นิพนธ์ต้นฉบับ

Comparison of the efficacy of 40 and 120 milligrams daily iron supplementation in normal pregnancy

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Objective *To compare the efficacy of 40 and 120 milligrams daily iron supplementation during normal pregnancy in term of preventing anemia .*

Methods *One hundred pregnant women with gestational ages of 16-20 weeks and initial hemoglobin concentrations of 11.0 grams per decilitre(g/dL) or more were randomized into two groups. The first group received ferrous sulfate with an elemental iron content of 40 milligrams per day. Second group received 120 milligrams per day. Both groups were followed until 36 completed weeks of gestation.*

Results *Sixty one women completed the study. Thirty women were in the first group and 31 in the second group. Mean hemoglobin concentration were 11.65 and 11.65 g/dL before iron supplementation, and 12.47 and 12.47 g/dL after iron supplementation in the first and second groups respectively. The difference in hematocrit and hemoglobin concentrations between the two groups had no statistical significance. The efficacy in preventing anemia at term pregnancy were 93.33 and 96.77 percent respectively. There was a higher incidence of nausea in the 120-milligram group. (p=0.028)*

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Conclusions *Forty milligrams daily iron supplementation is as effective as 120 milligrams daily dose in preventing iron deficiency anemia in normal pregnancy, and there are less side effects.*

Key words : *Iron supplementation, Ferrous sulfate, Pregnancy.*

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ศักนัน มะโนทัย, กำธร พฤกษานานนท์. ประสิทธิภาพของการให้เหล็กเสริมขนาด 40 และ 120 มิลลิกรัมต่อวันในสตรีตั้งครรภ์ปกติ. จุฬาลงกรณ์เวชสาร 2539 มกราคม; 40(1): 41-47

วัตถุประสงค์ *เพื่อเปรียบเทียบประสิทธิภาพของการให้เหล็กเสริมขนาด 40 และ 120 มิลลิกรัมต่อวันในสตรีตั้งครรภ์ปกติเพื่อป้องกันภาวะโลหิตจาง*

วิธีการวิจัย *สตรีตั้งครรภ์ปกติอายุครรภ์ 16-20 สัปดาห์ที่มาฝากครรภ์ที่หน่วยฝากครรภ์โรงพยาบาลจุฬาลงกรณ์ และมีค่าความเข้มข้นของฮีโมโกลบินตั้งแต่ 11.0 กรัมต่อเดซิลิตร จำนวน 100 รายถูกแบ่งโดยการการสุ่มออกเป็น 2 กลุ่ม กลุ่มที่ 1 ได้รับเหล็กเสริมในรูปของเฟอรัส ซัลเฟต โดยมีปริมาณธาตุเหล็ก 40 มิลลิกรัมต่อวัน กลุ่มที่ 2 ได้รับในขนาด 120 มิลลิกรัมต่อวัน และสิ้นสุดการศึกษาเมื่ออายุครรภ์ 36 สัปดาห์ขึ้นไป*

ผลการวิจัย *สตรีจำนวน 61 รายที่เก็บข้อมูลได้เมื่อสิ้นสุดการศึกษา เป็นสตรีในกลุ่มที่ 1 จำนวน 30 ราย กลุ่มที่ 2 จำนวน 31 ราย ค่าความเข้มข้นของฮีโมโกลบินก่อนการให้เหล็กเสริมมีค่าเฉลี่ย 11.65 และ 11.65 กรัมต่อเดซิลิตร ตามลำดับ และภายหลังการให้เหล็กเสริมมีค่าเฉลี่ย 12.47 และ 12.47 กรัมต่อเดซิลิตรตามลำดับ ซึ่งความแตกต่างระหว่างทั้ง 2 กลุ่มไม่มีนัยสำคัญทางสถิติ ประสิทธิภาพในการป้องกันภาวะโลหิตจางเมื่ออายุครรภ์ครบกำหนดเท่ากับร้อยละ 93.33 และ 96.77 ตามลำดับ ในสตรีกลุ่มที่ 2 พบว่ามีผลข้างเคียงได้แก่ อาการคลื่นไส้มากกว่ากลุ่มที่ 1 อย่างมีนัยสำคัญทางสถติ ($p=0.028$)*

สรุป *การให้เหล็กเสริมขนาด 40 มิลลิกรัมต่อวัน มีประสิทธิภาพในการป้องกันภาวะโลหิตจางจากการขาดเหล็กในสตรีตั้งครรภ์ปกติ ไม่แตกต่างจากขนาด 120 มิลลิกรัมต่อวัน โดยมีผลข้างเคียงน้อยกว่า*

Anemia is a common complication during pregnancy. The Center for Disease Control[1] defined anemia during pregnancy as a hemoglobin concentration of less than 11.0 grams per decilitre in the third trimester. By this definition, the prevalence of anemia in Thai pregnant women is 23-30 percent,[2,3] and 75% of the cases are caused by iron deficiency.[4] In pregnant women without iron supplementation, the incidence of anemia at term can reach 80 percent.[4] Iron supplementation has been demonstrated to be an effective way to prevent this complication. Scott et al[5] found that as little as 30 milligrams (mg) of daily elemental iron supplementation was enough to prevent anemia during pregnancy but in other series[6] as much as 120 mg daily dose was reported as necesssary.

