

The Baseline Serum Homocysteine Levels in Peri- and Postmenopausal Women

Hakan KIRAN¹, Gürkan KIRAN², Mustafa KAPLANOĞLU¹, Bülent KÖSTÜ², M. Turan ÇETİN¹

Adana-Turkey

OBJECTIVE: To investigate the effects of perimenopause, natural menopause and surgical menopause on the baseline serum homocysteine (Hcy) levels.

STUDY DESIGN: The baseline serum Hcy levels were measured in 33 perimenopausal and 153 postmenopausal women and were compared between groups

RESULTS: The mean Hcy levels of perimenopausal (n=33), natural menopausal (n=99) and surgical menopausal (n=54) women were 12,3 µmol/L, 13,4 µmol/L and 13,2 µmol/L, respectively. There were no statistically significant differences in the baseline levels of Hcy between the study groups (p=0.73).

CONCLUSIONS: The baseline Hcy levels of postmenopausal women were not higher than perimenopausal women. On the other hand, there were no significant differences in the baseline Hcy levels between the natural and surgical menopausal groups.

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Key Words: Homocysteine, Perimenopause, Natural menopause, Surgical menopause

Elevated homocysteine (Hcy) concentrations have been associated with increased atherosclerotic disease risk. Also mild hyperhomocysteinemia (i.e., fasting Hcy plasma levels >15 µmol/L) seems an independent risk factor for vascular diseases localized to the coronary, cerebral, and peripheral vessels.¹⁻⁴ Hormon therapy have been suggested to lower Hcy concentrations in postmenopausal women.⁵⁻⁹

Hcy is a thiol-containing amino acid produced by the demethylation of the dietarily obtained essential amino acid methionine.^{6,10} It is metabolized by transsulfuration via cystathionine to cysteine or by remethylation to methionine. The pathogenic role of Hcy as a cardiovascular risk factor is thought to be related to its influence on the coagulation system and the resistance of the endothelium to thrombosis. Hcy might also interfere with the vasodilator and antithrombotic functions of nitric oxide.⁵

Causes of hyperhomocysteinemia are multifactorial. Mild hyperhomocysteinemia may be the consequence of an impairment of the remethylation pathway due to a genetic (e.g., methylen-tetrahydrofolate reductase deficiency) and/or nutritional (deficiencies of folate, vitamin B6, and B12) deficit.^{5,6} Basal homocysteinemia is significantly higher in men than in women. After menopause, basal homocysteinemia levels increase significantly in women, approaching those in men.¹¹

¹Prof.Dr.M.Turan Cetin Women Health and IVF Center, Adana

²Department of Obstetrics and Gynecology, KSU School of Medicine, Kahramanmaraş

Address of Correspondence Hakan Kiran
M.Turan Çetin Kadın Sağlığı ve IVF
Merkezi 100. Yıl Mah. 132 Sok. No:1
Adana

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There are still many obscurities and controversial observations concerning the influence of menopause on Hcy levels in women. Investigations showed a significant increase in Hcy levels during postmenopause,¹¹⁻¹⁶ but this has not been confirmed by others.^{17,18}

Materials and Methods

A total of 186 healthy peri- and postmenopausal women with climacteric symptoms (hot flushes and/or outbreaks of sweating) were enrolled in the study. The mean Hcy levels of perimenopausal (n=33), natural menopausal (n=99) and surgical menopausal (n=54) women were measured. Ninety-nine natural menopausal (defined as amenorrhoeic for >6 months) women, aged 40 to 68 years, 54 surgical menopausal women, aged 42 to 59 years and 33 perimenopausal women with irregular cycles (generally oligomenorrhoeic), aged 36 to 48 years. Postmenopausal status was confirmed by serum FSH (follicle stimulating hormone) concentrations of > 30 mIU/L. There were no significant differences between the treatment groups at baseline levels of FSH, estradiol and Hcy (p > 0.05) (Table 1).

