

Copper and Zinc status in women with unexplained infertility

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الخلاصة

يعتبر الخارصين من أكثر العناصر التي تمت دراستها بما يتعلق بحالات العقم عند الذكور والإناث, حيث تم تثبيت العلاقة بين نقص الخارصين مع الكثير من حالات العقم. تم إجراء هذه الدراسة العشوائية القياسية في مركز معالجة العقم في مستشفى السامرائي في بغداد لتقييم التناسب بين مستويات الخارصين والنحاس في مصل الدم لدى النساء اللواتي يعانين من العقم غير المسبب, حيث تم تقييم مستوى كل من النحاس الخارصين في مصل الدم لستة وعشرون امرأة ممن يعانين من العقم غير المسبب وفي عشرين امرأة أخرى من النساء الطبيعيات كمجموعة سيطرة , باستخدام مطياف الامتصاص الذري. أظهرت النتائج وجود انخفاض معنوي في مستوى النحاس الطبيعيات كمجموعة سيطرة مقارنة بمجموعة العقم غير المسبب (6.63 mol/L ± 0.24 VS 9.0 mol/L ± 0.9, P=0.01) مقارنة بمجموعة السيطرة. وعند اعتماد النسبة نحاس / خارصين كمعيار للمقارنة وجد بان هذه النسبة مرتفعة وبقيمه ذات فرق معنوي واضح لدى النساء العقيمات مقارنة بمجموعة السيطرة (10.92 mol/L ± 0.4 VS 7.81 mol/L ± 0.38, P=0.01) مقارنة بمجموعة السيطرة (1.65 ± 0.014 VS 0.86 ± 0.011, P= 0.02).

من هذه النتائج يمكن الاستنتاج بان ارتفاع نسبة نحاس / خارصين في مصل الدم قد تكون عاملاً مسبباً مهماً في الفسلجة المرضية لحالة العقم غير المسبب , وان التدخل العلاجي لتصحيح هذه النسبة من خلال استخدام الخارصين بجرعات علاجية قد تكون ذات فائدة مما يعطي أملاً جديداً لعلاج هذه الحالة.

ABSTRACT

Zinc is the most widely studied element in term of fertility in both men and women; and zinc deficiency was reported to be associated with infertility. This prospective, randomized controlled study was conducted in the Infertility and IVF center, AL-Samarai Hospital Baghdad-Iraq, to evaluate the level of Cu/Zn ratio in the serum of women with unexplained infertility. Serum levels of copper and zinc were evaluated in twenty six women with unexplained infertility, and in twenty normal women served as control, using atomic absorption spectrophotometer. serum Zn levels were significantly lower compared to control group (6.63 mol/L ± 0.24 VS 9.0 mol/L ± 0.9, P= 0.01), serum Cu levels were significantly higher compared to controls (10.92 mol/L ± 0.4 VS 7.81 mol/L ± 0.38, P=0.01), Cu/Zn ratio was higher in infertile group (1.65 ± 0.014 VS 0.86 ± 0.011, P= 0.02).

From these results it was concluded that the increase in Cu/Zn ratio may have an important etiological role in the pathogenicity of unexplained infertility, and therapeutic intervention in this respect may be beneficial in the treatment of this condition.

INTRODUCTION :

Zinc is an essential element in the nutrition of human beings and animals. It is essential element for many biological functions including protein synthesis, cerebral function and stimulation of growth⁽¹⁾. Also, it has a therapeutic role in preventing prostatitis and treatment of menstrual irregularities and impotence⁽²⁾.

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It plays an important role in the regulation of gene function and immune responses⁽³⁻⁶⁾. Zinc is the most widely studied nutrient in terms of infertility in men and women, and zinc deficiency was reported to be associated with infertility⁽³⁾. It is found to be important in the homeostasis of reproductive hormones estrogen and progesterone⁽⁷⁾. The competition between zinc and copper for intestinal absorption and protein binding sites is well known, and there is a higher probability that copper deficiency might be induced in patients receiving high daily doses of zinc for months⁽⁸⁾. In this study zinc and copper levels in the serum of women with unexplained infertility measured and compared with those in normal fertile, age matched women.