While too low a dosage may not prevent anemia, excessive iron dosage may cause side effects such as nausea vomiting constipation or diarrhea. Poor patient compliance and public health expense are also increased. In this study we compared the efficacy and side effects of 40 and 120 milligrams daily iron supplementation. Ferrous sulfate was used because it was cheap, readily available, and was included in the National Drug List.

Materials and Methods

During the period of August 1992 to June 1993, one hundred pregnant women attending antenatal the clinic at Chulalongkorn Hospital were enrolled in the study. They aged between 18-35 years, had gestational ages of 16-20 weeks, and had initial hemoglobin concentrations of 11.0 grams per decilitre or more. Patients with severe nausea and vomiting, stool parasites, a history of hematologic diseases, medical or obstetric complications were excluded. The subjects were randomized by random number into two groups. The first group received ferrous sulfate tablets (200 mg) once daily (equivalent to 40 mg elemental iron), while the second group was instructed to take the same medication three times a day (equivalent to 120 mg elemental iron). The patient's compliance with the instructions was assessed by tablet count. Both groups were followed until 36 completed weeks. The hemoglobin concentration and hematocrit were tested at the beginning and end of the study. The hemoglobin concentration and hematocrit values were determined by an automated cell counter (Celldyne 1600). The unpaired T-test and Fishers Exact test were used for statistical analysis. Using data from Paintin et al[7], a sample size of 27 cases for each group was deemed necessary to detect a difference of hemoglobin concentration of 1 gram per decilitre at the end of study (alpha error 0.05, beta error 0.05).

Results

Sixty one women completed the study, 30 in the first group and 31 in the second group. The clinical characteristics of both groups are shown as mean $\pm$ standard deviation in Table 1. Hematocrit and hemoglobin concentrations before and after iron supplementation are shown as mean $\pm$ standard deviation in Table 2. Efficacy in preventing anemia at term pregnancy were 93.33 and 96.77 percent respectively. Two cases (6.7%) in the first group were found to be

anamic after iron supplementation and 1 case (3.2%) in the second group. This difference did not reach statistical significance (p = 0.37). Side effects found during study are shown in Table 3. The incidence of nausea was significantly higher in the second group.(p = 0.028)

Table 1. Clinical Characteristics

Clinical Characteristics	Group I (n=30)	Group II (n=30)	P value
Age (years)	25.6 ± 4.4	25.0 ± 5.4	NS
Gravidity	1.7 ± 0.9	1.6 ± 0.9	NS
Parity	0.3 ± 0.6	0.3 ± 0.8	NS
Gestational age (day at beginning)	128.2 ± 11.0	124.3 ± 9.1	NS
Gestational age (day at end)	260.5 ± 9.6	261.5 ± 9.6	NS
Duration of iron supplementation (days)	132.3 ± 14.9	137.3 ± 12.1	NS

NS:p>0.05

Table 2. Hematocrit and hemoglobin cocentration before and after study.

	Group I (mean ± SD)	Group II (mean ± SD)	P value
Hematocrit (Volume %)			
Before iron supplementation	34.83 ± 1.60	34.64 ± 1.79	NS
After iron supplementation	37.36 ± 2.96	37.25 ± 2.78	NS
Hemoglobin concentration (Grams per decilitre)			
Before iron supplementation	11.65 ± 0.73	11.65 ± 0.65	NS
After iron supplementation	12.47 ± 0.97	12.47 ± 1.16	NS

NS:p>0.05

Table 3. Side effects of iron supplementation found during study.

Side effects	Group I (n=30)	Group II (n=31)	P value
Nausea	0	5	0.028
Vomiting	0	2	NS
Constipation	1	0	NS
Diarrhea	1	1	NS

NS:p>0.05

Discussion

Approximately 1,000 milligrams of ele-mental iron are required during a normal pregnancy[8], 300 mg for the fetus and placenta, 500 mg for increased maternal red blood cell production and 200 mg for normal daily loss. On the average, there is only 300 mg of stored iron in young, healthy nulliparous women[9], so the necessity for iron supplementation is apparent. The results of many studies to define appropriate iron supplementation dosage to prevent anemia has varied from country to country[2,3], and these variations may be due to different socioeconomic backgrounds, dietary habits or ethnic variations.

The results of our study showed that daily 40-mg elemental iron supplementation was as effective as a 120-mg daily dose for the prevention of anemia during normal pregnancy in Thai women. Less side effects and a more convenient dosage schedule would definitely lead to better compliance for iron supplementation.

In Thailand, there were 905,837 live births recorded in 1989.[10] If every pregnant woman was given 120 mg elemental iron daily in the last 20 weeks of pregnancy, 380.4 million tablets of 200-mg ferrous sulfate would be needed annually. On the contrary, if only 40 mg elemental iron were given daily, only 126.8 million tablets would be sufficient. Routine 40 mg daily doses in normal pregnant women would save annual public health expenses of at least 25 million Baht (assuming a 200-mg ferrous sulfate tablet costs 0.10 Baht).

However it must be emphasized that in pregnant women who were initially anemic, had medical or obstetric complications, used drugs that may impede iron absorption or were late booking, the 40 mg daily dose may not suffice to prevent anemia during pregnancy and higher doses may be more appropriate.

For future studies, serum ferritin measurements are needed to define appropriate daily doses to prevent an iron deficiency state in pregnant women. A larger sample size will have higher sensitivity to detect subtle changes in hematocrit or hemoglobin concentrations. Continuing the study into the postpartum period may reveal effects of blood loss during delivery.

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