

Serum Zinc and Copper Changes in Male Infertility

التغيرات في مستوى الخارصين والزنك في الدم للرجال العقيمين

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المستخلص:

الهدف: تهدف الدراسة الحالية الى التعرف على العلاقة بين العناصر النادرة مثل الزنك والخارصين وعملية نشوء النطف وحيويتها وحركتها. **المنهجية:** تم جمع نماذج مصل الدم والسائل المنوي من (١٢٠) مريضاً يعانون العقم وبأعمار تراوحت ما بين عشرين وخمسين سنة، من الذين كانوا يراجعون معهد أبحاث الأجنة وعلاج العقم / جامعة بغداد، بالإضافة إلى (٣٠) رجلاً خصيباً استخدموا كمجموعة مقارنة، للفترة ما بين شهر حزيران إلى نهاية شهر تشرين الأول من عام ٢٠٠٤.

النتائج: صنفت نتائج السائل المنوي للذكور العقيمين اعتماداً على الحد القياسي لمنظمة الصحة العالمية (WHO) لعام 1999، إلى اربعة مجاميع: المجموعة المصابة بوهن النطفية (A) والمجموعة المصابة بوهن وتشوه النطفية (AT)، مجموعة قلة مع وهن وتشوه النطفية (OAT)، ومجموعة اللانطفية (AZOO). وكانت كل مجموعة مكونة من (٣٠) مريضاً. استخدمت عينات مصل الدم لقياس تركيز كلاً من الخارصين، النحاس، أظهرت الدراسة أن هناك نقص عالي المعنوية في تركيز الخارصين في مصل الدم لمختلف مجاميع مرضى العقم مقارنة بمجموعة السيطرة. وقد ظهرت زيادة طفيفة في تركيز النحاس في مختلف مجاميع العقم مقارنة بمجموعة السيطرة. مع تقدم العمر أظهرت جميع مجاميع العقم بالإضافة إلى مجموعة السيطرة، وجود انخفاض طفيف في تركيز الخارصين تقابلها زيادة طفيفة في تركيز كل من النحاس.

التوصيات: توصي الدراسة بضرورة اعداد دراسة اخرى يتم من خلالها قياس مستوى العناصر النادرة مثل الزنك والخارصين بين مصل الدم والسائل المنوي للرجال العقيمين.

Abstract:

Objective: The aim of this study to detect the correlation between trace elements such as zinc, copper and spermatogenesis, sperm viability and motility.

Methodology: Serum and semen samples were collected from one hundred twenty patients with age ranged (20-50 years) attending the high institute for Embryo Research and Infertility Treatment/ Baghdad University, in addition to thirty fertile males their age comparable to that of patients. The period of this study was from June 2004 until the end of October 2004.

Results: The result of routine seminal fluid analysis of all infertile males was divided according to WHO, (1999) limit into four groups: Asthenospermia(A), Asthenoteratospermia(AT), Oligoasthenoteratospermia OAT and Azoospermia(Azoo), each group includes thirty patient. Results showed highly significant decrease in serum zinc concentration in different infertile groups compared to control group, and a slight increase in serum copper concentration in different infertile group. With advancing age, all the infertile groups, as well as the control group, had a slight decrease in serum concentration of zinc, and a slight increase in serum copper concentration.

Recommendations: Further studies are needed to evaluate the levels of different biochemical parameters in seminal plasma of different infertile groups.

Keywords: Zinc, Copper , and Male Infertility.

Introduction:

Male infertility, the inability of a man to produce a pregnancy in a woman, is often caused by measurable defects in sperm function or sperm concentration⁽¹⁾.

Approximately 20 % of cases of infertility entirely due to a male factor, with an additional 30 % of cases involving both male and female factors⁽²⁾, therefore, roughly one half of infertile unions involve male factor infertility⁽³⁾. Sperm concentration may be declining worldwide over the last half century which may be related to increase of stress, lifestyle changes and environmental contaminates such as heavy metals, pesticides and hormone altering chemicals⁽⁴⁾.

On the other hand, certain substances such as zinc, calcium, magnesium and copper play an essential role in spermatogenesis and fertility⁽⁵⁾. These elements called mineral elements which are frequently classed as either macronutrients or micronutrients (trace elements), depending on the amount of each that is needed in the diet⁽⁶⁾. A large number of trace elements are recognized as essential sperm nutrients, they act independently or together in human sperm metabolism⁽⁷⁾. Dietary requirement of most of them are met by balanced diet, but certain population groups and specific diseases are likely to be associated with deficiency of one or more of those trace elements^(8,9).

So, according to the relationship between zinc and copper with the correlation between these elements and the spermatogenesis, sperm viability and motility, the aim of this study is to find the role of serum zinc and copper changes among different infertile groups in comparison with fertile men.

