

Editorial Commentary

Cavallini G, Ferraretti AP, Gianaroli L, Biagiotti G, Vitali G. Cinnoxicam and L-carnitine/acetyl-L-carnitine treatment for idiopathic and varicocele-associated oligoasthenospermia. *J Androl.* 2004; 25:771–772.

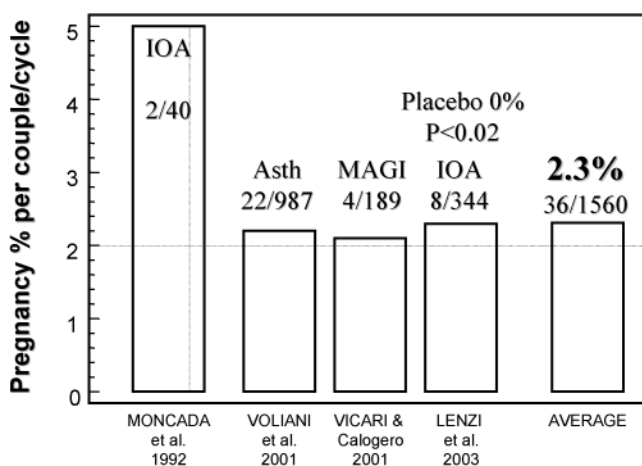
A male factor is detected in approximately half of the couples with infertility, defined as the inability to attain conception within 12 months of unprotected intercourse. More than 30% of men with subnormal semen quality present with varicocele, and between 20% and 25% are classified as having idiopathic oligo-, astheno-, and/or teratozoospermia. Evidently, any treatment that can improve the fertilizing potential of spermatozoa in these patients should be welcomed.

Varicocele treatment by means of retrograde embolization of the internal spermatic veins results in a more than threefold increase in the pregnancy rate when compared to that in couples in whom treatment was postponed (Comhaire et al, 1985; Dohle et al, unpublished). The recommended treatment of idiopathic oligozoospermia among patients without elevated gonadotropins is tamoxifen, either in association with testosterone undecanoate or not (Comhaire, 1976; Adamopoulos et al, 2003).

It has become increasingly clear that these treatments are more efficacious in terms of increasing the cumulative pregnancy rates among men with lower sperm concentrations than among those with only moderate oligozoospermia (eg, >10 million/mL). In the latter, it seems to be the functional impairment of spermatozoa rather than their number that is responsible for the decreased fertility. Such patients may benefit from complementary treatment with food supplements and/or anti-inflammatory medication.

Although several studies have evaluated the effect of carnitines on sperm parameters and pregnancy rates, very few address this treatment in a placebo-controlled design. In the present issue, Cavallini et al report the results of a double-blind randomized trial. They demonstrate that treating subfertile patients with low-grade varicoceles or idiopathic oligozoospermia and moderately decreased sperm concentration (average before treatment, 10–12 million/mL) with or without carnitines associated with the nonsteroidal anti-inflammatory drug ([NSAID] cinnoxicam) improves sperm quality and increases fertility. After 3 months of the combined delivery of the NSAID with carnitines, the pregnancy rate increased rather dramatically, suggesting that the effect of treatment was through interference with spermatogenesis itself.

There are some critical notes to be made to the results of this well-designed study. First, the treatment-independent pregnancy rate is lower (approximately 0.3% per couple per month) than that expected in couples with a relatively short duration of infertility (15 months) and moderate degree of sperm deficiency. In fact, such couples are estimated to have a 1.4% probability of conception per month at consultation and a cumulative pregnancy rate of 7.4% after 6 months (Collins et al, 1984; Comhaire, 1987). Second, the success rate among couples treated with carnitines alone is rather high, with an estimated 3.6% pregnancy rate per couple per month. In reviewing the literature on treatment with carnitines (Figure), we found 36 pregnancies among 1560 couples per month, equal to 2.3% per couple per month (Moncada et al, 1992; Vicari and Calogero, 2001; Lenzi et al, 2003; Voliani et al, unpublished). In a pilot double-blind randomized trial (unpublished), we were unable to show any favorable effect of complementary supplementation with carnitines on the outcome of World Health Organization–recommended conventional treatment (Rowe et al, 2000), either with respect to sperm characteristics or pregnancy rates. The most important finding is that NSAID treatment, given in conjunction with carnitines, seems significantly more efficient than carnitines alone, though several studies have failed to detect any effect of NSAIDs by themselves. The authors suggest that the NSAID they have administered is more efficient than other NSAIDs, whereby rectal administration is preferred because of supposedly higher bioavailability in the pelvic region. This may be of importance for the treatment of inflammatory



Therapy with carnitines: pregnancy rates. IOA indicates idiopathic oligoasthenozoospermia; Asth, asthenozoospermia; and MAGI, male accessory gland infection.

conditions of the pelvic organs, but it seems less relevant with regard to an alleged positive effect on spermatogenesis and increasing the sperm concentration.

Notwithstanding these critical notes, it must be emphasized that the results reported by Cavallini et al are of great interest and should stimulate complementary, preferentially multicenter trials. It is of the utmost importance to further increase the armamentarium of treatment options of subfertile men, particularly in view of the enormous economic cost and the increased health hazards to the offspring generated by techniques of assisted reproduction.

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