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Original Research Article

Effect of Atenolol and Enalapril on Oxidative Stress in Pre and Postmenopausal Women with Essential Hypertension

Raj Kumar Das[1], Vaishali R. Das[2*], Juilee D. Sawalakhe[3], Shailaja R. Raghatate[4]

[1]Assistant Professor, Department of Biochemistry,
Super Specialty Hospital and Government Medical College, Nagpur, Maharashtra, India.
[2*]Professor and Head, Department of Biochemistry,
Dr. Rajesh Ramdasji Kambe Dental College and Hospital, Kanheri, Akola, Maharashtra, India.
[3]M.Sc Biotechnology, Symbiosis International University, Pune, Maharashtra, India.
[4]Director, Greeno Biotech Lab, Nagalwadi, Hingna, Nagpur, Maharashtra, India.

ABSTRACT

Background: There is an increased risk of morbidity and mortality in pre and postmenopausal hypertensive patients due to metabolic abnormality which leads to formation of free radicals. Hence; we estimated the oxidative stress in pre and postmenopausal essential hypertensive patients before and after the treatment with atenolol and enalapril.

Materials and Methods: 348 outpatient essential hypertensive women were selected for the study. The subjects selected were between the age group 30 to 70 years. All the subjects were divided into two groups, premenopausal hypertensive women and postmenopausal hypertensive women. The subjects in the premenopausal hypertensive women group had age 30-50 years. The subjects in postmenopausal hypertensive group had age 50 to 70 years. Equal numbers of patients from each group were selected for antihypertensive drugs, atenolol and enalapril.

Results: An increase in the level of superoxide dismutase, glutathione peroxidase against parallel decrease in the levels of malondialdehyde was observed. Pre and postmenopausal hypertyensive women treated with enalapril had highly significant concentration of above given oxidative parameters as compoared to those who were treated with atenolol.

Conclusion: Increased production of nitric oxide from the lungs induced by ACE-inhibitor, enalapril may be mediated by inhibition of angiotensin II production.

Key words: Atenolol, Enalapril, Postmenopausal.

***Correspondence to:**

Dr. Mrs. Vaishali R. Das
'Nirupama', 287, Lokseva Nagar,
Opp. Mokhare College, Bhamti, Nagpur, Maharashtra, India.

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INTRODUCTION

There is an increased risk of morbidity and mortality in pre and postmenopausal hypertensive patients due to metabolic abnormality which leads to formation of free radicals. Free radicals are formed during routine metabolic processes and are very reactive oxygen species.[1-3] Normally, these are very efficiently scavenged from the body. The defence mechanism in our body against free radicals is Superoxide Dismutase (SOD) in association with glutathione peroxidase.[4-5] Deleterious reactions of these free radicals are initiated when their level is increased due to exhaustion of antioxidant enzymes. Free radicals have capacity of attacking healthy cells of the body and cause them to lose their functional cell structure. Degenerative diseases like insulin resistance, hypertension and cardiovascular diseases are very commonly related to oxidative stress which is developed due to cellular damage caused by free radicals.[6-7]

Various studies around the globe have observed that in the pathogenesis of essential hypertension, oxidative stress has very important role.[8-10] So, this study was planned to estimate the selected parameters of oxidative stress in pre and postmenopausal essential hypertensive patients by the measurement of the concentration of malandione, superoxide dismutase and glutathione peroxidase before and after the treatment with the most commonly prescribed drugs beta-blocker-atenolol and ACE-inhibitor-enalapril.

MATERIAL AND METHODS

The study was conducted in the medicine department of the medical institute. 348 outpatient essential hypertensive women were selected for the study. The subjects selected were between the age group 30 to 70 years. All the subjects were divided into

