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ORIGINAL ARTICLE

EFFECT OF ATENOLOL AND ENALAPRIL ON MICROALBUMINURIA IN PRE- AND POST-MENOPAUSAL WOMEN WITH ESSENTIAL HYPERTENSION

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ABSTRACT:

Background: The progression of renal, cardiovascular and cerebrovascular diseases is associated with increased Urinary Augmented Excretion (UAE) among hypertensive patients. Captopril is shown to reduce micro albuminuria and improve the insulin sensitivity in patients with essential hypertension. But, more study is needed to know about the efficacy of other non-sulfhydryl ACE inhibitor agents and β-blockers to have such action. In elderly patients with essential hypertension, micro albuminuria is now considered to be a marker for cardiovascular, cerebrovascular and renal risk. So, based on above subjects the present study was planned to study the effect of enalapril, non-sulfhydryl ACE inhibitor and atenolol, β-blocker on blood pressure and urinary albumin excretion in pre and postmenopausal women patients with essential hypertension. **Materials & methods:** The study included 30 pre and 30 postmenopausal women patients with mild to moderate essential hypertension and 60 normal controls for both the groups. The age group of premenopausal hypertensive women was 30-50 years and for postmenopausal hypertensive women it was 50-70 years. Clinical criteria were used for selection of all the patients. It was made sure that no patient had taken anti-hypertensive drugs before the study. Measurement of urinary creatinine was done to ensure completeness of the 24 hour urine collection and only those values were considered reliable with good urine collection that had values + 20% in comparison to expected values. All the results were recorded and analyzed. **Results:** The 24 hours urine samples of healthy premenopausal and postmenopausal normotensive subjects had 5.8 + 5.5 and 6 + 5.2 of UAE respectively In comparison to this, patients treated with enalapril showed less significant decrease in the level of UAE. In premenopausal women, UAE decreased from 31.51 + 5.45 to 14.77 + 3.1 mg/24 hours whereas in postmenopausal women UAE decreased from 33.15 + 5.8 to 18.22 + 2.8 mg/24 hours. **Conclusion:** Metabolic and homodynamic defects with pathogenic potentials regardless of the underlying mechanisms are signaled in hypertensive patients by micro albuminuria.

Key words: Atenolol, Enalapril, Hypertension

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INTRODUCTION

In patients with essential hypertension, the progression of renal, cardiovascular and cerebrovascular diseases is associated with increased Urinary Augmented Excretion (UAE).[1] 35% to 40% of patients with essential hypertension are reported having presence of microalbuminuria and it is considered as a strong marker for glomerular damage, which can be thought as an early sign for renal damage.[2] So, for the better understanding of role of assessment of microalbuminuria in hypertension it is significant to have information on the determinants of microalbuminuria.[3]

There should be an unsurprising dose response curve and an adequate, recognized profile for side effects for an ideal drug.[4]The ideal drug should have trial evidence to prove that it achieves the main purpose of treating hypertension, i.e, to reduce the incidence of hypertensive complications along with simply lowering the blood pressure.[5]

Itis shown by the investigators that captopril, a sulfhydryl containing Angiotensin Converting Enzyme (ACE) inhibitor reduces micro albuminuria and improves insulin

sensitivity in patients with essential hypertension.[6]But, more study is needed to know about the efficacy of other non-sulfhydryl ACE inhibitor agents and β-blockers to have such action. In elderly patients with essential hypertension, micro albuminuria is now considered to be a marker for cardiovascular, cerebrovascular and renal risk.[7]There are very few studies in the literature regarding long-term surveys of micro albuminuria in pre and postmenopausal women with essential hypertension.[8]

So, based on above subjects the present study was planned to study the effect of enalapril, non-sulfhydryl ACE inhibitor and atenolol, β-blocker on blood pressure and urinary albumin excretion in pre and postmenopausal women patients with essential hypertension.

MATERIALS AND METHODS

The study was conducted in the medicine department of the institution. For the study, selection of 30 pre and 30 postmenopausal women patients with mild to moderate essential hypertension and 60 normal controls for both the groups were selected. The age group of premenopausal hypertensive women was 30-50 years and for postmenopausal hypertensive women it was 50-70 years. Clinical criteria were used for selection of all the patients. It was made sure that no patient had taken anti-hypertensive drugs before the study.