Blood samples were collected between 8:00 and 10:00 a.m. after at least 12 h fasting from a peripheral vein at study entry. All specimens were collected in Vacutainer (Becton-Dickinson, Franklin Lakes, NJ) blood-collecting tubes according to standard hospital guidelines for venipuncture and sample collection. Hcy specimens were placed on ice and all specimens were transported to the laboratory within 30 minutes of collection. Serum was obtained after centrifugation at 2,000 x g for 10 minutes, frozen, and stored at -20 °C until analysis. Serum total Hcy concentrations were measured by using an IMX (Abbott Diagn. USA) Hcy assay. Assay is based on the fluorescence polarization immunoassay (FPIA) technology.

Table 1. Descriptive Characteristics at Baseline.

Variable	Natural menopausal group (n=99)	Surgical menopausal group (n=54)	Perimenopausal group (n=33)
Age (y)	51.2 ± 5	49 ± 4	43.4 ± 3.3
Body mass index (kg/m ²)	31 ± 5.2	31.4 ± 3.8	29.6 ± 4.1
FSH (mIU/mL)	70.2 ± 32.5	71.5 ± 34	63.4 ± 42
Estradiol (pg/mL)	32 ± 38.2	29.2 ± 53.8	47.4 ± 62.4
Homocysteine (µmol/L)	13.4 ± 4.9	13.2 ± 4.2	12.3 ± 2.2

Note: Values are expressed as mean ± SD. All comparisons are nonsignificant.

FSH: Follicle stimulating hormone

Statistical analysis: For normally distributed data ANOVA test (followed by post-hoc Bonferroni test), for non-normally distributed data Kruskal-Wallis test (followed by post-hoc Mann-Whitney U test) were carried out. P values < 0.05 were considered statistically significant. Analyses were performed by using SPSS software, version 9.05 for Windows (SPSS Inc., Chicago, IL).

Results

The mean Hcy levels of perimenopausal, natural menopausal and surgical menopausal women were 12.3 ± 2.2 µmol/L, 13.4 ± 4.9 µmol/L and 13.2 ± 4.2 µmol/L, respectively. There were no statistically significant differences in the baseline levels of Hcy between the study groups. (p=0.73). (Table 1).

Discussion

There are still many controversial observations concerning the influence of menopause on Hcy levels in women. Wouters et al investigated that the concentrations of plasma Hcy in premenopausal and postmenopausal women, and examined that a possible relationship between plasma Hcy and estrogen status. 12 They have found that fasting plasma Hcy concentrations were significantly higher in postmenopausal women as compared to premenopausal women as well as postmethionine plasma Hcy concentrations. Hak et al shown that total Hcy is significantly higher in postmenopausal women than in premenopausal women.¹³ Similarly, Marchesoni et al reported that surgically postmenopausal women have higher plasma Hcy concentrations than premenopausal women¹⁴.

In the other study, Christodoulakos et al studied that the Hcy levels in postmenopausal women. They reported that the Hcy levels increased significantly after 60 years and menopause duration increased significantly Hcy levels after >180 months duration. Hcy levels did not differ significantly between women with natural and surgical menopause.¹⁵ In a review, Moustapha et al reported that the Hcy levels increase after menopause and may be related to decreased estrogen concentrations.¹⁶

On the other hand, Andersson et al measured that both free

and total plasma Hcy concentrations both fasting and post-methionine load, in healthy subjects. Neither fasting nor post-load values of free or total Hcy were lower in premenopausal women than in postmenopausal women.¹⁷ Bruschi et al reported that age, and not menopausal status, was the main determinant of Hcy levels in women around menopause.¹⁸

Our data suggest that menopause or perimenopause did not have significant changes on serum Hcy concentrations. Effects of menopause on Hcy concentrations is unclear. Further research is needed to better understand the effect of menopausal status on Hcy metabolism.

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