Zinc Supplementation in Male Infertility

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Abstract:

Background: Infertile males have been shown to have lower levels of seminal plasma zinc which have been associated with reduced levels of zinc in their blood. Supplementation improve semen parameters by improving zinc level in blood. **Objective:** .To find out whether zinc supplementation is effective in improving semen parameters in oligo-asthenozoospermic patients. **Method:** The study was carried out in the Infertility unit of the Dept of Obs & Gynae, BSMMU during the period of March 2011 to February 2012. Seventy five oligo-asthenozoospermic patients having no history of medical treatment were recruited for the study. The patients were divided into two groups by odd and even numbers. Odd numbers received tablet zinc 20 mg twice daily (Group A) and even numbers received placebo (Group B).Serum zinc level and seminal zinc level estimation were done by Graphite Furnace Atomic Absorption Spectrophotometry and semen analysis was done according to WHO guidelines (1999). Data analysis was done using software SPSS (version 16) by applying ANOVA (PostHock) and Paired Student's't' test. **Results:** Serum zinc level was low in oligozoospermic patients which showed significant improvement with zinc supplementation (A+197.83 mmol/l, P<0.01). Mean (±SD) seminal plasma zinc level showed significant improvement in group A following zinc supplementation (+942.39 mmol/L, P<0.001). The mean increase in sperm count, sperm motility, sperm rapid linear motility, sperm morphology in group A following zinc supplementation for 12 weeks was 14.83 million/ml (P<0.01), 16.30% (P<0.01), 11.96% (P<0.01), 4.26% (P<0.001) respectively, which was statistically significant. **Conclusion:** The study shows zinc deficiency affects sperm count, sperm motility, rapid linear motility and sperm morphology and with zinc supplementation there can be significant improvement in semen parameters.

Key Words: Zinc deficiency, male infertility, oligoasthenozoospermia, zinc supplementation.

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Introduction:

Infertility affects millions of couples worldwide. Male factor is responsible for almost 50% of infertility. Possible role of environmental, nutritional and lifestyle factors in having negative impact on sperm quality, has opened up the possibility of prevention and treatment of male infertility. Zinc is a very important element in the reproduction. It plays an important role in normal testicular development, spermatogenesis, and sperm motility.[1] Zinc deficiency is abundant in the community and the possible association of zinc deficiency with reduced number of sperm and impotency in men is of concern in the management of infertility. Mild to moderate zinc deficiency is relatively common throughout the world[2]. Some authors claim low zinc level in infertile population[3]. Zinc is necessary for the formation and maturation of spermatozoa. Zinc maintains testicular development, spermatogenesis and sperm motility. Low serum level of zinc is usually associated with low sperm count and also impairment of its motility. It is seen that a low serum testosterone level with oligospermia in male is closely related to zinc restricted diet, which returned to normal after zinc

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supplementation[4]. Zinc therapy reduces asthenozoospermia through several mechanisms, such as, prevention of oxidative stress, apoptosis and sperm DNA fragmentation[5].

Zinc, copper, selenium and molybdenum are involved in many biochemical processes in supporting life. The most important of these processes are cellular respiration, cellular utilization of oxygen, DNA and RNA reproduction, and maintenance of cell membrane integrity and sequestration of free radicals[6]. Zinc is highly concentrated in the seminal plasma by the addition of the prostatic secretion and acts as an antibacterial and antioxidant. Zinc deficiency is likely to disrupt the normal sperm chromatin quaternary structure in which zinc plays a role by providing stability and resistance to DNA denaturation in situ[7]. Zinc deficiency is one of the ten biggest factors contributing to burden of disease in developing countries with high mortality[8]. Improving zinc intake has important preventive or curative benefits. The World Health Organization recommends zinc only as curative intervention but the importance of supplementation and food fortification has already been highlighted. It is known that the zinc concentration of seminal plasma is very high, at over 30 times than that found in blood. Many studies have found that seminal plasma zinc concentration is positively correlated with sperm count and increase seminal plasma zinc level increases sperm motility[9-12]. However there is no such controlled trial in Bangladeshi infertile males . The present study was designed to find out whether zinc supplementation is effective in improving semen parameters of infertile men with oligoasthenozoospermia.

