

Comparing Serum Follicle-Stimulating Hormone (FSH) Level with Vaginal PH in Women with Menopausal Symptoms

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Abstract

Objectives: Despite the important implication for women's health and reproduction, very few studies have focused on vaginal PH for menopausal diagnosis. Recent studies have suggested vaginal PH as a simple, noninvasive and inexpensive method for this purpose. The aim of this study is to compare serum FSH level with vaginal PH in menopause.

Methods: This is a cross-sectional, descriptive study, conducted on 103 women (aged 31-95 yrs) with menopausal symptoms who were referred to the Menopausal Clinic at Ghaem Hospital during 2006. Vaginal pH was measured using pH meter strips and serum FSH levels were measured using immunoassay methods. The data was analyzed using SPSS software (version 11.5) and results were evaluated statistically by the Chi-square and Kappa tests. $p \leq 0.05$ was considered statistically significant.

Results: According to this study, in the absence of vaginal infection, the average vaginal pH in these 103 menopausal women

was 5.33 ± 0.53 . If the menopausal hallmark was considered as vaginal $\text{pH} > 4.5$, and serum FSH as ≥ 20 mIU/ml, then the sensitivity of vaginal pH for menopausal diagnosis was 97%. The mean of FSH levels in this population was 80.79 mIU/ml.

Conclusion: Vaginal pH is a simple, accurate, and cost effective tool that can be suggested as a suitable alternative to serum FSH measurement for the diagnosis of menopause.

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Introduction

Menopause is the physiological cessation of menstruation which usually has a negative impact on the quality of life of most women.¹ It begins twelve months after the last menstruation and it is demonstrated by elevated levels of follicle-stimulating hormone (FSH). The average age of menopause has not changed from 600 B.C, the mean age has been 51.4 ± 3.8 yrs.^{2,3} In a study conducted by the "National Health Center", it was reported that the average age of menopause among Iranian women was 49.6 yrs, while among U.S women the average age of menopause was 51 ± 1 yrs.⁴ Increase in serum FSH, with or without a decrease of estradiol, has been observed in women over the age of 40 yrs who continue to cycle regularly.⁵ Moreover, abrupt fluctuation in serum FSH and estradiol may also be observed with postmenopausal levels returning to the normal reproductive range.⁶

Menopause is diagnosed by age, cessation of menstruation for more than one year and presence of symptoms. FSH can be used to confirm the diagnosis in the presence of the above and may not be necessary in most cases. Although recently, some studies have proposed vaginal pH as another method for this purpose.⁵ It has been known for decades that without vaginal infections, vaginal pH is ≤ 4.5 during the reproductive years and > 4.5 before menarche and after menopause. Contamination with cervical mucus, blood or semen leads to incorrect vaginal pH interpretation.⁷

There is a relationship between sufficient vaginal estrogen and the vaginal micro-organism and their metabolic products.^{8,9} In response to estrogen, vaginal epithelial cells proliferate, their glycogen content is increased and subsequently, lactobacillus produces lactic acid from glycogen and causes an acidic pH which maintains vaginal health.¹⁰ In the presence of vaginitis, vaginal pH of > 4.5 may indicate various infections such as bacterial vaginosis, trichomonas vaginalis, group B streptococcus or other pathogenic organisms.¹¹ In the absence of vaginitis, an elevated vaginal pH may reflect low circulating estrogen levels (estradiol < 40 pg/ml) or inadequate response of atrophic vaginal epithelium to estrogen therapy.¹²

However, like an elevated temperature at the time of ovulation, an elevated pH alone is only presumptive and not diagnostic. Menopause can be recognized by elevated serum FSH level, before the onset of symptoms. But this is an expensive test, and according to the patient's socioeconomic status, it is reasonable to choose a more cost effective, simple and noninvasive method.¹³ Some authors have suggested the evaluation of proposed vaginal pH as a good and inexpensive method. They reported that if vaginal $\text{pH} > 4.5$, then serum estradiol is more likely to be the same as menopausal level.¹⁴

In the absence of vaginitis, a vaginal pH of 6-7.5 strongly suggests menopause.¹³⁻¹⁵ Health care providers suggest routine vaginal pH examination as a part of well-woman examinations

and for diagnostic purposes in patients with symptoms of vaginitis or the request for hormone therapy.¹¹ The purpose of this study is to compare serum follicle-stimulating hormone (FSH) level with vaginal pH in women with menopausal symptoms (according to the inclusion criteria, all the women had menopausal symptoms).

