

Studies on Effect of Atenolol and Enalapril on Serum Electrolytes in Pre and Postmenopausal Women with Essential Hypertension.

Vaishali R. Das¹, Raj Kumar Das², Juilee D. Sawalakhe³, Shailaja R. Raghatate⁴

¹Professor and Head, Department of Biochemistry, Dr. Rajesh Ramdasji Kambe Dental College, And Hospital Kanheri (Sarap) Akola. (M.S.).

²Assistant Professor, Department of Biochemistry, Super Speciality Hospital and Government Medical College, Nagpur. (M.S.).

³M.Sc Biotechnology, Symbiosis International University, Pune (M.S.).

⁴Director Greeno Biotech Lab, Nagalwadi, Hingna, Nagpur (M.S.).

Received: January 2017

Accepted: January 2017

Copyright: © the author(s), publisher. It is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Essential hypertension is considered one of the major risk factors for morbidity and mortality in modern civilized life. Because of the involvement of ions in contraction of excitable tissues like vascular smooth muscles and myocardium, alteration in the cation transport across cell membrane plays a pivotal role in the pathogenesis of essential hypertension. The aim of this study was to assess the effect of β blocker, atenolol and ACE inhibitor, enalapril on the concentration of serum sodium, potassium and calcium in pre and postmenopausal hypertensive women as compared to normotensive women. **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 was done. The age group of premenopausal hypertensive women was 30-50 years and for postmenopausal hypertensive women it was 50-70 years. Venous blood sample was withdrawn from the study groups and serum was used for estimation of serum sodium, potassium and calcium. 'Systronic' flame photometer was used for estimation of serum sodium and potassium. **Results:** A significant decrease in the blood pressure of patients treated with both atenolol and enalapril was observed in groups of pre and postmenopausal women with essential hypertension. Significant variations were seen in the concentrations of serum sodium, potassium and calcium ($p < 0.01$) in pre and postmenopausal women with essential hypertension as compared to normal control. We observed significant decrease in the level of serum potassium, calcium and parallel increase in the level of serum sodium in the study subjects before treatment. In postmenopausal essential hypertensive patients, decrease in serum calcium was not found. **Conclusion:** The effect of β blocker, atenolol on the electrolyte balance shows that it lowers blood pressure by decreasing plasma renin activity. Status of renin in patient may be a marker for the responsiveness to β adrenoreceptor blocker, atenolol. Adenylatecyclase system is also activated in case of atenolol which leads to relaxation.

Keywords: atenolol, enalapril, sodium, potassium, calcium, hypertension

INTRODUCTION

Essential hypertension is considered one of the major risk factors for morbidity and mortality in modern civilized life. It is asymptomatic and considered a multifactorial disease occurring because of interaction between genetic and environmental factors.^[1]

Name & Address of Corresponding Author

Dr. Mrs. Vaishali R. Das
Professor and Head,
Department of Biochemistry,
Dr. Rajesh Ramdasji Kambe Dental College And Hospital
Kanheri (Sarap) Akola. (M.S.).

Because of the involvement of ions in contraction of excitable tissues like vascular smooth muscles and

myocardium, alteration in the cation transport across cell membrane plays a pivotal role in the pathogenesis of essential hypertension.^[2] Blood pressure is regulated at normal level by action of sodium, potassium, calcium and magnesium especially in controlling the arterial resistance. Also, fluid balance is regulated by these elements especially sodium and potassium which in turn affects cardiac output.^[3] Abnormalities in renal sodium clearance and influx of Na^+ in erythrocytes are commonly associated with patients of essential hypertension.^[4]

Also, disturbance in calcium metabolism in essential hypertensive patients is reported. Calcium ion acts as a second messenger in excitatory contraction of cardiac and smooth muscles and free intracellular calcium concentration regulates the peripheral

vascular resistance which is reported to be uniformly increased in essential hypertensive cases.^[5]

Potassium, along with sodium plays a pivotal role in every function of our body. Urinary excretion of calcium is also increased in potassium deficient subjects. Some of the studies have reported that urinary excretion of calcium is increased due to increased potassium depletion.^[6]

