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ORIGINAL ARTICLE

The effect of folic acid supplementation on serum homocysteine of egyptian post menopausal women: A randomized controlled trial

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KEYWORDS

Folic acid;
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Abstract *Objective:* To evaluate the effect of folic acid supplementation on serum homocysteine (HCY) level in Egyptian post-menopausal women.

Patients and methods: The current randomized controlled trial was conducted at the Ain Shams University Maternity Hospital, Cairo, Egypt. 100 included women were divided into three groups: group C; 20 premenopausal women while the rest 80 women were postmenopausal (who were randomly divided into two groups; group A who received 5 mg folic acid for 6 weeks and group B who received placebo). Blood samples were collected from 100 women. Other samples were collected from 80 women (postmenopausal) 6 weeks after treatment. Serum was analyzed for HCY.

Results: Serum HCY was significantly higher in postmenopausal than premenopausal women (14.7 ± 6.4 μmol/L versus 6.3 ± 1.4 μmol/L, in group A and group C, respectively) and (15.3 ± 5.4 μmol/L versus 6.3 ± 1.4 μmol/L, in group B and group C, respectively).

HCY was significantly reduced in postmenopausal women after receiving folic acid (14.7 ± 6.4 μmol/L versus 12.4 ± 6.4 μmol/L, before and after treatment, respectively), while there was a decrease in serum HCY level of postmenopausal women after receiving placebo but not to reach a statistical significant level (15.3 ± 5.4 μmol/L versus 14.9 ± 7.6 μmol/L, before and after placebo, respectively). There was a statistical significant reduction in serum HCY in group A after receiving 5 mg folic acid compared to group B after receiving placebo (12.4 ± 6.4 μmol/L versus 14.9 ± 7.6 μmol/L, respectively).

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Conclusion: Serum HCY level was significantly higher in Egyptian postmenopausal than premenopausal women. Postmenopausal Folic acid supplementation seems to reduce serum HCY, but not to premenopausal level.

Introduction

Hyperhomocysteinemia is an independent risk factor for atherosclerotic diseases including ischemic heart disease, stroke and peripheral vascular disease. This may be due to endothelial dysfunction and excessive oxidation of LDL cholesterol (1). Plasma homocysteine (HCY) is significantly lower in premenopausal women than young men but after menopause basal homocysteinemia increases significantly in women approaching those in men (1). Ischemic heart disease is largely a disease of postmenopausal women that may be related to advancement of age and change of hormonal milieu. Folic acid supplementation has also been associated with a reduction in carotid atherosclerosis progression (2). Moreover, Jalali et al. indicated that prescribing folic acid 2 mg/day for a short time (3 months) decreases significantly serum homocysteine levels and morbidity indices (3). The aim of the present study was to evaluate the effect of folic acid supplementation on serum HCY level in post-menopausal women.

Patients and methods

The current randomized controlled trial was conducted at the Ain Shams University Maternity Hospital during the period from June 2010 to June 2011.

Women who agreed to participate in the study were informed about the nature of the study, the investigations they will undergo and its timing. An informed consent was signed by every participant after approval of ethics and research committee of council of obstetric and gynecology department, Ain Shams university hospital. Twenty pre-menopausal women (age ranged from 38 to 45 years old) and eighty post-menopausal women (age ranged from 52 to 60 years old) were included in the study. Women with impaired liver or kidney function, diabetic patients, taking multivitamins, drugs affecting folic acid as anticonvulsant, oral contraceptive pills and or hormone replacement therapy were excluded from the study. Included women were divided into three groups: group C: included 20 premenopausal women while the rest 80 women were postmenopausal (at least for 2 years), by then, each enrolled subject was allocated the next available number in the concealed sequence in a computer-generated randomization plan and this was done by the first author who played no role in patients' enrollment, so all participants, authors and *statisticians* were blind to the group allocation. The included 80 menopausal women were randomized into two groups: the first group (group A) included 40 women who were given folic acid tablets (Folic acid®; Nile company, Egypt) 5 mg/day for six weeks; the second group (group B) included 40 women who received placebo tablets for the same period. A venous blood samples were collected from 100 women (pre- and post-menopausal) after an overnight fasting of 12–14 h in ethlenediamine tetraacetate (EDTA) vacutainer tube of 4 mL and centrifuged within 30 min at 3000*g* for 10 min. Other venous samples were collected from 80 women (postmenopausal) after an overnight fasting 6 weeks after treatment. Serum was separated and stored at −20 °C until finally analyzed for HCY assay. HCY concentrations were measured using enzyme linked immunosorbent assay (ELISA) using HCY IMMULITE 2000 (kit lot 264) Siemens Healthcare Diagnostics, Germany.

After 6 weeks visit, all women said that they had taken their tablets regularly. Counts of unused tablets in the containers showed a maximum of 3 (of 42 initially), and 75% of the patients had taken all their tablets.

Primary outcome measure was serum HCY level in premenopausal and postmenopausal women. Secondary outcome measure was serum HCY level in postmenopausal women before and after the 6 weeks treatment with 5 mg folic acid or placebo.

Sample size justification:

On line statistical calculation was used for sample size calculation, guided by the following:

Power of test = (1- beta) = 80%
Confidence level = (1- alpha) = 90%
Expected response rate = 70%
Total population = 10000.
Total sample size (minimum accepted) = 100 women.

They were divided as follow:

80 post menopausal women. They were equally subdivided to two groups. Group A received 5mg folic acid for 6 weeks and group B received placebo.
20 pre menopausal women(group C).

Statistical analysis

Statistical analysis was performed using Microsoft® Excel® version 2010 and Statistical Package for Social Sciences (SPSS®) for Windows® version 15.0. Data were described as mean and standard deviation (for numeric continuous variables), number and percentage (for categorical variables). Difference between two groups was estimated using student's *t* test or paired t test which was used to compare between 2 means and standard deviations of the same group. *P* value < 0.05 is considered significant.

Results

A total of 100 women were included in this study. Included women were divided into three groups: group C: included 20 premenopausal women while the rest 80 women were postmenopausal (who were randomly into two groups; group A who received 5 mg folic acid for 6 weeks and group B who received placebo for the same period). Flow chart of postmenopausal women is shown in Fig. 1.