Methodology:

Serum and semen samples were collected from one hundred twenty patients with age ranged (20-50 years) attending the high

institute for Embryo Research and Infertility Treatment/ Baghdad University, in addition to thirty fertile males their age comparable to that of patients. The period of this study was from June 2004 until the end of October 2004.

Routine seminal fluid analysis was done and the result of seminal fluid analysis of all infertile males was divided according to WHO⁽¹⁰⁾ limit into four groups: Asthenospermia(A): Percentage of normal sperm motility < 50 %, Asthenoteratospermia(AT): Normal sperm motility < 50 % and normal sperm morphology < 30 % ., Oligoasthenoteratospermia(OAT): Sperm concentration < 20 million / ml , Normal sperm motility < 50 % and normal sperm morphology < 30 % . , Azoospermia(Azoo) : No sperm in the ejaculate., each group includes thirty patient.

The serum samples were analyzed for zinc & copper by flame atomic absorption spectrophotometry (Shimadzu AA646)⁽¹¹⁾.

Patients were evaluated by full medical history to exclude any existing systemic diseases that may affect the parameters to be diagnosed particularly diabetes, hypertensive, liver disease, renal disease, cardiac disease and chronic drug intake, otherwise the patient was excluded from this study.

Computerized statistical analysis were performed using SPSS (statistical package of social science), version 10.5. Frequency distribution percentage and mean \pm standard error of the mean (S.E.M.) or selected variables were done first. The statistical significance of difference in the mean between more than two groups was assessed using one way analysis of variance (ANOVA) test .P value less than the point 0.05 level of significance was considered statistically significant⁽¹²⁾.

Results:**Table 1.** The Changes in Mean \pm S.D of Serum Biochemical Parameters in Control and Different Infertile Groups

Groups	Zn $\mu\text{mol/L}$	Cu $\mu\text{mol/L}$
Control	14.5 \pm 1.5	17 \pm 1.6
AT	** 6.5 \pm 1.4	17.6 \pm 3.5
Azoo	** 7.3 \pm 1.06	18 \pm 2.7
A	** 7.9 \pm 1.2	18.6 \pm 1.5
OAT	** 6.3 \pm 0.9	17.2 \pm 2

* Statistical significant ($P < 0.05$).** Highly significant ($P < 0.01$).

C : Control fertile men (n = 30), A : Asthenospermia (n = 30), AT: Asthenoteratospermia (n = 30).

Azoo: Azoospermia (n = 30), OAT : Oligoasthenoteratospermia (n = 30).

The results of serum zinc concentration determination in different infertile groups A, AT, Azoo and OAT revealed that there was a highly significant decrease ($p < 0.01$) in serum zinc concentration compared to control group as shown in table (1) and Figure (1).

In relation to the age of subjects, results showed that there was a slight decrease in the serum zinc concentration in control, A, AT, OAT and Azoo groups with age increase (table 2).

