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Autonomic Nervous System activity in Hypertensive patients under Calcium Channel Blockers treatment

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ABSTRACT

Introduction: Hypertension is a "silent killer" has multi-factorial underlying defect. A number of physiological derangements are involved in elevation of blood pressure. Along with excessive salt intake, obesity and dyslipidemia autonomic dysfunctions too take part in this. Present study was conducted to study autonomic disturbances in hypertensive subjects and role of calcium channel blockers in their alleviation and possible sustenance.

Material & Methods: Present study was conducted on 25 non-diabetic early hypertensive subjects of 1-2 years duration and who were put on single drug therapy (Calcium Channel Blockers) and their autonomic functions were tested before and after taking drug and also results were compared with age and sex matched 25 normotensive controls.

Results: Results showed mean value of pulse rate was lowest in group HT (82.04±14.73) which is statistically non significant when compared to group NT (77.78±5.55) while Systolic was at significantly higher value & Diastolic BP was not. Sympathetic functions tests in study group were significantly predominant while Parasympathetic functions were non-significant. This shows study group subjects were having higher mean values of sympathetic functions tests.

Conclusion: There is an increased sympathetic activity in the hypertensive individuals in comparison to normotensive subjects. The hypertensive patients receiving Calcium Channel Blockers showed significant rise of sympathetic activity when it is compared with normotensive subjects. but more significant rise was seen in Diastolic Blood pressure and GSR. There are no changes in parasympathetic activity of hypertensive groups in comparison to normotensive subjects.

Key words: Hypertension, Beta Blockers, Autonomic dysfunctions, autonomic function tests

INTRODUCTION

The sympathetic nervous system is an important regular of circulation. Its activity is increased in hypertension and heart failure and adversely affects prognosis.[1] Hypertension is a complex disease where the high blood pressure is only one of the numerous coronary risk factors. Sympathetic over activity in hypertension, independent of the blood pressure, may be conducive to premature atherosclerosis by inducing insulin resistance and dyslipidemia. Through its trophic effect on blood vessels, sympathetic over activity potentiates vasoconstriction. This, in turn, accelerates hypertension and the metabolic syndrome. The hypertrophy of small coronary

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arterioles decreases the coronary reserve and enhances coronary spasms. Tachycardia, which is due to increase sympathetic tone and a decrease parasympathetic tone, favors arrhythmias and sudden death in congestive heart failure and hypertension.[2] Judicious use of appropriate drug is important to further improve the efficacy of antihypertensive treatment in those patients who in addition to high blood pressure, also have other associated risk factors. The various classes of antihypertensive drugs act differently in relation to autonomic nerves system activity.

Hypertension is a complex disease where the high blood pressure is only one of the numerous coronary risk factors. The incidence of atherosclerosis too increases in hypertension and myocardial infarcts are common even when the heart is not enlarged.[3][4] The ability to compensate for the high peripheral resistance is exceeded eventually and the heart fails. The hypertensive individuals are also predisposed to thrombosis of cerebral vessels and cerebral hemorrhage[5]. Renal failure is another complication of hypertension. The overactive Renin-angiotensin-aldosterone system (RAAS) plays an important part in many pathologic conditions including hypertension, heart failure, and renal disease[6]. However, the incidence of heart failure, strokes and renal failure can be markedly reduced by active treatment of hypertension, even when the hypertension is relatively mild. Lifestyle modification is an important part of management of hypertension along with antihypertensive drugs.

The prevalence of autonomic imbalance found in hypertensive subjects can be assessed by various cardiovascular automatic function tests[7]. These tests have been divided to asses parasympathetic and sympathetic activities separately. Resting heart rate, resting blood pressure, cold pressor test and hand grip test are the measures of sympathetic nervous system activity. While standing/lying ratio, 30:15 ration, valsalva ration and tachycardia ration are the tests for evaluation of parasympathetic nervous system activity.

Various studies have been carried out to study the changes in automatic nervous system activity on hypertensive patients having different drug regime worldwide with variable inferences.

MATERIAL & METHODS

Present study was conducted on 25 non-diabetic early hypertensive subjects of 1-2 years duration and who were put on single drug therapy (Calcium Channel Blockers) which were grouped as Hypertensive group (HT). Their autonomic functions were tested before and after taking drug. Results were compared with age and sex matched 25 normotensive controls.

The examination of autonomic nervous system has been carried out in the following manner:

Heart rate,

Respiratory rate,

Pulse and temperature

Area of excessive sweating or anhydrosis.

Autonomic functions tests: The various autonomic function tests were carried out with the help of Cardiart-108T/MK-VI ECG machine (BPL make) using standard limb lead II. But for Galvanic Skin Resistance Polyrite-4 Medicare Machine was used. Polyrite recorder is a highly sensitive oscillography capable of simultaneously recording signals in the different modes from many sources.