Urinary calcium excretion is increased upto a greater extent in hypertensive subjects with higher salt sensitivity index.^[7] An increased concentration of serum sodium and decreased concentration of potassium and calcium is seen in essential hypertensive patients. According a study, estrogen is responsible for sodium and water retention by kidneys. Atenolol is now considered as an appropriate basis for antihypertensive therapy, when administered, metabolic disturbances induced by essential hypertension may or maynot be reduced.^[8] Enalapril is newer, long standing ACE-inhibitor that decreases plasma level of angiotensin and aldosterone and reduces sympathetic activity. For that reason some clinical data suggests that ACE inhibitor, enalapril could reduce the loss of potassium and calcium induced by essential hypertension.^[9]

The aim of this study was to assess the effect of β blocker, atenolol and ACE inhibitor, enalapril on the concentration of serum sodium, potassium and calcium in pre and postmenopausal hypertensive women as compared to normotensive women.

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 was done. 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. Venous blood

sample was withdrawn from the study groups and serum was used for estimation of serum sodium, potassium and calcium. 'Systronic' flame photometer was used for estimation of serum sodium and potassium.

The expression of data was done as mean + SD. The paired t-test was used for analysis of serum sodium, potassium and calcium 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

A significant decrease in the blood pressure of patients treated with both atenolol and enalapril was observed in groups of pre and postmenopausal women with essential hypertension.

In the present study, significant variations were seen in the concentrations of serum sodium, potassium and calcium ($p < 0.01$) in pre and postmenopausal women with essential hypertension as compared to normal control. We observed significant decrease in the level of serum potassium, calcium and parallel increase in the level of serum sodium in the study subjects before treatment. In postmenopausal essential hypertensive patients, decrease in serum calcium was not found. After treating the patients with prescribed dosages of atenolol and enalapril, a gradual decrease in serum sodium level and parallel increase in the serum potassium and calcium was observed after 3, 6, 12 months of treatment. Enalapril showed more significant decrease in the level of serum sodium [158 ± 30 to 139 ± 21 meq/l; $p < 0.01$ in premenopausal and 60 ± 29 to 139 ± 19 meq/l; $p < 0.01$ in postmenopausal women] and significant increase in the level of potassium [2.9 ± 0.31 to 4.2 ± 1 meq/l; $p < 0.01$ in premenopausal and 2.7 ± 0.30 to 4.1 ± 1.1 meq/l; $p < 0.01$ in postmenopausal] and calcium [7.3 ± 1.07 to 8.9 ± 1.9 meq/l; $p < 0.05$ in premenopausal and 9.1 ± 1.11 to 10.5 ± 1.15 meq/l; $p < 0.05$ in postmenopausal women].

Table 1: Effect of atenolol and enalapril on the level of serum sodium, potassium and calcium in Premenopausal women with essential hypertension

	Atenolol			Enalapril		
	Sodium (Meq/Lit)	Potassium (Meq/Lit)	Calcium (Mg/Dl)	Sodium (Meq/Lit)	Potassium (Meq/Lit)	Calcium (Mg/Dl)
BT	$154 \pm 37^*$	$2.6 \pm 0.22^*$	$7.2 \pm 1.06^*$	$158 \pm 30^*$	$2.9 \pm 0.31^*$	$7.3 \pm 1.07^*$
AT						
3 months	157 ± 31	3.0 ± 0.72	7.6 ± 1.09	154 ± 26	3.5 ± 0.40	7.8 ± 1.12
6 months	149 ± 26	3.2 ± 1.22	8.1 ± 1.20	143 ± 23	3.8 ± 0.99	8.1 ± 1.8
12 months	$146 \pm 20^{**}$	$3.4 \pm 1.52^{**}$	$8.5 \pm 1.31^{**}$	$139 \pm 21^*$	$4.2 \pm 1.2^*$	$8.9 \pm 1.9^{**}$