two groups, premenopausal hypertensive women and postmenopausal hypertensive women. The subjects in the premenopausal hypertensive women group had age 30-50 years. The subjects in postmenopausal hypertensive group had age 50 to 70 years. Equal numbers of patients from each group were selected for antihypertensive drugs, atenolol and enalapril. The dosage of atenolol prescribed to selected subjects was 10-40mg/day and the dosage of enalapril prescribed to selected subjects was 5-20 mg/day. The direct effect of antihypertensive drugs, atenolol and enalapril on the oxidative stress was examined by collecting venous 12 hour fasting blood samples before and after 3,6, 12 months of treatment. Estimation of plasma Malondialdehyde, superoxide dismutase and glutathione peroxidase was done for the estimation of oxidative stress. Superoxide Dismutase (SOD) was measured using the method given by Markland et al.[11] In this method inhibition of auto-oxidation of pyragallol by superoxide dismutase is utilised for the investigation.Glutathione Peroxidase was investigated by using method given by Pagalia et al.[12] This method utilises the property of Glutathione to catalyse the oxidation of glutathione (GSH) by cumene hydroperoxide.Lipid peroxidation was established by measuring plasma malondialdehyde (MDA) by method given by Okhawa et al.[13] Staistcal analysis was observed using paired 't' test for Malondialdehyde, Superoxide dismutase and Glutathione peroxidase in control and essential hypertensive women patients. Paired 't'test was also used for statistical anallysis before and after the treatment in both premenopausal and postmenopausal women patients. Statistical significance was considered as P<0.05.

Table 1: Effect of atenolol versus enalapril on the level of malondialdehyde, superoxide dimutase and glutathione peroxidase in pre and post menopausal women with essential hypertension

Premenopausal Women						
		ATENOLOL			**ENALAPRIL**	
	Malondi-aldehyde (nm/ml)	**Superoxide dismutase (U/ml)**	**Glutathione Peroxide (U/ml)**	**Malondi--aldehyde (nm/ml)**	**Superoxide dismutase (U/ml)**	**Glutathione Peroxide (U/ml)**
BT	6.89±0.84*	1.65±0.25*	1.26±0.12*	7.11±0.91*	1.66±0.28*	1.19±0.17*
AT						
3 months	5.9±0.77	1.67±0.29	1.48±0.15	5.8±0.85	2.10±0.31	1.7±0.20
6months	5.5±0.62	1.86±0.32	1.69±0.19	4.9±0.80	2.57±0.35	2.0±0.22
12 months	5.11±0.55	1.99±0.35	1.81±0.20	4.15±0.75**	2.90±0.39**	2.21±0.25**
Postmenopausal Women						
		ATENOLOL			**ENALAPRIL**	
	Malondi-aldehyde (nm/ml	**Superoxide dismutase (U/ml)**	**Glutathione Peroxide (U/ml)**	**Malondi-aldehyde (nm/ml**	**Superoxide dismutase (U/ml)**	**Glutathione Peroxide (U/ml)**
BT	7.25±0.88*	1.55±0.27*	1.29±0.13*	7.15±0.92*	1.71±0.27*	1.21±0.18*
AT						
3 months	6.8±0.78	1.70±0.29	1.52±0.15	5.7±0.86	2.05±0.30	1.70±0.20
6months	5.9±0.69	1.88±0.32	1.7±0.17	4.8±0.76	2.56±0.36	2.05±0.23
12 months	5.53±0.55	1.92±0.36	1.86±0.18	4.2±0.62**	3.0±0.40**	2.30±0.26**

*P<0.001; **P<0.01

Figure 1: Effect of Atenelol on oxidative stress in premenopausal women with essential hypertension.

