Letters to the Editor

Thrombophilic screening in clinical practice should be evidence-based

Sir,

We have read with much interest the article by Bellver et al. (2008), in which they examined the role of thrombophilia and thyroid autoimmunity in reproductive failure. The study is very important because it explores the relationship between thrombophilia and reproductive failures after excluding chromosomal abnormalities by preimplantation genetic screening. The authors conclude that "when embryo aneuploidy is ruled out, thrombophilia could constitute an etiologic factor in implantation failure". The logical consequence of this finding is that thrombophilic screening should be recommended in women who had experienced repeated IVF failures and that antithrombotic therapy should be evaluated in such patients.

We believe, however, that some points need to be clarified. Statistical analysis of results shows that the prevalence of different isolated or combined thrombophilia was not significantly different in the implantation failure (IF) group in comparison with the control group. The authors report a higher prevalence of the activated protein C resistance (APCR) in the IF group in comparison with the control group detected by chi-square test ($P = 0.035$). However, this was a statistical mistake because, applying chi-square test to data provided in the article (Table II, Bellver et al., 2008) the correct two-sided $P$-value is 0.0753 (not significant). The authors also report that there was a trend towards a higher prevalence of lupus anticoagulant (LA) in the IF group ($P = 0.056$). However, comparing the prevalence of LA in the IF and in the control group, chi-square test provides a two-sided $P$-value of 0.1685. Furthermore, the presence of LA and anticardiolipin antibodies (ACAs) was diagnosed by performing a single measurement and using a low positivity cut-off, in contrast with international criteria. In fact, international consensus recommends a second confirmatory test at least 12 weeks apart since an initial elevation in any of these tests may be transitory (Miyakis et al., 2006). LA and ACAs in medium or high titre are found transiently in many cases (de Moerloose and Reber, 2004). This can also explain the extremely high percentage of controls with ACAs IgM observed in this study. Finally, the authors report a trend towards a higher prevalence for combined thrombophilia in the IF group in comparison with the control group. In the Materials and Methods, the authors stated that APCR positive cases were only considered when Factor V Leiden was negative. However, one case of APCR plus Factor V Leiden was wrongly included in combined thrombophilia group (Table III, Bellver et al., 2008). Excluding this case, the prevalence of combined thrombophilia results similar in the IF and in the control groups. In fact, chi-square test provides a two-sided $P$-value of 0.7692.

In conclusion, the study failed to show any association between isolated or combined thrombophilia and IF. Therefore, at present, there is no evidence to suggest thrombophilic screening for patients with repeated IVF, as readers might be otherwise induced to think on the basis of the conclusions of the paper. Thrombophilic screening is very expensive and it has many implications, such as antithrombotic therapy in positive women and management of women carriers of mutations of uncertain pathological significance (Wu et al., 2006). Therefore, the introduction of thrombophilic screening in clinical practice should be evidence-based (Lindhoff-Last and Luxembourg, 2008).

References


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