The various autonomic function tests carried out were:

1. Standing to Lying Ration (S/L Ratio)
2. 30:15 ratio
3. Valsalva ratio
4. Tachycardia ratio

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5. Galvanic skin resistance (GSR)
6. Hand grip test (HGT)
7. Cold pressor test (CPT)

OBSERVATIONS AND RESULTS

TABLE I -PRE-TEST MEAN VALUES OF PULSE RATE AND BLOOD PRESSURE IN THE TWO GROUPS

Parameter	Group I (NT) Mean ± SD	Group II (HT) Mean ± SD	p-value	Significance
Pulse rate(per min)	77.78±5.55	82.04±14.73	>0.05*	Non Significant
SBP (mm Hg)	130.1±6.98	148.08±17.37	<0.05*	Significant
DBP (mm Hg)	75.92 ±5.67	87.6±9.11	>0.05*	Non Significant

Table I shows significant* higher mean values of Pulse Rate, Systolic Blood Pressure and Diastolic Blood pressure in case of HT (Hypertensive) group as compared to NT (Normotensive) group.

TABLE II- COMPARATIVE STUDY OF SYMPATHETIC FUNCTIONS IN TWO GROUPS (N=50)

Parameter	Group I (NT) mean±SD	Group II (HT) mean±SD	p-value	Significance
CPT				
Rise in SBP (mmHg)	11.84±4.75	7.68±5.28	<0.05*	Significant
Rise in DBP (mmHg)	8.24±4.90	5.88±5.40	<0.05*	Significant
HGT				
Rise in SBP (mmHg)	12.08±6.23	5.68±5.28	<0.05*	Significant
Rise in DBP (mmHg)	13.60±6.97	5.44±6.23	<0.05*	Significant
GSR	158.00±4.80	164.00±7.68	<0.05*	Significant

Table II shows significant higher mean values ($p<0.05$) of Cold Pressure test (CPT), Hand grip Test (HGT) and Galvanic Skin Response (GSR) in case of HT (Hypertensive) group as compared to NT (Normotensive) group.

TABLE III- COMPARATIVE STUDY OF PARASYMPATHETIC FUNCTION TESTS IN TWO GROUPS (N-50)

Parameter	Group I (N) mean ± SD	Group II mean ± SD	p-value	Significance
S/L ratio	1.13±028	1.09±0.23	>0.05	Non-significant
30-15 ratio	1.05±0.16	1.02±0.05	>0.05	Non-significant
Valsalva ratio	1.36±0.27	1.24±0.17	>0.05	Non-significant
Tachycardia ratio	0.87±0.10	0.87±0.10	>0.05	Non-significant

DISCUSSION

The present study showed that mean value of pulse rate in hypertensive group HT was (82.04±14.73) when compared to group NT (77.78±5.55) in Table I The heart rate variability is statistically non significant ($p>0.05$) among group I (HT) when intergroup comparison is done.

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The non significant change in heart rate in patients taking Calcium channel Blockers (group II) could be due to no action on beta-1 adrenergic receptors present in sinoaortic node. When stimulated they increase heart rate causing positive chronotropic effect and also cause increased ventricular contractility with positive ionotropic effect. There depression causes negative effect. This results in decreased sympathetic discharge. These results are consistent with earlier studies done on persons taking betablockers confirming that beta blockers reduce heart rate[8][9] but no change seen when taking Calcium Channel Blockers.

Table I further shows that pretest mean value for systolic blood pressure is statistically significant higher in group HT (148.08±17.37) when compared to normotensive subjects group (NT) (130.1±1.98) ($p<0.05$). This indicates a comparatively higher degree of sympathetic tone in all patients of hypertension despite various antihypertensive treatments.

The spontaneously occurring changes in central haemodynamics have been followed in young males with essential hypertension over a 17-year period. There was found a gradual increase in total peripheral resistance and blood pressure, and a gradual fall in cardiac output and stroke volume[10].

The pretest mean value for diastolic blood pressure group showed non significant variation in diastolic blood pressure (83.54±10.14) in hypertensive group (HT) when compared to normotensive group (NT) (87.6±9.11). The values are statistically non significant ($p>0.05$).This observation again indicates a relatively non significant changes in diastolic blood pressure in hypertensive groups taking Calcium channel blockers as compared to normotensive group.

This could be explained again due to sustained increase in sympathetic activity in patients of hypertension in spite of antihypertensive treatment. Since most current evidence suggests that, in humans, sustained increase in heart rate are basically due to decreased parasympathetic tone. These findings support the concept that autonomic imbalance contributes to the pathogenesis of hypertension. In addition since diastolic blood pressure relates more closely to vascular resistance than to cardiac function, these results also suggest that increased sympathetic tone may increase diastolic blood pressure by causing vascular smooth-muscle cell proliferation and vascular remodeling[11].

