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Study of Sympathetic Autonomic Functions in Stage 1 Essential Hypertensive Subjects

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Abstract
Background: *Essential hypertension may have a cause but our knowledge is not enough to recognize it. The sympathetic nervous system helps to control circulation. Increased incidence of tachycardia, arrhythmias in hypertension, suggests abnormality in sympathetic autonomic system. So the present study was aimed to study blood pressure and heart rate responses during sympathetic stress like 'cold pressor test' (CPT) and 'sustained hand grip test' (SHG) in stage 1 essential hypertensive subjects.*
Study Setting and Design: *Analytical, cross-sectional, comparative study in the Department of Physiology, B J medical college and Sassoon hospital, Pune.*
Materials and Methods: *50 newly diagnosed essential hypertensive male subjects in the age group of 35 - 50 years having stage 1 hypertension according to JNC 7 criteria were selected in study group. Healthy age and gender matched, 50 normotensive subjects were included in control group. After informed consent, blood pressure and heart rate responses were measured during sympathetic stress like 'cold pressor test' (CPT) and 'sustained hand grip test' (SHG) in the study group and the control group. Statistical analysis: Comparisons were performed using 'z-test' in the two groups.*
Results: *During cold pressor test and sustained hand grip test blood pressure and heart rate responses were significantly increased in stage 1 essential hypertensive subjects as compared to normotensive subjects. ($p<0.05$)*
Conclusion: *The sympathetic autonomic activity is increased in stage 1essential hypertensive subjects as compared to normotensive subjects.*
Keywords: *Hypertension, sympathetic autonomic function, cold pressor test (CPT), sustained hand grip test (SHG).*

Worldwide hypertensive prevalence is approximately 26%.[1] In India hypertensive prevalence is about 17% in urban population and 12% in rural population.[2] Worldwide 80 to 95% of hypertensive subjects have idiopathic hypertension called essential hypertension. Though essential

hypertension is called idiopathic, it may has a cause but our knowledge is not enough to recognize it.[3]The mechanism involved in the development of essential hypertension is still poorly understood. Increased incidence of tachycardia, arrhythmias and sudden death in essential hypertension suggest abnormal sympathetic nervous system activity.

The sympathetic nervous system helps to control the reaction of the body to stress. The sympathetic nervous system is also an important regulator of circulation. Hypertension may be associated with sensory neuropathy,[4] ischemic optic neuropathy.[5] Autonomic nerves supplying the heart may also be involved in hypertension causing cardiac autonomic neuropathy (CAN).[4,6] These facts also suggests that some abnormality in sympathetic autonomic function could be associated with essential hypertension. Sympathetic autonomic functions are less studied in stage 1 essential hypertension.

With this background, in the present study blood pressure and heart rate responses were measured during sympathetic stress like 'cold pressor test' (CPT) and 'sustained hand grip test' (SHG) in stage 1 essential hypertensive subjects and the same was compared with normotensive subjects.

Aim and Objectives

To measure sympathetic autonomic functions in newly diagnosed stage 1 essential hypertensive subjects and compare the same in age and gender matched normotensive controls.

Materials and Method

The study was designed as analytical, cross-sectional, comparative study in the Department of Physiology of BJGMC medical college, Pune. The synopsis of study protocol was submitted to the institutional ethics committee and approval was obtained. Study was conducted from December 2013 to September 2015. First screening was done according to inclusion-exclusion criteria.

Inclusion criteria

For study group newly diagnosed essential hypertensive male subjects in the age group between 35 - 50 years having stage 1hypertension as per JNC 7 criteria with systolic blood pressure upto159 mm of Hg, diastolic blood pressure up to 99 mm of Hg were included. For control group healthy normotensive age, gender and body mass index (BMI) matched 50 subjects with sinus rhythm on ECG were selected.

Exclusion criteria

For both study group and control groupobese person having BMI ≥ 30 were excluded. Subjects having history of cardiac diseases, renal or endocrinal diseases, peripheral nervous system diseases, peripheral vascular disorder like Reynaud's disease, diabetes mellitus, bronchial asthma, alcohol abuse and tobacco chewing or smoking, those who regularly practice yoga or exercise training, secondary hypertension, Subjects on drugs like β2 agonist, antagonist were excluded.

