A Comparative Study of Seminal Copper Zinc, Magnesium and Manganese Levels In Fertile and Infertile Men

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FIRTİL VE İNFERTİL ERKEKLERDE SEMİNAL BAKIR, ÇİNKO, MAGNEZYUM VE MANGAN DÜZEYLERİ ÜZERİNE KARŞILAŞTIRMALI BİR ARAŞTIRMA

Geliş Tarihi, 7 Nisan 1988

SUMMARY

In order to determine the effects of trace elements on fertility potential, we measured seminal coper, zinc, magnesium and manganese concentrations of 53 infertile and 16 fertile male referred to outpatient Ciinies of Urology, Ondokuz May is University School of Medicine by means of atomic absorption spectrophotometry. In all groups zinc and magnesium had the first and second highest concentration.

A weak correlation was also observed between sperm morphology and manganese concentrations in normospermic infertile group. Manganese and copper levels were higher in infertile cases. Moreover especially in fertile group we found statistically significant positive correlation (n=/6, r=0.76) between zinc and magnesium levels. Still a weak negative correlation was found between sperm density, motility and copper levels.

Key Words: Seminal copper, zinc, magnesium, manganese, fertility potential,

T JResoarcti Med Scl V.7, N.3, 1989. 200-205

ÖZET

Ondokuz Mayıs Üniversitesi üroloji Ana Bilim Dalı Polikliniklerine müracaat eden 53 infertil ve 16 fertil hastanın séminal bakır, çinko, magnezyum ve mangan düzeylerini absorpsiyon spektrofotometresinde ölçerek bu elementlerin fertilité potansiyeline etkileri incelendi. Semende sırasıyla çinko ve magnezyum en yüksek konsantrasyonda bulunmuştur. Mangan ve bakır düzeyleri infertillerde fertillere göre daha yüksek düzeyde idi. Ayrıca çinko ile magnezyum arasında özellikle fertil gurupta istatiksel anlamlı fn-16 r=0.76) pozitif, bakır düzeyi ile sperm sayısı ve motilite, normospermik infertil gurupta da sperm morfolojisi ile mangan düzeyleri arasında zayıf negatif bir korelasyon tesbit edildi.

Anahtar Kelimeler: Semina] bakır, çinko, magnezyum, mangan, fertilité potansiyeli

T Kİ Tıp Bil Aras Dergisi c.7, S.3.1989, 200-205

The association of seminal trace elements with problems of infertility was reported by Vladesco and Bertrand (25) in the early 1900' s. Since then many controversial reports have been published on the contribution of trace elements on fertility potential (1,5,10,18,19,22,23,25,26).

As accepted worldwide (10,18,25) Concentrations of seminal trace elements vary according to dietary habits, and mineral content of the soil.

In our study, in order to evaluate the effects of seminal trace element concentrations on fertility potential, we examined semens of 16 fertile and 53 infertile men referred to Ondokuz Mayıs University School of Medicine from East Black Sea Region by means of atomic absorption spectrophotometre.

MATERIAL AND METHODS

Selection criteria of subjects included in our study:

16 fertil and 53 infertile men referred to outpatient Clinics of Urology, School of Medicine, Ondokuz Mayıs University, Samsun Turkey, between January and October 1987 were included in our study. Their marital period and ages ranged from 19 to 50 (mean 35) years and 1 to 15 (mean 5) years respectively. By the term "infertile" we mean the marriages without conception within 1 year of normal sexual life. We excluded cases with apparent urogenital infection, history of medical infertility therapy, and whose wives having sterility problems.

In order to assess seminal parameters such as sperm count, motility and morphology, specimens were examined under 250x magnification within at most I hour of collection. A verage of three measurements taken at monthly intervals were taken into consideration.