PATIENTS AND METHODS :

This study was carried out on 46 women referred to the (infertility and IVF center, AL-samarai hospital, and family planning clinic in AL-Alwyia teaching hospital, Baghdad, Iraq) and those women were divided into two groups:

Group No.1 (study group): Involved 26 infertile women of unknown causes, and from each one blood sample was collected for the measurement of serum level of free Zinc (Zn) and copper (Cu) by using atomic absorption spectrophotometry⁽⁹⁾.

Also the following information was taken from each woman involved in this study:

Full name, age, address, parity, date of marriage, age of last baby, duration of infertility, regularity of menstrual cycle, abortion, primary infertility, secondary infertility, ultra sound, Hysterosalpingography, seminal fluid analysis, last menstrual period, laparoscopy, drugs history, intrauterine insemination, and in vitro fertilization.

Group No.2 (control group): Involved 20 normal fertile women, visiting the family planning clinic before using contraceptives, and from each one blood samples, and biodata were collected as in group I for the same purpose.

In this study, Comparison of means were performed using student's t-test with P values <0.05 considered significant.

RESULTS :

Serum level of Zn and Cu were analyzed using atomic absorption, and the amount calculated according to standard solution of ZnCl₂ and CuSO₄ used for this purpose, and Cu/Zn ratio were estimated.

The data presented in (table 1) showed that serum zinc levels were significantly lower than in infertile women (group I) those compared to fertile one. (26%, P=0.01)

Whereas plasma Cu was significantly higher in the infertile women compared to the control group. (40%, P=0.01)

Cu/Zn ratio was used to compare between the trace metals status in the two groups, this was found to be significantly higher in group I compared to group II. (48%, P=0.02)

Table 1 . The mean and standard deviation of Zinc and Copper values and the ratio between these two values in infertile and fertile group

	Zinc	Copper	Co/Zn ratio
	Mean ± S.D.	Mean ± S.D.	
Infertile women	6.63 mol/L ± 0.24	10.92 mol/L ± 0.4	1.65 ± 0.014
fertile women	9.0 mol/L ± 0.9	7.81 mol/L ± 0.38	0.86 ± 0.011
	P=0.01	P=0.01	P=0.02

Both groups had the same socioeconomic status, comparable age, and all investigations of infertility did not reveal any pathological abnormality.

DISCUSSION :

In this study the results presented in table (1) clearly showed that in women with unexplained infertility, serum level of free Zn were significantly lower, and free Cu were significantly higher compared to those who are normally fertile, and this situation was reflected as impaired Cu/Zn ratio.

Zinc deficiency can interfere with fertility by disrupting menstrual cycle, due to impairment in the synthesis and secretion of two important hormones, follicle-stimulating hormone (FSH) and lutenizing hormone (LH), and oral zinc supplementation has been found to correct such impairment^(10,11).

Moreover, it has been reported that Zn plays an important role in sex differentiation, spermatogenesis, as a first direct evidence for the role of Zn in growth and development⁽¹²⁾, and specifically, it was found to be vital for the function of the reproductive organs⁽¹³⁾.

Many studies reported that decreased serum Zn levels and low Zn/Cu ratio were observed in women suffering from premenstrual tension syndrome compared to controls^(14,15).

This may give an indication that imbalance in serum copper could be the major cause of unexplained infertility⁽¹⁶⁾, and elevated level of this element may interfere with fertility in many possible ways; first, excessive amounts of copper may interfere with neuronal signaling in CNS which are responsible for neuro-endocrine regulation of fertility⁽¹⁷⁾.

Second, excessive serum Cu out weights the role of zinc required for regulation of ovulation process.

Excessive elevation in serum copper levels in pregnant can adversely affect fetal brain growth, and subtle birth defects may occur⁽¹⁸⁾.

Supplementation of zinc gluconate 80mg/day is found to be of benefit for the function of the reproduction organs⁽¹⁹⁾.

In conclusion, the results of this study may give an indication about the involvement of zinc deficiency and/or copper overload as an important etiological role in the pathogenicity of unexplained infertility and therapeutic intervention with zinc supplement in a suitable formula may be beneficial and might give a promise in this respect.

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