Effect of Folic Acid Versus Placebo on Hot Flashes in Menopausal Women Attending a Rural Family Practice Centre in Egypt: A double-blind randomized controlled clinical Trial

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ABSTRACT

Background: Globally, the number of postmenopausal women is expected to reach 1.1 billion by 2025. Menopausal symptoms can be so severe that they affect the quality of life (QOL) of menopausal women. This study aimed to assess the effect of folic acid on the frequency, severity, and score of hot flashes in postmenopausal women. **Methods:** A double-blind randomized placebo-controlled clinical trial was conducted at El Mahsama Family Practice Centre, Ismailia, Egypt, between August 2019 and October 2020 on 100 postmenopausal women who were randomly allocated into two groups: a 5 mg/daily folic acid group or an identical-appearing placebo group for 4 weeks. Data on socio-demographic characteristics and obstetric history were gathered using a semi-structured questionnaire. A daily hot flash record was used to collect information about the frequency, severity, and score of hot flashes. The menopause-specific quality of life (MENQOL) was used to assess the QOL of post-menopausal women. **Results:** There was a statistically significant difference between both groups regarding hot flashe frequency, severity, and hot flashes score ($p = 0.015$, 0.001, and 0.002), respectively. The folic acid group shows 22% of participants were clinically improved compared with no clinical improvement among the placebo group ($\chi 2 = 12.360$, $p<0.001$). It was found that there was no statistically significant difference between the groups regarding their MENQOL domains after treatment. **Conclusion:** Folic acid was effective in reducing the frequency, severity, and hot flashes score in postmenopausal women, so it can be recommended as an accessible and affordable method of treating hot flashes.

Keywords: Folic acid, Hot flashes, Menopausal women.

Introduction

By 2025, the number of postmenopausal women worldwide is expected to reach approximately 1.1 billion. [(1)] The menopausal transition (MT) is defined as beginning with irregular menstrual cycles

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and a gradual increase in follicle-stimulating hormone (FSH), without a concurrent rise in luteinizing hormone (LH). This transition concludes with the final menstrual period, which is traditionally confirmed only after 12 consecutive months of amenorrhea. [2]

On average, natural menopause occurs at 48.8 years of age globally, with variations ranging from 47.2 years in Latin America to 51.3 years in Australia. Due to increased life expectancy, women now spend more than one-third to one-half of their lives after the menopausal transition. [3]

During this phase of post-reproductive life, most women experience various physiological changes influenced by a diverse array of social, racial, psychological, and cultural factors. [4]

Previous studies have indicated that women are more likely to experience various menopause-related symptoms during the menopausal transition, including central nervous system disorders, sexual dysfunction, urogenital atrophy, and changes in cardiovascular, metabolic, weight, and musculoskeletal health.

The prevalence of menopausal symptoms varies significantly among women of different ethnicities. [6] Vasomotor (VMS), which includes hot and/or night sweats, is the most common manifestation of menopause and affects up to 80% of women.[7] These symptoms can significantly impact women's quality of life (QOL). Postmenopausal women with VMS may suffer from fatigue, sleep disturbances, anxiety, and depression, which may affect their ability and carry out daily activities. Regarding women, it can be crucial to treat symptoms postmenopausal improving their QOL. A woman's control is controlling her symptoms proportional to the proportional level of her knowledge and awareness. [9] Previous research has the most common postmenopausal symptoms were joint include (96.3%), pain disturbances (89.0%), physical and mental tiredness (88.0%), fatigue flashes hot depressive mood (74.5%), heart discomfort (72.8%), and bladder problems. [10] problems.

A previous study reported that folic acid (5 mg) is recommended as a safe, acceptable, and affordable alternative to hormone replacement therapy (HRT) for women. [11] Folic acid does not exhibit adverse effects associated with excessive folate ingestion from food in humans. In healthy individuals, daily oral doses of 5-10 mg of folic acid are generally well tolerated and rarely result in side effects. [12] There have been limited studies investigating the potential adverse effects of excessive folic acid intake, making it difficult to establish a threshold for high

folic acid consumption in the absence of such research. More recent observational studies have suggested potential side effects related to birth outcomes, hypersensitivity symptoms, and cancer risk. [13] This study aimed to explore the effect of folic acid on alleviating hot flashes in postmenopausal women, as folic acid may provide a safer, more cost-effective, and more acceptable alternative to standard HRT for postmenopausal women experiencing hot flashes.