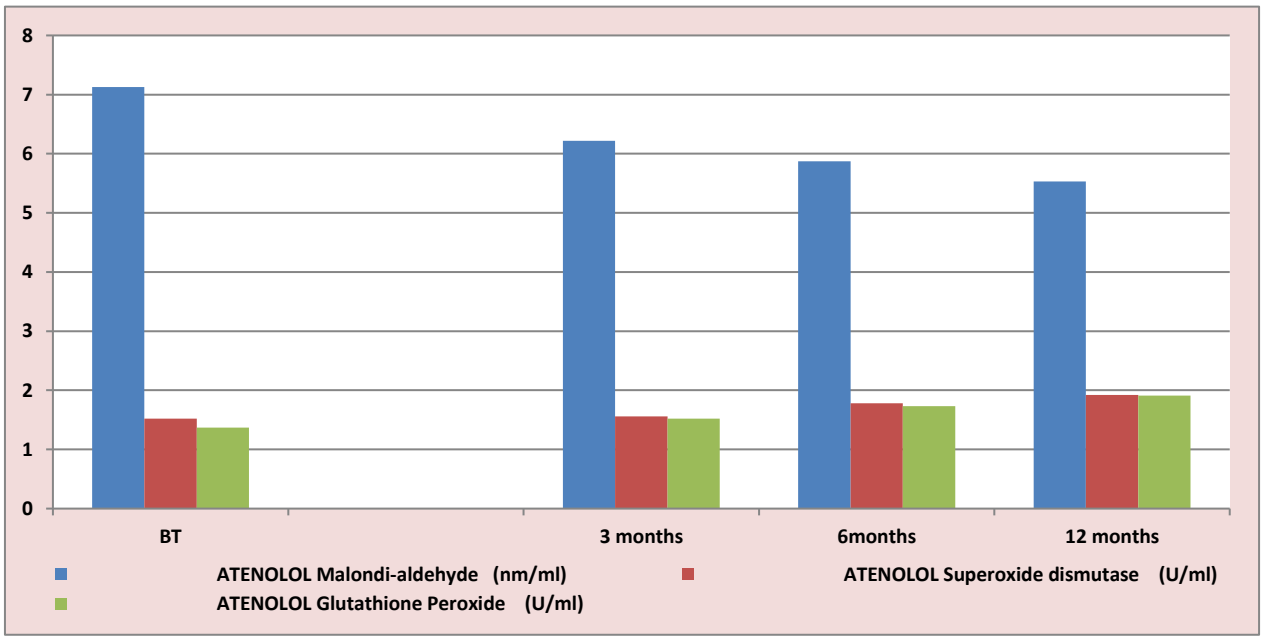
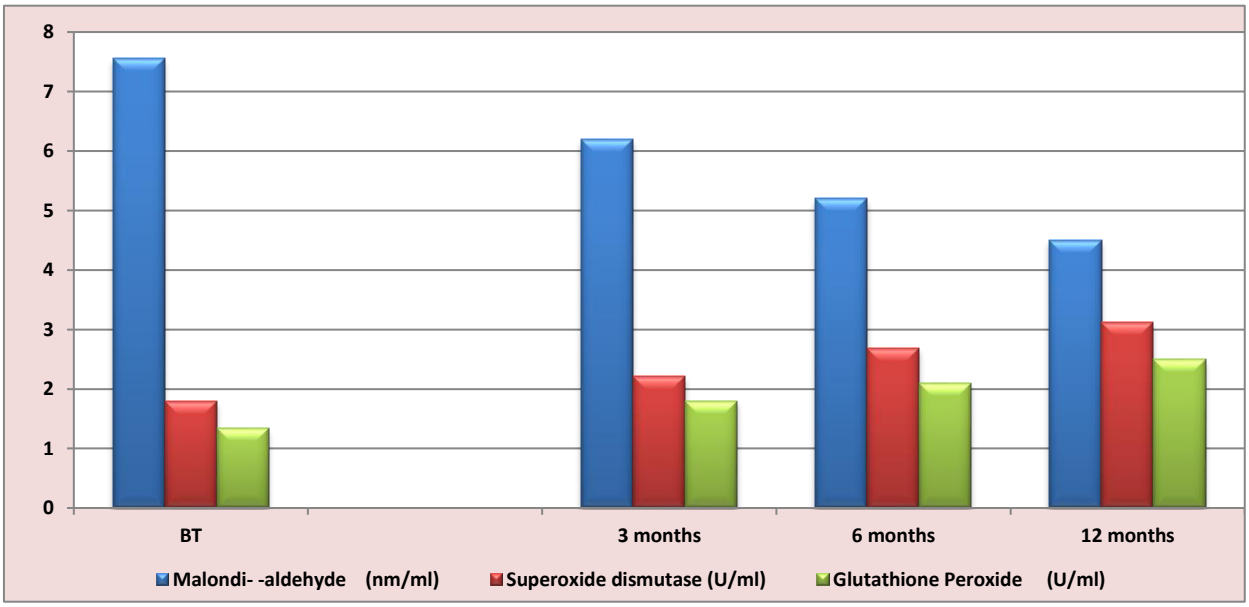


Figure 2: Effect of Enalapril on oxidative stress in premenopausal women with essential hypertension.



