

The Effect of Combined Supplementation of Iron and Zinc Versus Iron alone on Anemic Pregnant Patients in Dohuk

Melad A. Yalda, *¹ Aveen Akhram Ibrahiem²

Abstract

Background: Combined supplementation with iron and zinc during pregnancy may be effective in preventing deficiencies of these micronutrients.

Objective: To assess the effect of combined supplementation of Iron and Zinc versus Iron alone on anemic pregnant patients.

Design: Single blind randomized clinical control trial.

Setting: This study was carried out in Kurdistan region, Dohuk city/ Iraq from 1st of November 2005 to 31st of October 2006. Hundred anemic pregnant patients completed their first trimester assigned and divided randomly into two groups. First group (A) supplemented daily with 120 mg Iron. Second group (B) received 120mg iron + 22.5mg zinc. The therapy continued for six months. Three Venous blood samples were collected during the study.

Results: at time of booking, a baseline blood sample was collected, in which we estimated the hemoglobin, PCV, serum Iron, total serum iron binding capacity and serum zinc. Another two samples were collected three months apart. Collected data were analyzed by SPSS software; independent t-test was applied. Hemoglobin, PCV and serum iron had significantly influenced by the supplement therapy in both groups ($p < 0.001$). Group B had a significant improvement in their serum iron status ($p < 0.0001$). A desirable response in hemoglobin and PCV values have been observed in group B three months after treatment. This, however, did not stand between the two groups by the end of the study.

A sustained significant rise in zinc level was achieved in group B ($p < 0.00$). On the contrary, there was a decline in zinc level in group A, especially in the first three months. After that, zinc level started to build up again and showed a significant improvement in respect to the second reading but did not approach the first booking level.

Conclusion: The study clearly demonstrated the efficacy of the combined therapy for treating anemia and improving zinc status in pregnancy.

Keywords: Supplementation of Iron and Zinc, Iron alone, Anemic pregnant patient, Dohuk.

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Introduction

Nutritional iron deficiency is the highest in population segments that are at peak rates of growth, namely; infants, young children, and pregnant women.¹

Anemia through the lack of iron, affects more than 260 million women in the developing countries. It has been found that up to 75% of pregnant women in the developing countries have low hemoglobin levels.^{2,3}

Pregnancy is a time in which the risk for developing iron deficiency anemia is the highest, particularly during their late second and third trimester.⁴

Some scientists argue that it is not possible to maintain the iron status of a pregnant woman with normal dietary practices and that iron prophylaxis is necessary.⁵

Iron and zinc deficiencies may coexist in populations that consume diets with insufficient amounts of animal-source foods. In which, food fortification or supplementation programs may be needed.⁶

Low-to-moderate Zinc deficiency during pregnancy is likely to be a national problem. It has been estimated that 82% of pregnant women worldwide may have inadequate usual intakes of zinc.⁷

Adverse consequences of zinc deficiency during pregnancy were related to prolonged labor, increase in maternal mortality, low birth weight and late fetal development.^{7,8}

It is believed that iron and zinc compete for the same absorptive pathways.⁹

New aspects based on cell culture studies have shown that iron may inhibit zinc absorption in some cells at very high ratios of iron to zinc, but not the other way around.¹⁰

As these micronutrients have the capability to interact when supplemented given together, it is important to assess the biochemical and functional evidence from clinical trials before supplementation policies are established.

In the present study, we try to find whether simultaneous administration of zinc and iron can raise haematocrit level higher than what is achieved with iron alone. As well as we assessed the zinc status in both supplemented groups.

Methodology

This study was carried out between 1st of November 2005 to 31st of October 2006. A single blind randomized clinically-controlled trial was conducted in Kabat Primary Health Center in Dohuk city, in which anemic singleton pregnant women in their completed 12 weeks of gestation were enrolled.

All recruited patients were moderately anemic and their hemoglobin was less than 10g/dl.¹¹

Questionnaire regarding age, parity, past medical and surgical history, obstetrical and gynecological history was recorded.

Thoroughly, clinical examination was performed at the time of registration including height, weight, medical assessment and full obstetrical examination.

At enrollment, subjects were randomly assigned into two groups.