Cases were grouped according to their sperm densites.
Group 1. Fertile, 16 Cases.
Group 2. Cases with sperm counts more than 40 millions per ml, normospermic infertile 22 cases
Group 3. Cases with sperm counts 20 to 40 millions per ml. (Amelar (21). Mac Leod (14), Sherins (20) accepted this group as "normospermic") oligospermic 14 cases.
Group 4. Cases with sperm counts less than 20 milians per ml, severe oligospermic infertile group, 11 cases

We also classified the cases according to their 3 + progresisive motility and normal morphology percentages, with fertility limits being 40% and 60% respectively.

Due to scarcity of subjects (6 cases), azospermic cases weren't grouped separately. They were included in group I.

Urethral urine was examined and sterilized beforehand to detect an occult, asymptomatic prostatic infection.

Analysis of trace elements:

Specimens collected in clean plastic containers treated previously with 1 percent nitric acid were kept at 5±1°C till the day of examination. 2 ml of specimen was mixed overnight with 2 mis of concentrated nitric and perchloric acid.

Trace element analyses were carried out in Laboratories of Plant and Soil Sciences Faculty of Agriculture, Ondokuz Mayıs university in graphite furnace system single beam atomic absorption spectrophotometre.

Optic density values of sample solutions were determined for Zn, Cu, Mn, Mg at 374.7 nm, 285.2 nm. 279.5 nm, 313.9 nm wave lengths respectively and their concentrations were expressed in miligrams per I.

In order to minimize the risks of contamination, laboratory was kept clean and dust-free, specimens were collected in plastic jar cleansed with 1% nitric acid, and rubber or glass material weren't used in any stage of the experiment. Specimens were diluted with water demineralized using anion and cation holding recins.

Data obtained were subjected to Student-t test and regression-correlation analyses.

RESULTS

The results obtained are shown on table 1 and 2. In consideration of all groups, we found Zn and Mg as the first and second highest concentration. Seminal Zn, Mg, Cu, Mn, levels of fertile-and infertile men showed variations Manganese and copper concentrations were highest in group IV. (0.075*0.002 mg/1 and 0.109 0.056 mg/1 respectively (Table I). Zinc was at maximal concentariton in group 3.(74.6 30.4 mg/I) Table I).

Seminal Cu and Mn levels were found higher in infertile group (2-4) (Table I). Copper levels were significantly higher in asthenospermic cases (0.181* 0.29 mg/I vs 0.143» 0.42 mg/I) p<0.001 (Table II).

In regression - correlation analyses, especially in fertile group we found a statistically significant positive correlation between Mg and Zn concentrations (**n**©16, r=0,76) (figure 3).

Though not statistically significant, the relation between these two elements grows stronger as we go from group 2 to 4{Fig 2). In fertile group we detected a negative correlation between Cu and Z\" levels (pH0.005).

In addition a negative insignificant correlation was observed between Cu levels, and sperm density and motility in all groups. A negative correlation was also seen between sperm morphologies and Mn levels in normospermic infertile group.

DISCUSSION

Positive effects of zinc on fertility potential have been the subject of many reports (6,9,10.16). In zinc deficiencies hypophyser gonadotrophin hormone secretions such as follicle stimulating (FSH) and luteinizing hormones (LH) decrease (10), testicular atrophy and spermatogenetic arrest develop (10,22).

All of these disorders recorver with dietary zinc supplementation (6,9,15,24). Zinc also catalyses RNA and DNA biosynthesis (3). It plays an active role in cyclic adenosine mononhosphate (CAMP) catalysation of dihydrotestosterone and improves sexual potence (3,24).

Especially in fertile group some authors reported (3,9,15) a statistically significant positive correlation between sperm densities and seminal zinc concentration.

