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Oncofertility E Update: May 2019, Fertility Preservation Society (India)

Importance of AMH testing before and after chemotherapy

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In the E-news update of May 2019 we highlight a recent publication, which demonstrates significant fluctuations of Anti-Müllerian hormone (AMH) during the menstrual cycle. In the past AMH measurements at any time of the menstrual cycle were considered reliable. We know that AMH is an important ovarian reserve marker for baseline assessment and therapeutic strategy in fertility treatments. This paper thus raises a question whether a single measurement is reliable for clinical decision-making. In oncofertility because of time constraints, we have to rely on AMH values tested at any time in the menstrual cycle, but we must be aware about the inter-cycle variability.

Key Message:

There is significant intra- and inter-cycle variations in serum AMH concentrations throughout natural ovulatory cycles and between two consecutive menstruations using a fully automated AMH assay. Thus the current clinical practice of using a single random AMH measurement in determining ovarian reserve at any time of the menstrual cycle should be revisited. This will apply to all women undergoing evaluation of AMH to determine the ovarian reserve. However this may not be possible in women with cancer subjected to fertility preservation due to scarcity of time available before initiation of chemo or radiotherapy.

Anti-müllerian Hormone During Natural Cycle Presents Significant Intra and Intercycle Variations When Measured With Fully Automated Assay

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Introduction

Anti-Müllerian hormone (AMH) a dimeric glycoprotein is produced by granulosa cells of pre-antral and small antral follicles in the ovary and its production is independent of follicle stimulating hormone (FSH). AMH concentration in serum is proportional to the number of developing follicles in the ovaries making it an important clinical marker of ovarian reserve. AMH levels are used in IVF to predict ovarian response, individualize stimulation protocols and counsel patients. Use of hormonal contraceptives, gonadotropins for ovarian stimulation, pregnancy, high BMI and smoking and lead to alteration in AMH. Variability in AMH concentrations during the menstrual cycle described earlier by some authors were attributed to analytical variations caused by different conditions used for sample

storage and/or the assay method. Use of the fully automated highly sensitive and precise AMH allow for more efficient sample processing and reducing possible procedural errors.

Material and Methods: Twenty-two healthy volunteers aged ≥ 18 to ≤ 38 years, with regular 28 - 32 days cycles and BMI between ≥ 18 and ≤ 28 kg/m² were included in the study. Exclusion criteria included : the intake of hormonal contraceptives for a minimum of 2 months prior to study commencement, pregnancy, breastfeeding, and previous conditions which may adversely affect ovarian reserve (ovarian surgery, chemotherapy, pelvic radiation). Blood samples were obtained between 8 am and 2 pm and were processed immediately. During the natural cycle, samples were collected on day 2/3 (AMH_01), day 10 (mid follicular phase, AMH_MFP), day of LH rise (AMH_LHR), mid luteal phase (AMH_MLP), and day 2/3 of the subsequent menstruation (AMH_02). AMH analysis was performed with Elecsys[®] AMH automated assay.

Results: There was a significant longitudinal fluctuation in AMH levels, indicated by the coefficient of variation (CV) intra-cycle of 0.2070 ± 0.143 . A positive correlation between LH and AMH concentrations was found at the moment of LH rise ($p < 0.0001$). No correlation between AMH and FSH, E2 and P4 was observed at any time of the measurements. Absolute intra-individual inter-cyclic variability was 0.75 ng/mL (range: 0.03–2.81 ng/mL) and inter-cycle CV was 0.28 (Confidence interval: 0.16–0.39; $p < 0.0001$). The average of the AMH values obtained on each day of measurement for all the 22 participants varies significantly through the cycle as shown as boxplot graph in Figure 1.

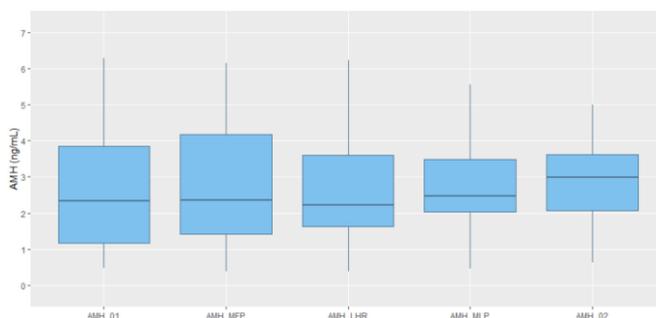


Figure 1: Average of the AMH values obtained on each day of measurement for all the 22 participants through the cycle

Conclusion: There is significant intra- and inter-cycle variations in serum AMH concentrations throughout natural ovulatory cycles and between two consecutive menstruations using a fully automated AMH assay.