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Original Article

The Effect of Simultaneous Administration of Zinc Sulfate and Ferrous Sulfate in the Treatment of Anemic Pregnant Women

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ABSTRACT

Background: Iron deficiency and its resulting anemia is a common problem among Iranian pregnant women. In spite of iron supplementation program, yet, this problem has not resolved in many parts of the country. Zinc deficiency also is very common in Iran. This study evaluated the efficiency of concomitant zinc and iron therapy in the treatment of anemic pregnant Iranian women.

Methods: A total of 118 anemic women were registered in this randomized controlled trial. Both groups received 100 mg elemental iron daily. The intervention group received an additional dose of 15mg zinc every day for a period of 12 weeks while the control group received placebo. Serum hemoglobin was measured at the beginig of study, after 12 weeks of treatment and at the end of 8 weeks follow-up. Collected data were analyzed with %95 significance level by ANOVA test for comparing baseline characteristics in the two groups and t-test was applied to assess hemoglobin changes in the intervention group.

Results: After 12 weeks of therapy, desirable response was obtained in 78.35% and 93.1% (CI=95%) of anemic women in control and intervention group, respectively which showed a significant difference (P<0.05). Increase in serum hemoglobin just after 12 weeks of treatment was 2.22 ± 0.77 and 1.5 ± 0.66 (gr/dl) in intervention and control group respectively, (P<0.001). Serum hemoglobin differences in the two groups 8 weeks later (step2) when iron alone was administered to both groups were 2.24 ± 0.77 and 1.49 ± 0.66 (gr/dl) respectively . (P<001)

Conclusion: this study clearly demonstrated the efficacy of this inexpensive and simple intervention in the treatment of anemia and prevention of its recurrence in anemic pregnant women.

Key words: Anemia, Pregnant women, Supplement, Isfahan, Zinc sulfate, Ferrous sulfate

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Iron deficiency anemia is recognized as the most prevalent nutritional problem in the world[1] . More than 90% of anemic patients are living in developing countries. In Iran, the prevalence of anemia is relatively high. 10.5% of high school female students in Lar city [2], 7.2% of 1-5 year old children in Kerman city [3] and 23.8% of women in reproductive ages in Ilam city [4] are suffering from anemia.

The prevalence of low ferritin level and low transferin saturation are more than anemia [3, 4]. Iron requirement in pregnant women is more than in other women. Iron deficiency anemia is common in pregnant women in India (56.6%), Iran (17.4%), Peru (50%) compared to Germany (2.2%) [5-8].

Anemic pregnant women are at risk of fatigue, reduction of mental and physical activity, high mortality rate, premature labor and low birth weight of their newborns [9, 10].

Despite policies advocating iron supplementation for high risk groups such as breast-fed children, pregnant and lactating women, few effective interventions have so far been identified [11].

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Two basic causes of this issue are: multiple micronutrient deficiencies and insufficient drug use

Imani's study in Zahedan showed that only 18% of mothers used iron supplements for their children[12] and study of Kalantary in Isfahan indicated that anemia persisted in 70% of pregnant women in spite of regular iron use[13] . Malekafzali et al evaluated the efficacy of iron supplementation in Varamin but there were not any increase in ferritin level [14].

Now researchers have paid more attention to zinc[15]. This element has a basic role in human metabolic activity, cellular mitosis, protein synthesis and the enzymatic processes [16]. It is also a component of enzyme "Aminolevolinate Dehydratase" which changes ALA to probilinogen in the heme synthesis pathway [17].

In 63% of pregnant women and 70% of lactating women in Isfahan, serum zinc level was below 60 µg/dl [18, 19].

In this study we tried to find weather simultaneous administration of zinc and iron can raise hemoglobin level higher than what is achieved with iron supplementation per se.

Subjects and Methods

In a double blind placebo controlled clinical trail, 130 anemic pregnant women from primary health care centers in urban and rural areas of Isfahan were selected. A hemoglobin level less than 11g/dl was defined as anemia [20]. Blood samples were tested by cyanomethemoglobin method. Laboratory tests were done at the end of the first trimester of pregnancy after history-taking and physical examination by a physician. Health center physicians observed blood exam results. They also sought past history of anemia and if positive, they evaluated clinical reasons for causes of anemia other than iron deficiency. Anemic pregnant women with evidence of iron deficiency anemia were referred to family health technicians.

Health centers were divided in two groups randomly by the health staff supervisor. (A and B) Drugs and placebo in similar shape were put in coded boxes (A and B) and delivered to family health care centers. Women who accepted to take zinc sulfate entered the research.

Health workers were informed of zinc importance. Patient education and data collection were carried out by trained health care staff. They instructed mothers in health care and correct way of drug use.