SUBJECTS AND METHODS

Study design and setting: A randomized, double-blind, placebo-controlled clinical trial was conducted in the EL Mahsama family practice center, affiliated with the Faculty of Medicine, Suez Canal University, Egypt.

Participants:

Participants were recruited for the study between January 2019 and August 2019. Eligible women were postmenopausal aged 45 to 65 years old (at least 12 months since their last menstruation), healthy (based on medical history, physical examination, and basic blood tests), experiencing hot flashes; at least 14 hot flashes or night sweats per week in the 1st two screening weeks. Hot flashes or night sweats rated as severe or at least bothersome on 4 or more days per week. [14]

Exclusion criteria: Women with a known history of gastrointestinal disease, hematological disorders (pathologic vitamin B12 deficiency, pernicious anemia, aplastic and normocytic anemia,), participants with depression, renal, liver, heart, and hypothyroidism disease, and participants with depression, renal, liver, heart, and hypothyroidism disease.

Women on the following drugs were also excluded: Non-steroidal anti-inflammatory drugs in large doses, anticonvulsants as phenytoin, Cholesterol-lowering agents as cholestyramine, drugs with antifolate activities as methotrexate and trimethoprim, any chemotherapy, estrogen, sulphonamide drugs, sulfasalazine, daily multivitamins, and any herbal or over-the-counter medications used to treat hot flashes in the previous 30 days.

SAMPLING

The following formula was used to determine the sample size:

$$n = 2\left[\frac{\left(Z_{\propto/2} + Z_{\beta}\right) * \sigma}{\mu_1 - \mu_2}\right]^2$$

Zα/2 = 1.96 for a 95% confidence level, Zβ = 0.84 for a power of 80%, σ = standard deviation in the intervention group = 3.68, μ1 = 2.83 mean change in frequency of hot flashes among the intervention group, [15] μ2 = 0.74 mean change in frequency of hot flashes among the placebo group. [15] After

adding 20% dropout, the total sample size was 30 participants in each group.

Which was extended to 50 participants per group. The sample size was calculated for all primary outcomes and the higher sample size was selected.

Randomization and Blinding: Eligible women were randomized in a 1:1 ratio to treatment groups of folic acid or identical-appearing placebo for 4 weeks by computer randomization. The allocation was carried out by sequential sealed envelopes containing a randomization code.

An independent statistician generated the randomization and the allocation. Participants, data collectors, and clinical center staff were blinded to the participants' treatment assignments.

Tools of the study: Baseline data on participants' demographics, including age, education level, and financial condition, were collected a week before the commencement of the intervention.

Daily hot flash record: Keep daily diaries to track the frequency, severity, and annoyance of heat flashes. [16] Participants were advised to record each hot flash as soon as it occurred to reduce errors due to memory recall. Night sweats were to be noted no later than the morning when you awoke to start the day. Hot flash frequencies were determined using the number of hot flashes observed daily.

The severity of the hot flashes was coded as 0=None, 1=Mild, 2=Moderate, and 3=Severe. Mean severity was calculated by adding individual severity ratings and dividing by the total number of hot flashes experienced. The hot flash scores were determined as hot flashes frequency times the severity of the hot flashes. [17]

Clinical improvement (defined as a 50% reduction in the frequency of hot flashes from baseline) was calculated at baseline and the 4th week of treatment.

Menopause menopause-specific quality of life questionnaire (MENQOL); is divided into four domains: physical (16 items), psychosocial (7 items), vasomotor (3 items), and sexual (3 items).

An eight-point Likert scale, ranging from one to eight for each of the 29 items, with scores of 2-4 considered mild, 5-6 moderate, and 7-8 severe symptoms. [18] The Alpha Cronbach test was 0.721 for the (MENQOL) Arabic version which indicates reliable results. [19]

Intervention

Participants in the intervention group (50 women) received one tablet containing of 5 mg of folic acid daily for four weeks, and the control group (50 women) received placebo

tablets. Both medications were taken daily at a certain time for four weeks.

