CORRELATION AMONG INHIBIN A AND B, ANTI-MÜLLERIAN HORMONE, FOLLICLE-STIMULATING HORMONE, LUTEINIZING HORMONE, AND ESTRADIOL HORMONES IN INFERTILE WOMEN

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Abstract

Objective: The main purpose of this study was to assess ovarian reserve in infertile women and whether hormonal status depends on anti-Müllerian hormone level.

Study Design: This retrospective study evaluated and compared inhibins A and B, follicle-stimulating hormone, luteinizing hormone, and estradiol concentrations in 67 infertile women with anti-Müllerian hormone level <600 ng/L and in 39 infertile women with anti-Müllerian hormone level >600 ng/L. Data were analyzed using SPSS version 20 (IBM, Armonk, NY, USA) and reported as mean±standard deviation or number and percentage. The data in the study groups were nonparametric.

Results: The mean concentrations of inhibin A and B and estradiol levels were lower (p<0.05) in infertile women with low anti-Müllerian hormone level. Serum inhibin A level (p<0.01) positively correlated with inhibin B level in women with anti-Müllerian hormone level <600 mg/mL. In women with anti-Müllerian hormone level >600 mg/mL, negative correlations were found between inhibin A and B levels (r=0.494, R²=0.13, p<0.01) and between anti-Müllerian hormone and inhibin B levels (r=-0.426, R²=0.149, p<0.01), but a positive correlation was demonstrated between inhibin A and anti-Müllerian hormone levels (r=0.545, R²=0.096, p<0.01). The analyses of correlations between follicle-stimulating hormone and estradiol showed a major coefficient of correlation (r=0.545, R²=0.287, p<0.05). There was no correlation between age and anti-Müllerian hormone.

Conclusion: Differences in correlation between inhibin A and B levels in groups with different anti-Müllerian hormone levels demonstrate their importance in the evaluation of ovarian reserve in infertile women. Hence, we conclude that ovarian reserve assessment in infertile women should include not only the anti-Müllerian hormone level but also the inhibin A and B levels.

Keywords
Anti-Müllerian hormone, estradiol, infertile women, inhibin A, inhibin B, ovarian reserve

Introduction

Despite many studies showing anti-Müllerian hormone (AMH) concentration as a marker of ovarian reserve, a wide range of tests of ovarian reserve suggests that no single test provides a sufficiently accurate result¹. Although various direct and indirect biochemical measures were used to provide an insight, none fulfills the criteria of a single parameter satisfactory for ovarian reserve assessment².

Inhibins play an important role in regulating follicle-stimulating hormone (FSH) secretion³⁴. Two forms of inhibins (A and B) have been identified. Based on tissue localization, as assessed by in situ hybridization⁵ and immuno cytochemical methods⁶ and serum patterns during the menstrual cycle¹⁰,¹¹, inhibin B is believed to be produced by recruited follicles, whereas inhibin A is primarily a product of the dominant follicle. These data suggested that inhibin B may be a suitable marker of ovarian follicle reserve in the assessment of in vitro fertilization (IVF) outcome in women¹²,¹³, whereas inhibin A may provide an alternative index to serum 17β-estradiol (E2) for dominant follicular development¹⁴. Inhibins A and B are released by the granulosa cells of the ovarian follicle. Early follicular inhibin B correlates inversely with early follicular FSH levels in perimenopausal women¹⁵ and has been nominated as an early indicator of decreasing ovarian reserve¹⁶. Although inhibin B increases in the follicular phase, inhibin A has a luteal peak and should be further studied before being used as an indicator of ovarian reserve. Inhibin B, however, has an early follicular phase elevation followed by a decrease before another brief peak just after the luteinizing hormone (LH) surge and subsequent lower values in the luteal phase¹². This pattern suggests that inhibin B, as a granulosa cell product, plays a role in follicular development with the possibility that serum concentrations reflect follicular function and oocyte number. Another study suggested that decreased inhibin B secretion reflects a diminished ovarian follicular pool in older women¹⁰.

Studies investigating factors influencing AMH level in infertile women are only few. The aim of the present

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study was to determine the factors related with AMH level and other factors such as age, BMI, hypothyroidism, and hyperprolactinemia in infertile women by measuring the AMH, prolactin, LH, FSH, E2, and inhibin A and B levels and determining the LH:FSH ratio.17

**Methods**

This retrospective study was conducted at XXXX Institute, from January 2016 to December 2016, in accordance with the approved guidelines of the Azerbaijan National Committee on Bioethics and Ethics of Science and Technology. All subjects provided written consent for participation in this study after receiving complete information on the study’s scope and purpose.

