ORIGINAL RESEARCH

THE ROLE OF VAGINAL MATURATION VALUE ASSESSMENT IN PREDICTION OF VAGINAL PH, SERUM FSH AND E2 LEVELS

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ABSTRACT

Introduction: The objective of this study is to detect the correlation between vaginal maturation value (MV) and vaginal pH measurement, serum FSH and E2 levels in women without vaginal infection.

Materials And Methods: Fifty women with vasomotor symptoms were enrolled at the present study. All women underwent vaginal pH assessment, measurement of serum FSH and E2 levels and vaginal MV measurement in addition to routine follow-up. For determination of vaginal MV, pap smear from lateral vaginal wall was obtained and evaluated.

Results: In women with atrophic symptoms, the age and vaginal pH levels were significantly higher than women without these symptoms. Highly significant correlation between vaginal pH, vaginal MV and serum FSH was detected. Similarly highly significant inverse correlation was present between vaginal pH levels and vaginal MV.

Discussion: In summary, this study confirms that vaginal pH and MV are similar to FSH in the identification of patients who have low estrogen levels or who are menopausal. Methods of deriving vaginal pH and MV are simple, practical, quick and economic. As a conclusion, the present study demonstrated that vaginal pH measurement and vaginal MV assessment is similar in diagnosis and monitoring of estrogen deficiency in women with urogenital atrophic symptoms.

Keywords: vaginal maturation value, pH, menopause

VAJİNAL PH, SERUM FSH VE E2 SEVİYELERİNİ ÖN GÖRMEDE VAJİNAL MATURASYON İNDEKSİNİN DEĞERİ

ÖZET

Giriş: Bu çalışmanın amacı vajinal enfeksiyonu olmayan kadınlarda vajinal maturasyon değeri (MV) ile vajinal pH, serum FSH ve E2 değerleri arasındaki korelasyonu saptamaktır.


Anahtar Kelimeler: vajinal maturasyon değeri, pH, menopoz

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INTRODUCTION

Menopause has great impacts on life-quality of all women and is defined as cessation of menstrual bleeding for at least 12 months, serum FSH value ≥ 40 mIU/ml, and serum E2 level < 20 pg/ml. 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. Only methods of deriving reproductive years and > 4.5 before menarche and the presence of inflammation are useful marker to examine vaginal maturation and postmenopausal symptomatic women. MV is a diagnostic feature of menopause. In this study we aimed to detect the correlation of vaginal pH with vaginal atrophy and estrogen deficiency in post-menopausal women. MV is a useful marker to examine vaginal maturation and reveal vaginal estrogen deficiency regardless of the presence of inflammation. After the introduction of vaginal pH device, it has been proposed that determination of vaginal pH in the absence of vaginitis in an outpatient setting might be a diagnostic feature of menopause. In this study we aimed to detect the correlation of vaginal MV with vaginal pH measurement, serum FSH and E2 levels in women with climacteric symptoms.

METHODS

Study population: Fifty peri-postmenopausal otherwise healthy women attending to our menopause outpatient clinic with climacteric symptoms for the first time were enrolled at the present study. Demographic characteristics including age, gravidity, parity and body mass index (BMI) and urogenital atrophic symptoms were questioned by the presence of vaginal dryness, dyspareunia, pruritus and dysuria. All women underwent vaginal pH measurement, measurement of serum FSH and E2 levels and vaginal MV measurement in addition to routine follow-up. Amine test was carried out simultaneously with vaginal pH measurement in order to rule out vaginal infections and exclude false positive pH values. Women who have surgical menopause, systemic diseases, positive amine test, previous vaginal surgery involving more than 1/3 of the vagina, and women with history of current or past therapy of estrogen-progesteron replacement are excluded.

Vaginal pH measurement: Vaginal pH levels are measured by Quickvue® Advance pH and Amines Test, developed by Quidel® Corporation (San Diego, USA). This device is composed of a foil wrapped test (contains nitazine yellow for pH test and bromocresol green for amines test), and sterile amine controlled cotton swabs. Cotton swabs are applied to the lateral vaginal wall, then rubbed over the entire surface of the tests. Results are interpreted by formation of blue “plus” or “minus” sign on each test. Afterwards, nitazine paper is contacted to the vagina for 5 seconds, and the color of the paper is compared with a colorimetric scale on an enclosed card, and the pH value is determined.

Vaginal MV assessment: Cytological evaluation was performed by vaginal smears collected from the mid-third of the vaginal lateral wall and evaluated in our Pathology Department. In a total of 100 exfoliation cells, parabasal cells (P), intermediary cells (I), and superficial cells (S) were counted and results were expressed as the maturation value (MV) of Meisels. Superficial cells were assigned a point value of 1.0, intermediate cells were assigned a point value of 0.5, and parabasal cells were assigned a point value of 0. The number of cells in each category was multiplied by the point value, and the 3 results were added to arrive at a maturation value. A value of 0 to 49 indicated low estrogen effect, a value of 50 to 64 indicated moderate estrogen effect, and a value of 65 to 100 indicated high estrogen effect. All examinations were interpreted by the same cytopathologist without prior knowledge of the subjects’ data.