After explaining study and taking written informed consent, blood pressure and heart rate responses were measured and compared in both the groups during cold pressor test (CPT) and sustained hand grip (SHG) test. All the subjects were called in the morning hours between 10 am to 12 noon to avoid diurnal variations in autonomic functions. The subjects were instructed to avoid drinking tea and caffeine containing beverages for minimum 8 hours prior to testing. Subjects were examined in quiet room at room temperature. Heart rate response and blood pressure response were measured after a mandatory 30 minutes rest period.

Sample size

In the present study after screening according to inclusion and exclusion criteria, 50 newly diagnosed essential hypertensive male subjects in the age group of 35 -50 years having stage 1 hypertension according to JNC 7 criteria were selected in study group. Healthy age and gender matched, 50 normotensive subjects were included in control group.

Classification of blood pressure according to JNC 7 report: [7]		
Category	Systolic BP	Diastolic BP
Normal	<120	<80
Prehypertension	120–139	80–89
Hypertension, Stage 1	140–159	90–99
Hypertension, Stage 2	≥160	≥100

The purpose of the study and the tests to be performed on subjects were explained to them in detail in their own language. Opportunity was given for adequate discussion and answering queries regarding the study. Written informed consent was obtained from each subject in study and control group. A detailed relevant clinical history was obtained from them. This was followed by a brief general physical examination including vital signs and complete systemic examination. All the subjects were called in the morning hours between 10 am to 12 noon to avoid diurnal variations in autonomic functions. The subjects were instructed to avoid drinking tea and caffeine containing beverages for minimum 8 hours prior to testing. Subjects were also advised to avoid strenuous exercise for at least 24 hours before the examination. Subjects were examined in quiet room at room temperature. Heart rate responses and blood pressure responses to CPT and SHG maneuvers were measured after a mandatory 30 minutes rest period.

1] Cold Pressor Test (CPT):[8]

Resting blood pressure was recorded with the subject sitting comfortably following which his hand is immersed in cold water upto wrist and the temperature was maintained at 4-6^0 C throughout the procedure. Blood pressure measurement was made from the other arm at 30 second intervals for a period of 2 minutes. After 2 minutes, the subject was asked to remove his hand. The maximum rise in the systolic and diastolic blood pressure and heart rate was recorded. Participants were instructed to maintain normal breathing patterns and avoid breath holding.

2] Sustained hand grip test (SHG):[9]

Recording of Maximum Voluntary Contraction (MVC):

Maximum voluntary contraction (MVC) was recorded by asking the subjects to squeeze the bars of hand grip dynamometer by dominant hand to produce a maximum effort as much as possible and maintaining the maximal effort for 2-3 sec. Three trials were given with interval of 10 sec between each trial to avoid fatigue.

Recording of BP at 30% of MVC:

The subject was asked to apply pressure on a handgrip dynamometer for 1 minute at 30% of maximal voluntary contraction and simultaneously the blood pressure changes were observed by using automatic digital machine. The difference between the systolic, diastolic blood pressure records (DBP) and heart rate just before the release of contraction and just before starting handgrip maneuver, was taken as a measure of the response.

Statistical Analysis

The results were given as Mean ± Standard Deviation. Comparisons were performed using z-test in the two groups. A p-value of less than 0.05 was considered as statistically significant. Statistical software SPSS (Statistical Package for the Social Science) version 20 was used for the analysis of data. Microsoft word and Microsoft excel have beenused to create text documents, graphs and tables etc

Table no.2: Comparison of change in sympathetic autonomic functions in cold pressor test (CPT) between hypertensive and normotensive groups.

Parameters	Hypertensive N=50	Normotensive N=50	z-value	p-value
SBP (mm of Hg)	20.06± 2.81	17.80 ± 3.33	3.67	<0.0001
DBP (mm of Hg)	16.92 ± 2.137	12.56 ± 2.23	9.98	<0.0001
HR (beats/min)	11.10 ± 2.44	7.68 ±1.88	7.95	<0.0001
p-value<0.05 : statistically significant*, p value<0.0001: statistically highly significant**, p value> 0.05 : not significant.				

Table no.3: Comparison of change in sympathetic autonomic functions in sustained hand grip (SHG) test between hypertensive and normotensive groups.

Parameters	Hypertensive N=50	Normotensive N=50	z-value	p-value
SBP (mm of Hg)	20.58± 3.37	18.20 ± 2.22	4.17	<0.001
DBP (mm of Hg)	18.78 ± 2.64	17.74 ± 2.23	2.13	<0.05
HR (beats/min)	13.52 ± 2.71	12.30 ±2.73	2.25	<0.05
p-value<0.05 : statistically significant*, p value<0.0001: statistically highly significant**, p value> 0.05 : not significant.				