We investigated 106 infertile women with mean age of 29.8±0.57 years (range, 20-41) years. All of the participants were seeking infertility treatment at the institute and were selected based on detailed history (including age, menstrual history, obstetric history, medication use, and addictions), clinical examination, and laboratory investigations. Standard anthropometric data such as age, height, and weight were measured, and the body mass index (BMI) was calculated as the weight (in kilograms) divided by the square of height (in meters). The exclusion criteria were male factor infertility, any obvious organic lesion such as ovarian tumor or cysts, tubal factor, any congenital anomaly of the urogenital tract, or any obvious organic lesion such as ovarian tumor or cysts.

The participants were divided into two groups based on serum AMH levels concentration: AMH level <600 ng/L and AMH level > 600 ng/L. Venous blood samples were collected from all participants in their early follicular phase of menstrual cycle, i.e., day 3. Serum AMH, inhibin A and B, FSH, LH, and E2 hormone levels were quantitatively measured through chemiluminescence immunoassay using AccuLite chemiluminescence immunoassay microwells (Monobind, Lake Forest, CA, USA).

**Statistical analyses**

Data were analyzed using SPSS version 20 (IBM, Armonk, NY, USA) and reported as mean±standard deviation or number and percentage. The data in the study groups were nonparametric. Significant differences between the groups were determined using the Mann-Whitney U test to assess differences in the levels of E2-, inhibin A- and B-, FSH-, and LH-specific antibodies. The same test was used to assess differences in the quantitative variables between groups. In all instances, significance was set at p<0.05.

Spearman’s correlation coefficient was calculated to find the relationship between non-normally distributed parameters, and p<0.05 was considered significant.

**Results**

The characteristics of the two groups are presented in Table 1. The concentrations of the ovarian polypeptide hormones inhibins A and B and E2 were low in women with AMH level <600 ng/L. A significant positive correlation (p<0.01) with mean coefficient r=0.546 was found, demonstrating a relationship between inhibin A and B levels.

Figure 2A–D shows the correlations in women with AMH level >600 ng/L. In women with AMH level >600 ng/L, negative correlations were found between inhibin A and B levels (r=-0.494, R²=0.13, p<0.01) and between AMH and inhibin B levels (r=-0.426, R²=0.149, p<0.01), but a positive correlation was demonstrated between inhibin A and AMH levels (r=0.545, R²=0.296, p<0.01). The analyses of correlations between FSH and E2 showed a major coefficient of correlation (r=0.545, R²=0.287, p<0.05). There was no correlation between age and AMH.

**Discussion**

The AMH, which is secreted by the granulosa cells of the small antral and pre-antral follicles in the ovary, diminishes...
Age is considered to be the single most important factor in determining the quality and quantity of ovarian reserve. Both the quantity and quality of ovarian follicles significantly decrease as a woman advances in age, and many women who postpone maternity may be infertile by the time they are willing to become pregnant. The probabilities of clinical pregnancy after intercourse on fertile days in women in age groups of 19–26, 27–34, and 35–39 years were approximately 50%, 40%, and 30%, respectively, with partners in the same age groups. In the present study, no difference was found in age depending on the level of AMH.

FSH and LH levels are commonly used for predicting ovarian reserve in the early follicular phase despite their lower predictive value. The day 3 LH/FSH ratio is relatively easy to obtain and shows more predictive power as the day 3 FSH level alone. As serum FSH increases during the early stage of reproductive aging and an increase in LH is observed at a later stage, the decreased basal LH/FSH ratio might be a sign of diminished ovarian reserve even with normal basal FSH. As the LH/FSH ratio may decrease as the ovarian reserve declines, the value of the LH/FSH ratio could play a significant role in determining the appropriate status of the ovarian reserve. However, although the LH/FSH ratio is clearly related to infertility, it is not related to AMH level in our study.

Serum inhibin A and B levels were lower in women with AMH level <600 ng/mL. These results demonstrate diminished ovarian reserve in these women.

Comment

This study determined a relationship among AMH, FSH, E2, and inhibin A and B levels in infertile women with AMH level >600 ng/mL. Differences in correlation between inhibin A and B levels in groups with different AMH levels demonstrate their importance in the evaluation of ovarian reserve in infertile women. Hence, we conclude that ovarian reserve assessment in infertile women should include not only the AMH level but also the inhibin A and B levels.

References


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