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Randomized Correlations of Trace Elements with Reproductive Hormones and Semen Quality among Sudanese Infertile Males

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Abstract

Background: The concentrations of trace elements significantly correlate with azoospermia, oligospermia, and abnormal sperm motility among infertile males. The reproductive hormones levels in male infertility reflect a positive relationship with trace elements concentrations in seminal and serum specimens; and specifically strongly correlated between the luteinizing hormone and seminal cadmium in azoospermic patients.

Objective: To correlate the serum and semen concentrations of trace elements with reproductive hormones and semen quality among infertile Sudanese males.

Materials and methods: Using atomic absorption spectrometry (AAS), the levels of the trace elements ZN, Cu, Co, and Se were estimated in semen and serum of 500 infertile married males. From these 150 were azoospermic, 150 were oligospermic, 100 were asthenozoospermic, and 100 had abnormal sperm morphology. **Another 100 fe**rtile, married males (normospermic) were estimated for these trace elements as a control group.

Results: In serum the levels of the trace elements were variable, but they were within the normal ranges when compared with control group ($p > 0.5$). However, in seminal plasma the Zn level was significantly reduced among all infertile groups ($p < 0.05$), Se level was also significantly reduced in both azoospermic and oligospermic males ($p < 0.05$). On the other hand, Co and Cu levels in semen showed no significant variations. Furthermore, the serum concentrations of the elements in the test group were higher than their concentrations in semen except for Zn level which was higher in semen than serum. Positive correlation was noticed between the Zn level and the seminal volume among azoospermic males, and significant correlation was also observed between the liquefaction time and the seminal Zn level among oligospermic males ($r < 0.05$). Another significant correlation was observed between the follicle stimulating hormone (FSH) and the seminal Se level among both oligospermic and asthenozoospermic males. Again significant correlation was noticed between the seminal Zn level and both the luteinizing hormone (LH) and the prolactin hormone among oligospermic males ($r < 0.05$).

Conclusion: The concentrations of the trace elements are higher in serum than semen except for Zn, which is higher in semen. There is a strong correlation between seminal trace elements

levels and seminal abnormalities and reproductive hormones among infertile patients.

Key words: Trace elements, Reproductive hormones, Semen quality, Infertile Sudanese males.

Introduction

Trace elements are needed in the range of micrograms to milligrams per day to maintain good health. They are functional components of numerous metabolic events. They have structural, physiological, catalytic and regulatory roles in the human body[1].

Trace elements can be essential or non-essential. An essential trace element is absolutely necessary for life. Deficiency or absence of such an element may cause severe function alteration and may eventually lead to mortality. Zinc has close interrelationships with the endocrine system, and is essential for normal growth, reproductive function, thyroid function and glucose metabolism[2].

Zinc deficiency in rats may lead to atrophy of the seminiferous tubules, failure of spermatogenesis and decreased testosterone secretion. Zinc deficiency also impairs the responsiveness of Leydig cells to gonadotrophins and may cause primary hypogonadism in humans as well as in experimental animals[3].

Zinc has many biologically significant interactions with hormones. It plays a role in the production, storage, and secretion of hormones as well as affecting the effectiveness of receptor sites and end-organ responsiveness. Among the most notable effects of Zn deficiency on hormone production and secretion are those related to testosterone, insulin and adrenal corticosteroids[4].

Selenium is one of the least abundant and most toxic of all essential elements. Selenium is vital for maintaining the integrity of sperm mitochondria[5]. Selenium deficiency leads to a reduced testicular growth[6]; and impairs the reproductive process in all animal species[7]. Cobalt is widely distributed in the human body, and its biological function is limited to vitamin B12 formation. It is present as a cobalt complex in cyanocobalamin[1].

The object of this study is to estimate the concentration of the trace elements: zinc (Zn), copper (Cu), cobalt (Co), and selenium (Se) in serum and semen of infertile Sudanese males, and to study their effects on fertility hormones and spermogram.

Materials and methods

This was a case finding, prospective, hospital and laboratory-based study. It is also a comparative, cross-sectional, quantitative study. 500 infertile males were enrolled in this study that was carried out in Khartoum (Sudan) within a period of two years. The patients studied were infertile males; divided into four groups: 150 azoospermic, 150 oligospermic, 100 asthenozoospermic, and 100 teratozoospermic patients. Control group included 100 fertile males. A structured interview was conducted to collect demographic and reproductive history. A complete physical and andrological examination was carried out.