Tablets were packaged in closed bottles similar in shape and size and coded A or B in the faculty of pharmacy, at Suez Canal University. The researcher and participants were not aware of the codes being used until the end of the study. Patient compliance was followed by returning empty strips to the researcher.

Statistical Analysis

The obtained data were entered, processed, and analyzed using SPSS (Statistical Package of Social Science) 20. The Shapiro-Wilk test was used to examine the normality of the distribution. Comparison between values of different variables in the two studied groups was examined by either the unpaired t-test or the Mann–Whitney test for quantitative variables.

The Friedman test with Post Hoc Test (Dunn's) compared between more than two periods or stages within groups for abnormally distributed quantitative variables. P value < 0.05 is considered significant.

Ethical consideration: The Ethics Committee of the Faculty of Medicine, Suez Canal University, approved the study in November 2018 (code 3941). All participants in the study provided informed consent after being explained the goal of the study and the fact that they could withdraw at any time.

Results

A total of 100 menopausal women were studied and treated in two groups: the folic acid group (50) and the placebo group (50). There was no significant difference between the two groups in terms of patient baseline characteristics (Table 1). The mean age of the intervention group was 53.18 ± 2.99 years compared with 53.54 ± 3.01 years in the control group. The mean menopausal duration was 3.16 ± 1.60 in the folic acid group and 3.12 ± 1.59 in the placebo group. Table (1)

There was no significant difference in hot flash frequency between the two groups in the first, second, and third weeks of treatment; however, this difference was significant in the fourth week of treatment (U = 896.0, p = 0.015). With hot flash, frequency means 5.70±2.7 in the folic acid group compared to 7.43±3.48 in the placebo group. There was a significant difference (p< 0.001) in the frequency of hot flashes within groups at baseline and during treatment weeks. Table (2) The folic acid group showed 22% clinical improvement, while the placebo group showed no relevant

clinical improvement ($\chi 2$ =12.360, p<0.001).

Table (3): demonstrates that there was no significant difference in hot flash severity between the two groups during the first, second, and third weeks of treatment; however, this difference was significant in the fourth week of treatment (U= 715.50, p<0.001). The hot flash severity means 1.66 ± 0.29 in the folic acid group compared to 1.89 ± 0.26 in the placebo group.

The severity of hot flashes changed significantly (p < 0.001) across groups at baseline and treatment weeks.

Table (4): shows that there was no significant difference in hot flash score between the two groups during the first, second, and third weeks of treatment; however, this difference was significant in the fourth week after treatment (U= 794.0, p=0.002). The mean hot flash score was (9.66 ± 5.25) in the folic acid group compared to (14.09 ± 7.14) in the placebo group. There was a significant difference (p <0.001) between groups in terms of hot flash scores at baseline and during treatment weeks.

It was found that there was no statistically significant difference between the interventional and control groups regarding their MENQOL domains after treatment. Table (5)

Discussion

This study reported that folic acid in a dose of five mg/day reduced mean hot flashes frequency, severity, and hot flashes score in participants after four weeks compared to those in the placebo group.

Regarding clinical improvement, a further 22% of folic acid participants were clinically improved compared with no clinical improvement among the placebo group. It was found that folic acid significantly decreases postmenopausal hot flashes frequency compared to placebo (p-value = 0.015).

Our findings were consistent with a study conducted by Bani *et al.* which showed improvement in mean hot flashes frequency after four weeks of its administration. Before treatment, it was (7.31±6.79) in the folic acid group and (6.35 ±3.98) in the placebo group.

In the fourth week, there was a statistically significant difference between both groups regarding the mean of hot flashes frequency. The mean was (4.48 ±3.68) in the folic acid group compared to (5.61 ±3.59) in the placebo group (p < 0.001).[15]

Also, Freeman *et al.* reported that the mean frequency of hot flashes at baseline was (9.88 ±6.24) in the intervention group and (9.66 ±4.88) in the placebo group. Hot

flashes frequency decreased after 4 weeks of treatment to (4.37 ±4.39) in the intervention group and (2.49 ±4.12) in the placebo group.[20]

In the current study, the folic acid group shows that 22% of participants are clinically improved to treatment compared with no clinical improvement in the placebo group ($\chi 2$ =12.360, p<0.001).