Diet with constant sodium content (80-100 meq/lit) was provided to all the patients. Instructions were provided to the subjects to collect early morning urine specimen for urinary albumin excretion determination for first 4 days and also instructed to collect 24 hours urine on 3 consecutive occasionsduring same period. Measurement of urinary creatinine was done to ensure completeness of the 24 hour urine collection and only those values were considered reliable with good urine collection that had values + 20% in comparison to expected values. If the mean of the three determinants of urinary albumin excretion (UAE)was between 30 - 300 mg/24 hours and that of urinary albumin/creatinine excretion rate was greater than 2 mg/mole than te patients was designated as having microalbuminuria. The measurement of urinary albumin excretion was done before and after treatment at 3,6,12 months by using ERBA test kits using pyragallol red, end point method in pre and postmenopausal hypertensive women on CIBA corning Express plus autoanalyser.[9] Urine samples for biochemical analysis were taken from the 24 hors collection, stored in glass tubes at 4^0C and analysis was done before 7 days of collection.

The expression of databwas done as mean + SD. The paired t-test was used for analysis of microalbuminuria in control and essential hypertensive pre and postmenopausal women. The paired t-test was also used for observing statistical significance before and after the treatment in both pre and postmenopausal women. $P < 0.05$ was considered as statistical significance.

RESULTS

The 24 hours urine samples of healthy premenopausal and postmenopausal normotensive subjects had 5.8 + 5.5 and 6 + 5.2 of UAE respectively [Table 1]. 30% of pre and postmenopausal women were seen to have microalbuminuria. Enalapril was observed to be more significant ($p<0.01$) in reducing the urinary albumin excretion (UAE) rate. In premenopausal women, the UAE decreased from 30.22 + 5.7 mg/24 hours to 6.8 + 2.0 mg/24 hours, $P < 0.01$ whereas in postmenopausal women, it decreased from 31.55 + 5.7 to 10.67 + 2.9 mg/24 hours, $P < 0.01$. In comparison to this, patients treated with enalapril showed less significant decrease in the level of UAE. In premenopausal women, UAE decreased from 31.51 + 5.45 to 14.77 + 3.1 mg/24 hours ($P<0.05$) whereas in postmenopausal women UAE decreased from 33.15 + 5.8 to 18.22 + 2.8 mg/24 hours ($P<0.05$). In the present study, we observed gradual decrease in the urinary albumin excretion. In either group of the patients, we did not observe any kind of statistically significant correlation between the reduction in urinary albumin excretion induced by atenolol, enalapril and changes in systolic, diastolic blood pressure. After administration of atenolol and enalapril for 3 months, there was a significant decrease in the blood pressure in both the groups and it remained lower over the course of the 12 months of therapy. The values of systolic or diastolic blood pressure between the pre and postmenopausal hypertensive patients had no significant differences. Whereas, in comparison to untreated subjects, the diastolic and systolic blood pressure decreased in pre and postmenopausal hypertensive women.

Table 1. Effect of Atenolo Vs Enalapril on Microalbuminuria (mg/24 hours) in pre and post menopausal women with essential hypertenion.

Mode of Treatment	**Premenopausal**		**Postmenopausal**	
	ATENOLOL	ENALAPRIL	ATENOLOL	ENALAPRIL
Normal control	5.8+5.5		6+5.2	
Before treatment	31.51+5.45*	30.22+5.7*	33.15+5.8*	31.55+5.7*
After treatment				
3 months	22.3+4.7	20.56+4.8	27.22+3.9	26.68+4.5
6 months	19.4+3.3	15.67+3.1	24.38+3.1	17.88+3.1
12 months	14.77+3.1 #	6.8+2.0**	18.22+2.8#	10.67+2.9**

