

ARTICLE (7)
MICRONUTRIENTS AND SPERMS DENSITY, MOTILITY AND VIABILITY
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Despite the growing number of studies on the effects of micronutrient supplementation on subfertility, inconsistencies in the literature relating to males and the lack of studies on females, preclude firm recommendations relating to their prescription and the specific dose or the optimum duration of treatment. In addition, no information is available on whether partners with specific subfertility issues will benefit more than others from supplementation. For example, aside from a few studies, the effects of oral Zn or Se supplementation on male subfertility has only been investigated in combination with other micronutrients, making it impossible to delineate the specific effects of Zn or Se. Importantly however, none of the studies identified any detrimental effects of Zn or Se on male or female fertility when administered below the recommended daily intake. Furthermore, most of studies to date involved small, heterogeneous cohorts, and interestingly, the administration of supplements comprising several micronutrients matched results for single micronutrients, with no apparent synergistic effects on the outcome variables. Many reviews highlight that when taking combinations of micronutrients, it is vital to pay attention to the doses and number of ingredients used. Thus, it is recommended that large randomised clinical trials, with controls, be undertaken in which Zn or Se supplementation alone is administered to investigate their potential effects on pregnancy rate in both fertile and especially subfertile populations.

Reference: Micronutrient (Zinc and Selenium) supplements and subfertility. Your Fertility Organization is a national public education campaign funded by the Australian Government Department of Health and Ageing under the Family Planning Grants Program. (October 2015)

The following are a brief description of few key publications on the subject.

1. ZINC

A. SYSTEMATIC REVIEW AND META-ANALYSIS

Zinc is an essential trace mineral for the normal functioning of the male reproductive system. Current studies have investigated the relationship between seminal plasma zinc and male infertility but have shown inconsistent results. Hence, authors systematically searched PubMed, EMBASE, Science Direct/ Elsevier, and the Cochrane Library for studies that examined the relationship between seminal plasma zinc and male infertility, as well as the effects of zinc supplementation on sperm parameters. Twenty studies were identified, including 2,600 cases and 867 controls. The meta-analysis results indicated that the seminal

plasma zinc concentrations from infertile males were significantly lower than those from normal controls.

Zinc supplementation was found to significantly increase the semen volume, sperm motility and the percentage of normal sperm morphology. Zinc supplementation could significantly increase the sperm quality of infertile males.

Reference: Jiang Zhao et al. Zinc levels in seminal plasma and their correlation with male infertility: A systematic review and meta-analysis. www.nature.com/scientificreports/ (02 March 2016).

B. CLINICAL

The present study was conducted to study the effect of zinc supplementation on the quantitative and qualitative characteristics of semen, along with enzymes of the NO pathway in the seminal plasma of asthenospermic patients.

Semen samples were obtained from 60 fertile and 60 asthenozoospermic infertile men of matched age. The subfertile group was treated with zinc sulfate; each participant took two capsules (220 mg per capsule) per day for 3 months. Semen samples were obtained (before and after zinc sulfate supplementation).

Workers found that treatment of asthenospermic patients with zinc supplementation leads to restored peroxynitrite levels, arginase activity and NO synthase activity to normal values and gives a statistically significant improvement of semen parameters compared with controls.

Reference: Hadwan et al. Study of the effects of oral zinc supplementation on peroxynitrite levels, arginase activity and NO synthase activity in seminal plasma of Iraqi asthenospermic patients *Reproductive Biology and Endocrinology* 2014, 12:1

C. CLINICAL

The aim of the study was to examine the relationships between concentrations of zinc in blood and seminal plasma and sperm quality among infertile and fertile men. One hundred seven male (infertile group) who were undergoing investigation for infertility with no known cause for the infertility and 103 men (fertile group). The subjects' blood and seminal plasma concentration of zinc were determined. Except for semen volume, all the other semen parameters for the infertile men were significantly lower than those for the fertile group. The geometric means of the seminal plasma zinc concentration were significantly lower in the infertile group compared with those in the fertile group. There were no significant differences in the geometric means of the blood zinc concentration between the two groups. Seminal plasma zinc concentration was significantly correlated with sperm density, motility, and viability. Based on the findings of this study and

those of other reports, zinc may contribute to fertility through its positive effect on spermatogenesis.