A study conducted in Egypt by Gaweesh et al. reported about a 65% improvement in hot flashes frequency in the folic acid group compared to a 16% improvement in the placebo group. [11]

This study revealed that there is a noticeable decrease in mean hot flashes severity. There was a statistically significant difference between both groups in the fourth week after treatment (p < 0.001) and this is consistent with the study of Bani *et al.* stated that the difference between the two groups regarding mean hot flash severity was observed in the second, third, and fourth weeks (p< 0.001).[15]

Also, Freeman *et al.* showed a statistically significant difference regarding mean hot flashes severity (p<0.003) after four weeks of intervention. [20]

In the current study, there was a statistically significant difference between the two groups in the fourth week regarding the mean hot flash score (p = 0.002). Consistent with our research, Ewies *et al.* found that folic acid is more effective in reducing the hot flash score in postmenopausal women when compared to placebo.

However, the difference between the two groups did not achieve statistical significance. [21]

According to Gaweesh *et al.* using folic acid 5 mg for 4 weeks significantly reduced the severity of hot flashes compared to the control group. [11]

This study found that there was an unexpected response to placebo regarding the hot flashes. In the placebo group, there was also a statistically significant improvement in the hot flash frequency that started to be more remarkable from the third and fourth weeks in comparison to the first week. Ewies *et al.* were unable to show that folic acid was significantly superior to placebo in lowering the hot flashes Score over 12 weeks in postmenopausal women, which may be due to a greater than expected response to placebo. [21]

The effectiveness of hormone therapy was demonstrated in a Cochrane review of 9 placebo-controlled trials of oral estrogen therapy for menopausal hot flashes, however, it also revealed that those receiving

placebo treatment experienced a mean reduction of 58 % in hot flash frequency. [22]

This study reported, there was no statistically significant difference between both groups in terms of their MENQOL domains after treatment. This finding may be attributed to the lengthy recall period since MENQOL change was only assessed at the beginning and the fourth week of the intervention.

Furthermore, finding significant differences in the MENQOL requires a larger sample. In England, Ewies *et al*. found that, according to the Greene Climacteric Scale, folic acid had a greater benefit in ameliorating menopausal symptoms compared with placebo; however, the difference wasn't statistically significant.[21]

This study may have some limitations. First, because the questionnaire was self-reported, reporting and recall bias were unavoidable. The second limitation was selection bias, as women were recruited from one primary healthcare setting, which did not represent a truly community-based sample. The third limitation is the duration of the study.

Conclusion

According to the findings of the current study, daily treatment with 5mg of folic acid for postmenopausal women resulted in better hot flash frequency and intensity control than placebo. However, there was no noticeable effect on QOL. More research is needed to determine the efficacy and safety of long-term folic acid supplementation in menopausal women.

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Table (1). Comparison between the two studied groups according to patient characteristics

Parameter	Folic Acid (n = 50)	Placebo (n = 50)	Test of Sig.	P- Value
Age (years)	53.2 ± 3	53.5 ± 31	t=0.600	0.550
BMI (kg/m^2)	34.5 (30 –36)	33 (31 –36)	U=1195.0	0.703
Education				
Read and write	28 (56%)	31 (62%)	χ^2= 0.579	0.943 [a]
Primary	14 (28%)	12 (24%)		
Secondary	4 (8%)	3 (6%)		
University	4 (8%)	4 (8%)		
Occupation				
Housewife	44 (88%)	47 (94%)	χ^2= 1.099	0.487 [b]
Employee	6 (12%)	3 (6%)		
Marital Status				
Married	35 (70%)	39 (78%)	χ^2= 0.962	0.665 [a]
Divorced	5 (10%)	3 (6%)		
Widow	10 (20%)	8 (16%)		
Socioeconomic status				
High	7 (14%)	4 (8%)	χ^2= 1.840	0.606 [a]
Moderate	18 (36%)	15 (30%)		
Low	14 (28%)	16 (32%)		
Very Low	11 (22%)	15 (30%)		
Residency				
Rural	48 (96%)	47 (94%)	χ^2= 0.211	1.000 [b]
Urban	2 (4%)	3 (6%)		
Smoking				
No	48 (96%)	49 (98%)	χ^2= 0.344	1.000 [b]
Yes	2 (4%)	1 (2%)		
Parity				
Nulli Parous	0 (0%)	0 (0%)	χ^2= 1.010	1.000 [b]
Primi Parous	1 (2%)	0 (0%)		
Multi Parous	49 (98%)	50 (100%)		
Median (IQR)	4.50 (3 –6)	4 (3 –6)	U=1213.0	0.796
Menopause duration	3 (2 –4)	3 (2 –4)	U=1230.5	0.891
Menopause type				
Natural	49 (98%)	47 (94%)	χ^2= 1.042	0.617 [b]
Induced	1 (2%)	3 (6%)		

