Oral antioxidants and male infertility

Dear Sir,

We read with great interest the recent paper (Rolf et al., 1999), on the antioxidant treatment of patients with asthenozoospermia or moderate oligoasthenozoospermia. This randomized, placebo-controlled study showed that the combination of high dose Vitamin (Vit) C and VitE had no effect on basic semen characteristics in 14 treated cases after an observation period of 8 weeks. No pregnancies occurred in either the treated or control groups.

Both in-vitro experiments and an in-vivo pilot study (Hughes et al., 1998) have proven that VitC and VitE could protect the DNA of spermatozoa from oxidative damage when given separately, but induced DNA damage when given in combination. VitC can indeed act as pro-oxidant in certain circumstances (Burkitt and Gilbert 1989; Murakami et al., 1991; Podmore et al., 1998) by reducing Fe^{3+} to Fe^{2+}. The Fe^{2+} formed triggers the Fenton reaction which results in the formation of free hydroxyl radicals which are strong oxidizing agents and highly toxic. This phenomenon occurs with greater intensity in persons who have a higher circulating concentration of the [Ferritine–Fe^{3+}] complex, related to the fact that their haptoglobin belongs to type 1–2 or type 2–2 (Langlois et al., 1997). Since the iron-shuttle which occurs in the Sertoli cells plays an important role in spermatogenesis (Sylvester and Griswold, 1994), it is conceivable that the pro-oxidant effect of (high dose) VitC can also occur at that level.

Antioxidants are expected to exert their effect, if any, in cases with an elevated initial level of reactive oxygen species (ROS), but ROS was not measured in this study, neither was the effect of treatment on this variable monitored. Furthermore, the authors provide no data concerning the number of white blood cells in semen which are a major source of ROS (Aitken et al., 1992).

It should hardly be astonishing to record no pregnancies, since the number of couple-months of observation was no more than 28 in the treated group. Since the authors did not give any useful information on the duration of infertility (except that was >12 months) it is impossible to estimate the expected spontaneous conception rate.

Several publications have demonstrated that conventional, also called basic, semen characteristics (with the exception of sperm motility), are not influenced by the oxidative state of the semen (Aitken et al., 1995). This does not exclude effects from occurring on the lipid composition of the sperm membrane which may change the acrosome reactivity and fusogenic capacity of spermatozoa. Also, oxidative damage to DNA is not reflected in changes of the basic sperm characteristics. However, none of these variables were tested in the present study.

It is generally accepted that conventional sperm characteristics are poorly correlated with the fertilizing capacity of spermatozoa and that both the inter- and intra-assay variability of these characteristics is high, even in centres that participate in quality control programmes. Hence, it is hardly astonishing that the study has yielded no results.

The authors concluded from their ‘observation’ that timing sexual intercourse with a prolonged abstinence does not improve the probability of conception and they recommended frequent sexual intercourse during the fertile period. How the results of their study lead to this conclusion and recommendation is not clear.

In summary, the ‘evidence base’ generated by this study is poor, except for the observation that the period of abstinence does influence sperm characteristics. However, this has been known for a long time (Baker et al., 1981).

References


Ahmed M.A. Mahmoud1, Frank H.Comhaire2 and Armand B.Christophe

University Hospital Gent, Department of Internal Medicine, Section Endocrinology, De Pintelaan 185, B-9000 Gent, Belgium

1On leave of absence from Department of Dermatology and Andrology, Assiut University Hospitals, Egypt

2To whom correspondence should be addressed
Dear Sir,

We welcome the opportunity to rebut the claims by Mahmoud et al. that the evidence base generated in our recent paper (Rolf et al., 1999) might be poor.

With respect to his remarks, we have the following comments. Our results agree well with the results of another study (Hughes et al., 1998). However, this study was published in your journal only 1 month prior to our study and, therefore, we were not aware of this study. We appreciate this new scientific explanation for our disappointing results. As already discussed in our paper we are aware of the limitations of our study, and in the discussion we explained extensively the problems of this study.

References

C.Rolf, T.G.Cooper and E.Nieschlag

*Institute of Reproductive Medicine, Münster University,
Domagkstrasse 11, D-48129 Münster, Germany*

*To whom correspondence should be addressed*