RESULTS

Pre and postmenopausal hypertensive women had significant variations in the level of malondialdehyde, glutathione peroxidase and superoxide dismutase as shown in table 1. Before the treatment, significant increase in the level of malondialdehyde and parallel decrease in antioxidant enzymes, superoxide dimutase and glutathione perooxidase was obserevd in pre and postmenopausal women. On the contrary, there was a gradual decrease in malondialdehyde levels and parallel increase in the activity of superoxide dismutase and glutathione peroxide after treatment with atenelol and enalapril at 3, 6 and 12 months. There was a non-significant decrease observed in the level of malondialdehyde with treatment of atenelol (6.89±0.84 to 5.11±0.55 nm/ml in premenopausal and 7.25±0.88 to 5.53±0.55 nm/ml in postmenopausal hypersensitive subjects). Also, there was a non-significant increasewith atenolol in the level of superoxide dismutase (1.65±0.32 to 1.95±0.35 U/ml in premenopausal and 1.55±0.34 to 1.92±0.36 U/ml in postmenopausal essential hypertensive women) and glutathione peroxidase (1.26±0.12 to 1.81±0.20 in premenopausal and 1.29±0.13 to 1.86±0.18 in postmenopausal essential hypertension).In contrast to atenolol, pre and postmenopausal hypertensive subjects treated with enalapril had significant increases in the level of malondialdehyde (7.11±0.91 to 4.15±0.75 nm/ml,P<0.001 in premenopausal and 7.15±0.92 to 4.2±0.62 nm/ml, P<0.01 in postmenopausal women); Superdioxide dismutase (1.66±0.28 to 2.90±0.39 U/ml, P<0.001 in premenopausal and 1.71±0.27 to 3.0±0.40 U/ml, P<0.01 in postmenopausal women) and glutathione peroxidase (1.19±0.17 to 2.21±0.25 U/ml, P<0.001 in premenopausal and 1.21±0.18 to 2.30±0.26 U/ml. P<0.01 in postmenopausal women).

DISCUSSION

In the present study, we observed that oxidative metabolic dysfunction was present in pre and postmenopausal women with essential hypertension. This was evident from the decreased serum level of antioxidants versus increased serum level of oxidative products. This results in the decreased synthesis of nitric oxide. Studies have shown that due to decreased activity of endothelial nitric oxide, reduced endothelial dependent vasodilation is observed in pre and postmenopausal women with essential hypertension. This indicates that increased vascular resistance that is characteristic to hypertensive process may be caused due to endothelail dysfunction.[14] Also,oxidative stress is documented as potentially important contributor to endothelial dysfunction.[15]

Sex hormones have an important role in cardiovascular diseases because normal premenopausal women have lower risk of cardiovasuclar disease as compared to postmenopausal women. A study conducted by Daniel J et al reported that there is a direct role of estrogen in decreasing oxidative stress. Oxidised low density lipoprotein cholesterol might be removed by estradiol and induce antioxidant enzyme nitric oxide synthase in the endothelium of arterial cells.[16] The frequent association of essential hypotension with postmenopause was observed in study conducted by Yanes et al. The abrupt interruptions of estrogen that have direct effect on vessel functions might be the risk related to postmenopause. Estrogen have infact vasodilator action due to nitric oxide release, calcium antagonist like action and anti-proliferative effect on smooth muscle cells which determines an increase in systemic vascular resistance. So, the prevelance of hypertension in postmenopausal women is more as compared premenopausal women because of increased oxidative stress due to estrogen deficiency in postmenopausal women.[17]

In the present study, we observed an increase in the level of superoxide dismutase, glutathione peroxidase against parallel decrease in the levels of malondialdehyde. Pre and postmenopausal hypertyensive women treated with enalapril had highly significant concentration of above given oxidative parameters as compoared to those who were treated with atenolol. So,it is confirmed from our study that with an increase in oxidative stress, there is resultant dysfunction of vascular endothelium in essential hypertension which is consistent with other reports.[18,19]

In the study conducted by Griendling et al, it has been shown that with Angiotensin II increased production of superoxide occurs, which quenches nitric oxide. On the contrary, peroxynitrite is yielded with the combination of superoxide with nitric oxide which

has high oxidising power and can oxidise arachdonic acid and thus release a potent renal vasoconstrictor 8-iso-prostaglandin F_2 (isoprostane).[20] Accordingly, the vasopressor effect of angiotensin II is enhanced due to vasoconstrictor effect of reduced nitric oxide increased isoprotane. This might be the reason for maintenance of hypertension in pathological situations.[21] An imortant observation that links superoxide production to an increased level of angiotensi-II shows how inhibition by angiotensin converting enzyme inhibitor, enalapril is responsible for the positive alteration of oxidative stress in pre and postmenopausal women with essential hypertension.[22]

CONCLUSION

Increased production of nitric oxide from the lungs induced by ACE-inhibitor may be mediated by inhibition of angiotensin II production. A special advantageous action of ACE inhibition not shared by other main anti-hypertensive class on conduit artery endothelium dependent vasodilation in patients with essential hypertension. Although endothelial dysfunction is an independent promotor demonsrate that the reversal of endothelail dysfunction can improve the prognosis of patients with hypertension.

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