ARTICLE (8)
MULTI INGREDIENTS STUDIES

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As it has been discussed in article seven "Micronutrients and Sperms Density, Motility, And Viability", there are incnsistencies in the literature which prevent firm recommendations related 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. In this article, we present few key clinical studies on the subject, but with the use of multi micronutrients combined.

1. **CLINICAL: ZINC & SELENIUM**

   This study was to determine glutathione (GSH) concentrations, trace element levels (zinc and selenium) and the lipid peroxidation end-product, malondialdehyde (MDA), in the seminal plasma of men with different fertility potentials.

   Semen samples from 60 fertile men (normozoospermics) and 190 infertile patients (74 asthenozoospermics, 56 oligozoospermics, and 60 teratozoospermics) were analyzed for physical and biochemical parameters. Study results showed that Zn and Se concentrations in seminal plasma of normozoospermics were more elevated than the three abnormal groups. This report revealed that decreased seminal GSH and trace element deficiencies are implicated in low sperm quality and may be an important indirect biomarker of idiopathic male infertility. Study results sustain that the evaluation of seminal antioxidant status in infertile men is necessary and can be helpful in fertility assessment from early stages.

   Reference: Atig et al. Impact of seminal trace element and glutathione levels on semen quality of Tunisian infertile men. BMC Urology 2012, 12:6

2. **CLINICAL: SELENIUM & VITAMIN E**

   Selenium (Se) is an essential element for normal testicular development, spermatogenesis, and spermatozoa motility and function. The predominant biochemical action of Se is to serve as an antioxidant via the Se-dependent enzyme glutathione peroxidase and thus protect cellular membranes and organelles from peroxidative damage. Workers explored the efficacy of Se in combination with vitamin E for improving semen parameters and pregnancy rates in infertile men.

   The study included 690 infertile men with idiopathic asthenoteratospermia who received supplemental daily Se (200 μg) in combination with vitamin E (400 units) for

at least 100 days. The mean age of cases was 28.5 years. These cases had presented with male factor infertility (primary or secondary) for at least one year.

Workers observed that 52.6% (362 cases) total improvement in sperm motility, morphology, or both, and 10.8% (75 cases) spontaneous pregnancy in comparison with no treatment. No response to treatment occurred in 253 cases (36.6%) after 14 weeks of combination therapy. Based on paired *t*-test results, combination therapy with oral Se and vitamin E was effective for treatment of asthenospermia or asthenoteratospermia or induction of spontaneous pregnancy. It was concluded that Se and vitamin E may improve semen quality and have beneficial and protective effects, especially on sperm motility. Authors support their use for the treatment of idiopathic male infertility diagnosed with asthenoteratospermia or asthenospermia.

Reference: M. K Moslemi, et al. Selenium–vitamin E supplementation in infertile men: effects on semen parameters and pregnancy rate. International Journal of General Medicine 2011:4 99–104

3. **CLINICAL: FOLATE, ZINC, AND VITAMIN E**

Dietary intake of antioxidants was compared between thirty-two men with oligolastheno/ teratazoospermic (cases) and 32 normospermic volunteers (controls) attending fertility clinic in Mirza Koochak-khan Hospital in Tehran, Iran. Semen samples were collected and were assessed by measuring volume, concentration, motility and morphology. It was concluded that a low intake of folate, zinc, and vitamin E were related to poor sperm concentration and motility.

Reference: Nadjarzadeh, et al. The association between dietary antioxidant intake and semen quality in infertile men. Medical Journal of the Islamic Republic of Iran, Vol. 27, No. 4, Nov 2013, pp. 204-209.

4. **CLINICAL: COPPER, CHROMIUM AND ZINC**

Copper, chromium and zinc concentrations were determined in semen samples. The concentration of these metals was determined in **43** infertile men and 27 fertile men. Semen quality was evaluated based on the norm established by the World Health Organization. Statistical analysis of the seminal parameters showed significant differences among fertile and infertile men regarding sperm concentration, progressive linear motility and normal morphology. Heavy metal concentrations showed no significant correlation when comparing the results obtained for semen from fertile and infertile men. Overall, the comparison between semen quality and heavy metal concentration showed no correlation; the copper, chromium and zinc concentrations found in the semen samples do not seem to affect sperm quality. This is the first report in Venezuela about the semen concentration of heavy metals.

Reference: Luz Marina Foglietta et al. Copper, chromium and zinc content in human semen and Its possible effect on sperm quality of fertile and infertile men in the city of Caracas, Venezuela. CIENCIA 6(1), 31-38,1998. Maracaibo, Venezuela

5. IRON AND COPPER

Iron and copper play indispensable roles in the physiology as well as pathology of male reproduction. Published studies highlight the crucial roles these micronutrients play in cellular respiration, spermatozoa development and metabolism as well as their ability to protect against oxidative stress in male gametes. Unfortunately, clinical as well as research data drawing a clear line between the beneficial and toxic effects of both trace elements are still lacking. Thus, the assessment of iron and copper concentrations in both seminal fractions should become more routine in clinical settings to understand their complex two-sided roles in male infertility associated with diverse diseases.

Reference: Eva Tvrda et al. Iron and copper in male reproduction: a double-edged sword. J Assist Reprod Genet (2015) 32:3–16

6. CLINICAL: COMBINATION OF EIGHT MICRONUTRIENTS

This study was carried out to compare the short-term effects of a combination of eight micronutrients including L-carnitine vs. a mono-substance (L-carnitine alone) on sperm parameters. This was a prospective, open-labelled, non-randomized study that included male subjects with at least one year of subfertility and at least one pathological semen analysis who received 3 months treatment with a mono-substance (500 mg l-carnitine / twice a day, n = 156) or a combined compound (***440 mg l-carnitine + 250 mg l-arginine + 40 mg zinc + 120 mg vitamin E + 80 mg glutathione + 60 µg selenium + 15 mg coenzyme Q10 + 800 µg folic acid/once a day, n = 143)*** for the same time period. Sperm parameters were analyzed before and after treatment and groups comparisons performed. Workers found that Semen parameters (volume, density, overall progressive motility [including slow and fast motility) and percentage of sperm with normal morphology improved after 3 months in both groups as compared to baseline. However, relative change (expressed as % increase of absolute values) for sperm density and overall progressive motility (including fast motility) was found to be higher for the combined micronutrient treatment group as compared to the mono-treatment using L-carnitine alone.

Reference: Lipovac et al. Comparison of the effect of a combination of eight micronutrients versus a standard mono preparation on sperm parameters. Reproductive Biology and Endocrinology (2016) 14:84