Does the time interval between antimüllerian hormone serum sampling and initiation of ovarian stimulation affect its predictive ability in in vitro fertilization–intracytoplasmic sperm injection cycles with a gonadotropin-releasing hormone antagonist? A retrospective single-center study

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Objective: To investigate whether the time interval between serum antimüllerian hormone (AMH) sampling and initiation of ovarian stimulation for in vitro fertilization–intracytoplasmic sperm injection (IVF-ICSI) may affect the predictive ability of the marker for low and excessive ovarian response.
Design: Retrospective cohort study.
Setting: University-based tertiary center.
Patient(s): Five hundred and forty women with AMH values measured before their first IVF-ICSI cycle.
Intervention(s): Eligible patients treated with 150–225 IU recombinant follicle-stimulating hormone (FSH) in a gonadotropin-releasing hormone (GnRH) antagonist protocol.
Main Outcome Measure(s): Predictive ability of AMH for low and excessive ovarian response in relation to the time interval between serum AMH sampling and initiation of ovarian stimulation for IVF-ICSI.
Result(s): All patients had their AMH concentration measured up to 12 months before initiation of stimulation. The level of AMH demonstrated a statistically significant positive correlation with number of oocytes retrieved. The time interval between AMH measurement and initiation of stimulation had no influence on this correlation. The area under the receiver operator characteristic curve (ROC AUC) of

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AMH was high for both poor (0.72) and excessive response (0.80). The ROC regression analysis demonstrated that the time interval from sampling did not affect the performance of either poor response or excessive response prediction.
Conclusion(s): A time interval up to 12 months between AMH serum sampling and initiation of ovarian stimulation does not appear to affect the correlation between AMH level and the number of oocytes retrieved and the predictive ability of AMH to identify women at risk of low or excessive ovarian response. (Fertil Steril® 2013;100:438–44. ©2013 by American Society for Reproductive Medicine.)
Key Words: AMH, AMH variability, excessive responders, OHSS, ovarian response, poor responder, stimulation, time interval

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Antimüllerian hormone (AMH) is increasingly being established as the serum biomarker of choice for predicting ovarian response to stimulation during in vitro fertilization–intracytoplasmic sperm injection (IVF-ICSI) cycles (1). Several large cohorts using long-course gonadotropin-releasing hormone (GnRH) agonist stimulation protocols have shown a strong correlation of AMH with the number of oocytes retrieved, with a very high predictive ability for poor and excessive ovarian response, equivalent to that of the antral follicle count (AFC) (2–4). Even when the analyses are restricted to cycles that have used GnRH antagonist–based strategies, with the inherent differences in follicular recruitment, these strong associations persist (1).

Given the ability of AMH to predict both a poor and excessive ovarian response, using AMH to tailor ovarian stimulation has been proposed by several investigators (5–7). The ability of AMH to accurately identify women at risk of ovarian hyperstimulation syndrome (OHSS) is potentially its greatest utility, as we now have a variety of techniques available to us to reduce or completely eliminate the risk of this potentially fatal complication (8–10). Initial studies using an AMH stratified approach to individualize treatment have demonstrated a significant reduction in OHSS (6) while not compromising live-birth rates (11).

However, as the use of AMH has become more common, when it is measured in the fertility workup has also changed. In the initial studies, AMH was primarily assessed during the menstrual cycle immediately preceding the cycle of ovarian stimulation (4, 12, 13). However, now AMH is increasingly measured much earlier, during the initial fertility workup and even by primary care physicians before referral to specialist services. In fertility centers, this assessment frequently takes place significantly earlier than the initiation of ovarian stimulation. This delay may be even be more pronounced in centers that have a high volume of patients, or when the initial plan is intrauterine insemination, with ensuing IVF-ICSI in case of treatment failure.

Given that serum AMH levels decline with age (14, 15), and that this decline may be as much as 15% per annum (16), a key question is whether the interval between AMH serum measurement and initiation of stimulation may adversely affect the performance of AMH for predicting ovarian response. To address this question, we have examined in a large, single-center cohort study of women undergoing their first IVF cycle whether the time interval between serum AMH sampling and initiation of ovarian stimulation affects the correlation of AMH and oocyte yield. More importantly, we also assessed whether a delay of up to 12 months affects the ability of AMH to predict both poor and excessive ovarian response.

MATERIALS AND METHODS

Institutional review board approval was obtained for the current study (B.U.N. 143201111492), and all patients gave written authorization at the time of treatment for the future use of their clinical data. The eligible cohort were all consecutive patients who fulfilled the following criteria: [1] having at least 2 years of infertility, [2] undergoing their first IVF-ICSI attempt from 2010–2011, [3] being treated with a fixed GnRH antagonist protocol followed by recombinant follicle-stimulating hormone (FSH), and [4] having AMH values tested in our laboratory with the Immunotech Beckman Coulter AMH enzyme-linked immunosorbent assay (ELISA) kit during the preliminary fertility workup at their first consultation.

Antimüllerian Hormone Measurement

Serum AMH samples were obtained during the initial fertility workup. Samples were obtained at the first consultation, regardless of the day of the menstrual cycle. Blood was drawn in plain serum tubes, centrifugation was performed within 1 hour, and the serum was separated and immediately stored at −80°C until analysis. All samples were measured with the Immunotech Beckman Coulter AMH ELISA kit. The AMH assay has demonstrated stable intra-assay and interassay coefficients of variation of <9.5% and a functional sensitivity of 0.35 ng/mL. All values are presented in ng/ml (to convert to pmol/L multiply by 7.14).

Interval between AMH Serum Sample and Initiation of Stimulation

The time interval between AMH measurement and initiation of stimulation was calculated in days. This time interval was calculated by taking into account the exact date of AMH sampling and the first day or initiation of stimulation and was analyzed as a continuous outcome. No restriction was applied regarding this time interval, and all patients who had an AMH serum sample before stimulation were considered eligible, regardless of the duration of this interval.