Methods

This study is a cross-sectional descriptive study. The study subjects included 103 women with menopausal symptoms who were selected randomly from women referred to the Menopausal Clinic at Ghaem Hospital related to Mashhad University of Medical Sciences during 2006. A complete menstrual, sexual, medical and family history of early menopause was obtained and a questionnaire was completed for each woman including demographic characteristics (age, parity and body mass index), gynecological disorders and clinical manifestation of menopause. The patients' age ranged between 31- 95 yrs.

The inclusion criteria specified women who had clinical symptoms of menopause (no menstrual bleeding for at least one year with exclusion of other causes of amenorrhea or FSH>20 mIU/ml). The exclusion criteria comprised of; pregnancy, vaginitis, hormone replacement therapy, and sexual intercourse within the previous three days. The protocol was approved by the Ethics Committee at Mashhad University and all the women gave an informed consent.

The two quantitative variants were serum FSH level and vaginal pH. Serum FSH level was measured using the Radio immunoassay (Wakeman, UK). All the women were referred to a specific laboratory where the results were given. Vaginal pH was measured using pH meter strip (Macherey nagel, Germany). During vaginal examinations, after the insertion of a non-lubricated sterile vaginal speculum, a 2 cm of the strip was applied directly to the lateral vaginal wall at the outer third of the vagina until it became wet. Color changes of the strip were immediately compared with the colorimetric scale and the measurements were recorded. The spaces between colors on the pH meter was 0.03, which was more accurate compared to conventional pH meters in which the spaces are 0.5 in pH unit. Care was taken to avoid cervical mucus or anything that may affect the vaginal pH.

After data collection, statistical analysis was performed using SPSS software (version 11.5). Mc Nemar and Kappa tests were used to analyze the convergence of the two methods for the diagnosis of menopause. Moreover, Receiver operating characteristics (ROC) curve was used for the determination of cutoff point of pH with the highest sensitivity and specificity in regard to FSH test as a basic test. The Chi-square test was applied to compare different groups and $p \leq 0.05$ was considered statistically significant.

Results

On the basis of the results from this study, the mean age of the patients was 54.28 ± 8.59 yrs (ranging between 31-95 years) and 95% of the patients were below 70 years old. The length of amenorrhea was between 1 to 30 years. The mean and standard deviation for FSH level was 80.79 ± 6.42 mIU/ml (ranging from 18.6 to 349 mIU/ml). The mean vaginal pH for the women was 5.33 ± 0.53 (ranging from 4.1 to 5.9). According to this study, 97% of patients were determined to be menopausal on the basis of two criteria if FSH level was higher than 20 mIU/ml or if vaginal pH was ≥ 4.5 (all the women had menopausal symptom, but this test showed accurately that 97% of them were menopausal). In this study, by considering the FSH level as the base test and vaginal pH ≥ 4.5 with the sensitivity of 97% and confidence limit of 100, 93.6 of the patients were menopausal (Table 1). Kappa and Mc Nemar tests also confirmed the convergence of the two methods ($p=0.001$).

Table 1: The evaluation of sensitivity of vagina pH in diagnosis of menopause in 103 individuals studied in Menopause Clinic of Mashhad at Ghaem Hospital during 2006-2006.

Vagina PH FSH Level	pH \leq 4.5	pH>4.5	Total
FSH<20	2	1	3
FSH \geq 20	3	97	100
Total	5	98	103

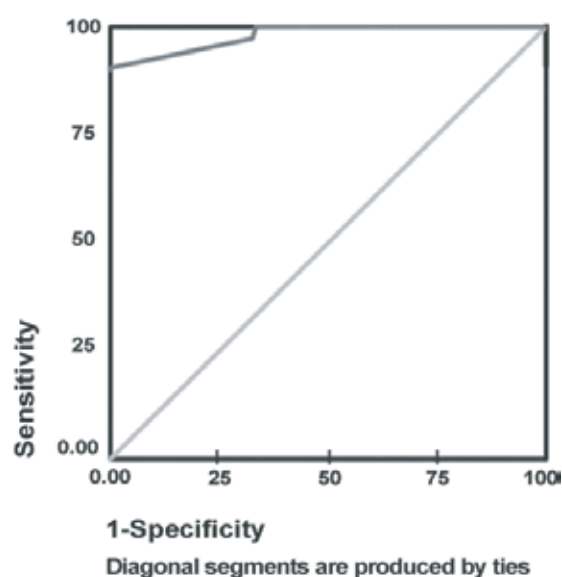


Figure 1: ROC curve for determining the best cut off point in order to determine the highest sensitivity for vaginal pH test