Normally quantitative data was expressed in Mean ± SD while abnormally distributed data was expressed in Median (IQR), and qualitative data was expressed using Number (%)

[a]: χ^2: Chi-square test [b]: FE: Fisher Exact

t: Student t-test U: Mann Whitney test p: p-value for comparing between the studied groups

Table (2). Comparison between the two studied groups in hot flash frequency change over time from baseline to week 4 of intervention.

Hot flash frequency	**Baseline**	**First week**	**Second week**	**Third week**	**Fourth week**	**Fr**	**P-Value**
Folic Acid	(n = 50)	(n = 50)	(n = 50)	(n = 50)	(n = 50)	153.025*	<0.001*
Mean ± SD.	8.47±3.47	8.30±3.52	7.38±3.20	6.82±3.04	5.70±2.71		
Median (IQR)	8.64 (5.7-11.4)	8.57 (5.3-11.4)	7.29 (5.0-10.1)	6.43 (4.3-9.4)	5.07 (3.4-7.6)		
p_0		0.137	<0.001*	<0.001*	<0.001*		
p_1			<0.001*	<0.001*	<0.001*		
Sig. bet. Wks.			p_2=0.014*, p_3<0.001*, p_4=0.003*				
Placebo	(n = 50)	(n = 50)	(n = 50)	(n = 50)	(n = 50)	24.734*	<0.001*
Mean ± SD.	7.72±3.58	7.79±3.66	7.69±3.48	7.50±3.44	7.43±3.48		
Median (IQR)	8.14 (4.3-10.3)	7.71 (4.0-11.1)	7.36 (4.3-10.9)	7.64 (4.0-10.4)	7.29 (3.9-10.0)		
p_0		0.155	0.924	0.023*	0.007*		
p_1			0.129	<0.001*	<0.001*		
Sig. bet. Wks.			p_2=0.029*, p_3=0.010*, p_4=0.681				
Difference between the 2 studied groups U P_5		1090.0 0.270	1150.0 0.490	1183.0 0.644	1108.0 0.327	896.0* 0.015*	

IQR: Inter quartile range SD: Standard deviation U: Mann Whitney test

*: Statistically significant at $p \leq 0.05$

Fr: Friedman test, Sig. Bet. periods were done using Post Hoc Test (Dunn's)

p: p-value for comparing between the studied time divisions

p_0: p-value for comparing between baseline and each other weeks

p_1: p-value for comparing between the First week and each other week

p_2: p-value for comparing between Second week and Third week

p_3: p-value for comparing between Second week and Fourth week

p_4: p-value for comparing between Third week and Fourth week

P_5: p-value for comparing between the studied groups (folic acid and placebo groups)

*: Statistically significant at $p \leq 0.05$

Table (3). Comparison between the two studied groups in hot flash severity changes over time from baseline to week 4 of intervention.