The 1st group (A) received daily supplements of 120mg iron as (Ferrous sulfate). The 2nd group (B) received the same amount of iron with 22.5 mg of zinc as (zinc sulfate).

Supplementation started at 12 weeks of gestation and continued up to 36 wk gestation. The aim was to avoid the side effects of the medication at the first trimester and to have uniform results. The tablets were given out monthly during the ante-natal visits with the recommendation to take the tablets daily, between meals, with lemonade, water, or a juice rich in ascorbic acid.

A total number of 132 pregnant women was initially enrolled in the study. Ten patients had dropped out of the study because they have changed their place of stay, eighteen declined to participate shortly after enrolling and four had abortion. So, we have succeeded to assign 100 patients in this study.

Three venous blood samples were collected from each recruited patient.

The first blood sample was obtained at 12 weeks of gestation. The second and the third samples were withdrawn at 24 and 36 completed weeks of gestation, respectively. The amount of blood withdrawn was 10 ml.

Hemoglobin concentration was measured by the cyanomethemoglobin method. This was done by using a kit Arcomex/Amman/NO.11110.

PCV was measured by usual microhaematocrit method. The above two procedures needed 2ml of blood.

The rest of the blood (8ml) was allowed to clot for 15-25 minutes and then centrifuged at 3000 rpm for 15-20 minutes. The clear serum was separated and the collected samples were used to estimate the levels of serum iron, total iron binding capacity and serum zinc.

Iron and TIBC were assayed by using a kit from Biolabo /France/ No.92108, 92308. Estimation of serum zinc was carried out by a kit provided by Giesse/ Italy /NO.0033.

Collected data were analyzed by SPSS software; independent t-test was applied.

Results

The selected characteristic features of the participants are presented in Table (1). There were no significant differences between the two treated groups at enrollment, with regard to parity, weight, height and body mass index (BMI in kg/m²). However, women consuming supplements containing iron and zinc were significantly younger than those who received

only iron.

Table (1): Characteristic features of the study groups.

<i>Characteristic</i>	<i>Iron + zinc (n=50)</i>	<i>Iron alone (n=50)</i>
<i>Age(y)</i>	23.54±5.719	26.32±5.343
<i>Height (cm)</i>	1.591±0.046	1.589±0.047
<i>Weight (kg)</i>	61.644±4.281	61.648±5.03
<i>BMI (kg/m²)</i>	24.395±2.176	24.003±4.265
<i>Parity (%)</i>		
<i>0</i>	22%	18%
<i>1-4</i>	58%	62%
<i>>4</i>	20%	20%

The initial readings were described in Table (2). The first blood sample was considered to be the base line assessment for the next readings.

At the end of the first trimester (first blood sample) the recruited patients had hemoglobin level < 10 g/dl, with a Mean equal to 9.179 ± 0.375. The Mean PCV was 27.99 ± 1.63. The serum iron status was low, with a Mean of 42.166 ± 4.572. Normal iron serum range's between 50-170 µg/dl.¹²

In general, the zinc values have showed mild-to-moderate zinc deficiency. The Mean zinc level was 62.121 ± 3.658. The normal range of zinc is between 70 – 114 µg/dl.¹³

At the end of 24 weeks gestation, a desirable response was obtained in hemoglobin and PCV levels among both groups particularly group B, which was statistically significant (P <0.02), (P < 0.01), respectively.

At the same time, it has been noticed that there was an increase in serum iron level in both groups. However, the difference was statically insignificant. (Table 3)

By completing 36 weeks gestation, the hemoglobin and PCV have shown an excellent improvement in their values. Although group B (Mean 12.26 ± 0.799) had a minimal higher levels than group A (Mean 12.042 ± 0.9364), but it was of no considerable significance. (Table 4)

Table (2): At 12 weeks gestation sample reading.