Discussion

'Essential hypertension' is idiopathic hypertension with no clear etiology. Over the past decade lots of efforts have been made in evaluating pathogenesis of essential hypertension. Increased incidence of tachycardia, arrhythmias and sudden death in essential hypertension, suggests abnormal sympathetic autonomic functions. So in the present study we comparedchange in sympathetic autonomic functions between hypertensive study group and normotensive control group during cold pressor test (CPT) and sustained hand grip test.

CPT stimulates adrenergic receptors of sympathetic nervous system increasing peripheral vasoconst-riction leading to increased blood pressure.[10] The afferent limb of the reflex pathway is by somatic fibers whereas the efferent pathway is by sympathetic fibers.[11] The pressor reaction to a cold stimulus was mediated through a neurogenic reflex arc.[12]

In our study the increase in blood pressure and heart rate response was significantly more in stage 1 essential hypertensive subjects than normotensive subjects during cold pressor test ($p<0.05$). It suggests that there may be increased sympathetic activity in stage 1 essential hypertensive group than normotensive group.

During sustained hand grip also the increase in blood pressure and heart rate response was significantly more in stage 1 essential hypertensive subjects than normotensive subjects.

During the static contraction intramuscular pressure increases due tothe thickening and stiffening of the active muscle fibers within their connective tissues heaths. Thus a slight shortening of the muscle fibers takes place even instatic exercise. The increased pressure is transferred to the intramuscularblood vessels which squeezes blood out of the veins and hinders blood fromentering the intramuscular arteries. This totally blocks the blood flow duringthe contraction period of maximal static exercise. So there is initiation of themetaboreflex in an attempt to restore blood flow, since isometric contractionsimpair blood flow even at low intensity levels.[13]

There is increase in metabolites like lactic acid and adenosine which are detected by metabolic sensitive nerve endings within the skeletal muscle interstitium. These substances increase the discharge of group IV (metaborecetors) afferent fibers and initiate a potent reflex increasing sympathetic nerve activity. This leads to vasoconstriction which increases blood pressure.[14]

In sustained hand grip test, increase in diastolic blood pressure is due to exercise induced increase in sympathetic activity mediated by the alpha adrenergic receptors of the autonomic nervous system.[1] Recruitment of new motor units to maintain muscle tension expands the excitation of the central nervous system also to the cardiovascular centers. Thus the voluntary activity increases the excitatory state of thecentral nervous system and results in a possible increase in sympathetic outflow, which explains increased blood pressure response.[15] Due to muscle fatigue there is increased voluntary effort to produce a certain force. This increased effort stimulates central nervous system. As a result of this effect on the central nervous system, sympathetic stimulation increases leading to an increased heart rate and blood pressure.[15]

In the present study, we observed that cardiovascular autonomic functions are significantly altered in essential hypertensive group than in normotensive group. There is increased sympathetic activity in stage 1essential hypertensive group as compared to normotensive group.

This type of autonomic dysregulation in stage 1 essential hypertension may be due to some abnormalities either in –

1. Brainstem control centers of autonomic nervous system[16]: In essential hypertension, repeated increase in dopamine neuron activity strengthens synaptic transmission of the hypothalamic defence pathway. This lowers the threshold for eliciting the sympatho-adrenal changes responsible for the chronic elevation of blood pressure.17

2. Afferent pathways which modify the response of central controllers by feedback mechanism like baroreceptors and chemoreceptors- Baroreflexes contribute to virtually all aspects of circulatory control. In the intact organism the responses depend on the combined changes in arterial, cardiac and pulmonary baroreceptor activity. In hypertension there is a chronic increase in cardiopulmonary load, which gives rise to vagal deficit. This vagal deficit is evoked through serotonergic neurons stimulated by an increase in activity from medium-high threshold baroreceptors.[17]

3. There may be cardiac autonomic neuropathy in hypertensive subjects like peripheral neuropathy in diabetes, leading to myelin degeneration and axonal degeneration due to hypoxia, chronic inflammation, oxidative stress, free radical damage to autonomic nerves.[18]

Application of the study-

1. It will also help clinically treating the hypertensive patients and preventing the complications in high risk patients.

2. If any abnormality is detected in sympathetic autonomic functions in early stage of hypertension, future progression and complication can be prevented.

3. People with autonomic dysfunction can undergo yoga and lifestyle modification to prevent further damage and complications.

Conflict of interest:

There was no any conflict of interest.

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