Methods:

This study is a descriptive type of clinical trial done in the Infertility unit of the Department of Obstetrics & Gynaecology, Bangabandhu Sheikh Mujib Medical University, Dhaka, during the period of March 2011 to February 2012.

A total of 75 oligospermic male partners of infertile couples attending the infertility unit of BSMMU were enrolled for the study. Only those male partners with oligoasthenozoospermia who were within the age range of 20-50 years and who agreed to participate in the study were included. The oligoasthenozoospermia patients receiving any supplements within previous three months or receiving any treatment for any medical disorders like diabetes mellitus and hypertension were excluded from the studie. The participants were divided into two groups by odd and even numbers. Odd numbers received zinc tablets 20 mg twice daily (Group A) and even numbers received placebo (Group B).

After taking written informed consent to participate in the study data collection was done by entering the information in preformed questionnaire. Blood were collected in metal free container from all study population for estimation of zinc in blood serum. Semen samples were collected by masturbation following 3 days abstinence. Semen analysis of both groups were done for volume, sperm count, sperm morphology and motility, according to WHO protocol (1999). Serum zinc level, seminal plasma zinc levels was measured in the Department of Biochemistry BSMMU by Graphite Furance Atomic Absorption Spectophotometer. Semen analysis was done at booking and at 12 weeks after supplementation. Thirty eight oligozospermic male partners took 20 mg zinc tablet twice daily for 3 months and 37 oligozoospermia male partners received placebo tablet (which consisted of glucose) twice daily for 3 months. The patients were blinded to whether they received the drug or placebo. Zinc levels both in semen and blood were analyzed at booking and after 12 weeks of zinc supplementation.

Data processing and statistical analysis were done using software SPSS (Statistical Package for Social Science) version 16. The test statistics used to analyze the data were descriptive statistics, ANOVA (PostHock), Paired Student's 't' test. Level of significance was considered at 0.05 and $P<0.05$ level was considered significant.

Results:

Mean (±SD) age of group A and B study subjects were 34.70±4.76 and 36.04±5.27 years, respectively. The mean (±SD) duration of marriage of group A and B subjects were7.78±4.76 and 7.06±5.30 years, respectively.

Table I shows comparison of serum zinc level of the study subjects at 0 week and 12 week. The mean (±SD) serum zinc level at 0 week for group A and B were 658.70±217.24 mmol/L and 727.78±175.05 mmol/L respectively. At 12 weeks serum zinc level of group A and B were 856.52±245.55 mmol/L and 798.15±219.91 mmol/L respectively. The mean increase was highest in group A (197.83 mmol/l) than in group B (70.37 mmol/L). Statistically, the increase of serum zinc level at 12 week from 0 week was significant in group A (P<0.001) but not significant in group B who received placebo. Group A patients who were given zinc supplementation,showed significant improvement in serum zinc level .

Table II shows the mean (±SD) seminal zinc level of group A and B subjects at 0 week were 1414.13±475.47 and 1352.78±518.89, and at 12 week were 2356.52±580.81 and 1977.78±580.01 mmol/L respectively. The higher mean increase in seminal zinc level was in group A (942.39 mmol/L) who received zinc supplementation compared to group B (625 mmol/L) who did not . The increase in seminal zinc levels at 12 week from 0 week was significant in both study groups (P<0.001 and P<0.001).

Table III shows that the mean increase of sperm concentration at 12 week was 5.44 million/ml in group B which was not significant. However, the increase in group A (14.83 million/ml) was statistically significant (P<0.01). Zinc supplementation had significant impact on sperm concentration in oligoasthenozoospermic patients.

The mean increase of sperm motility was higher in group A (16.30%) than in group B (13.70%). At 12 week, the increase was statistically significant in both groups (A, P<0.01, and B, P<0.05). There was significant improvement of sperm motility in group A.

The mean increase of sperm rapid linear motility was significant in group A (11.96%) but not significant in group B (6.78%). The mean increase of normal sperm morphology at 12 week was highest in group A (4.26%, P<0.001) but not significant in group B (2.22%). Zinc supplementation may have impact in improving sperm morphology and sperm rapid linear motility.