Treatment Code	N	Mean	SEM	Sig. (2-tailed)	95% Confidence Interval of the difference	
					Lower	Upper
HB1 Iron	50	9.156	0.051	0.543	-0.1957	0.1037
Iron + Zinc	50	9.202	0.055	0.543	-0.1957	0.1037
PCV1 Iron	50	27.76	0.224	0.159	-1.104	0.184
Iron + Zinc	50	28.22	0.234	0.159	-1.104	0.184
TIBC1 Iron	50	390.038	3.287	0.071	19.9082	0.8242
Iron + Zinc	50	399.580	4.059	0.071	19.9138	0.8298
Fe1 Iron	50	41.870	0.687	0.520	-2.4122	1.2282
Iron + Zinc	50	42.462	0.607	0.520	-2.4125	1.2285
Zn1 Iron	50	61.764	0.549	0.332	-2.1664	0.7384
Iron + Zinc	50	62.478	0.484	0.332	-2.1667	0.7387

SEM Standard Error of Mean

Table (3): Readings at 24 completed weeks gestation.

Treatment Code	N	Mean	SEM	Sig. (2-tailed)	95% Confidence Interval of the difference	
					Lower	Upper
HB2 Iron	50	10.530	0.0946	0.022	-0.7510	-0.0450
Iron+Zinc	50	10.838	0.0928	0.022	-0.5710	-0.0450
PCV2 Iron	50	30.42	0.260	0.010	-1.722	-0.238
Iron+Zinc	50	31.40	0.268	0.010	-1.722	-0.238
TIBC2 Iron	50	401.924	4.0931	0.404	4.9924	6.0884
Iron+Zinc	50	406.376	3.3849	0.404	4.9970	6.0930
Fe2 Iron	50	49.468	0.5228	0.063	2.7624	0.0744
Iron+Zinc	50	50.812	0.4873	0.063	2.7625	0.0745
Zn2 Iron	50	60.854	0.5593	0.000	0.5772	7.8748
Iron+Zinc	50	70.080	0.3883	0.000	0.5793	7.8727

Table (4): Readings at completed 36 weeks gestation.

Treatment Code	N	Mean	SEM	Sig. (2-tailed)	95% Confidence Interval of the difference	
					Lower	Upper
HB3 Iron	50	12.042	0.132	0.214	-0.5636	0.1276
Iron+Zinc	50	12.260	0.113	0.214	-0.5637	0.1277
PCV3 Iron	50	34.54	0.355	0.405	-1.350	0.550
Iron+Zinc	50	34.94	0.321	0.405	-1.350	0.550
TIBC3 Iron	50	407.328	4.300	0.534	-15.5050	8.0850
Iron+Zinc	50	411.038	4.102	0.534	-15.5053	8.0853
Fe3 Iron	50	56.386	0.558	0.000	-4.3154	-1.3486
Iron+Zinc	50	59.218	0.497	0.000	-4.3156	-1.3484
Zn3 Iron	50	61.494	0.552	0.000	-15.4016	-12.8224
Iron+Zinc	50	75.606	0.342	0.000	-15.4048	-12.8192

Serum Iron level had showed a significant rise in group B when compared to group A (P< 0.001). (Table 5)

It was obvious in table (6) that the level of zinc raised significantly with the progress of treatment

in patients who received combined supplementation (P< 0.001).

Concerning zinc status in group A, it was found that there was a considerable significant drop in its level, mainly the second reading.

Then, it started to build up again in the third reading. The improvement of the zinc status in the last reading was of significance in respect to the second reading ($P < 0.001$) but it's still far from the booking visit. (Table 7)

Although there was a relative increase in TIBC throughout the treatment course in both groups. But, the raised value was within the normal range of this primary iron-transport protein. No significant value was observed in comparison between the two studied groups. The normal value range of TIBC is between 358- 543 $\mu\text{g/dl}$.¹² (Table 8)

Table (5): Measurements of iron status.

Treatment Code	N	Mean	SEM	Sig. (2-tailed)	95% Confidence Interval of the difference	
					Lower	Upper
Fe1 Iron	50	41.870	0.687	0.520	-2.4122	1.2282
Iron +Zinc	50	42.462	0.607	0.520	-2.4125	1.2285
Fe2 Iron	50	49.468	0.522	0.063	-2.7624	0.0744
Iron +Zinc	50	50.812	0.487	0.063	-2.7625	0.0745
Fe3 Iron	50	56.386	0.558	0.000	-4.3154	-1.3486
Iron +Zinc	50	59.218	0.497	0.000	-4.3156	-1.3484

Table (6): Level of zinc in Patients who have received iron and zinc supplementation.