There are basically two fundamental haemodynamic changes in an established case of hypertension. There is an increased total peripheral resistance and subnormal blood flow particularly during exercise or activity. Antihypertensive drugs which act on central and peripheral adrenergic receptors cause regaining of normal vascular resistance, cardiac output, and thus blood pressure[12].

Data reveals that rise in systolic blood pressure in response to stress induced by CPT is less in group II (7.68±5.28), as compared to normotensive group I (N) (11.84±4.75). These results are statistically significant ($p.<0.05$). Table II also shows that magnitude of rise of diastolic blood pressure in response to CPT is less in group II (5.88±5.40) when compared to normotensive subjects group I (N) (8.24±4.90). This value too is significant statistically ($p<0.05$). Also there is significant fall in rise of diastolic blood pressure in response to HGT in group HT (5.44±6.23), group when compared to normotensive subjects group I (N) (13.60±6.97). Values are significant ($p<0.05$). In case of galvanic skin resistance (GSR) the hypertensive group HT showed mean values of (164.00±7.68) showed significant variation ($p<0.05$) in comparison to normotensive subjects (158±4.80).

These finding indicate that Calcium Channel Blocking drugs like Beta blocking drugs suppress sympathetic activity consequently resulting in less increase in systolic as well as diastolic blood

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pressure in response to CPT in patients of hypertension on drugs regime which include beta blockers rise of systolic as well as diastolic blood pressure in response to CPT.

Calcium Channel blockers due to a reflex decrease in total peripheral resistance index due to vasodilator effect, blood pressure is unchanged or only slightly reduced[13]. With long term use total peripheral resistance drops towards pretreatment level and pressure falls. During exercise heart rate and cardiac output are reduced, but less with conventional beta blockers and resistance is unchanged or slightly reduced[14].

Table III depicts the results obtained after performing various parasympathetic function tests on subjects of both groups.

Data revealed that there is no significant change in S/L ratio hypertensive group HT (1.09±0.23) when compared to normotensive subjects group I (NT) (1.13±0.28). The mean value for 30:15 ration in hypertensive group HT(1.02±0.05) also show statistically insignificant changes when compared to normotensive group (NT) (1.05±0.16) ($p>0.05$). Intergroup comparison of the hypertensive patients on different drug regime also show insignificant variation 30:15 ration among themselves.

The mean value for valsalva ratio in group HT (1.24±0.17) show statistically insignificant ($p>0.05$) variation when compared to normotensive group (1.36±0.27). Even the intergroup comparison of the hypertensive patients on different drug regime shows no remarkable variation among themselves in valsalva ratio.

The mean value for techycardia ratio again showed statistically insignificant variation ($p>0.05$) in group HT (0.87±0.10), compared to normotensive subjects group (NT) (0.87±0.10). The intergroup comparison in techycardia ratio also shows insignificant variation ($p>0.05$).

Thus, these tests on parasympathetic activity (S/L ratio, 30:15 ration, valsalva ration, tachycardia ration) in hypertensive groups HT and normotensive group (NT) show statistically insignificant variations.The overall present study in hypertensive patients have shown that there is an increased sympathetic activity in all the hypertensive patients with no alteration in parasympathetic activity when intergroup subjects were compared.

Greater sympathetic drive has been established in the early stages of essential hypertension, suggesting that neuro-hormonal dis-regulation may be key to its etiology the progression of hypertension and subsequent end-organ damage, such as raised arterial stiffness and left ventricular hypertrophy[15].

The sympathetic and parasympathetic nervous systems are not “opposites”; rather, the interactions are complex.A dynamic interaction occurs between them; these interactions are modulated partially by secondary messengers (cAMP and cGMP). The parasympathetic nervous system can inhibit sympathetic nerve traffic presynaptically. Likewise, sympathetic activation can inhibit parasympathetic activation presynaptically[16].

SUMMARY AND CONCLUSIONS

The hypertensive patients receiving calcium channel blockers show minimum depression of sympathetic activity when it is compared with other antihypertensive groups on different drug regime and against normotensive subjects.

There is no change in parasympathetic activity of hypertensive groups in comparison to normotensive subjects.

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ABBREVIATIONS

CPT: Cold pressor test; HGT: hand Grip test; GSR: Galvanic skin resistance; SBP: Systolic blood pressure; DBP; Diastolic blood pressure

ETHICAL CONSIDERATIONS

Ethical considerations were given due regard in this study. Patients and subjects were asked to volunteer for test by signing proper Performa. They were told about the pain and distress they would undergo while performing autonomic function tests.

