drug in males with high sperm DNA fragmentation values announced by Alvarez.

In our clinics we have recently tested another conservative approach to the problem of sperm DNA fragmentation, based on combined oral treatment with two antioxidants, vitamins C and E. In a prospective randomized study we found that the oral treatment with these two antioxidants for 2 months significantly alleviates DNA damage to ejaculated sperm (Greco et al., 2005b). The effect of this treatment on clinical outcomes of ICSI performed with ejaculated sperm from men whose initially elevated DNA fragmentation values return to normal values after treatment is currently under study.

References

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Ermanno Greco1,3, Filomena Scarselli1, Marcello Iacobelli1, Laura Rienzi1, Filippo Ubaldi1, Susanna Ferrero1, Giorgio Franco1, Nazareno Anniballo1, Carmen Mendoza2 and Jan Tesarik2
1Centre for Reproductive Medicine, European Hospital, Via Portuense 700, 00149 Rome, Italy and 2MAR&Gen, Molecular Assisted Reproduction and Genetics, Gracia 36, 18002 Granada, Spain
3To whom correspondence should be addressed.
E-mail: cmendoza@ugr.es
doi:10.1093/humrep/deh815

Request for information on unreported cases of severe ovarian hyperstimulation syndrome (OHSS)

Sir,

On various occasions, at conferences, I have been invited to speak about the epidemiology of OHSS. Occasionally after these talks, some of our colleagues have told me about severe complications with sometimes fatal outcomes, which have never been mentioned in the scientific literature. This suggests an underreporting of OHSS. Currently I am writing a paper about the mortality related to OHSS. Some cases with a fatal outcome were reported during the 1950s. Although more recent anecdotal cases have been discussed in workshops, no publication has ever described their circumstances in detail. We believe that some information is particularly pertinent: (i) when and where the death occurred (how long after stimulation, in a reference centre, time lapse between diagnosis and treatment, type of treatment, admission in an intensive care unit?); (ii) what was the cause of death, which may have been different in earlier days (renal failure) as compared to today (thromboembolic disorders)? We feel certain that additional data regarding these circumstances could help us to define safer treatments for our patients. Obviously, our goal is not to criticize, after the fact, the therapeutic decisions made by our colleagues. We will ensure anonymity to those who wish it. They can reply to E-mail: http://users.skynet.be/sky98426/survey.html. On the other hand, those who would like to be mentioned will be acknowledged for their help and can contact me directly on E-mail: annick_delvigne@stpierry-bru.be.

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Annick Delvigne
IVF Clinic, St Pierre Hospital, Free University Brussels, Hospital Universitaire Saint-Pierre, Rue Haute 322, B-1000 Bruxelles, Belgium
E-mail: annick.delvigne@yucom.be
doi:10.1093/humrep/deh816

The effects of the human immunodeficiency virus on semen parameters and intrauterine insemination outcome

Sir,

We have read with great interest the paper about the effects of the human immunodeficiency virus (HIV) on semen parameters by Nicopoulouls et al. (2004).

The authors performed a case–control study, comparing semen parameters of 106 asymptomatic HIV-I infected men with semen parameters of 234 HIV negative men requiring IVF, because of a partner with tubal infertility. In addition, the study compared 133 pre-wash semen parameters on the day of intrauterine insemination (IUI) of HIV positive men with 222 pre-wash semen parameters on the day of IUI of non-infected men. Finally, the authors attempted to analyse which factors predict IUI outcome in HIV-infected men. Based on their analysis, the authors conclude that semen parameters are impaired in the presence of HIV infection and that both viral load and antiretroviral therapy predict IUI outcome in HIV infected men. However, there are several problems with the study that make us question whether these conclusions are justified.

First, the conclusions are based on a comparison between a group of HIV positive men with an unmatched group of HIV negative men. It is thus unclear if differences other than the presence of an HIV infection exist in these cases and controls that could explain the observed differences in semen quality. Furthermore, the variability of semen parameters between individuals limits the conclusions of a case–control study design (Guzick et al., 2001). The ideal situation to
study the effects of HIV infection on semen parameters is a comparison of semen parameters before and after infection with HIV. Interestingly, we recently described semen parameters before and after infection with HIV from a sperm donor, who became seropositive (van Leeuwen et al., 2004). However, this represents a unique case and larger studies of this kind are not feasible. The best study design feasible for larger patient numbers is a longitudinal cohort study, describing semen parameters during the course of an HIV infection.

