. Venezuela.

RESULTS

Only 38 patients were followed throughout pregnancy, until confinement, since 2 patients suffered spontaneous abortion in the first trimester and one in midtrimester, due to cervical incompetence, ten women developed anemia or iron deficiency during the second trimester and were removed from the study and another nine patients were excluded from the program due to a variety of causes, such as failure to show at the clinic, changes of residence, etc. Only twenty four patients of the 38 studied returned to the clinic six weeks after delivery.

Mean values for hemoglobin and nutrients in maternal blood, during the study, were within normal ranges (Table I); although when the student's test was applied, there was a significant difference between the values found in the third trimester and those of early pregnancy for hemoglobin, iron and transferrin saturation. Six weeks after delivery, hemoglobin reached values similar to those of the first trimester, but serum iron and tranferrin saturation were significantly lower. The same was true for serum folate.

A high frequency of nutrient deficiency was found in the third trimester (Table II), with the exception of red cell folate, which according to the X^2 test was not significantly different from the first trimester rate. When the comparison was made between the first trimester and the post-partum frequencies of deficit, it was observed that six weeks after delivery all the nutrients were on shortage in a significant proportion of the population, although there was no difference in hemoglobin concentration.

Hemoglobin values were normal in cord blood (Table III), and no significant differences were encountered when compared to the results of a similar population (28 cases), where the mother received, ferrous fumarate 130 mg per day, throughout pregnancy (4). Only red cell folate deficiency was significantly higher in the "placebo" group.

The bone marrow specimens of eight patients, taken six weeks after delivery, showed megaloblastic changes in four cases, and absence of hemosiderin in one which was also megaloblastic.

DISCUSSION

The present study shows that in a population of middle class, pregnant women, apparently well nourished, who started their pregnancy with

TABLE I

CONCENTRATION OF HAEMOGLOBIN AND NUTRIENTS DURING PREGNANCY AND POST-PARTUM

PARAMETERS	FIRST TRIMESTER MEAN ± S.D.	THIRD-TRIMESTER (LABOR) MEAN ± S.D.	SIGNIFICANCE FIRST VS THIRD TRIMESTER* P	POST-PARTUM (SIXTH WEEK) MEAN ± S.D.	SIGNIFICANCE FIRST TRIMESTER VS. POST-PARTUM* P
HAEMOGLOBIN g/100 ml	12.8 ± 0.9	11.5 ± 1.3	0.001	12.6 ± 1.4	N.S.
SERUM IRON µg/100 ml	109.0 ± 26.0	80.0 ± 42.0	0.001	75.0 ± 34.0	0.001
TRANSFERRIN SATURATION INDEX %	28.0 ± 9.0	12.0 ± 6.0	0.001	21.0 ± 10.0	0.01
SERUM FOLATE ng/ml	6.5 ± 4.0	5.3 ± 4.0	N.S.	3.9 ± 2.0	0.01
RED CELL FOLATE ng/ml	239.0 ± 91.0	232.0 ± 170.0	N.S.	224.0 ± 137.0	N.S.
No. OF CASES	38	38	—	24	—

* STUDENT'S t TEST

TABLE II

DEFICIENCY OF HAEMOGLOBIN AND NUTRIENTS IN MATERNAL BLOOD

PARAMETERS	FIRST TRIMESTER	THIRD-TRIMESTER	SIGNIFICANCE FIRST VS. THIRD TRIMESTER * P	POST-PARTUM	SIGNIFICANCE FIRST TRIMESTER VS. POST-PARTUM* P
HAEMOGLOBIN < 11g/100 ml %	3	34	< 0.001	13	N.S.
SERUM IRON < 50µg/100 ml %	0	32	< 0.0005	26	< 0.001
TRANSFERRIN SATURATION INDEX < 15% %	5	71	< 0.0005	24	< 0.05
SERUM FOLATE < 3 ng/ml %	13	39	< 0.0005	39	< 0.01
RED CELL FOLATE < 160/ml %	18	34	N.S.	47	< 0.01

