Anti-Müllerian Hormone (AMH) in Gynecological Endocrinology

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Abstract: *Anti-Müllerian Hormone (AMH) is largely known as an indicator of ovarian reserve. This review discusses the different uses of AMH in gynecological endocrinology including guiding and monitoring of assisted reproduction treatment, the debate of AMH levels in polycystic ovary syndrome (PCOS), the role of AMH measurements in premature ovarian failure (POF), as well as its value in pediatric endocrinology.*

Keywords: *Anti-Müllerian Hormone, AMH, Gynecological Endocrinology, Ovarian Reserve, Assisted Reproduction*

1. INTRODUCTION

Anti-Müllerian hormone (AMH), also known as Mullerian inhibiting substance (MIS), is a dimeric protein member of the TGF-β subfamily (1). AMH is produced by the granulosa cells of pre-antral and small antral follicles. Follicular growth is modulated by AMH, which inhibits recruitment of follicles from the primordial pool by modifying the FSH sensitivity of those follicles. As a follicle matures, AMH production disappears allowing the follicle to complete the development process (2).

2. DISCUSSION

2.1. Ovarian Reserve

Ovarian reserve represents the remaining population of primordial and resting follicles; and is generally defined as the quantity and quality of the follicles present in the ovary (3). Although chronological age is the major determinant of ovarian reserve, there is considerable individual variability in the rate of ovarian ageing (4). Therefore, accurate evaluation of ovarian reserve may allow individualized patient management.

Traditionally, other than age, basal (day 3) serum follicle stimulating hormone (FSH) level and antral follicle count (AFC) assessed by trans-vaginal sonography are often used as tests of ovarian reserve. FSH is not considered highly accurate due to inter-cycle variations (3). AFC correlates with the number of oocytes (5); and is considered to be one of the best tests of ovarian reserve, and much better than FSH or inhibin B assays (6).

2.2. Assisted Reproduction

Assisted reproduction (IVF/ICSI) treatment of infertility results in reasonably high pregnancy rates; however, the variability in patient response dictates the need for personalized diagnostic and therapeutic approach to optimize efficacy and safety outcomes (7).The ovarian response to gonadotrophin stimulation depends primarily on the ovarian reserve; and is a major determinant of the success of assisted reproduction (8).

The clinical significance of AMH determination was first proven in assisted reproduction, as AMH levels reflect the ovarian reserve potential with high accuracy (9-12). There is also a strong correlation basal AMH level and the number of retrieved oocytes (10, 12). The fact that AMH is secreted without dependence on other hormones, particularly the gonadotropins; and at a constant level, independent of cycle day, makes AMH very attractive as a direct measure of ovarian reserve (13).

Compared to other ovarian reserve biomarkers, Themmen(14) found AMH to be a better marker to predict the ovarian response to gonadotropin stimulation than age, day 3 FSH, estradiol, and inhibin B. Gleicher et al. (15)also concluded that women with normal FSH and abnormal AMH

will have reduced oocyte yield, and women with normal FSH and normal AMH will have the best oocyte yield; showing again that AMH is a better marker than FSH.

Compared to AFC, Broer et al. (16) concluded that both AMH and AFC have the same accuracy level in predicting ovarian response and outcome after IVF. This was confirmed by another study that showed that small AFC (2-6 mm) and AMH are equally accurate predictors of ovarian response to controlled ovarian hyperstimulation (17). In addition to being a good marker for the quantity of follicles, AMH is also suggestive of the quality of the remaining oocytes (18).

Furthermore, AMH has the ability to predict both poor response and excessive response to gonadotropins. Compared to AFC, AMH concentrations could reliably and equally predict poor response to ovarian stimulation in IVF cycles (19). On the opposite end of the spectrum, it was reported that AMH levels could recognize those women prone to ovarian hyper stimulation syndrome (OHSS) during ovulation induction with gonadotropins (20).

2.3. Polycystic Ovary Syndrome (PCOS)

Since AMH levels reflect the number of developing follicles, their measurement may be used as a marker of ovarian follicle impairment in PCOS. It has been shown that circulating AMH levels are higher in PCOS patients, and that AMH levels correlate with the severity of the syndrome (21). However, AMH has not proven as a diagnostic marker of PCOS (22).

2.4. Premature Ovarian Failure (POF)

AMH could be a marker for women at risk for POF. In cancer survivorsafter chemotherapy and/or radiotherapy, AMH levels correlate with the extent of gonadal damage (23). Early diagnosis of POF can prevent expensive ways of fertility treatment. AMH is a slightly better marker of POF than FSH; having more sensitivity (24).

2.5. Turner Syndrome

AMH levels can serve as a useful marker of the follicle pool in patients with Turner syndrome. AMH levels in these patients are related to karyotype, pubertal development and growth hormone treatment (25). A low AMH level can predict failure to enter puberty in young patients and imminent POF (26).

2.6. Precocious Puberty

AMH levels in girls with precocious puberty are usually in the normal range. However, AMH levels decrease at the early stages of GnRH agonist treatment, but return to pretreatment levels after discontinuation of the treatment, indicating GnRH treatment does not affect fertility (27).

2.7. Female Virilization

AMH levels can indicate if the virilization originates from testicular tissue or of a granulosa cell tumor -- AMH levels in the male reference range, or from adrenal androgens, as in the case of congenital adrenal hyperplasia -- AMH levels in the female reference range (28).

3. CONCLUSION

AMH measurement is of proven value for estimating ovarian reserve and guiding and monitoring of assisted reproduction treatment. The use of AMH as a diagnostic marker in PCOS is still controversial. AMH measurements to predict POFafter chemotherapy and/or radiotherapy of cancer are promising. It is also a useful tool in the field of pediatric endocrinology.

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