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Perspectives and Editorials: Letter to the Editor

Responsiveness to Tamoxifen Citrate and Testosterone Undecanoate Is Independent of the Severity of Idiopathic Oligozoospermia

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To the Editor:

In their recent article, "Cinnoxicam and L-Carnitine/Acetyl-L-Carnitine Treatment for Idiopathic and Varicocele-Associated Oligoasthenospermia," Cavallini et al (*J Androl.* 2004;761-770) made a reference to our recent publication (Adamopoulos et al, 2003), citing this article on 3 occasions, with a fourth citation coming from the ensuing "Editorial Commentary," by Comhaire and Mahmoud–(*J Androl.* 2004;771-772).

In the discussion of their paper, Cavallini et al stated that "A survey of the data of Adamopoulos et al (2003) and Wong et al (2002) indicated that their trial predominantly treated patients with isolated alterations of motility, morphology or both who have normal concentration of sperm." This was a rather misguided interpretation of our clinical trial and, to put the record straight, we present unpublished details of the study, summarized in Tables 1 and 2.

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Table 1. *Distribution of cases according to basal 1) sperm concentration and 2) total sperm number*

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Table 2. *Response to therapy according to basal 1) sperm concentration and 2) total sperm count*

To begin with, all patients included in our trial (106 men for each of the 2 treatment groups) had sperm concentrations below the 20.0 million spermatozoa per milliliter mark and, as defined by arbitrary World Health Organization (WHO) (1999) criteria, were classified as oligozoospermic. This selection procedure was followed regardless of the total sperm number, which, on certain occasions (placebo, 39.6%; tamoxifen citrate [TMX] + testosterone undecanoate [TU], 27.3%), exceeded that of 40.0 million per ejaculate, the lowest limit proposed by the WHO (1999). In table 1 of our article (Adamopoulos et al, 2003), the mean values for total sperm number were 27.1 (range, 9.4-54.0) and 32.0 (range, 14.1-70.0) million per ejaculate for active and placebo treatments, respectively. At the same time, sperm concentration was 7.9 (range, 3.7-12.1) and 9.1 (range, 3.4-10.9) million per milliliter in the 2 groups. Finally, the means for good motility were 29.7% ± 12.0% and 29.6% ± 15.7%, and those for conventional normal morphology were 41.2% ± 14.0% and 45.5% ± 16.5% for active and placebo treatment groups.

Moreover, the greatest proportion of men with idiopathic oligozoospermia as defined by their sperm concentration was distributed to the 1.0 to 4.9 x 10^6/mL (placebo 25.5%; TMX & TU 35.8%) and the 5.0 to 9.9 x 10^6/mL (placebo 28.3%; TMX & TU 34.9%) subgroups (table 1). A similar, although not quite identical, situation was evident regarding the total sperm number in our clinical material. Therefore, the distribution of our cases in terms of sperm concentration and total number was not skewed toward the upper end of this set of values.

Regarding the response to treatment with TMX and TU, as judged by more than a doubling of the original (basal) sperm concentration and total number, the picture emerged is given in table 2. It is noted that the successful response to treatment was relatively evenly distributed in all sperm concentration subgroups of men treated with this combination, with the exception of the relatively higher first subgroup (1.0-4.9 x 10^6/mL).

As is obvious from the evidence presented, all the men with idiopathic oligozoospermia included in our study had low sperm concentrations, and most of them had additional aberrations of morphology and motility, but definitely, there were no patients with "isolated alterations of motility, morphology or both who have normal concentrations of sperm," as stated by Cavallini et al.

This clarification is most important for prescribing practitioners, since Cavallini's statement may mislead them to exclude from treatment men with very low sperm concentrations who may also have a chance to respond favorably to this treatment, as did patients with higher concentrations in our study. Such an exclusion is most certainly not justified, given the evidence presented. On the contrary, this kind of treatment may be beneficial to the couple since, as has been shown (Comhaire et al, 1995), a sizable improvement in sperm concentration has been linked to disproportionately higher increases in effective cumulative pregnancy rates in men with idiopathic oligozoospermia.

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