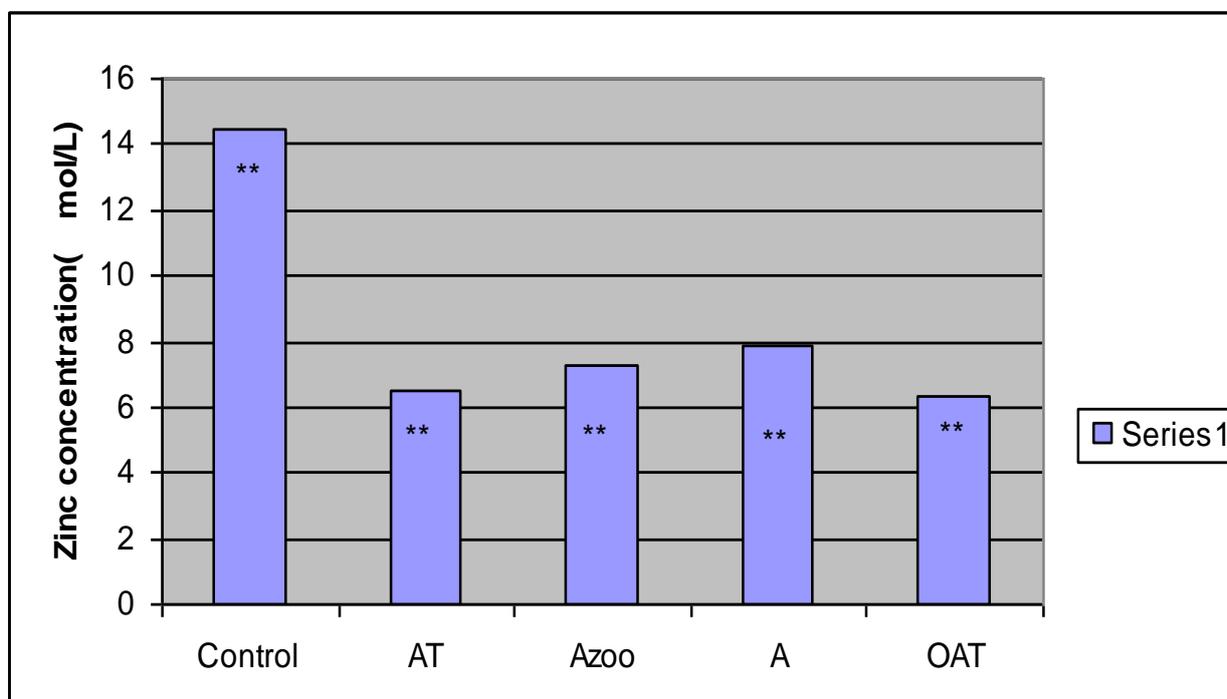
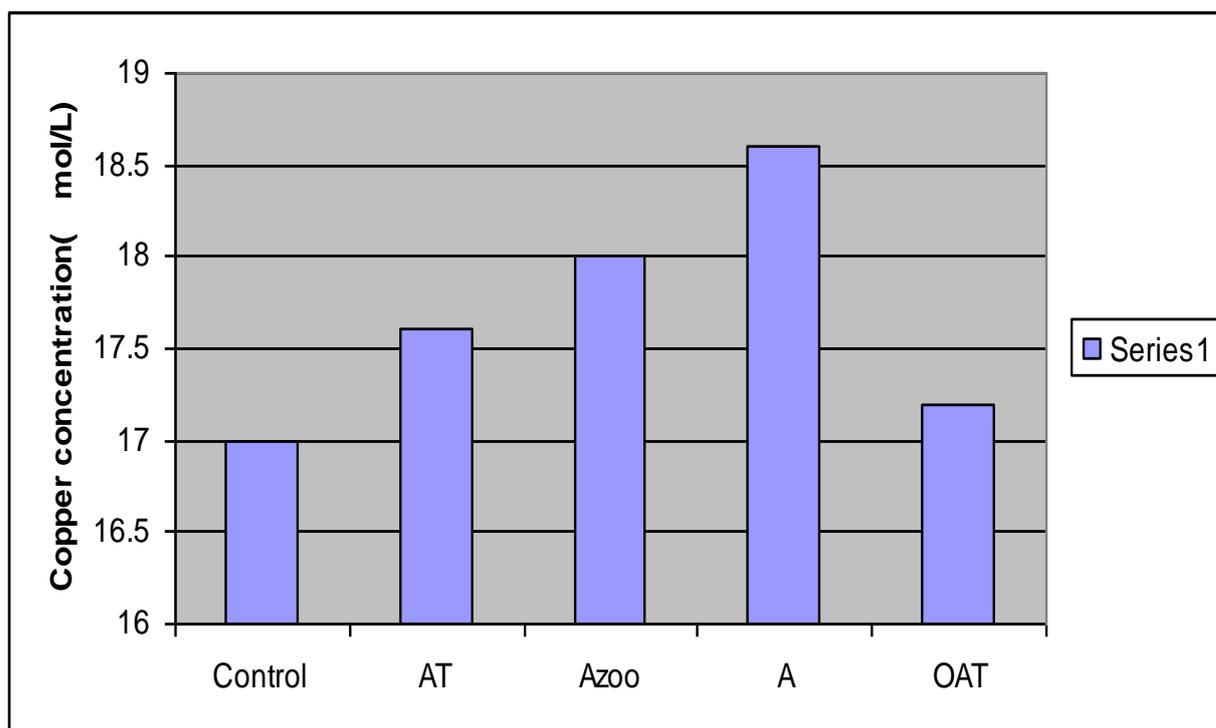
**Figure 1.** Serum Zinc Concentration of Control and Different Infertile Groups** Highly significant ($P < 0.01$).

Table 2. Difference in Mean \pm SD of Serum Zinc Concentration $\mu\text{mol/L}$ between Different Groups in Different Age Groups

Age/Years	C	A	AT	OAT	Azoo
20-29	14.8 \pm 1.5	8.2 \pm 0.8	7.4 \pm 1.1	6.5 \pm 0.6	7.5 \pm 0.9
30-39	14.7 \pm 1.8	7.9 \pm 1.3	6.5 \pm 1.3	6.1 \pm 0.9	7.4 \pm 1.2
40-49	13.8 \pm 1.2	7.8 \pm 1.5	5.8 \pm 1.5	6 \pm 0.9	7.0 \pm 1.0

In table (1) and Figure (2), there is a slight increase in serum copper concentration in all the studied groups, and it was more obviously in Asthenospermic patients followed by Azoospermic patients when compared to control group, but statistically this increment was not significant ($p>0.05$).

