2005; Cilt: 2 Sayı: 2 Sayfa: 107-110

THE EFFECT OF ESTROGEN REPLACEMENT THERAPY ON PARAOXONASE, ERYTHROCYTE CATALASE AND ERYTHROCYTE MDA IN POSTMENOPAUSAL WOMEN

Fatih ŞENDAĞ*, Yasemin Delen AKÇAY, Kemal ÖZTEKİN*, Eser Yıldırım SÖZMEN****

* Department of Obstetrics and Gynecology,
** Department of Biochemistry, School of Medicine, Ege University, İzmir

SUMMARY

Objective: *Antioxidant and protective effect of high density lipoprotein (HDL) cholesterol for atherosclerosis is well known. The decrease of HDL concentration in postmenopausal women can be a reason for increased coronary artery disease due to atherosclerosis. The paraoxonase (PON) enzyme in blood is related with the antioxidant effect of HDL. Catalase (CAT), besides superoxide dismutase and glutathione peroxidase, is a natural antioxidant enzyme. Erythrocyte lipid peroxidation can be determined by the measurement of MDA, which is an index of oxidative damage. The objective of this study was to determine whether postmenopausal oestrogen replacement therapy has some effects on lipid peroxidation and antioxidative enzymes.*

Desing: *Thirty women, who had undergone menopause after surgery for a benign disease, were included in this prospective study. Mean age of the patients was 49.30+-4.16 years. Every patient was given conjuge equine estrogen 0.625mg p.o. daily for 6 months. PON, CAT and MDA were measured before the therapy (baseline), at the first month and sixth month of the therapy. We used paired-t-test to evaluate our findings.*

Setting: *University hospital*

Patients: *Thirty women who had undergone menopause after surgery for a benign disease INTERVENTION: Women were administered conjugated equine estrogen 0.625mg p.o. daily for 6 months*

Main Outcome Measure: *PON, CAT and MDA were measured before the therapy (baseline), at the first month and sixth month of the therapy*

Results: *The level of PON at baseline (PON1) was 65.79+-34.76 U/l, at the first month (PON2) was 34.76+-27.76 U/l and at the sixth month (PON3) was 76.93+-27.12 U/l. The p values for PON1-PON2, PON1-PON3 and PON2-PON3 were 0.308, 0.779 and 0.572; respectively. The level of erythrocyte CAT at baseline (CAT1) was 4600.88+-1056.04 U/g Hb, at the first month (CAT2) was 4675.74+-1487.01 U/g Hb and at the sixth month (CAT3) was 4393.31+-750.97 U/g Hb. The p values for CAT1-CAT2, CAT1-CAT3 and CAT2-CAT3 were 0.526, 0.448 and 0.689; respectively. The level of erythrocyte MDA at baseline (MDA1) was 27.85+-7.96 nmol/mg protein, at the first month (MDA2) was 30.33+-9.66 nmol/mg protein and at the sixth month (MDA3) was 24.92+-6.16 nmol/mg protein. The p values for MDA1-MDA2, MDA1-MDA3 and MDA2-MDA3 were 0.375, 0.147 and 0.179; respectively. There was no significant difference between any of the pairs above.*

Conclusion: *Our study demonstrated no increase of PON and erythrocyte CAT activities and no change in erythrocyte MDA level due to oestrogen replacement therapy in postmenopausal women. On the other hand, some other studies showed beneficial effects of oestrogen replacement in preventing atherosclerosis. More detailed studies are necessary to investigate this subject.*

Key words: *catalase, estrogen replacement therapy, paraoxonase*

Adress for Corresponding: Fatih ŞENDAĞ. Ege University Faculty of Medicine Department of Obstetrics and Gynecology
Bornova, 35100 İzmir, TURKEY
Tel: +90 (232) 388 19 63-300
Fax: +90 (232) 343 07 11
e-mail:sendag@med.ege.edu.tr
Alındığı tarih: 29. 04. 2005, kabul tarihi: 16. 05. 2005

ÖZET

Postmenopozal Kadınlarda Östrojen Replasman Tedavisinin Paraoksonaz, Eritrosit Katalaz ve Eritrosit MDA üzerine olan etkisi

Giriş ve Amaç: *Yüksek dansiteli lipoproteinin (HDL) antioksidatif ve ateroskleroza karşı koruyucu etkisi bilinmektedir. Postmenopozal kadınlarda HDL konsantrasyonunun düşmesi, ateroskleroza bağlı koroner arter hastalıklarında görülen artışın sebeplerinden biri olabilir. Serumdaki paraoksonaz (PON) enzimi, HDL'nin antioksidatif etkisiyle ilişkilidir. Süperoksid dismutaz ve glutatyon peroksidaz'ın yanı sıra, katalaz (CAT) enzimi de doğal antioksidan enzimlerden birisidir. Oksidatif hasarın bir belirteci olan malondialdehid'in (MDA) ölçülmesi, eritrositlerdeki lipid peroksidasyonunu belirlemede kullanılabilir. Bu çalışmanın amacı; postmenopozal östrojen replasman tedavisinin, lipid peroksidasyonu ve antioksidan enzimler üzerinde bir etkisinin olup olmadığının saptanmasıdır.*