In our cases, though not statistically significant, a positive corelation was also found between these 2 **parameters.**

As **Stanwell** - Smith (22) noticed in group with **sperm densites of** 20-40 **milions**/ml, seminal **zinc** con**centration attained the highest** level. In this group

Table - I

Average Seminal Zn, Mg, Cu, Mn Concentrations in Fertile and infertile Men Expressed in miligrams per 1

	Group 1 Fertile	Group 2 >40 millions/ml	Group 3 20-40 millions/ml	Group 4 <20 millions/ml	Infertile Groups 2-4	Groups (1-4)
In	63.14+21.54	72.93+26.29	74.6+30.4	71.29±31.42	72.81+27.21	70.57+27.25
vlg	46.62+20.62	60.61+29.69	58.29+22.18	60.7 3 + 13.48	60.10+22.75	56.95+22.26
::u	0.086+0.057	0.096+0.066	0.106+0.06	0.108+0.056	0.102+0.063	0.099+0.061
Vln	0.040+0.027	0.0495+0.033	0.060+0.036	0.075±0.018	0.080+0.039	0.055+0.036

Table - II

Average Seminal Zn Mg. Mn, Cu Concentrations Grouped According to Motility and Morphology indices

	Motility <40	Percentages >40	Morphology Percentages <60	 >60
Zn	80.98+32.70	66.21 + 19.64	76.97+24.7	88.44+11.46
Mg	69.71+39.70	55.8 + 41.5	80.95±42.42	68.76+49.6
Mn	0.077±0.05	0.06 + 0.05	0.107±0.024	0.089+0.012
Cu	0.098+0.05	0.09 + 0.05	0.160+0.07	0.167+0.024

osmotically fragile sperms rupture sportaneosuly or during centrifugation, and high zinc content of sperms (18.22) (1429 ug/ml as compared to 122.9 ug/1 seminal fluid raises the seminal concentration.

In addition, zinc prevents the excessive oxidation of thiol chains of caudal keratinoid protein and thus stimulates sperm motility (10,15.23). We, in accordance, with Skandhan (25) Umeyama (25) and Wood (26), didn't notice statistically significant correlation between sperm motility and seminal zinc levels.

Zinc concentrations is asthenospermic cases were higher than normomotile cases (8.98+32.70 vs. 66.21+19.64 mg/1.).

Spermatotoxic effects of copper have been known for a long time. It has been used as a contraceptive material in intrauterine device and intravas contraceptive in animal experiments (12). Folowing intravenous copper administration in rats a decrease in hypophyser luteinizing hormone relaese leading to falling testosterone levels had been observed (10). Normalization of seminal copper levels after human chorionic gonadotropin injections supports previous observations (1,10). Morever, copper inactivates delta-3-ketosteroid isomerase, one of the catalysers of testosterone synthesis, ensuing in infertility (4).

All these observations anticipate higher seminal copper concentrations in infertile men.. In accordance with Skandhan (21), Pleban (18), Umeyama (25)