Mean hot flash Severity	Baseline	First week	Second week	Third week	Fourth week	Fr	P-Value
Folic Acid	(n = 50)	(n = 50)	(n = 50)	(n = 50)	(n = 50)	85.019*	<0.001*
Mean ± SD.	1.96 ± 0.21	1.95 ± 0.23	1.86 ± 0.24	1.79 ± 0.24	1.66 ± 0.29		
Median (IQR)	1.95 (1.80 –2.10)	1.90 (1.80 –2.10)	1.90 (1.80 –2.0)	1.80 (1.70 –2.0)	1.70 (1.50 –1.90)		
p_0		0.950	0.027*	<0.001*	<0.001*		
p_1			0.032*	<0.001*	<0.001*		
Sig. bet. Wks.			p_2=0.040*, p_3<0.001*, p_4=0.005*				
Placebo	(n = 50)	(n = 50)	(n = 50)	(n = 50)	(n = 50)	21.256*	<0.001*
Mean ± SD.	1.89 ± 0.22	1.91 ± 0.23	1.91 ± 0.22	1.88 ± 0.22	1.89 ± 0.26		
Median (IQR)	1.90 (1.70 –2.10)	1.90 (1.80 –2.0)	1.90 (1.80 –2.0)	1.80 (1.80 –2.0)	1.80 (1.70 –2.10)		
p_0		0.137	0.164	0.467	0.174		
p_1			0.924	0.027*	0.004*		
Sig. bet. Wks.			p_2=0.034*, p_3=0.006*, p_4=0.527				
Difference between the 2 studied groups U P_5	 1050.0 0.164	 1107.0 0.309	 1121.0 0.367	 1053.0 0.169	 715.50* <0.001*		

IQR: Inter quartile range SD: Standard deviation U: Mann Whitney test

*: Statistically significant at $p \leq 0.05$

Fr: Friedman test, Sig. Bet. periods were done using Post Hoc Test (Dunn's)

p: p-value for comparing between the studied time divisions

p0: p-value for comparing between baseline and each other weeks

p1: p-value for comparing between the First week and each other week

p_2: p-value for comparing between Second week and Third week

p_3: p-value for comparing between Second week and Fourth week

p_4: p-value for comparing between Third week and Fourth week

P_5: p-value for comparing between the studied groups (folic acid and placebo groups)

*: Statistically significant at $p \leq 0.05$

Table (4). Comparison between the two studied groups in hot flash score change over time from baseline to week 4 of intervention.

Mean hot flash score	Baseline	First week	Second week	Third week	Fourth week	Fr	P-Value
Folic Acid	(n = 50)	(n = 50)	(n = 50)	(n = 50)	(n = 50)	158.368*	<0.001*
Mean ± SD.	16.63 ± 6.92	16.23 ± 6.94	13.69 ± 6.09	12.22 ± 5.76	9.66 ± 5.25		
Median (IQR)	16.51 (11.43 – 23.14)	16.31 (11.10 – 21.60)	14.21 (8.40 –18.21)	11.74 (7.20 –17.29)	8.63 (4.71 –14.57)		
p_0		0.071	<0.001*	<0.001*	<0.001*		
p_1			0.001*	<0.001*	<0.001*		
Sig. bet. Wks.			p_2=0.016*, p_3<0.001*, p_4<0.001*				
Placebo	(n = 50)	(n = 50)	(n = 50)	(n = 50)	(n = 50)	19.200*	0.001*
Mean ± SD.	14.55 ± 6.92	14.78 ± 7.07	14.61 ± 6.68	14.04 ± 6.59	14.09 ± 7.14		
Median (IQR)	14.66 (7.71 – 20.0)	14.62 (7.71 –19.81)	14.01 (7.87 –19.43)	14.14 (8.54 –18.51)	14.80 (7.23 –18.0)		
p_0		0.155	0.776	0.137	0.015*		
p_1			0.255	0.004*	<0.001*		
Sig. bet. Wks.			p_2=0.077, p_3=0.007*, p_4=0.343				
Difference between the 2 studied groups							
U	1038.5	1115.0	1149.5	1055.0	794.0*		
P_5	0.145	0.352	0.488	0.179	0.002*		

IQR: Inter quartile range SD: Standard deviation U: Mann Whitney test

*: Statistically significant at $p \leq 0.05$

Fr: Friedman test, Sig. Bet. periods were done using Post Hoc Test (Dunn's)

p: p-value for comparing between the studied time divisions

p0: p-value for comparing between baseline and each other weeks

p1: p-value for comparing between the First week and each other week

p_2: p-value for comparing between Second week and Third week

p_3: p-value for comparing between Second week and Fourth week

p_4: p-value for comparing between Third week and Fourth week

P_5: p-value for comparing between the studied groups (folic acid and placebo groups)

*: Statistically significant at $p \leq 0.05$

Table (5). Comparison between the two studied groups according to score for each MENQOL domain before and after treatment.