Reference: Sin-Eng Chia et al. Comparison of Zinc Concentrations in Blood and Seminal Plasma and the Various Sperm Parameters Between Fertile and Infertile Men. J Androl 2000; 21:53-57

2. SELENIUM

CLINICAL (DOUBLE-BLIND CLINICALLY CONTROLLED TRIAL)

To determine whether the decline in selenium intake and selenium status in men in the West of Scotland might be a contributory factor to male subfertility. Two semen samples were collected from patients attending a subfertility clinic and those patients with samples showing reduced motility were invited to participate in a double-blind controlled trial. Sixty-nine patients were recruited and received either placebo, selenium alone or selenium plus vitamins A, C and E daily for 3 months.

Plasma selenium concentrations were significantly higher in both selenium-treated groups than in controls. No significant effect of treatment on sperm density was recorded. Sperm motility increased in both selenium-treated groups, in contrast to a slight decline in the placebo group, but the difference was not significant. However, as the provision of additional vitamins had no effect on any variable measured it was considered justified to combine the two selenium-treated groups and compare them with the placebo treatment. On this basis, selenium treatment significantly increased plasma selenium concentrations and sperm motility but sperm density was again unaffected. Five men (11%) achieved paternity in the treatment group, in contrast to none in the placebo group.

This trial confirms the result of an earlier study, that selenium supplementation in subfertile men with low selenium status can improve sperm motility and the chance of successful conception. However, 56% showed a positive response to treatment.

Reference: Scott R, et al. The effect of oral selenium supplementation on human sperm motility. Br J Urol. 1998 Jul;82(1):76-80.

3. VITAMIN E

A. CLINICAL: DOUBLE-BLIND CLINICALLY CONTROLLED TRIAL

In a study to determine the effectiveness of the in vivo administration of vitamin E as treatment for reactive oxygen species-associated male infertility. A double-blind randomized placebo cross-over controlled trial was conducted on thirty healthy men with high levels of reactive oxygen species generation in semen and a normal female partner. Patients were allocated to two groups according to the blinded randomization. Each patient received either 600 mg/d of vitamin E or

identical placebo tablets for 3 months. Then after a 1-month wash-out period the patients were crossed-over to the other treatment. It has been concluded that oral administration of vitamin E significantly improves the in vitro function of human spermatozoa as assessed by the zona binding test.

Reference: Kessopoulou E, Powers HJ, Sharma KK, Pearson MJ, Russell JM, Cooke ID, Barratt CL. A double-blind randomized placebo cross-over controlled trial using the antioxidant vitamin E to treat reactive oxygen species associated male infertility. Fertil Steril. 1995 Oct;64(4):825-31.

B. CLINICAL (MULTI-CENTERED RANDOMIZED CONTROLLED STUDY)

In a prospective multi-centered randomized controlled study on 64 infertile men with oligospermia, workers in China found that vitamin E can improve sperm concentration, the percentage of progressively motile sperm, and finally the rate of natural pregnancy.

Reference: Chen X, Li Z, Ping P et al. Efficacy of natural vitamin E on oligospermia and athenospermia: a prospective multicentered randomized controlled study of 106 cases. *Natl J of Androl* 2012; 18:428-431. (Abstract, Article in Chinese]

4. FOLATE

CLINICAL

This is an observational study to determine associations between vitamin B status, homocysteine (tHcy), semen parameters, and sperm DNA damage. Two hundred fifty-one men of couples undergoing in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) treatment, with subgroups of fertile and subfertile men defined according to semen concentration and proven fertility.

The DNA fragmentation index (DFI) as marker of sperm DNA damage determined using the sperm chromatin structure assay (SCSA), and semen parameters assessed according to World Health Organization criteria; tHcy, folate, cobalamin, and pyridoxine concentrations determined in seminal plasma and blood. In the groups of fertile and subfertile men, all biomarkers in blood were statistically significantly correlated with those in seminal plasma. No correlation was found between the biomarkers in blood and the semen parameters. In seminal plasma, both tHcy and cobalamin positively correlated with sperm count. Folate, cobalamin, and pyridoxine were inversely correlated with ejaculate volume. In fertile men, seminal plasma folate showed an inverse correlation with the DNA fragmentation index. Conclusion: Low concentrations of folate in semin plasma may be detrimental for sperm DNA stability.

Reference: Jolanda C. Boxmeer et al. Low folate in seminal plasma is associated with increased sperm DNA damage. *Fertil Steril*_ 2009;92:548-56. (by American Society for Reproductive Medicine.)