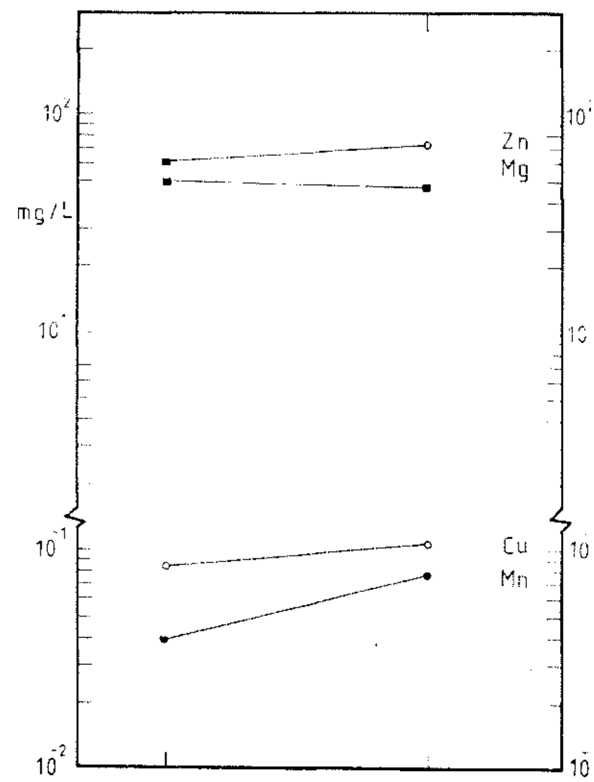
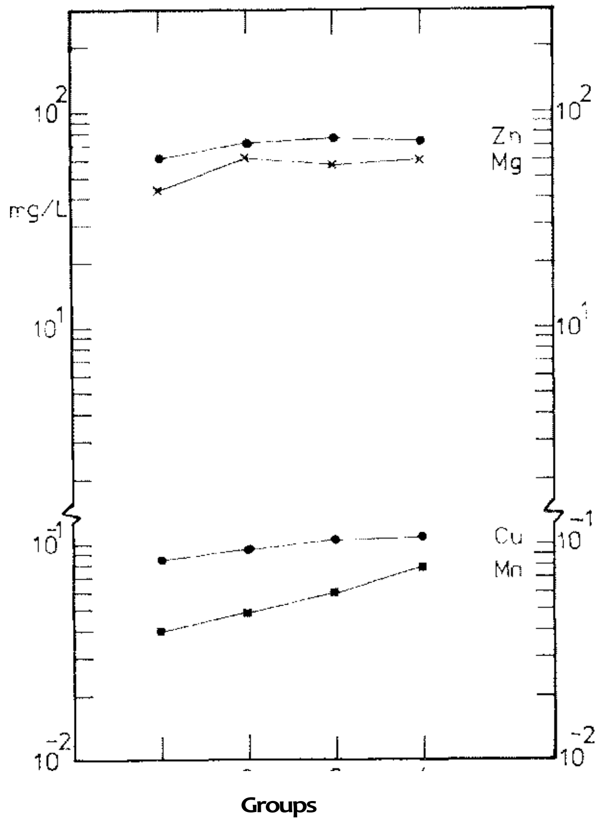


Figure: 1



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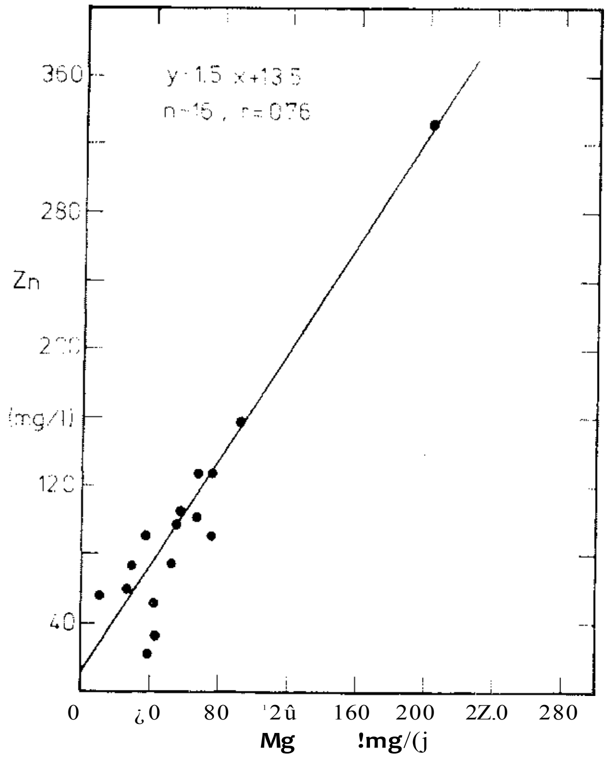

Figure : 3

copper concentrations in infertile group (2-4) were higher with respect to fertile group (0.103±0.06 vs. 0.086±0.057 mg/l).

As reported by Stanwell-Smith (23) copper reachead its highest value in oligospermic infertile group (0.106+ 0.06. mg/l).