Semen samples were obtained by masturbation. Part of the seminal fluid was centrifuged to separate spermatozoa and decanted into a metal-free polypropylene container for measurement of the trace elements. Semen analysis was performed as per the guidelines of World Health Organization (WHO). In both serum and seminal fluid, four trace elements: zinc (Zn), selenium (Se), copper (Cu), and cobalt (Co) were measured by atomic absorption spectrometry (AAS) with Zeeman-background correction method. Analytical quality control was performed daily by analyzing three certified, reference trace elements samples. Settlement and calibration of AAS were made with blank and working standards. Samples and control specimens were analyzed according to the procedure described in 1996 by Bishop and his co-workers[1]. Serum reproductive hormones were assayed by the enzyme-linked immuno-sorbent assay (ELISA).
Most of the data were expressed in mean, standard error, and standard deviation. Analysis was done by student t-test program, one-way analysis of variance (ANOVA), and coefficient of correlation (r) with a significance fixed at $p = 0.05$.
Complete information regarding risk factors was given to all patients under the study without any concealment what so ever. Confidentiality of information obtained from patients under the study was maintained. Valid consent of patients under the study was taken. Results of samples collected were donated to all patients included in the study and some sample results were dispatched to patients' physicians for treatment. Approval to run the study was obtained from Al Neelain University (Khartoum, Sudan). Approval to collect the samples was granted by the authorities of the different hospitals and centres included in the study.

Results:

Five hundred Sudanese infertile males were enrolled in the study. They were divided into four groups, according to the result of semen analysis as follows:
* Azoospermic males (had no sperm in their semen even after centrifugation).
* Oligospermic males (had sperm density < $20x10^6$ per ejaculation).
* Asthenozoospermic males (had sperm motility < 30% after 2 hours examination).
* Teratozoospermic males (had more than 35% deformed sperms).

Control fertile males (had normal spermogram and had fathered a child during the last 2 years).
Duration of infertility ranged from 2-15 years among azoospermic patients, from 4-18 years among oligospermic patients, from 3-14 years among asthenozoospermic patients, and from 2-11 years among teratozoospermic patients.
Significant correlation was noticed between seminal zinc level and LH, prolactin, and testosterone in oligospermic patients. Seminal zinc level was found significantly reduced among azoospermic and oligospermic patients. Also positive correlation was noticed between seminal Zn level and seminal volume in azoospermic patients ($r = 0.08$). A significant correlation was again observed between liquefaction time and seminal Zn level among oligospermic patients ($r = 0.04$). As regard selenium, a significant serum reduction was observed among azoospermic and oligospermic patients. Significant correlation was also observed between FSH and seminal levels in both oligospermic and asthenozoospermic patients. Concentrations of cobalt and copper showed no significant variations in semen or serum. Also no significant difference was observed

between infertile patients and control group as regard the levels of seminal cobalt and copper (Table 1).

Table (1): Variances of seminal trace elements among infertile males and the control group (µg/L)

Trace elements	Control group (m ± .se)	Azoo Patients (m ± .se)	Oligo Patients (m ± .se)	Asth Patients (m ± .se)	terato Patients (m ± .se)
Co Not Sig	0.082 ± 0.01	0.083 ± 0.08	0.081 ± 0.07	0.06 ± 0.06	0.07 ± 0.01
Zn Sig	19.5 ± 0.6	11.5 ± 0.25	11.3 ± 0.27	12.6 ± 0.45	12.8 ± 0.40
Cu Not Sig	58.4 ± 2.3	58.1 ± 2.1	58.7 ± 11.6	63.8 ± 2.0	61.9 ± 1.8
Se Sig	0.28 ± 0.01	0.22 ± 0.007	0.21 ± 0.006	0.26 ± 0.011	0.25 ± 0.01

Seminal zinc level among the infertile patients had been significantly reduced, and this was markedly noticed among azoospermic and oligospermic patients (Fig. 1).