On the other hand, the copper concentration showed a slight increase in control, A, AT, OAT and Azoo groups with increasing age of subjects although, these increment was not significant statistically ($p>0.05$), as shown in table (3).

**Figure 2.** Serum Copper Concentration of Control and Different Infertile Groups.**Table 3.** Difference in Mean \pm SD of Serum Copper Concentration $\mu\text{mol/L}$ between Different Groups in Different Age Groups

Age/Years	C	A	AT	OAT	Azoo
20-29	16.4 \pm 1.5	17.9 \pm 1.2	16.6 \pm 3.7	16.6 \pm 1.4	17.5 \pm 2.8
30-39	17.1 \pm 1.5	18.8 \pm 1.1	17.9 \pm 3.6	17.1 \pm 1.9	18.5 \pm 2.9
40-49	17.3 \pm 1.9	19.1 \pm 1.8	17.9 \pm 3.5	17.3 \pm 2.2	17.9 \pm 2.6

Discussion:

In the present study results showed highly significant decrease in serum zinc concentration of different infertile groups when compared with control group. The possible explanation for

these findings could be related to nutritional and / or conditional factors.

Regarding nutritional factors, mild to moderate zinc deficiency common in several developing countries, because the commonly consumed staple foods have low zinc contents

and are rich in phytates (inositol phosphates), cellulose, hemicellulose and other dietary fibers which inhibit zinc absorption⁽¹³⁾. Thus, the prevalence of zinc deficiency is likely to be high in a population consuming large quantities of cereal proteins^(14,15). Reports showed that zinc deficiency known to exist in several areas of the Middle East as Egypt, Iran, Syria, and Turkey^(16, 17); the reason may be attributed to dietary habits prevailing in these countries. Similarly, in Iraq most of the population consumes large amount of bread, rice, cereal proteins, grains and vegetables which contain phytic acid and organic compounds which form complex substances with zinc, rendering it unavailable for absorption with low meat, fish and poultry product in their meals, while conditional factors including: alcoholism, malabsorption, chronic renal failure and chronically debilitated diseases are known to be predisposing factors for zinc deficiency⁽¹⁸⁾. It is clear that the mean serum zinc concentration showed highly significant decrease in all infertile groups when compared to control group. Zinc plays an important role in reproductive physiology, zinc deficiency impaired male fertility because testosterone synthesis is dependent on dietary zinc level⁽¹⁹⁾, and as the testosterone has an important role in spermatogenesis and promotion of sexual maturation at puberty⁽²⁰⁾, so the deficiency of zinc is characterized by decreased testosterone levels and sperm count^(9,21). In addition, the prostate and semen are one of the tissues and fluids which are rich in zinc, and are sensitive to zinc depletion⁽²²⁾, zinc is most critical trace mineral for male sexual function, it is in virtually involved every aspect of male reproduction including hormone metabolism, normal testicular development, sperm formation, sperm motility, prevention of spermatozoa degradation, and in sperm membrane stabilization^(9,23) and this is supported by other study that showed seminal plasma zinc concentration was significantly correlated with sperm density, motility and viability between fertile and infertile groups⁽²⁴⁾.

In our study results revealed slight increase was recorded specially with Azoo and A groups, this may be related to the reduction in the zinc concentration, since both of them are absorbed in the small intestine⁽²⁵⁾, and normally zinc inhibits copper absorption⁽¹³⁾, this gives a chance to the copper to be absorbed all mostly completely.

Age also plays a role in decreasing serum zinc concentration; this effect has been attributed to the decline of dietary zinc intake with advancing age⁽²⁶⁾. The low zinc intake in elderly people is probably related to the increase of preference to cereal proteins, decreased energy intake, low income and disease status⁽²⁷⁾. In Iraq, these factors are at an increasing rate and expected to be more prevalent, because of the economic sanction imposed by the United Nations on our country for several years. On the other hand, the copper concentration also increased in all subject groups with the increasing of age, this may be related to the reduced zinc intake. Thus, estimation of serum copper concentration could be a helpful indicator of zinc status; these findings are in agreement with other reports^(28, 29) that proved that there is an inverse relationship between serum zinc concentration and serum copper concentration in old ages.

Recommendations:

1. Further studies are needed to evaluate the levels of different biochemical parameters in seminal plasma of different infertile groups.
2. Additional studies are needed to assess the correlation between these elements and male reproductive hormones.

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