Protective Influence of Zinc on Serum LH, FSH, Prolactin and Testosterone in Male Albino Rats

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Abstract

This study was performed to determine the effect of dietary zinc on male sex hormones in male albino rats. Rats with body weights between 200-250 gms were randomly allotted into five treatment groups with 8 animals each. The control group (I) received food and water *ad libitum*. Groups II-V received 30g, 40g, 50g and 60 g of zinc sulphate respectively. At the end of the trial, the rats were euthanized and blood samples assayed for Luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin (PL), testosterone (T), progesterone and oestradiol.Serum levels of testosterone in groups II, III and IV were statistically significantly increased. We also observed significantly decreased in sperm motility and morphology in groups compared with control ($p<0.05$). It was also shown that zinc sulphate has beneficially effect on male sex hormones and sperm quality.

Keywords: zinc sulphate, male sex hormones

Introduction:

Several trace elements have been shown to be essential for testicular development and spermatogenesis. It is the second most abundant transition metal after iron and it is the only metal which appears in all enzyme classes (Boran et al, 2004). The gonads are the fastest growing tissues in the body, with zinc essentially involved in nucleic acid and protein synthesis (Hambidge, 2007). In human, zinc plays an important role in the physiology of spermatozoa, in sperm production and/or viability, in the prevention of spermatozoa degradation, and in sperm membrane stabilization (Hsieh H et al, 2014). High levels of zinc are required to maintain hormone synthesis, spermatogenesis, and sperm chromatin structure (Chib, j et al, 2000). The concentration of zinc in seminal plasma is known to influence the regulation of fertility, although the exact mechanisms are unclear (Hambidge, 2007) .Although some beneficial effects of zinc on semen have been accepted, controversies continue regarding zinc levels between different subfertile groups as well as the relationship between zinc and semen parameters(Liu,T.Y,et al 1992). Zinc deficiency cause a reduction in the structural parameters of seminiferous tubules influences serum levels of testosterone (T) and prolactin (PRL) in rats (Gilbert, 1996). On the other hand, high zinc levels have negative effects on sperm quality. Excessive zinc intake in mice has indicated a negative effect of increasing doses of zinc on sperm count and motility (Turgu G, Abban G, Turgut S, Take G, 2003). On the other hands investigation showed that the metal ion such as zinc administered in vivo decrease serum testosterone concentration and change serum concentration of pituitary hormones in animal models (Kim, 2005). In addition it has been shown that in vitro zinc administration, at high dose, can be toxic to cells and can cause their death (Bancroft et al, 1984) but other studies showed growth acceleration, testicular development and increase in FSH, LH and testosterone serum levels after zinc supplementation (Mauss et al, 1970). More over investigation showed that zinc compounds were more potent for promotion of release of gonadotropins hormone in the ovariectomized animals which pretreated by estradiol and progesterone in a treatment period for 30 days (Kochman et al, 1992). Zinc is a voltage sensitive calcium channel blocker, accumulates in central nervous system and interferes with biological function of calcium ion and since FSH, LH and testosterone secretion is dependent on calcium ion (Marubayashi et al.,1992), hence alteration in secretion of these hormones will be expectable after administration of zinc. High intake of zinc after first prescription could induce some unknown effect in body systems. Infertility is a major clinical problem, affecting people medically and psychologically (Raghuveer et al, 2010). In Southeastern Nigeria, a positive male factor alone was found in133 (42.4%) couples and female factor alone in 81 (25.8%) couples of the three hundred and fourteen couples evaluated for the cause of infertility (Ikechebelu et al, 2003).

Material and Methods:

A total of forty male albino rats weighing between 200-250gms were obtained from the Laboratory Animal Resource Unit, Institute for Medical Research (IMR) Hamadan from August 2011 to December 2013. Rats kept in a well-ventilated animal house under natural dark light cycle (temperature 27-30 C, humidity; 50-55%) and had free access to water and food for acclimatized for two weeks. Animals were housed in groups (eight per group) and their bedding was changed every two days. The experiment lasted for six weeks. Zinc as zinc sulfate ($ZnSO_4$) was added to the feed. The control and test group received 12 Kg of feed. The feed for test group was divided into four of 3Kg and each was supplemented with 30g, 40g, 50g, and 60g of zinc sulphate before it was palletized. The rats were divided in 5 with 8 rats in each group. Group I is control and access to feed and water *ad libitum*. Groups II-V were given diet with 30g, 40g, 50g, and 60g zinc sulphate respectively for six weeks. At the end of the experiment, after an overnight fasting (12-14h), all animals were weighed then sacrificed under deep diethyl ether (Merck Germany) anesthesia and blood samples were collected from cervical vessels. 2ml of blood were collected from four rats in each group. The samples were carefully introduced into lithium containers free from anticoagulant and. The blood samples were allowed to clot, retract and then centrifuged for 5minutes at a speed of 5000 revolutions per minute. The plasma was then collected, refrigerated at -20C and later assayed for Prolactin, oestradiol, progesterone, LH, FSH and testosterone using ELISA Hormone Test kits, the average was recorded. Progressivity was determined by the grading system as described by WHO (1999).