		Mean	N	SEM	Sig.(2-tailed)
Pair 1	Zn1	62.478	50	0.484	0.000
	Zn2	70.080	50	0.388	
Pair 2	Zn2	70.080	50	0.388	0.000
	Zn3	75.606	50	0.342	
Pair 3	Zn1	62.478	50	0.484	0.000
	Zn3	75.606	50	0.342	

Table (7): Measurement of zinc in patient received only iron supplement.

		Mean	N	SEM	Sig.(2-tailed)
Pair 1	Zn1	61.764	50	0.549	0.000
	Zn2	60.854	50	0.559	
Pair 2	Zn2	60.854	50	0.559	0.000
	Zn3	61.494	50	0.552	
Pair 3	Zn1	61.764	50	0.549	0.000
	Zn3	61.494	50	0.552	

Table (8): Measurements of TIBC levels.

		Mean	N	SEM
Pair 1	TIBC1	399.580	50	4.059
	TIBC2	406.376	50	3.384
Pair 2	TIBC2	406.376	50	3.384
	TIBC3	411.038	50	4.102
Pair 3	TIBC1	399.580	50	4.059
	TIBC3	411.038	50	4.102

Discussion

There is worldwide global agreement that micronutrients deficiencies coexist during pregnancy particularly in the developing countries.^{6, 7, 14, 15}

In fertile communities, similar to ours, the numbers of deliveries are growing fastly. So, it was essential to create antenatal programs capable of improving maternal health during pregnancy.

Clinical trials can probably deal with the expanding problems of pregnancies and participate in the improvement of their outcomes.^{16- 18} They are essential to establish the efficacy of the used medications.

This study has found that joint supplementation generally does not negatively affect the biochemical outcomes expected from individual supplementation. Even in the presence of zinc, the benefit of iron supplementation on iron indicators was significant and important.

Christa Fischer Walker et al.⁶ reviewed randomized trials that assessed the effects of iron and zinc supplementation on iron and zinc status. On the basis of these reviews, however, when zinc is given with iron, iron indicators do not improve as greatly as when iron is given alone. In most of these studies, iron supplementation did not affect the biochemical status of zinc. They have clarified that, no strong evidence to discourage joint supplementation.⁶

On the contrary, our study had demonstrated a significant improvement in serum iron status seen in the combined supplemented group ($P < 0.001$).

In Mexico, the trial of Munoz EC(2000) has revealed that hemoglobin level increased in both the iron-only and iron with zinc supplemented groups by 14.0 g/L and 13.0 g/L, respectively and these were significantly greater than in the placebo group ($P < 0.05$).

Both the iron-alone ($P < 0.05$) and the iron-plus-zinc ($P < 0.0001$) groups had significant increases in plasma ferritin concentrations from baseline to post follow-up.¹⁹

These findings were coinciding to our results. Both groups in our trial had a significant increase in their hemoglobin ($P < 0.0001$) and iron indicators.

Our results were comparable to Kolsteren.²⁰ He suggested that the addition of zinc to the treatment for anemia can increase hemoglobin level and improved iron parameters more than with iron alone.²⁰

A study conducted in Iran, a country neighbor to our territory, found that there was a significant improvement in the hematological states with patients receiving iron and zinc during pregnancy in comparison to single iron therapy.²¹

In Peru,^{15, 22, 23} 1295 pregnant women were assigned to different daily supplementations. There were no differences between the groups supplemented with iron versus iron and zinc on maternal hemoglobin or serum ferritin concentrations throughout the gestation.

