

*FARIDA V. ABDIYEVA***ASSOCIATIONS BETWEEN SERUM FOLIC ACID LEVEL AND THE RISK OF ENDOMETRIAL HYPERPLASIA IN PERIMENOPAUSE**

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Doi: <https://doi.org/10.52340/jecm.2023.05.37>*ФАРИДА В. АБДЫЕВА***ВЗАИМОСВЯЗЬ МЕЖДУ УРОВНЕМ ФОЛИЕВОЙ КИСЛОТЫ И РИСКОМ РАЗВИТИЯ ГИПЕРПЛАСТИЧЕСКИХ ПРОЦЕССОВ ЭНДОМЕТРИЯ В ПЕРИМЕНОПАУЗЕ**

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РЕЗЮМЕ

Результаты нашего исследования показали, что у 100% женщин с гиперплазией эндометрия уровень фолиевой кислоты в сыворотке крови находился в пределах нормы. Наличие приливов в перименопаузальном периоде можно предотвратить приемом фолиевой кислоты в форме лекарственных препаратов или пищевых добавок. Проанализировав полученные результаты исследования, можно сделать вывод что у больных было достигнуто улучшение физического здоровья и социального качества жизни.

Introduction. In most countries, there is an increase in the aging population as a result of both longer life expectancy and declining fertility rates [1]. The World Health Organization has adopted a Global strategy and action plan on ageing and health to ensure adults live not only longer but healthier lives. Demographic data have shown that every year, 25 million women worldwide experience the menopause. This will result in 1.2 billion postmenopausal women worldwide by 2030 [2]. The menopause in Caucasian women occurs on average at age 51 [3]. Endometrial hyperplasia is diagnosed histologically in the presence of a proliferation of the endometrial glands resulting in an increase in gland-to-stroma ratio [4]. While endometrial hyperplasia can progress to endometrial cancer, the rate of progression depends on factors such as the degree of architectural abnormality and the presence or absence of nuclear atypia [5]. Endometrial cancer is the 6th most commonly diagnosed cancer in women worldwide, with the highest rates observed in developed countries, including the United States [6] with beyond 60,000 new cases in 2019 [7].

Endometrial hyperplasia is thought to evolve into endometrial carcinoma by first developing endometrial intraepithelial neoplasia (EIN)/atypical endometrial hyperplasia (AH), a histomorphologically defined process [7,8].

Most cases of EH are due to unopposed, prolonged exposure of the endometrium to estrogen hormone. Commonly reported concerns in perimenopause include hot flashes, dryness, depression, irritability, night sweats, headaches and sleep disorders, muscles and joint pains urinary frequency, cognitive impairment. Hot flash is the most common concern of perimenopausal women.

Hot flashes start by a sudden redness of neck, chest and is associated with a feeling of intense heat in the upper body; sometimes it ends with extreme sweating. Hot flashes usually last about 1 to 6 minutes. Despite the many studies that have been conducted on understanding the mechanisms involved in hot flash, its exact pathology is not known yet. Estrogen plays an important role in the etiology of hot flash, but it is not the only reason for its occurrence. Decline in estrogen activity increases the activity and stimulates of serotonin receptors (5-HT_{2A}) in the hypothalamus. Activation of these receptors results in changes in the regulation center and raises autonomic responses such as increased body temperature and sweating. These actions conclude in shivering and cooling of the body, which are a result of hot flash [9].

Today, there is limited information about perimenopausal women with endometrial hyperplasia and folic acid supplementation in other countries of the world and in particular, there are a few published studies about symptoms and quality of life in Baku, Azerbaijan.

Aim. The objective of this study was to investigate serum folic acid levels and their affect to hot flashes in perimenopausal women with endometrial hyperplasia.

Materials and methods. The study was approved by the Ethical Committee of Azerbaijan Medical University and was conducted on women visiting Obstetrics and Gynecology Department II and Oncology Department of Azerbaijan Medical University, situated in Baku.

Several menopausal symptoms experienced were taken into account and collected by the Menopause Specific QOL (MENQOL) – Intervention Questionnaire. A review of the assessment of questionnaires evaluating the QoL in perimenopausal women concluded that Menopause Specific Quality-of-Life (MENQOL) questionnaire was the often-used specific tool for assessing QoL in menopausal women. The questionnaire is translated into Azerbaijani and has 29 items spread over four domains: physical (16 items), vasomotor (3 items), psychosocial (7 items), and sexual (3 items) on a 7-point Likert scale ranging from 0 - not at all bothered to 6 – extremely bothered. For the analysis, score 1 for “No” and 2 for “Yes” given. The 41 perimenopausal women with endometrial hyperplasia who had concerns about hot flashes and AUB, were chosen to participate in the study. Morning fasting blood was drawn annually on days 2–7 of the menstrual cycle (follicular phase) for regularly cycling women. Detailed clinical history and gynecological examination including speculum and vaginal examination has done for all participants. Body mass index (BMI) was also calculated. Transvaginal ultrasonography (TVS) was performed in all patients. All women with endometrial hyperplasia (endometrial thickness >13 mm in pre-menopausal uterine bleeding) presented with pain, bleeding, hot flashes and tiredness. Women on hormone-replacement therapy, women with medically or surgically induced menopause, pregnant or breastfeeding women were excluded from the study.