* $P < 0.01$; ** $P < 0.001$; # $P < 0.05$

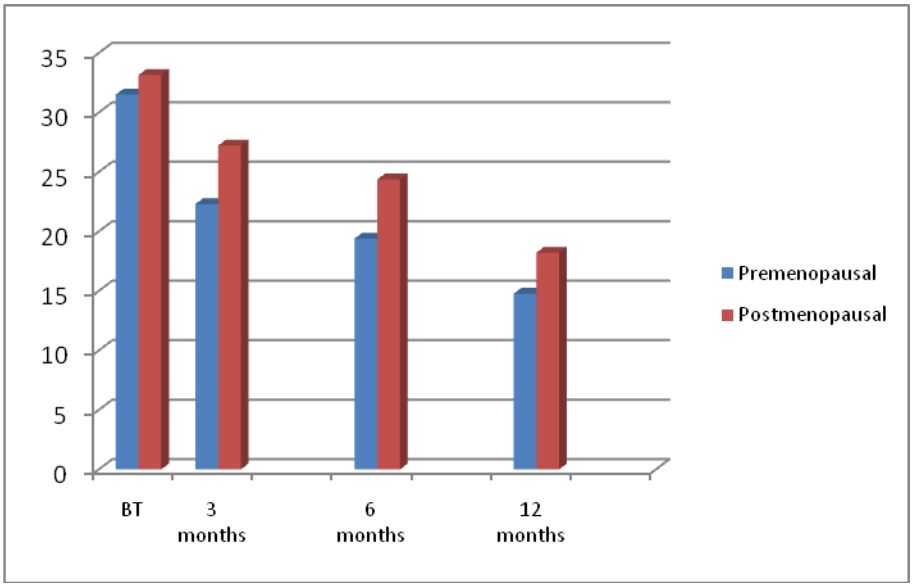

Figure 1: Effect of Atenolol on Urinary Albumin Excretion(UAE mg/24 hour) before and after treatment in pre and postmenopausal women with essential hypertension.

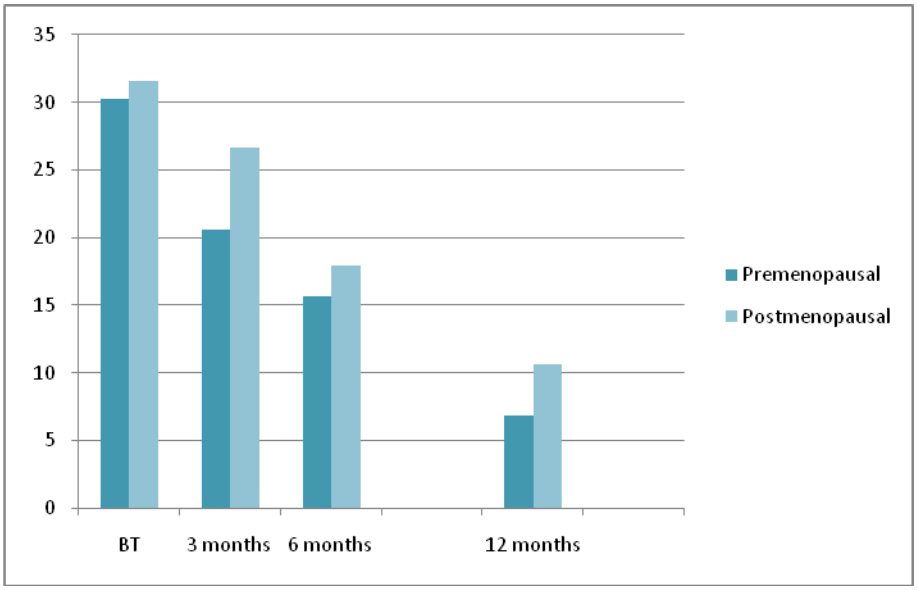

Figure 2: Effect of Enalapril on Urinary Albumin Excretion(UAE mg/24 hour) before and after treatment in pre and postmenopausal women with essential hypertension.

DISSCUSSION

Association of microalbuminuria with preclinical cerebrovascular damage in patients with essential hypertension is one of the most important finding of recently conducted studies.[10] Glomeruli are directly affected by increased blood pressure. With elevation of blood pressure, extension of pre-glomerular (afferent) vessels occurs so that more blood is forced into the glomeruli. The hemodynamic load on the glomeruli is increased which leads to glomerular hypertension, glomerulo sclerosis and loss of nephrons eventually. Loss of nephrons lead to increased renal resistance, which results in reduced perfusion of remaining glomeruli with increased velocity and pressure.[11] Despite the reduced renal blood flow, the hyperfiltration in the remaining glomeruli means that the glomerular filtration rate (GFR) appears to be normal for a time. The direct indication for damage to glomerulus is the onset of microalbuminuria. In patients