An important observation was noted in our sample, regarding zinc statues. In contrast to zinc replete patients, maternal serum zinc concentrations declined more rapidly as evidenced by significantly lower serum zinc concentrations in iron supplemented patients. Laura E Caulfield had clarified substantially the same findings.¹⁵

Plasma zinc concentration in pregnant women is different from that in the non-pregnant state. It begins to decline in early pregnancy and continues to decline till term, when it is about 35 % below the concentration found in non-pregnant women. The decline has been attributed to haemo-dilution, decrease in levels of zinc binding protein and active transport of zinc from the mother to the fetus.²⁴

Similar findings were observed by Carmen.²⁵ In his study, plasma zinc concentrations decreased

25% from early pregnancy to late pregnancy ($P<0.01$) and returned nearly to the early pregnancy concentration at early lactation.²⁵

O'Brien KO²⁶ found that iron supplementation during pregnancy and lactation may have an effect on zinc absorption. In their cross-sectional studies done during pregnancy, zinc absorption was significantly lower in iron-supplemented women than in non-supplemented women.²⁶

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تأثير المكملات المركبة في الحديد والزنك على الحوامل المصابات بفقر الدم مقابل جرعات الحديد بشكل منفرد في دوهوك

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الملخص

الخلفية: المكملات المركبة من عنصرَي الزنك والحديد خلال الحمل قد تكون فعالة في محاربة العوز في هذه المغذيات الدقيقة.

الهدف: تهدف الدراسة إلى تقييم أثر المكملات المركبة من عنصرَي الزنك والحديد بدلاً من الحديد بمفرده على الحوامل المصابات بفقر الدم.

التصميم: تجربة على مجموعة المراقبة الوحيدة التي أختيرت بعشوائية.

ظروف التجربة: تم تنفيذ الدراسة في منطقة كردستان، مدينة دوهوك، العراق ابتداءً من 2005/11/1 وحتى 2006/10/31. 100 امرأة حامل مصابة بفقر الدم واللواتي أكملن الثلاثة شهور الأولى من الحمل تم تحديدهن للتجربة وتقسيمهن عشوائياً إلى مجموعتين؛ تم تزويد النساء في المجموعة الأولى A بجرعة مقدارها 120 مغ من الحديد يومياً؛ بينما حصلت المجموعة الثانية B على 120 مغ من الحديد مضافة إلى 22.5 مغ من الزنك. استمرت التجربة لمدة 6 شهور تم خلالها أخذ 3 عينات وريدية من الدم.

النتائج: في بداية التجربة، تم أخذ عينة دم أساسية من الجميع، حيث خضعت للتحليل لقياس نسب الهيموغلوبين، و PCV، ونسبة الحديد في المصل، والنسبة الكلية الاستيعابية للحديد في المصل، ونسبة الزنك في المصل. ثم تم أخذ عينتين أخريين من الدم كل 3 أشهر. حللت البيانات التي جمعت بواسطة برنامج SPSS للإحصاء الحاسوبي، ثم تطبيق اختبار (t-test) المستقل. أشارت نتائج التحليل أن نسب الهيموغلوبين و PCV، والحديد في المصل قد تأثرت بشكل ملحوظ في كلتا المجموعتين ($P < 0.001$).

هناك تحسن ملحوظ في نسبة الحديد في المصل بالنسبة للمجموعة الثانية B ($P < 0.0001$)، بينما لوحظ حصول استجابة إيجابية في مستويات الهيموغلوبين و PCV في أفراد المجموعة B بعد مرور 3 أشهر على التجربة. ومع ذلك لم يشكل ذلك فرقاً مؤثراً بين المجموعتين عند نهاية الدراسة. وأيضاً لوحظ حصول ارتفاع مستدام ذو أهمية في مستوى الزنك في المجموعة B ($P < 0.00$). بينما على العكس من ذلك، لوحظ حصول انخفاض في مستوى الزنك عند المجموعة A، خاصة في الأشهر الثلاثة الأولى من التجربة. ولكن بعد ذلك بدأ مستوى الزنك بالارتفاع تدريجياً مرة أخرى ليظهر تحسناً ملحوظاً بالنسبة للقراءة الثانية؛ ولكنه مع هذا لم يصل إلى القراءة الأولى منذ بداية التجربة.

الخلاصة: بينت الدراسة بوضوح فعالية العلاج بالمكملات المركبة للحوامل المصابات بفقر الدم حيث ساعدت على تحسين مستوى الزنك خلال فترة الحمل.

الكلمات الدالة: المكملات المركبة من الحديد والزنك، الحديد بمفرده، الحوامل المصابات بفقر الدم، دوهوك.