Statistical analysis: In women with negative amine test, chi-square test, Pearson correlation test and logistic regression test were used where appropriate to assess vaginal pH levels and vaginal MV with menopausal status and urogenital atrophic symptoms. For statistical analysis SPSS 11.5 (SPSS, Inc, Chicago, IL, U.S.A.) was used.

RESULTS

Out of 50 women enrolled, 2 had positive amine test and remaining 48 women were included into the statistical analysis. The mean age was 54.7 years (range 47-70 years), mean body mass index was 25.5. Of the 48 women 18 (37.5%) had serum FSH levels < 40mIU/ml. The mean FSH value, E2 value, and MV were 53.3 mIU/ml; 17.4 pg/ml and 49.1 respectively. The percentage of women with pruritus was 18.7% (n=9); dysuria was 27% (n=13), vaginal dryness was 64.6% (n=31) and dyspareunia was 70.8% (n=34). All of the women with urogenital atrophic symptoms had vaginal pH values > 5.2 (mean value 6.5±0.48), MV < 65 (mean value 34.7±16.2), serum FSH levels > 40 mIU/ml and E2 levels < 20 pg/ml. The
The role of vaginal maturation value assessment in prediction of vaginal pH, serum FSH and E2 levels

demographic and hormonal characteristics of the women according to the presence of any of the questioned urogenital atrophic symptoms are listed in Table 1.

In women with atrophic symptoms, the age and vaginal pH levels were significantly higher than women without these symptoms (p<0.003; p<0.001 respectively). In addition, women with atrophic symptoms had significantly lower serum E2 levels, and vaginal MV (p<0.001; p<0.01 respectively) (Figure 1). However, serum FSH levels were statistically similar between groups probably due to high standard deviation values. There was no significant difference between groups according to gravidy, parity and body mass index.

Table 1: The demographic and hormonal characteristics of the women according to the presence of vaginal atrophic symptoms

<table>
<thead>
<tr>
<th>General Features</th>
<th>(+)</th>
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<tbody>
<tr>
<td></td>
<td>n=34 (70.8%)</td>
<td>n=14 (29.2%)</td>
<td>n=48 (100%)</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Gravidi</td>
<td>56.4 ± 5.1¹</td>
<td>50.1 ± 4.8¹</td>
<td>54.7 ± 5.5</td>
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<tr>
<td>Parity</td>
<td>3.3 ± 2.5</td>
<td>4.1 ± 2.2</td>
<td>3.5 ± 2.4</td>
</tr>
<tr>
<td>BMI</td>
<td>1.8 ± 1.2</td>
<td>2.2 ± 0.8</td>
<td>1.1 ± 3.5</td>
</tr>
<tr>
<td></td>
<td>25.1 ± 3.4</td>
<td>26.4 ± 3.7</td>
<td>25.5 ± 3.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hormonal Features</th>
<th>Mean ± SD</th>
<th>Mean ± SD</th>
<th>Mean ± SD</th>
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</thead>
<tbody>
<tr>
<td>Serum FSH (mlU/ml)</td>
<td>70.1 ± 23.2</td>
<td>12.6 ± 3.7</td>
<td>53.3 ± 32.8</td>
</tr>
<tr>
<td>E2 (pg/ml)</td>
<td>11.2 ± 5.4⁴</td>
<td>32.2 ± 15.5⁴</td>
<td>17.4 ± 13.4</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Vaginal</th>
<th>Mean ± SD</th>
<th>Mean ± SD</th>
<th>Mean ± SD</th>
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<tbody>
<tr>
<td>Maturation Value</td>
<td>34.7 ± 16.2³</td>
<td>83.8 ± 9.4³</td>
<td>49.1 ± 26.7</td>
</tr>
<tr>
<td>Parabasal</td>
<td>49.7 ± 27.7</td>
<td>4.6 ± 7.4</td>
<td>15.3 ± 24.5</td>
</tr>
<tr>
<td>Intermediate</td>
<td>75.6 ± 26.9</td>
<td>32.8 ± 35.3</td>
<td>63.1 ± 35.2</td>
</tr>
<tr>
<td>Superficial</td>
<td>4.7 ± 9.4</td>
<td>62.5 ± 34.1</td>
<td>21.5 ± 33.1</td>
</tr>
<tr>
<td>pH</td>
<td>6.5 ± 0.48²</td>
<td>4.6 ± 0.31²</td>
<td>5.9 ± 0.95</td>
</tr>
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</table>

¹ = p<0.003; ² = p<0.001; ³ = p<0.01; ⁴ = p<0.001

Figure 1: A-B) Different examples of atrophic vaginal smear (Pap stain x 100)
Pearson correlation analysis showed highly significant inverse correlation between vaginal MV and serum FSH ($r=-0.87; p<0.01$) (Figure 2). Similarly highly significant inverse correlation was present between vaginal pH levels and vaginal MV ($r=-0.9; p<0.01$) (Figure 3). Calculated correlation was moderate between vaginal MV and serum $E_2$ levels ($r=0.55; p<0.01$). MV significantly decreased concomitant with increasing serum FSH levels and increasing vaginal pH values. On the other hand, the decrease in MV only moderately correlated with decreasing circulating $E_2$ values. Linear regression analysis was performed and showed significant increase of vaginal pH and significant decrease of MV with rising serum FSH levels. In the present study the positive and negative predictive values for vaginal MV < 65 to predict serum FSH levels $\geq 40$mIU/ml was calculated as 100% and 83% respectively.