Statistical analysis

Data were analysed statistically for testosterone, LH, FSH, Oestradiol, prolactin, progesterone by two-way Analysis of Variance (ANOVA) using SPSS version 17.0 with significant level fixed at $p<0.05$.

Result

Our results showed that after six weeks of oral zinc supplementation in albino wistar rats, statistically significant increase in serum levels of follicle stimulating hormone (FSH) was observed in group II when compared with the control (0.562a IU/L). The result showed that significant decrease in Prolactin hormone (PLT) in group III (0.600ab).The results also revealed statistically significant increase in the serum levels of testosterone in groups V with 1.905a ng/ml when compared with the control with 0.36b ng/ml. The increase in testosterone levels were dose dependent as there were consistent increment in groups II and III after which the levels decreased with increasing zinc concentrations. No significant differences were observed in the other sex hormones studied ($P>0.05$) (Table 1).

Table1. Effect of Zn supplementation on male sex hormones after six weeks

	I (Control)	II (30g)	III (40g)	IV(50g)	V (60g)	SEM	P Value
LH (IU/L)	0.387a	0.441a	0.412a	0.387a	0.441a	0.0103	0.2473
FSH (IU/L)	0.562c	1.187a	0.887abc	0.675bc	1.075ab	0.0731	0.0260
PLT (IU/L)	1.187a	0.700b	0.600ab	1.100ab	1.200a	0.0714	0.1506
Prog (ng/ml)	0.150a	0.139a	0.126a	0.137a	0.134a	0.0048	0.6557
ESt (pg/ml)	22.90a	23.63a	26.90a	24.642a	22.862a	0.5949	0.1690
Test (ng/ml)	0.356b	1.892a	1.866a	1.880a	1.905a	0.1097	<0.0001

LH=Leuteinizing hormone, FSH=Follicle stimulating hormone, PLT=Prolactin, Prog=Progesterone, Est=Estradiol, Test=Testosterone.

DISCUSSION

Our study was done to assess the effects of oral zinc supplementation on male sex hormones in male albino wistar rats over a period of six weeks. The results obtained from the present study showed that statistically significant increase in serum levels of follicle stimulating hormone (FSH) compared with the control group I. The observed increase in testosterone levels in group V was less when compared with groups II and III that were given lower doses of zinc supplementation. This result agrees with the works of Ratnasooriya et al (2004) and Abdella et al (2011). The study of Karaca et al. indicated that administration of zinc supplementation increased serum FSH and testosterone values. The tolerable upper limit of 40mg of daily intake of zinc has been recommended (Institute of Medicine, 2001). Zinc supplementation activates secretion and action of testosterone (Pizent et al, 2003 and Abdella et all, 2011). Thus oral zinc supplementation within tolerable level has beneficial effects. Zinc deficiency lowers plasma testosterone levels but over supplementation has no effect on testosterone level (Blundle et al, 2013).The results also revealed statistically significant decrease in serum concentrations of Progestrone (Prog) in all groups ($P < 0.05$).The increase in serum levels of FSH and non-significant effect on Luteinizing hormone (LH) following the increased levels of testosterone may be due to the negative feedback effect of testosterone on the hypothalamus which in turn causes decrease in the secretion of FSH and LH by the gonads of the anterior pituitary gland (Grahl et al, 2007). Gonadotropins production is under the feedback control of sex hormones (Ganong, 2003). It has been observed that zinc is required for normal functioning of the hypothalamic -pituitary-gonadal-axis (Lei et al, 1976). Hypogonadism and lack of secondary sexual characteristics have been noted in severely undernourished young men and these abnormalities tend to respond to dietary supplementation of zinc (Prasad, 1991). Zinc is an essential element in some reproductive process (Mills, 1988). This work also agrees with Danscher et al (1978); Carpino et al,(1998); and Günfer et al,(2003). In conclusion, zinc supplementation within tolerable limits can improve fertility but detrimental at higher doses. Evaluation of dietary supplements containing trace elements such as zinc should form part of the management strategies in cases of infertility.

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