MENQOL domains	MENQOL domain before treatment				MENQOL domain after treatment			
	Folic Acid (n = 50)	Placebo (n = 50)	U	p	Folic Acid (n = 50)	Placebo (n = 50)	U	p-Value
Total Vasomotor Median (IQR)	13.0 (7.0 –16.0)	12.0 (7.0 –15.0)	1187.0	0.663	10.0 (6.0 –13.0)	11.50 (7.0 –15.0)	1010.0	0.097
Psychosocial Median (IQR)	30.50 (21.0 –42.0)	33.50 (22.0 –44.0)	1145.5	0.471	30.50 (20.0 –42.0)	33.0 (23.0 –44.0)	1121.0	0.373
Physical Median (IQR)	70.0 (43.0 –103.0)	74.50 (49.0–105.0)	1173.0	0.595	74.0 (40.0 –102.0)	70.0 (50.0 –100.0)	1134.5	0.426
Sexual Median (IQR)	6.0 (3.0 –6.0)	6.0 (3.0 –6.0)	1217.0	0.809	6.0 (3.0 –7.0)	6.0 (3.0 –6.0)	1130.5	0.384

IQR: Inter quartile range U: Mann Whitney test

p: p-value for comparing between the studied group's statistical significance $p < 0.05$

MENQL: The Menopause-Specific Quality of Life

الملخص العربي

تأثير حمض الفوليك مقابل الدواء الوهمي على الهبات الساخنة لدى النساء في سن اليأس اللاتي يزرن مركز طب أسرة ريفي في مصر: تجربة سريرية عشوائية مزدوجة التعمية.

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الخلفية: على الصعيد العالمي، من المتوقع أن يصل عدد النساء بعد انقطاع الطمث إلى ١,١ مليار بحلول عام ٢٠٢٥. يمكن أن تكون أعراض انقطاع الطمث شديدة لدرجة أنها تؤثر على جودة الحياة (QOL) للنساء بعد انقطاع الطمث. كان الهدف من هذه الدراسة هو تقييم تأثير حمض الفوليك على تواتر وشدة ودرجة الهبات الساخنة لدى النساء بعد انقطاع الطمث. **الطرق:** أُجريت تجربة سريرية عشوائية مزدوجة التعمية مُضبوطة بالعلاج الوهمي في مركز طب الأسرة بالمحسمة، الإسماعيلية، مصر، في الفترة ما بين أغسطس ٢٠١٩ وأكتوبر ٢٠٢٠ على ١٠٠ امرأة في مرحلة ما بعد انقطاع الطمث، وتم تقسيمهن عشوائيًا إلى مجموعتين: مجموعة حمض الفوليك بجرعة ٥ ملجم/يوميًا. ومجموعة علاج وهمي متطابقة المظهر لمدة اربعة أسابيع. تم جمع البيانات حول الخصائص الاجتماعية والديموغرافية وتاريخ الولادة باستخدام استبانة شبه منظم. تم استخدام سجل الهبات الساخنة اليومي لجمع معلومات حول تواتر الهبات الساخنة وشدتها ونتيجتها. تم استخدام جودة الحياة الخاصة بانقطاع الطمث (MENQOL) لتقييم جودة الحياة للنساء بعد انقطاع الطمث. **النتائج:** كان هناك فرق ذو دلالة إحصائية بين المجموعتين فيما يتعلق بتكرار الهبات الساخنة، وشدتها، ونقاط الهبات الساخنة (P = ٠,٠١٥، ٠,٠٠١، و٠,٠٠٢)، على التوالي. تظهر مجموعة حمض الفوليك أن ٢٢% من المشاركين قد تحسنوا سريريًا مقارنة بعدم وجود تحسن سريري بين مجموعة الدواء الوهمي($\chi 2 = 12.360$ P< 0.001) ، وقد وجد أنه لا يوجد فروق ذات دلالة إحصائية بين المجموعتين فيما يتعلق بمجالات MENQOL الخاصة بهم بعد العلاج. **الخلاصة:** كان حمض الفوليك فعالا في الحد من تكرار وشدة ودرجة الهبات الساخنة لدى النساء بعد انقطاع الطمث، لذلك يمكن التوصية به كوسيلة سهل الوصول إليها وبأسعار معقولة لعلاج الهبات الساخنة.