Second, only the first semen analyses from the HIV positive men were used, to avoid the bias of repeated sampling according to the authors. However, most studies investigating semen parameters and fertility use the average of all available semen analyses, mainly because of the well-established high variability of semen parameters between different ejaculates from the same individual (Alvarez et al., 2003).

Third, the group of HIV positive men undergoing IUI examined by Nicopoullos et al. was extremely heterogeneous, consisting for instance of both men with and without antiretroviral therapy. The authors conclude that no effect of antiretroviral therapy on semen parameters was seen. This is not surprising since normozoospermia was an inclusion criterion for men to enter the IUI programme. It remains unclear how many HIV positive men were refused entry to the IUI programme because of poor semen quality, possibly due to the use of antiretroviral therapy. Furthermore, it is also unclear how many of the original 105 HIV positive men provided the 133 samples that were analysed.

Finally, although the idea itself is innovative, we question the methods used to analyse which HIV characteristics can predict IUI success in an HIV-infected population. The continuous variables such as year since diagnosis, viral load and CD4 count were not analysed as continuous variables by the authors, but instead were dichotomized with apparently randomly chosen thresholds. Such dichotomization is only appropriate if a spline analysis has demonstrated that this represents a proper correlation of the two variables. The authors then demonstrate by univariate analysis that the outcome of IUI is dependent on both viral load and antiretroviral therapy. However, parameters such as duration of infection, CD4 count, viral load and antiretroviral therapy are well-established dependent variables. Therefore, one should analyse the predictive capacity of these individual variables using a multivariable approach.

In conclusion, we have identified several flaws in the study design that make us question the conclusions of this study. In our opinion, a longitudinal study in a cohort of HIV-infected men is necessary to determine whether HIV infection itself and/or antiretroviral therapy affect semen quality. Furthermore, a multivariable approach is needed to determine which factors independently predict IUI outcome for HIV-infected men desiring genetically own offspring.

References


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E.van Leeuwen1, J.M.van Weert, F.van der Veen and S.Repping
Center for Reproductive Medicine, Department of Obstetrics and Gynecology, Academic Medical Center, Amsterdam

1To whom correspondence should be addressed at: Academic Medical Center, Obstetrics and Gynecology, H4-205, Meibergdreef 9, 1100 DD Amsterdam, The Netherlands.
E-mail: e.vanleeuwen@amc.uva.nl
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Reply to ‘The effect of human immunodeficiency virus on semen parameters and intrauterine insemination outcome’

Sir,
We read with great interest the letter by van Leeuwen et al., and thank them for their interest in our research. We will address their comments in turn.

First, they suggest that differences other than the presence of an human immunodeficiency virus (HIV) infection may exist between our study group and controls that could explain the observed differences in semen quality. However, as Table I of our paper demonstrated, there was no significant difference in age between the groups (37.3 and 37.2 years respectively) and although the data are not presented, there was no significant difference in alcohol, tobacco or recreational drug use reported between the two groups (Nicopoullos et al., 2004). Furthermore, both groups would have undergone similar pre-treatment investigation. Although Guzick et al. (2001) do suggest ‘that caution must be used in interpreting the significance of any given subfertile or indeterminate semen measurement’, this is with regard to the ability of a given parameter to predict fertility potential per se.

Although their case report (van Leeuwen et al., 2004) is able to demonstrate a series of semen variables in an individual prior to, and following, HIV seroconversion and diagnosis, it also highlights the difficulties of longitudinal studies. First, they were only able to present such interesting data as a semen donor happened to seroconvert during the course of donation. The use of larger longitudinal cohort studies to assess the effect of the diagnosis of HIV on semen parameters would therefore be impossible. Second, longitudinal studies would, as they suggest, be of use in assessing the effect of ‘disease progression’ on parameters but would not in