Dilation and curettage are still common procedure performed for women with abnormal uterine bleeding in this transitional period. Endometrial tissue histopathological examination (HPE) was performed in all patients at the Department of Pathology. Informed written consent was obtained from each patient for the procedure.

Out of these 41 women, 39 were married, 2 divorced. Endometrial hyperplasia was diagnosed in patients of 45–55 years age group. The age of study population was distributed 25 women (61%) in the range of 45–50 years, follows by 16 women (39%) in the age group of 51–55. The age of menarche presented in range of 10-19 years. Under the observation 12 patients had high BMI. All patients were divided to 3 groups according to the BMI and degree of obesity, among them 8 patients with obesity grade I (66,66%), 2 patients with grade II (16,67%) and 2 patients grade III (16,67%) obesity.

All patients presented with complaints of pain, bleeding, dysuria. In our study, 41 perimenopausal women with endometrial hyperplasia were examined and evaluated by the MENQOL. Vasomotor symptoms were observed in perimenopausal women in the form of hot flashes (80%), sweating (70%) and night sweats (62%). TVS and EHP examination are important tools for detecting early endometrial carcinoma in perimenopausal women suffering with endometrial hyperplasia. TVS was performed in all patients revealed endometrial thickness in range of 13-27 mm.

On TVS 21 (51,2%) women with endometrial hyperplasia had endometrial thickness 13–17 mm and 18 (43,9%) women had endometrial thickness 18–21 mm, 2 (4,9%) women had endometrial thickness between 22 and 27 mm. Additionally, on TVS we found 21 cases of uterine fibroids and 8 cases of endometrial polyp.

According to the aim of our study we also investigated the folic acid levels in this group of patients. Interestingly, the present study demonstrated that endometrial hyperplasia was also characterized by unchanged levels of folic acid. The findings of our study are necessary in understanding the significance and role of vitamins in the endometrial hyperplasia. We found that folic acid administration for 8 weeks at a dosage of 1 mg/d for women with EH improved vasomotor symptoms. This suggests that folic acid supplementation may have advantageous therapeutic potential for women with EH.

Conclusion. In conclusion, we found that folic acid levels in our study group remained unchanged in women with endometrial hyperplasia in perimenopausal period. In our research we observed that folic acid in minimal dose had no side effects; therefore, it can be used for reducing hot flashes and improving the women’s quality of life. Future research should focus on understanding of mechanisms how folic acid affect nutrient status in perimenopausal women with endometrial hyperplasia, and how folic acid supplementation influence risk.

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Conflicts of Interest: The authors declare no conflict of interest.

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SUMMARY

The results of our study demonstrated that endometrial hyperplasia was also characterized by unchanged levels of folic acid. The findings of our study are necessary in understanding the significance and role of vitamins in the endometrial hyperplasia. We found that folic acid administration for 8 weeks at a dosage of 1 mg/d for women with EH improved vasomotor symptoms. This suggests that folic acid supplementation may have advantageous therapeutic potential for women with EH.

Keywords: Folic acid, endometrial hyperplasia, perimenopause

ფარიდა ვ. აბდიევა

ასოციაციები შრატში ფოლიუმის მუავის დონესა და ენდომეტრიული ჰიპერპლაზიის რისკს შორის პერიმენოპაუზაში

აზერბაიჯანის სამედიცინო უნივერსიტეტის მენობა-გინეკოლოგიის დეპარტამენტი, ბაქო, აზერბაიჯანი

რეზიუმე

ჩვენი კვლევის შედეგებმა აჩვენა, რომ ენდომეტრიუმის ჰიპერპლაზიას ასევე ახასიათებდა ფოლიუმის მუავის უცვლელი დონე. ჩვენი კვლევის დასკვნები აუცილებელია ვიტამინების მნიშვნელობის როლის გასაგებად ენდომეტრიუმის ჰიპერპლაზიაში. აღმოვაჩინეთ, რომ ფოლიუმის მუავას მიღება 8 კვირის განმავლობაში დოზით 1 მგ/დღეში ქალებისთვის EH-ით აუმჯობესებს ვაზომოტორულ სიმპტომებს. ეს მიუთითებს იმაზე, რომ ფოლიუმის მუავას დამატებას შეიძლება ჰქონდეს ხელსაყრელი თერაპიული პოტენციალი EH-ის მქონე ქალებისთვის.

