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Abstract

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HEMATOLOGICAL STUDIES ON IRON- AND FOLATE-REQUIREMENTS IN PREGNANCY

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Abstract: Hematological changes and serum iron, vitamin B_{12} and folate levels after administration of iron plus folic acid were compared with changes and levels after supplement of iron alone in 100 pregnant women. No hematological benefits by adding folic acid was revealed. It is concluded that folic acid deficiency in pregnant women is mild and routine supplementation of folic acid is not necessary except for proved cases of folate deficiency. As to the reason why folic acid deficiency is so mild and megaloblastic anemia is so rare in Japan, uniformity of dietary habits, *i.e.* boiled rice as basic food, was discussed.

Anemia is one of common complications of pregnancy. In Japan, the majority of anemias related to pregnancy have been thought to be due to iron deficiency (1). The incidence of megaloblastic anemia in pregnancy is very rare in Japan (2). Therefore, folic acid status of Japanese pregnant women had not been studied before our report (3). This indicated that mild folic acid deficiency masked by iron deficiency was not infrequently seen among pregnant women. Some reports (4, 5, 6) confirming also high incidence of low serum folate levels in pregnant women appeared afterwards.

Megaloblastic anemia is seen in 1-4% of pregnant women in Europe and North America (7). In the countries where high incidence of megaloblastic anemia is seen, prophylactic supplement has been recommended during pregnancy (8, 9).

The present study was designed to observe the effect of prophylactic folic acid on hematological values during the late stage of pregnancy and to elucidate whether or not folic acid is necessary during pregnancy.

MATERIALS AND METHODS

A total of 101 pregnant women visiting the Hakuaikai Hospital at Okayama city were studied. These subjects were divided at random into two groups at 28th week of pregnancy.

Group I received 48.5 mg of iron preparation as ferrous fumarate daily from 28th week to term, and group II, in addition, 5 mg of folic acid.

The following tests were carried out at 28th and 36th weeks of pregnancy and one month after delivery; red blood corpuscles (RBC), hemoglobin concentration (Hb), hematocrit (Ht), serum iron level by the orthophenanthroline method, serum vitamin B_{12} level by L. leichmannii (10) and serum folate level by L. casei (11).

RESULTS

As shown in Table 1, the initial mean levels of each test in both groups showed no significant differences. In group I, the mean values of RBC, Hb and Ht increased significantly after taking iron for 8 weeks. In group II, these values also increased at 36th week, though no significant difference was seen between the two groups. One month after delivery, increase of these values compared to those of 28th week was also examined, but the differences were small and were not stastically significant between the two groups.

TABLE 1 RESULTS OF HEMATOLOGICAL EXAMINATIONS

Mean±S.E.

Group		28th week	36th week	one month after delivery
RBC	I	382.4±28.0(49)	432.8±45.3(48)	450.7±41.3(45)
	II	368.6±37.2(52)	418.3±45.3(47)	447.8±44.0(33)
Hb	I	11.2±0.85(49)	12.4±1.0 (49)	12.8±2.22(46)
	II	10.6±1.0 (52)	11.8±1.0 (47)	12.8±1.0 (35)
Ht	I	33.8±2.6 (49)	38.0±2.8 (48)	39.8±2.5 (45)
	II	32.7±2.5 (43)	36.6±3.1 (46)	39.4±2.9 (34)

Group I: Iron, Group II: Iron plus folic acid
In parenthesis are the numbers of the women examined.

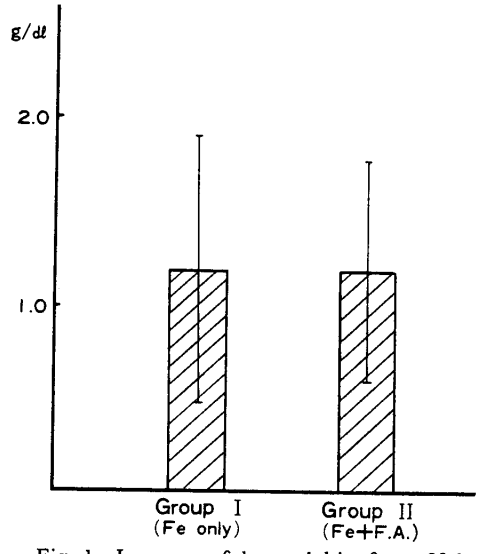

Fig. 1. Increase of hemoglobin from 28th to 36th week

In Table 2, results of serum iron, vitamin B_{12} and folate levels are shown. Serum iron levels in-

