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INVITED COMMENTARY

Male Infertility

Lycopene and male infertility: do we know enough?

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There has been a recent renewed interest in the medical treatment of male subfertility. Although, intracytoplasmic sperm injection can surmount many of the reproductive challenges imposed upon couples struggling with male infertility, it remains an invasive and expensive treatment modality.

Infections and inflammation, smoking, environmental exposure to toxins and heat, anatomic abnormalities such as varicocele and cryptorchidism, may all result in oxidative stress.[1] Oxidative stress leads to the production of reactive oxygen species (ROS). Antioxidants present in seminal plasma and spermatozoa serve to maintain a balance and protect against damage caused by ROS. Excessive amounts of ROS can cause structural damage to the sperm deoxyribonucleic acid, reduce motility and damage the sperm membrane, leading to abnormal semen parameters and possibly, infertility.[2] Thus, the use of antioxidant therapy has garnered attention in the treatment of reversible causes of male infertility. In this issue of the journal, Durairajanayagam *et al*.[3] present an exhaustive review of animal and human data associating a lycopene-enriched diet with an improvement in markers of oxidative stress in semen and other parameters. The authors indicate the potential for lycopene supplementation in idiopathic male infertility.[3]

Lycopene, a lipid soluble carotenoid found in tomato-rich diets, is a powerful scavenger of free radicals preventing lipid peroxidation.[4] Data suggest the beneficial effect of lycopene-rich diets on chronic disease states by upregulating gap-junction communication and modulation of growth factors.[4] A recent publication suggested the protective effect of lycopene against polychlorinated biphenyl induced epididymal toxicity in a rat model.[4] To study differences in the nutrient intake of men with normal semen parameters and those with low sperm numbers, motility or morphology, Mendiola *et al*.[5] examined specific nutrient intake of men attending infertility clinics in Spain. The authors demonstrated a positive association between lycopene intake and semen quality.[5] The present data linking lycopene to an improvement in semen parameters is primarily observational, with small sample sizes under investigation. The limitations conferred by bias and confounding in current literature makes it difficult to look beyond an association, despite biological plausibility.

Supplementation of diet with antioxidants has been studied in other areas of medicine. Sommer *et al*.[6] discuss the example of Vitamins E and C, which have been associated with a reduced risk of cataract formation in observational studies. The seemingly beneficial effect of a reduction of cataract formation with Vitamin C or E supplementation was not replicated in a well-designed randomized controlled trial.[6] Similarly, epidemiologic studies suggest a beneficial effect of lycopene on cardiovascular health.[7] However, in a randomized controlled trial, lycopene supplementation in moderately overweight, disease-free, middle aged adults (an appropriate target population for lycopene supplementation in clinical practice) showed no significant changes in markers of cardiovascular disease.[7] These findings do not justify potential health claims that lycopene supplementation has a cardioprotective effect.[7]

The review by Durairajanayagam *et al*.[3] underscores the need for prospective and randomized controlled trials in male subfertility treated with lycopene as a nutritional supplement. This is because observational studies cannot establish cause and effect. Clinical associations do not always hold up when subjected to the rigors of a randomized controlled trial. Until then, we must tread cautiously.

COMPETING INTERESTS

The authors have no competing interests.

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