Table-I

Effect of zinc supplementation on serum zinc level

	Serum zinc level (mmol/L)	
	Group A (n=38)	Group B (n=37)
0 week	658.70±217.24	727.78±175.05
12 week	856.52±245.55	798.15±219.91
P value	0.003**	0.097ns
Mean change at 12 week from 0 week	+197.83	+70.37

Group A : Oligozoospermia, zinc supplementation

Group B : Oligozoospermia, placebo

Paired Student's 't' test

** = P<0.01.

Table-II

Effect of zinc supplementation on semen zinc level

	Seminal plasma zinc level (mmol/L)	
	Group A (n=38)	Group B (n=37)
0 week	1414.13±475.47	1352.78±518.89
12 week	2356.52±580.81	1977.78±580.01
P value	0.0001***	0.0001***
Mean change at 12 week from 0 week	+942.39	+625.00

Group A : Oligozoospermia, zinc supplementation

Group B : Oligozoospermia, placebo

Paired Student's 't' test

*** = Significant (P<0.001)

Table-III

Effect of zinc supplementation on semen parameter

Mean change at 12 week from 0 week	Group A (n=38)	Group B (n=37)
Sperm concentration (million/ml)	+14.83**	+5.44
Sperm motility (%)	+16.30**	+13.70*
Sperm rapid linear motility (%)	+11.96**	+6.78
Sperm morphology (%)	+4.26***	+2.22

Group A : Oligozoospermia, zinc supplementation
Group B : Oligozoospermia, placebo
Paired Student's 't' test
** = P<0.01, *=P<0.05, ***=P<0.001

Discussion:

Zinc has been shown to have an important role in male reproductive health. Prostrate has important relation with zinc concentration in semen. The zinc content has been quoted to be 87 times more concentrated in semen than that in the serum[13]. In our study also the zinc level of seminal plasma was higher than the serum zinc level. In the study done by Madding CI,[14] serum zinc levels were significantly lower in the infertile men which is consistent with our findings . Saaranen et al (1987) found zinc concentrations in semen to increase with increasing sperm density,[15] which is similar to our findings that with zinc supplementation when there was significant improvement in seminal plasma zinc levels the sperm count improved significantly. Stankovic and Mikac-Devic[16] reported increased sperm motility with increased seminal plasma zinc concentrations which is consistent with our findings that when the seminal zinc level increases with zinc supplementation motility of the sperm also significantly improved in oligoasthenozospermia.

Tikkiwal in 1987[17] reported that with zinc administration serum zinc levels remained essentially unaffected, and seminal zinc levels increased significantly, where as in our study there was significant improvement in zinc levels both in the serum and seminal plasma. In a study done by Akinloye,[18] the seminal plasma zinc was higher than serum zinc in the oligoasthenozospermic group which is consistent with our result. Serum zinc is thought to be a reasonable indicator of zinc status. Serum zinc level was lower in patients having oligoasthenozospermia, where as the seminal plasma zinc level was higher. This results are contradictory in several previous studies.[19,20] Correlation between zinc concentration in seminal plasma and semen quality is controversial also. Kvist et al. reported that seminal zinc concentrations is lower in patients with idiopathic infertility.[21] Several studies have reported that oral zinc therapy improves seminal quality in idiopathic infertility.[17,22] According to a study conducted in five middle-aged men following a Zn-restricted diet, the men underwent Zn depletion and their sperm counts dropped from a mean of 283 million/ml to 45 million/ml within 2 to 14 months.[23] In our study following zinc supplementation for 12 week the mean increase in sperm count, sperm motility, sperm rapid linear motility, sperm morphology in oligoasthenozoospermic patients showed statistically significant improvement in semen parameters. In a study Lewis-Jones has suggested that zinc therapy is unlikely to yield any improvements in patients with normal zinc concentrations.[18]

According to Lewis-Jones et al[18] seminal zinc was significantly lower in the infertile group which was not the case in our patients. There was significant rise of serum and seminal zinc level in our patients with zinc supplementation.

Conclusion: In conclusion, oral zinc supplementation results in significant improvement in semen parameters (sperm total count, motility, rapid linear motility and morphology) in infertile oligoasthenozoospermia men. Male infertility is influenced by zinc in several different

ways. Seminal plasma zinc concentration has been significantly correlated with sperm density, possibly contributing a positive effect on spermatogenesis. Twenty five percent of the world's population is at risk of zinc deficiency. Oral zinc supplementation appears to be an important step in the management of male infertility especially in cases of low sperm production.

Recommendation: Zinc therapy has significant role in the medical management of male infertility.

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