* $P < 0.01$

** $P < 0.005$

Table 2: Effect of atenolol and enalapril on the level of serum, potassium and calcium in Postmenopausal women with essential hypertension

	Atenolol			Enalapril		
	Sodium (meq/lit)	Potassium (meq/lit)	Calcium (mg/dl)	Sodium (meq/lit)	Potassium (meq/lit)	Calcium (mg/dl)
BT	155±29*	2.8±0.24*	9.0±1.05*	160±29*	2.7±0.30*	9.1±1.06
AT						
3 months	155±26	3.1±0.68	9.3±1.07	158±25	3.4±0.42	9.3±1.09
6 months	150±24	3.3±1.26	9.7±1.10	144±21	3.9±0.78	9.8±1.12
12 months	146±21**	3.7±1.44**	10.2±1.14**	139±19*	4.1±1.1*	10.5±1.15**

* P < 0.01
** P < 0.005

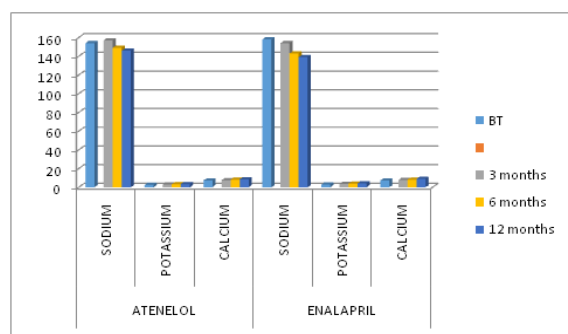


Figure 1: Effect of atenolol and enalapril on the level of serum sodium, potassium and calcium in Premenopausal women with essential hypertension

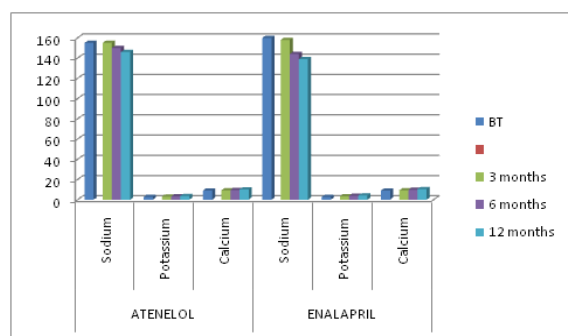


Figure 2: Effect of atenolol and enalapril on the level of serum, potassium and calcium in Postmenopausal women with essential hypertension

On the contrary, atenolol showed less significant decrease in the serum sodium (156 ± 33 to 146 ± 20 meq/l; $p < 0.05$ in premenopausal and 158 ± 29 to 146 ± 21 meq/l in postmenopausal subjects) as compared to enalapril. We also observed significant rise in the level of potassium [2.6 ± 0.22 to 3.4 ± 1.52 meq/l; $p < 0.05$ in premenopausal and 2.8 ± 0.24 to 3.7 ± 1.44 meq/l; $p < 0.05$ in postmenopausal women] and calcium [7.2 ± 1.06 to 8.5 ± 1.31 mg/dl; $p < 0.05$ in premenopausal and 9.0 ± 1.05 to 10.2 ± 1.14 mg/dl; $p < 0.05$ in postmenopausal subjects].

DISCUSSION

Association of ions and electrolytes in the pathogenesis and treatment of hypertension has been widely studied.^[10] Ionic homeostasis in the cardiovascular system is regulated by ion

transporters and ion channels. Involvement of these transporters is noted in not only in physiological regulation but also in pathological aspects of myocytes functions in cardiac diseases and hypertension. Activity of sodium transport channel is increased in hypertensive subjects.^[11] The mineral sodium, potassium and calcium, play a pivotal role in the normal regulation of blood pressure. Studies have observed that despite being involved in normal regulation of blood pressure, sodium is also an important factor in the pathogenesis of hypertension. This is supported by studies that indicate modifications in the level of angiotensin and aldosterone due to excess sodium which results in direct alteration of vascular resistance.^[12,13]