Besides in asthenospermic cases average seminal copper level was higher than normomotile group reflecting spermatotoxic property of this trace element (0.098* 0.058 vs 0.090+ 0.05 mg/l) (Table 2).

We also noticed a negative correlation between seminal copper and zinc levels in infertile men ($p< 0.001$). In fact copper and zinc antagonize each other's resorption from the intestinal lumen at the receptor level (8,9.17). In support of this argument, Cousins (7), Fischer (9), Oestreicher (17) managed to reduce intestinal resoption of copper by dietary zinc supplementation.

Manganese plays a vital role in oxidativephosphrylation of testosterone precursor, cholestero-Ie (1). It also enters in the synthesis of piruvate corboxylase, an active enzyme of glyconegonesis (10). It also facilitates protein synthesis by activating RNA polimerase (1,10,18). In maganese deficiency, oligo-and asthenospermia due to seminifer tubuli degeneration, atrrophy of accessory sex organs, sterility, loss of libido, and spermatogenetic arrest are commonly observed (10). Indeed following manganese supplementation, serum testosterone rises, to normal levels (1).

In manganese deficiency a rise in amorphous sperms is the result of defective oxidative process and detonation of spermic nuclear RNA structure (10). In group with higher amorphous sperm percentage, seminal maganese concentaritons were found increased with respect to the overall average value (0.107.125± 0.0688 mg/l) vs. (Table 2).

Magnesium acts as a catalyser in synthesis of adenosine triphosphate at the sperm organel membrane level (23) and in that way it enhances sperm motility (23). Among the trace elements magnesium stimulates sperm motility at the maximum (16). Therefore it is expected to be higher in fertile men (25). In our cases, in accordance with the previous reports, seminal magnesium levels were observed to be increased in normomotile group in comparison with asthenospermic cases (69.71+39.71 vs 72.76 mg/l).

Detrimental effects of higher zinc concentrations in semen have been reported previously (10,11,13, 23) Holland (11), Henkin (10), Stegmayr (23) had found out that higher seminal zinc levels inhibited sperm motility.

Kvist (13) claimed that zinc inhibits sperm motility by preventing decondensation of sperm nuclear chromatine. Besides in prostatic inflammations prostate organel factor (forward motility protein) increases the passage of zinc across sperm mebrane in order to inhibit motility (15,21).

Especially in normospermic infertile group we observed a negative correlation between seminal zinc concentrations and leukocyte counts (r=-56p<0.01). Paradoxically low levels of zinc in normomotile cases (66.21 19.64 mg/1 vs. 80.97 32.70 mg/1) may be due to an asymptomatic occult prostatic infection. Indeed Marmar (15), Nelson (16) confirmed bactericidal activity of zinc against gram positive and gram negative bacteria, They found extremely low seminal zinc concentrations in cases of bacterial prostatitis (<50 ug/ml vs normal 350 ug/ml).

We noticed a statistically positive correlation between zinc and magnesium levels in fertile group as reported by Umeyema (25) (Figure 3).

Though not statistically significant, a weak positive correlation still exists between the two elements in infertile group (Figure 2).

This synergism between magnesium and zinc seems to reflect secretory function of prostate and vesiculoseminalis rather than fertility potential (25). In reality prostate contains the maximum amount of zinc in the body indeed prostate is the depot organ of zinc (720 mg Zn per 100 gm dry weight) and regulates seminal zinc level so as to keep its concentration in balance with the other trace elements (25).

In Conclusion, though seminal, zinc, magnesium, maganese and copper concentrations reflect some features of semen, they are far from being a sound, reliable index of fertility potential and they must be evaluated in context with the other spermiogramic parameters.

Acknowledgements: We would like to express our deepest gratitude to Hikmet Acuner MD: Giilsevin Şeşen MD in Özel Samsun Tıbbi Tahlil Laboratuvarı and Mustafa Aydın in Computer Center Ondokuz Mayıs University for their close cooperation.

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