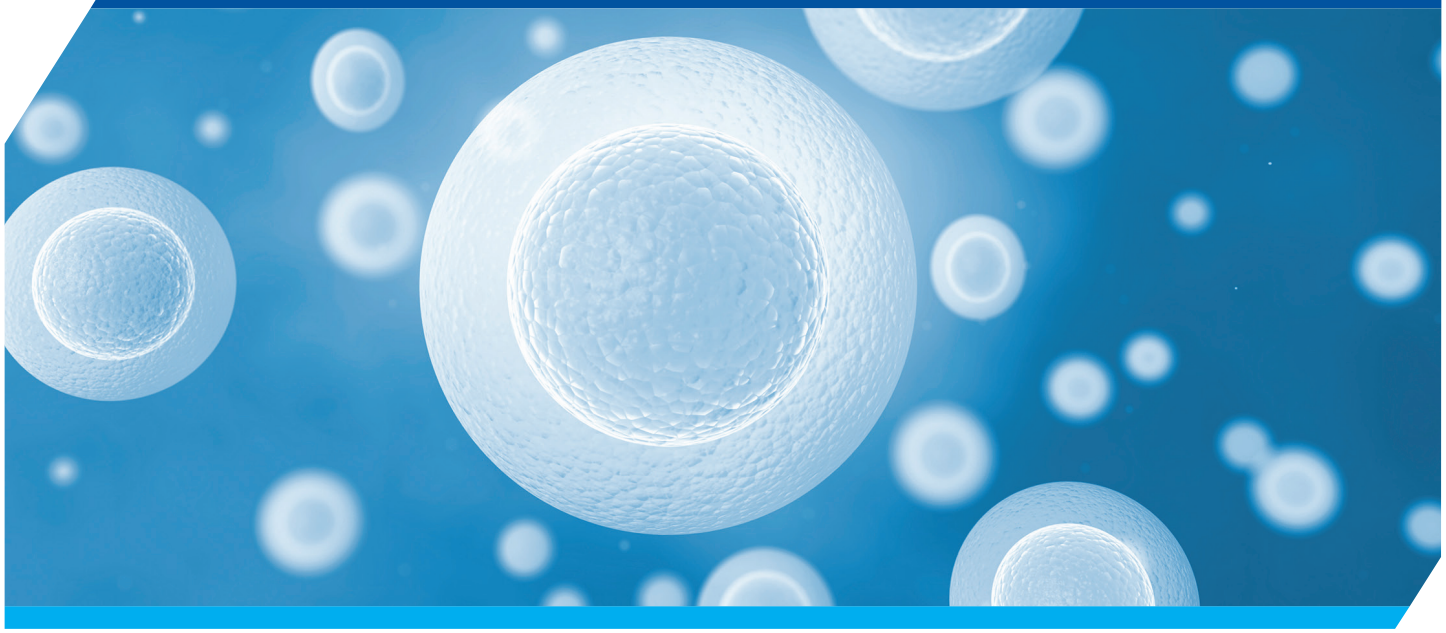
The Fertility Society of Australia

Pre-Conception Health Special Interest Group



Micronutrient (Zinc and Selenium) supplements and subfertility

Recent systematic reviews of the effects of micronutrients on male fertility have identified clear positive effects on basic sperm characteristics [1-3]. The vast majority of studies reviewed found that micronutrients, particularly those that are antioxidants or aid their function, significantly reduce sperm oxidative stress or DNA damage in subfertile males but greater evidence is required to clearly state whether these improvements translate to improved fertility [1-3]. Despite clinical trials and systematic reviews having been undertaken in males, very few, if any, clinical studies have thoroughly investigated the effects of micronutrient supplementation on female fertility. There is also a paucity of research investigating the role of micronutrients in women who are undergoing infertility treatment. Several recent reviews, based mainly on observational studies, have however identified that micronutrient concentrations in the peri-conception period influence female fertility and embryogenesis, and may prevent adverse pregnancy outcomes [4-6]. The possible effects on subfertility of two micronutrients (Zinc and Selenium), components of antioxidant enzymes which are commonly included in oral supplements, are discussed here.

Your fertility

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Evidence review

Zinc (Zn) - The recommended daily intake of Zn for an average weight female (61kg) and male (76kg) living in Australia and New Zealand is 8mg/day and 14mg/day respectively, with a recommended maximum intake for both sexes of 40mg/day [7]. These recommendations account for losses through menstruation in women and ejaculation in males; especially as semen has a high Zn concentration.