Group 1 received daily supplements of 100 mg of iron (as ferrous sulfate) and placebo similar to zinc sulfate pills. Group 2 received the same amount of iron along with 15 mg of zinc (as zinc sulfate) for 3 months. This regimen was begun between 16th and 20th weeks of pregnancy. After 3 months of treatment, both groups received 50 mg iron alone for two months thereafter.

They referred to health care centers once or twice every month for prenatal care. Health workers monitored their drug compliance, and recorded information in the forms. In case of failure to use the drugs regularly or if a complication occurred, the subject was excluded from the study. After 3 and 5 months intervention, hemoglobin concentration was measured, and information was recorded.

Data were entered into SPSS software and were analyzed. Independent t-test was used to compare baseline characteristics in the two groups with 95% significance level and repeated measurement. ANOVA was used to compare hemoglobin changes in the two groups by intervention type.

Results

From the total 118 pregnant woman who completed the first step, 115 could finish step 2 of the study.

Selected characteristics of anemic women are presented in Table 1. Past history of pregnancy, abortion and anemia are presented in table 2. At the beginning of intervention, there were no significant differences between the two groups ($p>0.05$).

After 12 weeks of therapy, desirable response was observed in 78.3% and 93.1% of anemic women in the control and intervention groups, respectively which demonstrated significant differences. ($X^2 = 5.8$, df = 1, $P<0.05$).

Changes in hemoglobin concentration during the course of treatment are presented in Table 3. As shown, there are significant differences in hemoglobin concentration according to the type of treatment in both steps. (p< 0.001)

Table 1. Baseline characteristics of anemic pregnant women

Charecteristics	group 1 (n=58)	Group 2 (n=60)	Mean difference	95% CI
	(Mean ± Standard deviation)	(Mean ± Standard deviation)		
Weight (Kg)	65.43 ± 9.18	63.6 ± 11.07	1.82	1.89 – 5.53
Height (cm)	158.88 ± 6.07	159.08 ± 6.03	0.20	2 – 2.41
BMI (kg/m^2)	25.26± 3.91	25.82± 4.00	0.14	0.88 – 1.99
Hemoglobin (kg/dl)	10.44± 0.2	10.46± 0.2	0.77	0.100 – 0.105

Table 2. Past history of pregnancy, abortion and anemia

Charecteristics	Group 1 (n=58)	Group 2 (n=60)	Mean diffrence	95% CI
Pariety	0.16	0.57 - 0.24		
1	%19.0	%25.3	--	--
2	%39.6	%36.7	--	--
3	%24.1	%19.7	--	--
>3	%15.3	%18.3	--	--
Abortion (Past history)	%6.9	%8.3	0.01	0.11 – 0.07
Anemia (Past history)	%8.6	%8.3	0.0	0.100- 0.105

Table 3. Hemoglobin concentration before and after the treatment

Group \ Hemoglobin	Before treatment	After 3 months (step 1)	After 5 months (step 2)
Iron	10.44 ± 0.24	11.94 ± 0.90	11.93 ± 0.94
Zinc + iron	10.46 ± 0.24	12.68 ± 1.01	12.70 ± 1.01

repeated measure ANOVA : P <0.001

Discussion

In the present study, the administration of zinc besides iron in the treatment of anemic pregnant woman affected hematological response in 12 weeks of treatment and persisted 8 weeks after withdrawal of zinc sulfate. The same finding was observed in Nishiyama's study [21]. In contrast, no benefit resulted from co-administration of zinc and iron to the same group in Zavalta's study in Peru [22]. Maybe, Such differences are related to the zinc status in the Peruvian people's diet compared to other nations such as Iranian people.

In our study, 93.1% of zinc plus iron group and 78.3% of iron plus placebo group responded to treatment as hemoglobin increased to more than 11 g/dl. It appears that multiple micronutrient deficiency is the most important cause of insufficient anemia treatment response.

Kolesteren compared the use of vitamin A and iron versus iron alone in the treatment of anemia and Ravanshad added vitamin C to iron [23, 24] . Both of those studies found benefitial effects of co-admistration.

There are other data and experiences that showed zinc administration relieves symptoms

such as fatigue, anorexia, hair loss and nail dystrophy in many patients.

Zinc content of soil is depleted in many areas of the world. In addition, high zinc foods such as meat, egg, milk and etc are used less than recommended, and incorrect processing of bread decreases zinc absorption. It is also proved that oral iron can decrease zinc absorption and serum zinc level [25].

In conclusion, we suggest that more attention should be paid to zinc deficiency and zinc supplementation in pregnant women.

Moreover, people should be educated on nutrition and dietary sources of zinc through health programs on mass media.

We also recommend more studies in this field to highlight the advantages of zinc supplementation in health care programs.

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