In the present study, results demonstrated that pre and postmenopausal women with essential hypertension were undergoing electrolyte metabolism dysfunction indicated by high concentration of serum sodium and decreased serum potassium, which is beneficial to pathogenesis of essential hypertension.^[14] From the previous studies it was observed that hypertensive patients have decreased tubular reabsorption of calcium, lower serum ionized calcium, lower phosphate, higher serum parathyroid hormone and higher concentration of free cytosolic calcium in their platelets in comparison to normotensive subjects. In the development of pathogenesis these irregularities might play a primary pathogenic role. Also, potassium intake and hypertension risk were inverse proportionally related.^[15] In hypertensive patients, natriuretic ability and calcium excretion are modified due to potassium depletion which might be responsible for the increased risk of hypertension. Potassium depletion might also be responsible for inducing pressure effects in hypertension by changes in systemic and renal vascular resistance. Recent studies have claimed that intake of salt is increased in humans having even mild calcium deficiency.^[16] The present study showed significant reduction in serum calcium in premenopausal hypertensive patients which is in agreement to other research findings.^[17] An increase in concentration of serum calcium was observed in postmenopausal hypertensive women and this may be due to higher filtered load of calcium mainly because of their reduced reabsorption of calcium. A direct effect of

calcium is reported on the peripheral vascular tone. A highly significant correlation between serum calcium concentration and the systolic and diastolic blood pressure was reported in recent epidemiological studies. It was also observed that the subjects with hypercalcaemia have increased risk for hypertension.^[18] A research study by Nordin et al have stated that urinary calcium in post-menopause is increased because of two components increased filtered load and reduced tubular re-absorption.^[17]

A rise in the level of serum calcium, potassium and parallel decrease in the level of serum sodium was observed after supplementing ACE-inhibitor, enalapril and β -blocker, atenolol which is necessary for decreasing blood pressure in pre and postmenopausal women.^[19] A study conducted for analysis of relationship between sodium status and ACE-inhibitor efficacy reported that sodium depletion boosts renin secretion from the juxtaglomerular cells which leads to increase in the hypotensive effect of ACE-inhibitor.^[20] Postmenopausal women are especially salt sensitive. Tubular reabsorption of sodium is increased in these patients, which inhibits renin release, which decreases efferent arteriolar vasoconstriction leading to increased renal blood flow due to increased sodium excretion. Also, angiotensin-II formation is decreased which leads to lower level of aldosterone to promote sodium diuresis. Hence, ACE-inhibition is associated with aldosterone reduction and has potential natriuretic and potassium retaining effect.^[21]

Recent study conducted reported that the risk of hypertension is increased with potassium depletion which might be due to modified natriuretic ability and calcium excretion in hypertensive subjects. Changes in systemic and renal vascular resistance may also be responsible for induction of pressure effect in hypertension due to potassium depletion.^[22] Though, patients treated with enalapril have normal levels of sodium and potassium which suggest that levels of angiotensin and aldosterone may be modified by Na^+ and K^+ . This may alter vascular resistance directly or through an effect of autonomic adrenergic system.^[23]

CONCLUSION

The effect of β blocker, atenolol on the electrolyte balance shows that it lowers blood pressure by decreasing plasma renin activity. Status of renin in patient may be a marker for the responsiveness to β adrenoreceptor blocker, atenolol. Adenylatecyclase system is also activated in case of atenolol which leads to relaxation.

REFERENCES

1. K Sudhakar, M Sujatha, S Ramesh Babu et al. Serum calcium levels in patients with essential hypertension and their first

