Letters to the Editor

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...date have assessed the response of the ovary to gonadotrophin stimulation and that these tests were, therefore, only an indirect measurement of ovarian reserve. In their study, the number of follicles (defined as ‘ovarian reserve’) was directly assessed by histology in women >35 years who underwent oophorectomy. Therefore, the study is based on the assumption that ovarian reserve is the number of follicles stored in the ovaries.

Studies by Faddy, Gosden and Gougeon have shown that during a woman’s life there is a continuing decline in the number of follicles at a variable rate. However, they have also shown different pools of ovarian follicles defined by Faddy and Gosden as stage I-II and III and by Gougeon as non-growing follicles (NGF) and early growing follicles (EGF) subject to a specific intra-ovarian dynamic (Gosden, 1987; Gougeon et al., 1994; Faddy and Gosden, 1995). Their model however has not proved to be accurately predictive since women who were expected to have the menopause advanced by seven years after unilateral oophorectomy have instead reached the menopause with no apparent advancement (te Velde, 1993). In some circumstances, such as early menopause, follicular depletion was not necessarily found (Board et al., 1979; Airman and Smentek, 1985). Patients who responded poorly to previous stimulation for IVF have had a sufficient number of oocytes retrieved at subsequent attempts using different drug regimens (Faber et al., 1998).

Therefore, all these data appear to address the issue that ovarian reserve is not a simple static anatomic number of follicles but rather a dynamic process, the mechanisms of which are not yet fully understood (te Velde, 1993).

In their study, Gülekli et al. have shown a large variety of follicular concentration and found no correlation with the tests performed (Gülekli et al., 1999). However, would the study have shown the same results had the authors correlated the tests performed with the response to stimulation instead of the number of follicles counted in the ovaries? Further, based on their results will the authors be able to predict which patients will or will not have responded to ovarian stimulation?

An accurate test of ovarian reserve has always been an attractive proposition to clinicians because of the attendant advantages of assessing the likelihood of a sufficient ovarian response prior to commencing IVF treatment, and optimising drug regimens for individual patients. All the studies performed up to date have correlated screening tests with ovarian response to stimulation. In 1998 we published a study on 177 patients comparing accuracy of the main predictors of ovarian reserve (Ranieri et al., 1998). Basal FSH, basal 17 β-oestradiol, FSH/LH ratio, increase in FSH level (ΔFSH) and 17 β-oestradiol (ΔE₂) after the commencement of GnRH analogue stimulation, were correlated with the ovarian response of patients undergoing IVF. The results of the simple regression and of the receiver operating characteristic curves (ROC), showed that all the possible predictors considered, except for day 2 17 β-oestradiol level and the ΔFSH, correlated significantly with the ovarian response. The best single correlation was between the number of follicles and the ΔE₂ (GAST). We also showed that when the FSH was evaluated simultaneously, the correlation was strengthened, resulting in a better negative predictive value. Gülekli et al. concluded in the article that the GAST

Ovarian reserve: A simple mathematical problem?

Dear Sir,

The study by Gülekli et al. ‘Accuracy of ovarian reserve tests’ showed an interesting observation, correlating the results of basal serum FSH, clomiphene citrate challenge test (CCCT) and gonadotrophin-releasing hormone agonist stimulation test (GAST) with the number of follicles in the ovaries (Gülekli et al., 1999). The authors state that all studies performed to
was expensive, invasive and required further standardization (Gülekli et al., 1999). Performing GAST simultaneously with an IVF treatment entails taking a blood sample before and after starting the GnRH analogue and this can hardly be perceived as being invasive or expensive. With regard to standardization we have previously shown that the predictive accuracy of the GAST is improved by assessing the cut-off level of the ∆E₂ at 180 rather than relying solely on the doubling of the 17β-oestradiol after GnRH analogue administration. We also gave other suggestions to standardise this test (Ranieri et al., 1998). This approach can reduce cancelled cycles, resource wastage, and emotional stress to the patient and result in a reasonable pregnancy rate (Faber et al., 1998, Ranieri et al., 1999).

Consequently we do not believe that the results of the study by Gülekli et al. (1999), admittedly on a low number of patients, justify the conclusion regarding the accuracy of the ovarian reserve tests. In our opinion, in view of the complexity of ovarian dynamics, the ovarian reserve cannot simply be equated with a static observation of the number of follicles.

References


Dear Sir,

We thank Ranieri and Serhal for their interest in our paper (Gülekli et al., 1999). We have two points to make in response.

(i) The main purpose of our study, as stated in the paper, was to examine the accuracy of the various ovarian reserve tests in predicting the number of follicles within ovaries removed from women of proven fertility. It was not our aim to examine the usefulness of these tests in predicting the response to ovarian stimulation. Many such studies have been performed previously as discussed both in our paper and Ranieri and Serhal’s letter. (ii) As regards gonadotrophin-releasing hormone agonist stimulation test (GAST), we used the criteria as described by Winslow et al. (1991). The test was considered normal for ovarian reserve if the serum oestradiol value on day 3 was double that on day 2. We do not know whether using modified criteria, such as those suggested by Ranieri et al. (1998), would have improved the value of GAST in our study. Again, whilst Ranieri et al.’s study demonstrated that GAST was of use in predicting the response to ovarian stimulation in IVF patients, this was not the intention of our study.

References


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