* x^2 TEST

TABLE III

HAEMATOLOGIC VALUES IN CORD BLOOD IN RELATION WITH ANTIANAEMIC PRENATAL THERAPY

PRENATAL ANTIANAEMIC THERAPY	HAEMOGLOBIN		SERUM IRON		TRANSFERRIN SATURATION INDEX		SERUM FOLATE		RED CELL FOLATE	
	g/100 ml mean ± s.d.	< 13.7 g/100 ml %	μg/100 ml mean ± s.d.	< 80 μg/100 ml %	percentage mean ± s.d.	< 40% %	ng/ml mean ± s.d.	< 2 ng/ml %	ng/ml mean ± s.d.	< 380 ng/ml %
PLACEBO	15.3 ± 2.3	21	160 ± 58	10	49 ± 19	33	18.3 ± 8.9	26	382 ± 198	55
IRON*	15.5 ± 1.3	13	171 ± 60	11	49 ± 18	35	23.4 ± 9.9	11	589 ± 283	32
p **	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	< 0.04

* Data obtained from a similar population, Diez Garcia et al. Invest. Clin. 14: 59-73, 1973.

** Student's t test for comparison of concentrations and χ^2 test for comparison of percentages.

satisfactory hematological status, neither the nutrients contained in their diets, nor the iron and folate body stores, are sufficient to satisfy the new requirements of pregnancy and avoid the hemoglobin decline at the end of gestation.

It is true that such values as hemglobin, could be low because of the physiologically increased plasma volume, but six weeks after partum, the deficiency of hemoglobin was still 13% and the deficit of serum iron was close to deficit at term of pregnancy. The high deficit of transferrin saturation could also be explained, in part, by the transferrin increase that occurs in pregnancy, (8) but again, an important deficit still remains after the levels of this protein have dropped.

The rate of folate deficiency was similar to findings in a similar population who received iron salts during gestation, (10). This and the high proportion of megaloblastic changes in patients with normal iron status gives another proof of the independence of folate metabolism in relation to iron (3).

Although the hematologic values of cord blood in the placebo group were generally lower in comparison with those found in a group treated with iron during pregnancy (4), no significant statistical difference was found between them, with the exception of red cell folate, which showed a low degree of significance. Sturgeon (12) sustains that the hematological status of the mother does not influence that of the newborn, but in other reports (6,4) a signficant positive correlation was found between maternal and newborn, iron and folic acid concentrations. The present results could be explained by the fact that the deficiency of the mothers was not so severe as to cause a high deficiency in the child; but we can notice that the deficit of red cell folate was significantly higher in the placebo group, indicating that possibly the stores were small too. Bone marrow studies would have been necessary in order to know how the tissue iron stores were, but this was not suitable for us. It is difficult in our media to accomplish follow up studies in the infant, mainly because of lack of cooperation from the mother's part. In this respect, the results of Sturgeon (12) showed no hematologic differences at 6-12 and 18 months of age, between the infants who received prenatal supplemental iron and those who did not, but in that study children were fed with iron fortified foods from 2-3 months of age.

In the light of these results, we can conclude that, iron and folic acid stores, in a well nourished population, are sufficient to maintain an acceptable hematological status in the fetus, but a high proportion of the mothers will confront the risks of labor and delivery in an anemic state, which 16 weeks after delivery will not be completely corrected.

RESUMEN

Se estudió el efecto hematológico de la falta de hierro suplementario durante el embarazo, en treinta y ocho mujeres bien alimentadas, de clase media, tratadas con placebo. Se encontró una alta frecuencia de anemia y deficiencia de hierro y folato, al final del embarazo. Seis meses después, a pesar de que la hemoglobina era normal, el hierro y el folato permanecían bajos. La frecuencia de anemia y la deficiencia de nutrientes, en sangre del cordón umbilical, no fué significativamente diferente de otros grupos que recibieron sales de hierro en el período prenatal. Se sugiere que, los depósitos de hierro y folato, en mujeres embarazadas bien nutridas, son insuficientes para mantener su estado normal hematológico; pero el recién nacido no está en mucha desventaja en relación con aquellos cuyas madres recibieron hierro durante la gestación.

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