Effects on male subfertility - Zn concentration in seminal plasma is known to correlate with sperm count, motility and viability, although studies report conflicting findings about the magnitude of these correlations [8-10] and whether concentrations are higher or lower in subfertile compared to fertile men; probably explained by between-study differences in inclusion criteria. Although the underlying mechanisms by which Zn affects spermatogenesis remain unknown, the positive effects of Zn on sperm count and parameters (morphology and motility) are documented [11-16]. Recently, the ability of Zn to reduce oxidative stress in sperm was also identified [16], although this was negatively associated with sperm decondensation [17]. Even when Zn supplementation far exceeds the recommended daily intake, a concurrent increase in circulating or local concentrations of Zn or FSH and testosterone are not always evident; possibly explained by the absence of Zn deficiency or high excretion by the prostate [14]. Unfortunately to date, no studies have measured secondary outcomes, so the effect of Zn on fertility remains unknown in both fertile and subfertile populations.

Effects on female subfertility - Serum Zn concentrations are almost twice as high as follicular concentrations, although the high expression of Zn transport genes in the oocyte suggests active Zn transport during the first stages of pre-implantation development [18]. Similar to studies on males, studies report conflicting findings as to whether differences exist in serum Zn concentrations between infertile and fertile women [19, 20]. Lower follicular fluid and serum Zn and selenium levels were found in IVF patients than in fertile women [19], with normalisation to those of fertile women following multivitamin supplementation [19], although the effect on pregnancy rate was not investigated.

Selenium (Se) - The recommended daily intake of Se for an average weight female (61kg) and male (76kg) living in Australia and New Zealand is 60µg/day and 70µg/day respectively, with a recommended maximum intake for both sexes of 400µg/day [7].

Effects on male subfertility - Only one double-blind, placebo controlled, randomised clinical trial has investigated the effects of Se supplementation (200µg/day orally) on sperm characteristics of subfertile men [21]. None of these men were deficient in Se but after 26 weeks of Se supplementation the mean total sperm count, concentration, normal morphology percentage and motility increased from baseline relative to placebo treatment [21]. These improvements were coupled with changes in hormone concentrations, although all parameters returned to baseline after supplementation ceased. What is not known is whether the beneficial effects on semen parameters were accompanied by improved fertility, as pregnancy rates were not determined. In a contrasting study, higher Se supplementation (300µg/day orally) increased serum and seminal plasma Se concentrations but did not affect sperm Se, serum androgen concentrations or sperm parameters [22]. The lack of an increase in sperm Se suggests that testicular Se stores are unresponsive to dietary Se concentrations [22]. In fact, excessive (>400µg/day) dietary Se can reduce motile spermatozoa in fertile men [23]. Thus, oral Se supplementation appears to be beneficial at 200µg/day [21] but not at 300µg/day [22] or above [23] in improving sperm characteristics in subfertile males.

Data are available from several studies on the supplementation of Se in combination with other antioxidants [21,24-27]. Improvements were evident in sperm motility [21,24,25,27], concentration [21], morphology [21,27] and pregnancy rate [26,27]. When Se was taken for three months as part of a combined antioxidant treatment (MenevitTM one daily dose) no differences were identified in basic sperm parameters (count, motility, morphology, semen volume) or hormone concentrations relative to baseline [28], though MenevitTM only contains 26µg of Se per dose; far below the recommended daily intake. Decreased DNA fragmentation, apoptosis and reactive oxygen species (ROS) production were however observed in subfertile men [28], potentially due to other micronutrients included in the supplement.

Effects on female subfertility - Nearly all published studies in both humans and animals have focussed only on the potential effects of Se concentrations during pregnancy and lactation. No studies were found on the effects of Se, endogenous or supplemented, around the peri-conception period in fertile or subfertile females. This statement also generally applies to animals studies, with a few exceptions in sheep, in which Se supplemented females had higher conception rates than non-treated females [29].

Summary

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. To date, no clinical studies have thoroughly investigated the effects of Zn or Se supplementation on female fertility. Furthermore, no studies have investigated the effects of Zn or Se supplement on pregnancy rate, in either fertile or subfertile populations. The majority 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.

Recommendations

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 cohorts with specific subfertility issues will benefit more than others from supplementation. 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. There may well be some benefit in Zn and Se supplementation, although data is currently unavailable to substantiate this claim. Thus, it is recommended that large randomised clinical trials, with appropriate 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.

For more information about pre-conception health visit

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Your fertility

www.yourfertility.org.au

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