BIBLIOGRAPHY

1. Low PA, Benarroch EE.. Clinical autonomic disorders, 3rd ed. 2008; Philadelphia: Lippincott Williams & Wilkins.
2. Raine AEG, Pickering TG. Cardiovascular and sympathetic response to exercise after long-term beta-adrenergic blockade. Brit Med. J 1977; 2: 90-92.
3. Waks JW, Sitlani CM et al, Global Electrical Heterogeneity Risk Score for Prediction of Sudden Cardiac Death in the General Population: The Atherosclerosis Risk in Communities (ARIC) and Cardiovascular Health (CHS) Studies. Circulation 2016 Apr 14. pii: CIRCULATIONAHA.116.021306. [Epub ahead of print] http://www.ncbi.nlm.nih.gov/pubmed/27081116
4. William F. Ganong. Cardiovascular homeostasis in health and disease. Review of Medical Physiology 22nd Edition. McGraw-Hill 2005; p. 641-642.
5. Iencean SM et al, Cerebral venous etiology of intracranial hypertension and differentiation from idiopathic intracranialhypertension. Kaohsiung J Med Sci 2015 Mar;31(3):156-62. doi: 10.1016/j.kjms.2014.12.007. Epub 2015 Jan 19.http://www.ncbi.nlm.nih.gov/pubmed/25744239
6. Rastogi A et al, New Agents in Treatment of Hyperkalemia: an Opportunity to Optimize Use of RAAS Inhibitors for Blood Pressure Control and Organ Protection in Patients with Chronic Kidney Disease. Curr Hypertens Rep, 2016 Jul;18(7):55. doi: 10.1007/s11906-016-0663-4. http://www.ncbi.nlm.nih.gov/pubmed/27230070
7. Low PA, Benarroch EE.. Clinical autonomic disorders, 3rd ed. 2008; Philadelphia: Lippincott Williams & Wilkins.
8. Raine AEG, Pickering TG. Cardiovascular and sympathetic response to exercise after long-term beta-adrenergic blockade. Brit Med. J 1977; 2: 90-92.https://www.researchgate.net/publication/23116947_Cardiovascular_and_sympathetic_response_to_exercise_after_long_term_beta_adrenergic_blockade
9. Dreslinski GR, Messerli FH, Dunn FG, Suarez DH, Reisin E and Frohlich ED. Hemodynamics, Biochemical and reflexive changes produced by atenolol in hypertension. Circulation 1982; 65: 1365-1368. http://www.ncbi.nlm.nih.gov/pubmed/6122514
10. Lund-Johansen P, Pharmacology of combined alpha-beta-blockade. II. Haemodynamic effects of labetalol.Drugs ,1984;28 Suppl 2:35-50. http://www.ncbi.nlm.nih.gov/pubmed/6151890
11. Suzanne Oparil, M. Amin Zaman, David A. Calhoun, Pathogenesis of Hypertension Ann Intern Med. 2003;139:761-776. http://www.the-aps.org/mm/publications/journals/pim/oparil-pdf.pdf

ISSN: 0975-3583,0976-2833 VOL11, ISSUE 04, 2020

12. Michael R. Ruggieri, et al,Combined use of α-adrenergic and muscarinic antagonists for the treatment of voiding dysfunction J Urol. 2005 Nov; 174(5): 1743Urol. 2005 Nov; 174(5): 1743–1748.doi: 10.1097/01.ju.0000176460.62847.23
13. Graziela Z Kalil and William G Haynes. Sympathetic nervous system in obesity -related hypertension Sympathetic nervous system in obesity-related hypertension: mechanisms and clinical implications,Hypertension Research 35, 4-16 (January 2012) | doi:10.1038/hr.2011.173 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3902842/
14. Lund-Johansen P, Omvik P, Acute and chronic hemodynamic effects of drugs with different actions on adrenergic receptors: a comparison between alpha blockers and different types of beta blockers with and without vasodilating effect,Cardiovasc DrugsTher, 1991 Jun;5(3):605-
15. http://www.ncbi.nlm.nih.gov/pubmed/1678963 20.Palatini P, Julius S,The role of cardiac autonomic function in hypertension and cardiovascular disease. Curr Hypertens Rep, 2009 Jun;11(3):199-205. http://www.ncbi.nlm.nih.gov/pubmed/19442329
16. Goldberg ND, Haddox MK,Biologic regulation through opposing influences of cyclic GMP and cyclic AMP: the Yin Yang hypothesis. **Adv Cyclic Nucleotide Res, 1975;5:307-30. http://www.ncbi.nlm.nih.gov/pubmed/165672?dopt=Abstract**