TABLE 2 RESULTS OF ESTIMATIONS OF IRON, VITAMIN B_{12} AND FOLIC ACID LEVELS

Group		28th week	36th week	one month after delivery (Mean±S.E.)
Iron	I	68.3±45.3(49)	114.3±62.6(47)	87.9±38.9(45)
	II	62.8±25.8(50)	91.9±50.3(47)	90.0±33.2(36)
Vit. B_{12}	I	288.9±148.6(49)	333.7±188.2(48)	428.0±187.0(46)
	II	351.4±260.2(52)	295.5±168.9(47)	440.7±208.0(37)
Folic acid	I	4.8±2.3(49)	4.5±2.0 (48)*	5.3±3.3(42)*
	II	4.4±1.9(52)	21.3±18.3(47)	12.1±10.4(31)

Group I: Iron, Group II: Iron plus folic acid. In parenthesis are the numbers of the women examined. * $p<0.001$

creased in the both groups at 36th week and remained at normal level one month after delivery, but the differences were not stastically significant. The serum vitamin B_{12} levels were similar throughout the period of pregnancy irrespective of the type of supplementation. In Group II, serum folate levels increased prominently after the administration of folic acid and high levels were maintained even after delivery.

DISCUSSION

It was revealed that in the present study, the routine supplementation of iron plus folic acid had no significant effect on the hematological status compared to that of iron alone. Therefore, improvement of Hb and Ht was due to iron. Folic acid might be less concerned with anemias in the women studied. Serum folate levels showed significantly high levels at 36th week and one month after delivery, but this is merely a reflection of supplemented folic acid. It would appear that the anemia in large group of subjects during pregnancy in Japan is dependent mainly on the state of iron nutrition. The present results suggest that prophylactic supplementation of folic acid may not be necessary in Japan. These results are similar to those of recent studies in white populations (12, 13, 14) and in other countries where folate intake is low (15, 16).

The present study also suggests that folic acid deficiency observed in high percentage judged from serum folate levels in pregnant women (3, 4, 5, 6) is so mild that it played little role for the cause of the anemia. This may be a reason why megaloblastic anemia is rare in Japan. Megaloblastic anemia may develop in the individuals whose folic acid intake is extremely low or with whom some other factors causing folic acid deficiency are associated.

Among the factors which cause folic acid deficiency, nutrition is thought

to be most important as previously reported by the authors (3, 17).

Recently HIBBARD *et al.* (18) studied anemia and folate status in the late stage of pregnancy in Singapore and obtained very interesting results. In the three ethnic groups studied (Chinese, Malay and Indian), folate depletion and megaloblastic anemia occurred most frequently among Indian and most rarely among Chinese. The reason for this may be as follows; Meal taken by Chinese women contain plentiful fresh green vegetables. Many Indian have a diet poor in vitamins and prolonged cooking may reduce them. As suggested by them, nutritional status of the women is very important for discussing the different incidence of megaloblastic anemia in pregnancy in different populations.

Folic acid contents in food taken by Japanese are reported to be enough for daily requirement (3, 19, 20). In addition, Japanese have very uniform dietary habits, *i. e.* boiled rice as basic food. Folic acid content in rice after cooking by the way usually prepared in Japan were assayed by the authors (21), revealing that free folate was 5.5 μg/100 g and total folate was 36.5μg/100g.

As a large part of diet is constituted of rice, folic acid intake by Japanese is maintained in satisfactory levels except for very unusual cases whose dietary intake is extremely low.

HERBERT (22) is rather against our suggestion described above; he mentioned the ethnic groups around the world whose diet consisted primarily or exclusively of rice or together with rice as classic examples of lack of folate. He stated that rice was finely particulated to begin with, and cooking in a large quantity of water allowed boiling water to get to the very core of rice grains and destroy folate in their center as well as periphery. This statement was based on his experiment in man (23) in which folic acid deficiency was produced by feeding a man with diet mainly composed of rice boiled three times with large quantity of water. His assumption that folic acid deficiency is prevalent among the people taking mainly rice is not justified, because megaloblastic anemia is extremely rare among Japanese (2) (3), Chinese (18) and Siamese (24) and rice is prepared in different ways from his experiment in these countries.

It is concluded that folic acid deficiency in Japanese pregnant women is very mild in the majority of cases, owing to uniform dietary habits composed mainly of boiled rice, and supplementation of folic acid is only indicated for pregnant women developing megaloblastic anemia.

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