Opinion

Markers of Female Reproductive Ageing and for Assessing Ovarian Function and Ovarian Stimulation Outcome

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Woman's fertility begins to decline at age 30 and worsens at age 35 due to a decrease in the quantity of eggs as well as in the quality of the eggs. This drop in the quality and quantity of eggs occurs thanks to the programmed cell apoptosis process known as apoptosis and also the genetic changes in that egg. Although this fall in the ovarian reserve is known with age, it is difficult to predict how the decline in fertility of each woman will be.

At 4 months of gestation, the female fetus has 6 - 7 million eggs. At birth, it decreases to 1 to 2 million and at puberty it has approximately 400,000 eggs. Around 37 years old, this amount is 25,000 and at the age of 51 a maximum of 1000 eggs.

This fall in the ovarian reserve is more significant at age 35, and there is a decrease in this reserve between 12 and 15% each year after this age. Therefore, markers of expression of ovarian activity are essential for family planning and medical conduct.

Several markers of ovarian reserve have already been evaluated as FSH, Inibine B, AMH (antimullerian hormone) and the amount of antral follicles (AFC). Nowadays it is known through evidence-based medicine that the three pillars of the evaluation of the quantity and/or quality of the egg are age, AMH and AFC.

Female age drastically affects the gene expression of the eggs, demonstrating a significant increase in genetic alterations and, consequently, embryos with aneuplodia.

The quantity of antral follicles also demonstrates a direct relationship with the quality of eggs as the quantity. The higher the AFC, the better the prognosis of a woman getting pregnant.

Anti-Müllerian hormone, also known as Müllerian inhibiting substance, is a member of the TGF-ß family most commonly known for its role in the regression of Müllerian ducts during male fetal sex differentiation. In females, AMH is produced by small antral and pre-antral follicles, and has been shown to inhibit excess recruitment of primordial follicles through reducing responsiveness to FSH. AMH serum concentration has been shown to be correlated with the ovarian follicular pool, so it is considered to be a marker of ovarian reserve as well as a marker of ovarian follicular activity. Numerous studies have demonstrated that AMH is associated with ovulatory disorders, such as primary ovarian insufficiency, polycystic ovary syndrome (PCOS), and ovarian hyperstimulation syndrome.

AMH, like AFC, relates to the quantity of eggs and has recently also shown a relationship with the quality of the eggs. This hormone appears to be a marker of ovarian aging and together with age and/or AFC it clearly demonstrates the female ovarian reserve.

These three markers of the ovarian reserve help in determining the quantity and quality of the eggs, stimulation protocols, prognosis of becoming pregnant by natural or induced means. Soon these markers are indispensable tools in the evaluation of female health.

The simplicity of evaluating these three markers; age, based on date of birth; AFC, based on the ultrasound evaluation of the ovaries and AMH through blood tests, it is mandatory to study the reproductive health of all women of childbearing age.

Deepening the benefits of AMH

Advantages

- Good predictive value for the number of oocytes retrieved and stimulation response.

- May help guide protocol and other treatment decisions.

- Well-characterized across adolescent and reproductive ages.

- Can be performed at any point during a cycle (low intra-cycle variability). AMH remains relatively stable through- out the menstrual cycle, with the fluctuations reported in some studies appearing to be of small amplitude

- Good inter-cycle consistency.

- Good inter-operator and inter-centre consistency.

- Relatively low cost (depending upon the specific anti-Müllerian hormone assay).

But like all exams, there are also their disadvantages

- **Problems of AMH measurements:** Yet from a practical standpoint, in addition to cost, problems related to AMH measurements have raised doubts about their clinical soundness. These problems essentially are attributed, on the one hand, to an uncoordinated development of AMH assays, which displayed different callibration and standards and, on the other hand, to the compulsory operator- and technique-dependent manipulations. Recently, to overcome these limitations and to improve quality of AMH measurements, fully automated AMH assays (Access AMH [Beckman Coulter] and Elecsys AMH [Roche Diagnostics International]) have been developed and commercialized.

The assessment of the ovarian reserve must be as reliable as possible, so as to avoid unnecessary treatments and psychological problems in women. Therefore, the association of these markers is essential to avoid incorrect and inaccurate diagnoses. It is known that the evaluation of at least two markers is already sufficient for guidance and medical conduct.

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