**DISCUSSION**

In the present study vaginal MV assessment and vaginal pH measurement correlates with serum FSH and $E_2$ levels. Accordingly estrogen deficiency in women can be detected by simply determining MV in vaginal smear specimens as well as measuring vaginal pH performed during routine gynecologic follow-up. The menopausal transition period lead to the development of certain signs and symptoms adversely affecting the life-quality of most women due to systemic estrogen deficiency. Most prominent of these symptoms are vasomotor hot flushes, insomnia, urogenital atrophy and problems in sexual function. In spite of the fact that vaginal dryness due to atrophic vaginitis is known to be present in up to 40% of postmenopausal women, the real incidence might be even higher since women, especially in advanced ages, regard these symptoms as age specific. Capewell et al, proposed that some clinical characteristics can predict the atrophy degree. In their study of 120 postmenopausal women, they found a correlation, among the atrophy degree at the vaginal cytology and the vaginal dryness at physical examination, low parity and physical thinness. However, Davila et al demonstrated weak correlations between symptoms scores and objective measures of genital atrophy. They concluded that vaginal pH is the solid predictor of maturation value and may be the most reliable indicator of urogenital atrophy. In the present study, the strong inverse correlation between vaginal pH and MV confirms the previous findings. According to the results of the present study, MV measurement can aid the clinicians to predict serum FSH levels and vaginal pH values. MV assessment alone could be a guide for the diagnosis and management of a woman with urogenital atrophy regardless of the presence of atrophic symptoms.

The positive correlation between vaginal pH and serum FSH has been demonstrated previously in the meta-analysis of 16 reports by Roy et al. In their study they confirmed that vaginal pH reflects circulating estradiol levels. Therefore, with the
use of vaginal pH values, it is possible to monitor the introduction dose, change the continuation dose and route of therapy in women receiving estrogen replacement therapy (ERT). In women with urogenital atrophic symptoms, who receive ERT, elevated vaginal pH decrease to lower levels resulting in partially or completely relief of the symptoms. In a postmenopausal woman who is on ERT, vaginal pH value of > 4.5 indicates low circulating estradiol levels, which suggests the need for an adjustment of dose or route of hormone therapy. However in the present study decreasing serum E2 levels were only moderately correlated with increasing vaginal pH values and decreasing MV. It has been demonstrated previously that in some women although serum E2 levels are sufficient, vaginal atrophy may persist. For them, augmenting oral therapy with topical vaginal estrogen may be necessary. In the present study the demonstrated inverse correlation between vaginal pH and MV point out that MV < 65, similarly, suggests vaginal estrogen deficiency although sufficient circulating E2 levels might be detected, and administration of ET or adjustments in dose or route of ET would be necessary.

In women with vaginitis, vaginal pH measurement has increased false positive results due to overgrowth of facultatively and obligately anaerobic bacteria, and is useful only for monitoring antimicrobial therapy. Therefore, amine test is preferably performed simultaneously with the vaginal pH measurement to rule out vaginal inflammation even in asymptomatic women. Conversely, MV is not adversely affected and can be safely used to document estrogen deficiency in women with vaginal inflammation.

From previous studies it is known that body mass index can influence serum E2 values and consecutively vaginal pH. In the present study body mass index of women without vaginal atrophic symptoms was similar to women with vaginal atrophy. Therefore body mass index was not a confounding factor in the present study.

The positive and negative predictive values should be calculated by epidemiologic population-based studies. The power of this study is not obviously enough to calculate a solid predictive value of vaginal pH or MV for menopausal status. On the other hand, percentages mentioned reflect the population referring to our clinic and might aid the clinicians in diagnosis and follow-up. It should also be noted that the population included into the present study was perimenopausal and early postmenopausal women; therefore results classified according to urogenital atrophic symptoms might not be generalized for older women who regard these symptoms as age specific.

In the present study we concluded that vaginal MV is similar to vaginal pH in the identification of patients who have low estrogen levels or who are menopausal. In postmenopausal women receiving ET, vaginal MV calculation would aid the clinicians, in the same manner as vaginal pH, to monitor the therapy, change the dose or route of administration, or augment the therapy with a topical vaginal estrogen. Methods of deriving vaginal MV and pH are simple, practical, quick and economic. Moreover, MV can be obtained simultaneously with Pap smear test, which is a part of routine follow-up, does not require additional intervention, and easily interpreted at office setting. As a conclusion the present study demonstrated that vaginal maturation value assessment, unlike serum E2 levels, is similar to vaginal pH values in diagnosis and management of estrogen deficiency in perimenopausal and early postmenopausal women with urogenital atrophic symptoms regardless of receiving past or current estrogen replacement therapy.

REFERENCES