with severe hypertension and hypertensive complications, there is generalized functional disturbance of endothelial barrier which leads to excessive loss of albumin throughout the entire microvascular system in addition to that found in the glomeruli as microalbuminuria.[12] Increased carotid intima-media thickness and microalbuminuria are strongly associated which suggests that increased urinary excretion of albumin may indicate an abnormality in systemic vascular permeabilityand may thus be a marker of early endothelial dysfunction and atherosclerosis.[13]Since, micro albuminuria is a useful and cost effective test, so this data can be exploited in clinical practice for identification of sub-groups at highest risk for cardiovascular, reno-vascular and cerebrovascular complications from large group of hypertensive patients.[14]

In the present study, we compared the effects of beta-adrenoreceptor blocker, atenolol and angiotensin converting enzyme inhibitor, enalapril on microalbuminuria in pre and postmenopausal women with essential hypertension. The effectivity of both the drugs was found to be adequate in lowering blood pressure.It was observed that after 3 months of therapy with atenolol and enalapril, there was a substantial and comparable reduction in systolic and diastolic blood pressure in both pre and postmenopausal women with essential hypertension and it remained lower over the course of the study. In both pre and postmenopausal women, urinary albumin excretion rate was signifcantly decreased with atenolol and enalapril. The ACE-inhibitor enalapril was observed to be more effective in reducing the blood pressure and the level of microalbuminuria as compared to β-blocker atenolol (**Table 1**). Acccording to some studies, the decrease in microalbuminuria was accompanied by reduction in blood pressure values through the use of antihypertensive drugs and the reduction in microalbuminuria was proportional to the reduction in blood pressure.[15]

Recent studies have stated that instead of lowering the circulating levels of blood pressure, blockade of renin-angiotensin system (RAS) at the tissue level might of more significance.[16]Significant inhibtion of the tissue renin-angiotensin system in heart, kidney and lungs is obtained by enalapril which is a non-sulfhydryl ACE inhibitor.[17] The conversion of angiotensin-I to angiotensin-II, which is stimulator of aldosterone release and a potent vasoconstrictor is blocked by ACE inhibtor. Very few side effects due to these drugs are reported to occcur. By selectively dilating the efferent arteriole and reducing glomerular capillary pressure without bargaining blood flow, proteinuria is reduced and glomerulosclerosis is retarded by ACE inhibitors in patients with diabetic nephropathy and this expalins its prolonged antihypertensive action.Treatment withenalapril in comparison to atenolol had significant and comparable reduction in urinary albumin excretion in both pre and postmenopausal women with essential hypertension (**Table 1**). Elevation in intraglomerualr haemodynamics is considered to result into increased urinary albumin excretion which inclines the patient towards renal failure.

The development of micro-vascular complications in postmenopausal women is due to the higher blood pressure in them as compared to premenopausal women. Also, increased activity of renin angiotensin system in essential hypertension has been linked to development of micro albuminuria. Usually, the moderate and gradual elevation of blood pressure has been associated with vascular hyalinization.[18]Increase in peripheral resistance associated with essential hypertension is observed which occurs because of thickening of vessel walls by hyaline material which results into decreased lumen of vessel.[19]

High level of estrogen in fertile period provides protection against risk factor in premenopausal condition and is also good for health of arterial walls.[20]So, vasodilation mediated by nitric oxide and other vascular relaxation mechanisms that depend on endothelium are regulated by high level of estrogen in premenopausal women which might be the reason for decreased incidence of hypertension in them.[21]

Cardiovascular events are predicted in patients with essential hypertension by micro albuminuria. Leaking of albumin through excessively permeant glomeruli exposed to the harmful impact of subclinical atherogenesis.[22]

CONCLUSION

So this can be concluded that metabolic and homodynamic defects with pathogenic potentials regardless of the underlying mechanisms are signaled in hypertensive patients by micro albuminuria. Closed association between micro albuminuria and cardiovascular, atherosclerotic, cerebrovascular and renal risk related to pre and postmenopausal hypertensive women is suggested by these observations. Micro albuminuria in essential hypertension may reflect systemic dysfunction of vascular endothelium. Some very important pathophysiological consequences are based on this abnormality.

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