Discussion

Many menopausal women experience irregular menses and an array of symptoms long before they meet the definition of menopause.¹⁶ During menopause, two factors influence vaginal pH; menopausal status and the presence of potentially pathogenic organisms. In normal fertile women, lactobacilli maintain the normal acidic vaginal pH that protects the vagina against colonization.¹⁷ Some strains of lactobacilli produce hydrogen peroxide that prevents vaginal colonization with uropathogens.¹⁸ Therefore, the exclusion of vaginitis is essential for the vaginal pH to reflect the state of the menopausal vagina.

According to previous studies, there was a strong correlation between aging and increasing vaginal pH. During perimenopause, there is decreased number of functional follicles with less recruitment of oocytes upon FSH stimulation. Over time, as the aging follicles become more resistant to gonadotrophin stimulation, circulating FSH and leutinizing Hormone (LH) increase leading to stromal stimulation of the ovary, with an increase in estrogen and a decrease in estradiol levels. With the beginning of menopause and loss of follicles, the most significant change in the hormonal profile is the decrease in circulating estrogen levels.¹⁹ In menopausal women with urinary symptoms (such as dysuria) and raised vaginal pH, hormone replacement therapy can lead to normal vaginal pH and decreased symptoms.

In most postmenopausal patients who receive hormone replacement therapy, a vaginal pH of >4.5 may indicate low circulating levels of estradiol, which suggests the need for an adjustment of dose or route of hormone therapy. However, some patients with vaginal atrophy do not replenish their vaginal epithelium while receiving oral therapy, despite suitable circulating estradiol levels. For them, combining oral therapy with topical vaginal estrogen may be necessary. Atrophic vaginal epithelium permits greater absorption of estrogen compared with estrogenized epithelium.²⁰ Some review articles indicated that serum FSH and vaginal pH have similar sensitivity in indentifying menopausal status.¹⁴

In a large epidemiologic study conducted in Costa Rica, vaginal pH was a functional index of aging and menopause.¹⁶ They reported that $\text{pH}>5$ has the sensitivity of 64-67% for the diagnosis of menopause.

In the current study, the sensitivity of vaginal pH in the diagnosis of menopause was 97%. Cailloutte et al. assessed vaginal pH and serum FSH level among 172 postmenopausal women. They reported that the sensitivity of vaginal pH in predicting estradiol status was 88%.¹³ Roy and colleagues reported that in the absence of vaginitis, a vaginal $\text{pH}>4.5$ indicated menopause with

a sensitivity of 74%.¹¹ The reported sensitivity of vaginal pH in the present study (97%) was more than the reported results in previous studies, perhaps because of the decrease in sexual activity or the decrease of intervention effect on vaginal pH.

Contradictory to the results from this study, Burger et al. reported that serum FSH was unsuitable to determine the presence menopause. They evaluated FSH levels among 150 women aged between 45-55 yrs for 6 years on the 4th and 8th day of every menstrual cycle and after three months of amenorrhea.²¹ In another study, Burger showed that both serum FSH and LH were of little diagnostic value in the assessment of menopause.⁶ Moreover, Gow et al. indicated that biochemical parameters do not guarantee menopausal status and cannot distinguish the early postmenopausal period from the period preceding menopause.²²

In brief, according to this study, like serum FSH levels, vaginal pH is sensitive in the diagnosis of menopause, or low estrogenic status (97%).²³ If vaginal pH is >4.5 in a menopausal woman, she can benefit from hormone therapy.²⁴⁻²⁵

Conclusion

In the absence of vaginitis, vaginal pH is a simple, accurate, and cost effective tool that can be suggested as a suitable alternative to serum FSH in diagnosing age-related hormonal changes. This method facilitates evaluation of the patient's baseline estrogen status and can be used for menopausal women to show the therapeutic efficacy and patient compliance with estrogen replacement therapy. However, further studies are required in appropriate design to evaluate the method of vaginal pH measurement for diagnosing menopause as a reliable and good replacement for FSH measurement.

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