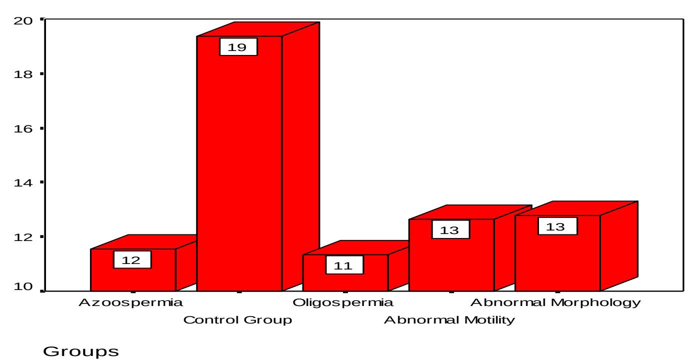

Fig. (1): Mean seminal zinc concentration among infertile patients and control group

Discussion

Pizent and his colleagues (2003) suggested that age, smoking habits, and alcohol consumption may decrease serum zinc concentration, and to a lesser extent, copper concentration[8].
In this study serum trace elements concentrations were slightly reduced among the infertile patients. Also in our study zinc deficiency was found linked with oligospermia. Generally zinc plays an important role in testicular development, spermatogenesis, and sperm motility. Supplementation with dietary zinc has been shown to improve sperm counts. Prescribing zinc supplement in combination with other nutritional supplements has been shown to improve sperm motility[2].
Mammalian spermatozoa are coated by a membrane rich in polyunsaturated fatty acids. These fatty acids are extremely susceptible to oxidative damage by free radicals or reactive oxygen species (ROS) through a process called lipid peroxidation (LPO). Lipid peroxidation damages the sperm cell membrane. It is considered to be the key mechanism of ROS that induces sperm damage and leads to male infertility . Selenium and zinc protect the human body from this toxicity and increase utilization of these elements. Selenium plays a role in the regulatory function of the testes and the accessory sex glands. Being an antioxidant, it has a protective role to spermatozoa. Selenium has been shown to improve sperm motility on its own or in conjunction with vitamin E.
Abbasi and his co-workers[9] (2000) revealed strong effect of seminal trace element on sperm production and function. Zinc is the most critical trace element for male sexual function. It is involved in virtually every aspect of male reproduction including hormonal metabolism, sperm formation, and sperm motility. In this study, decreased seminal zinc concentration was observed among the infertile males studied when compared with the control group. It is associated with decreased testosterone level that affected sperm production and function. Decreased seminal Se concentration was observed among the infertile patients and this had affected the fertilization capacity of the sperms. This effect may lead to oligospermia or even azoospermia. Reduction of seminal Zn and Se may be attributed to a decrease in testosterone level. Furthermore, Zn is utilized by the body for normal requirement and for neutralization of the toxicity of other trace elements. Zinc deficiency may impair the responsiveness of Leydig cells to gonadotrophins and may cause primary hypogonadism. Decreased Se level may impair male reproductive performance, may affect the integrity of sperm mitochondria, and may cause degenerative changes in the epididymis which is responsible for sperm maturation.
The secretary activities of the sexual, accessory glands are decreased by the concentrations of the two antioxidant seminal trace elements zinc and selenium. This phenomenon had revealed a strong positive relation between Zn level and seminal volume among the azoospermic and the oligospermic infertile patients studied. Testosterone is essential for all steps in spermatogenesis, hence reduction in testosterone concentration may affect sperm count and quality. Some studies confirmed the importance of zinc in testosterone production and its action in spermatogenesis. They observed a positive relation between testosterone and zinc levels, after feeding healthy male volunteers a zinc-restricted diet. As a consequence of zinc deficiency,

serum testosterone concentration and seminal volume had decreased per ejaculate.
The reproductive hormones levels among the infertile subjects enrolled in our study, revealed a proportional relationship with seminal trace elements levels. There is an inverse correlation between FSH and seminal Se. A decrease in Se level may cause many changes that affect FSH function and metabolism. The positive correlation of prolactin with Zn level in our study, indicates the stimulatory effect of prolactin on the prostate gland leading to secretion of Zn in semen.
The inverse correlation of LH with seminal Zn among the oligospermic subjects studied, may explain the feed-back stimulation of Zn deficiency on LH secretion by the pituitary gland. The levels of the fertility hormones among the infertile patients of our study were altered when compared with the control group. This may explain the positive effect of seminal Se and Zn concentrations on the fertility hormones, since Zn and facilitate the binding of these hormones to their receptors.
Conclusion: The concentrations of the trace elements were generally higher in serum than in semen of the patients studied, except for zinc which was higher in semen. Also the spermogram and reproductive hormones were affected by Zn and Se concentrations in semen of the infertile patients.

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