Planlama: *Cerrahi menopozda olan sağlıklı 30 hasta, bu prospektif çalışmaya dahil edildi. Hastaların ortalama yaşı 49.30+-4.16 idi. Tüm hastalara 6 ay boyunca her gün konjuge ekin östrojen 0.625mg p.o. verildi. Tedavi öncesi, tedavinin birinci ayında ve tedavinin altıncı ayında PON, CAT ve MDA ölçümleri yapıldı. Sonuçları değerlendirmek için paired-t-test kullanıldı.*

Ortam: *Üniversite hastanesi*

Hastalar: *Cerrahi menopozda olan 30 hasta*

Girişim: *Hastalara 6 ay boyunca 0.625 mg/gün konjuge ekin östrojen verildi*

Ölçülen Parametreler: *Tedavi öncesi, tedavinin 1. ve 6. aylarda paraoksanaz, katalaz ve malondialdehit düzeyleri ölçüldü.*

Sonuçlar: *Ortalama PON seviyeleri; tedavi öncesinde (PON1) 65.79+-34.76 U/l, tedavinin birinci ayında (PON2) 34.76+-27.76 U/l ve tedavinin altıncı ayında (PON3) 76.93+-27.12 U/l idi. PON1-P0N2, PON1-PON3 ve PON2-PON3 çiftleri için p değerleri sırasıyla 0.308, 0.779 ve 0.572 idi. Ortalama CAT seviyeleri; tedavi öncesinde (CAT1) 4600.88+-1056.04 U/g Hb, tedavinin birinci ayında (CAT2) 4685.74+-1487.01 U/g Hb ve tedavinin altıncı ayında (CAT3) 4393.31+-750.97 U/g Hb idi. CAT1-CAT2, CAT1-CAT3 ve CAT2-CAT3 çiftleri için p değerleri sırasıyla 0.526, 0.448 ve 0.689 idi. Ortalama MDA seviyeleri; tedavi öncesinde (MDA1) 27.85+-7.96 nmol/mg protein, tedavinin birinci ayında (MDA2) 30.33+-9.66 nmol/mg protein ve tedavinin altıncı ayında (MDA3) 24.92+-6.16 nmol/mg protein idi. MDA1-MDA2, MDA1-MDA3 ve MDA2-MDA3 çiftleri için p değerleri sırasıyla 0.375, 0.147 ve 0.179 idi. Yukarıdaki eşleşmelerin hiçbiri arasında anlamlı fark saptanmadı.*

Tartışma: *Çalışmamızdaki bulgulara göre; postmenopozal kadınlardaki östrojen replasman tedavisine bağlı olarak, PON ve eritrosit CAT aktivitelerinde artış ya da eritrosit MDA seviyesinde değişiklik saptanmadı. Öte yandan diğer bazı çalışmalarda östrojen replasmanının aterosklerozu önlemede faydalı etkileri gösterilmiştir. Bu konuyu incelemek için daha fazla çalışma gereklidir.*

Anahtar kelimeler: *katalaz, östrojen replasman tedavisi, paraoksanaz*

INTRODUCTION

Oxidative stress has an important role in the pathophysiological mechanisms of some diseases, including cancer, atherosclerosis, cardiovascular diseases and aging. Lipid peroxidation is a free radical chain reaction of unsaturated fatty acids with molecular oxygen or reactive oxygen radicals. When exposed to oxidative stress, proteins and lipids, especially low density lipoprotein (LDL) cholesterol, are subject to oxidation. Modified LDL has a key function in the development of atherosclerotic processes. However, human organism has an effective antioxidant system with numerous mechanisms for protection against free radicals. These include superoxide dismutase (SOD), catalase (CAT), gluthatione peroxidase and reductase, paraoxonase (PON), metalloproteins, ascorbic acid, vitamin E, etc. Antioxidant and protective effect of high density lipoprotein (HDL) cholesterol for atherosclerosis is well known. The PON enzyme is related with the antioxidant effect of HDL. PON prevents LDL oxidation by removing oxidized phospholipids from LDL. Erythrocyte lipid peroxidation can be determined by the measurement of malondialdehyde (MDA), which is an index of oxidative damage.

Women before menopause are protected from the toxic effect of free radicals to the greater extent than men. Serum lipid peroxide levels are lower in women than in men. The difference in the protective action of female and male hormones against lipid peroxidation may explain this situation. Coronary arterial disease due to atherosclerosis is a more common cause of death in postmenopausal women. Decrease of HDL concentration in postmenopausal women can be a reason for increased atherosclerotic processes.

The objective of this study was to determine whether postmenopausal oestrogen replacement therapy has some effects on lipid peroxidation and antioxidative enzymes.