- degree relatives. Indian J ClinBiochem. 2004 Jan; 19(1): 21–23.
2. Loris Borghi, Tiziana Meschi, Angela Guerra et al. Essential arterial hypertension and stone disease. Kidney International , 55(6): 2397 – 2406.
3. C. Beretta-Piccoli, D. L. Davies et al. Relation of Arterial Pressure with Body Sodium, Body Potassium and Plasma Potassium in Essential Hypertension. Clinical Science Sep 01, 1982; 63(3): 257-270.
4. Sullivan JM. Salt sensitivity. Definition, conception, methodology, and long-term issues. Hypertension. 1991 Jan; 17(1 Suppl):161-8.
5. Taddei S, Mattei P et al. Effect of potassium on vasodilation to acetylcholine in essential hypertension. Hypertension. 1994 Apr; 23(4):485-90.
6. Patki PS, Singh J et al. Efficacy of potassium and magnesium in essential hypertension: a double-blind, placebo controlled, crossover study. BMJ. 1990 Sep 15;301(6751):521-3.
7. Zidek W, Losse H et al. Intracellular sodium and calcium in essential hypertension. Klin Wochenschr. 1982 Aug 16;60 (16): 859-62.
8. Krishna GG, Miller E, Kapoor S. Increased blood pressure during potassium depletion in normotensive men. N Engl J Med. 1989 May 4;320(18):1177-82.
9. Safar, Michel E et al. Hypertension in Postmenopausal Women. Centro die Fisiologia, Clinica e Iperensione, Milano, Italy.
10. Hvarfner AI, Bergström R et al. Changes in calcium metabolic indices during long-term treatment of patients with essential hypertension. ClinSci (Lond). 1988 Nov;75(5):543-9.
11. Maxwell MH, Waks AU. Cations and hypertension: sodium, potassium, calcium, and magnesium. Med Clin North Am. 1987 Sep;71(5):859-75.
12. Morimoto A, Uzu T. Sodium sensitivity and cardiovascular events in patients with essential hypertension. Lancet. 1997 Dec 13;350(9093):1734-7.
13. Weinberger MH, Fineberg NS. Sodium and volume sensitivity of blood pressure. Age and pressure change over time. Hypertension. 1991 Jul;18(1):67-71.
14. Kimura G, Uzu T et al. High sodium sensitivity and glomerular hypertension/hyperfiltration in primary aldosteronism. J Hypertens. 1996 Dec; 14(12):1463-8.
15. Sowers JR, Zemel MB. Calcium and hypertension. J Lab Clin Med. 1989 Oct; 114(4):338-48.
16. Coruzzi P, Brambilla L. Potassium depletion and salt sensitivity in essential hypertension. J Clin Endocrinol Metab. 2001 Jun; 86(6):2857-62.
17. Nordin BE, Need AG et al. Biochemical variables in pre- and postmenopausal women: reconciling the calcium and estrogen hypotheses. Osteoporos Int. 1999;9(4):351-7.
18. Christensson T, Hellström K, Wengle B. Blood pressure in subjects with hypercalcaemia and primary hyperparathyroidism detected in a health screening programme. Eur J Clin Invest. 1977 Apr; 7(2):109-13.
19. Orshal JM, Khalil RA. Gender, sex hormones, and vascular tone. Am J Physiol Regul Integr Comp Physiol. 2004 Feb; 286(2):R233-49.
20. Webster J, Petrie JC. Enalapril in moderate to severe hypertension: a comparison with atenolol. Br J Clin Pharmacol. 1986 May; 21(5):489-95.
21. Freis ED. Veterans Administration Cooperative Study Group on Hypertensive Agents: effects of age on treatment results. Am J Med. 1991 Mar; 90(3A):20S-23S.
22. Nishimura M, Uzu T. Cardiovascular complications in patients with primary aldosteronism. Am J Kidney Dis. 1999 Feb; 33(2):261-6.
23. Schreij G, van Es PN. Renal extraction of atrial natriuretic peptide in hypertensive patients with or without renal artery stenosis. Hypertension. 1996 Jun; 27(6):1254-8.

How to cite this article: Das VR, Das RK, Sawalakhe JD, Raghatare SR. Studies on Effect of Atenolol and Enalapril on Trace Elements in Pre and Postmenopausal Women with Essential Hypertension. Ann. Int. Med. Den. Res. 2017; 3(2):BC01-BC05.

Source of Support: Nil, **Conflict of Interest:** None declared