MATERIALS AND METHODS

The study was carried out in the Ege University Hospital, Department of Gynecology and Obstetrics, Izmir, Turkey. A total of 30 healthy hysterectomised postmenopausal women with climacteric complaints were enrolled in this prospective study. The study authorized by the Ethical Committee of the hospital and written informed consent was obtained from each subject. Postmenopausal status was confirmed by measurement of gonadotropin levels (follicle stimulating hormone >40 mU/mL and oestradiol <20 pg/mL) . None were taking drugs known to affect lipid metabolism and none had ever received sex steroid pellets (implants), or steroids by any other route within the previous six months. All were nonsmokers and consumed less than 300 gm alcohol per week. None had undiagnosed vaginal bleeding, severe metabolic, endocrine or gastrointestinal diseases, neoplasms, or hypertension. All were within 20% of their ideal body weight (as defined by Metropolitan life tables)

Mean age of the patients was 49.30+-4.16 years. Every patient was given conjugated equine estrogen (Premarin) 0.625mg p.o. daily for six months. PON, CAT and MDA were measured before the therapy (baseline), at the first month and at the sixth month of the therapy. We used paired-t-test and mean+-SD to evaluate our findings.

RESULTS

The results related to the influence of postmenopausal oestrogen replacement therapy on PON, CAT and MDA are shown in Table 1. As seen below, there was no significant difference in any of the parameters with regard to PON, CAT and MDA.

Table I: *Values are presented as mean value +- standard deviation. CAT: Catalase; PON: Paraoxonase ; MDA: Malondialdehyde. (1)=Baseline level ; (2)=Level at the first month of therapy ; (3)=Level at the sixth month of therapy.*

	Enzyme pairs	Mean	Std. deviation	p-value
	CAT(1)	4600.88	1056.04	0.526
	CAT(2)	4675.74	1487.01	
CAT (U/g Hb)	CAT(1)	4600.88	1056.04	0.448
	CAT(3)	4393.31	750.97	
	CAT(2)	4675.74	1487.01	0.689
	CAT(3)	4393.31	750.97	
	PON(1)	65.79	34.76	0.308
	PON-2	34.47	27.76	
PON (U/l)	PON(1)	65.79	34.76	0.779
	PON(3)	76.93	27.12	
	PON(2)	34.47	27.76	0.572
	PON(3)	76.93	27.12	
	MDA(1)	27.85	7.96	0.375
	MDA(2)	30.33	9.66	
MDA	MDA(1)	27.85	7.96	0.147
(nmol/mg	MDA(3)	24.92	6.16	
protein)	MDA(2)	30.33	9.66	0.179
	MDA(3)	24.92	6.16	

CONCLUSION

In many studies in the last few decades, postmenopausal oestrogen replacement therapy have been associated with reduced risk of coronary events. Oestrogens seemed to have some beneficial effects on plasma lipids and LDL oxidation. But more recent reports have suggested contradictory results about this subject. Sack et al reported an increase in the resistance of LDL to oxidation in postmenopausal women after administration of transdermal or i.v. oestrogen[1] . However in a different study, there was no significant increase in the lag time to oxidation in postmenopausal women after treatment with transdermal 17beta-oestradiol (0.1mg/day)[2].

Oestrogens are shown in many studies to have an inhibitory effect on antioxidants of LDL in vitro[3,4,5]. But it is important to evaluate whether this effect occus also in vitro. In the study of Mc Manus et al, the results does not support the role of oestrogen as an antioxidant in vivo. There may be some explanations for the opposite results in vivo and in vitro. First of all, the oestrogen concentration in vitro is 104-106 times greater than the level found in postmenopausal women

receiving HRT (in vivo). Also oestrogens have an effect on LDL particle size which results in increased proportion of small dense LDL particles. These particles have increased susceptibility to oxidation[6]. Our study demonstrated no increase of PON and erythrocyte CAT activities, and no change in erythrocyte MDA level due to oestrogen replacement therapy in postmenopausal women. Replacement therapy seems to have no effect on antioxidant enzyme activities. This study may not have enough power to make an exact statement on this subject because of small sample size. More detailed studies are necessary to investigate this subject.

REFERENCES

1. M.N. Sack, DiJi Rader and R.O. Cannon, Oestrogen and inhibition of LDL in postmenopausal women. Lancet 343 (1994), pp. 269-270
2. V. Guetta, J.A. Panza, M.A. Waclawiw and R.O. Cannon, Effect of combined 17b-oestradiol and vitamin E on LDL oxidation in postmenopausal women. Am J Cardiol 75 (1995), pp. 1274-1276
3. V.A. Rifici and A.K. Khachadurian, The inhibition of LDL oxidation by 17b-oestradiol. Metabolism 41 (1992), pp. 1110-1114
4. M.T. Ravi Subbiah, B. Kessel, M. Agrawal, R. Rajan, W. Abplanalp and Z. Rymaszewski, Antioxidant potential of specific oestrogens on lipid peroxidation. J Clin Endocrinol Metab 77 (1993), pp. 1095-1097.
5. J. Mc Manus, J. Mc Eneny, I.S. Young and W. Thompson, The effect of various oestrogens and progestogens on the susceptibility of LDL cholesterol to oxidation. Menopause 2 (1995), p. 275.
6. D. L. Tribble, L. G. Holl, P. D. Wood and R. M. Krauss, Variations in oxidative susceptibility among six LDL subfractions of differing density and particle size. Atherosclerosis 93 (1992), pp. 189-199.