

EFFECT OF ISOMETRIC HAND GRIP ON HEART RATE VARIABILITY IN NORMOTENSIVE HEALTHY OFFSPRING OF HYPERTENSIVE PARENTS

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Abstracts: Background and objectives: One of the primary pathologies associated with hypertension is a complex autonomic malfunction with evidence of sympathetic hyperactivity and/or vagal withdrawal. The goal of present study was to assess the possibility for early detection of essential hypertension in the subjects with genetic predisposition on the basis of analysis of effect of Isometric Hand Grip (IHG) and heart rate variability. **Methods:** 45 young, normotensive male offspring of normotensive parents (control group) and 45 young, normotensive male offspring of hypertensive parents (test group) of similar body mass index participated in this study. Heart rate variability was recorded at baseline, during Isometric hand grip and after 5 minutes after isometric hand grip. **Results:** There was no significant difference in baseline parameters of heart rate variability in both groups. Low frequency in normalised unit (LFnu), Low frequency/ High Frequency (LF/HF) ratio were significantly increased and High frequency in normalised units (HFnu) was significantly decreased during isometric hand grip in test group. HFnu was significantly decreased during recovery in test group. **Conclusion:** Finding first indicates hyper responsiveness of sympathetic nervous system to isometric hand grip. Finding second indicates reduced vagal reactivation on recovery from isometric hand grip in test group. These results indicate the early existence of malfunctions in both branches of autonomic control in individuals at increased risk of hypertension.

Key Words: Essential hypertension, Heart rate variability, Isometric hand grip (IHG)

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Introduction:

Essential Hypertension is a multifaceted progressive disease process spanning several decades of life. In all, 25% of children with one hypertensive parent and 50% of children with two hypertensive parents will eventually become hypertensive^{1,2} demonstrating that hereditary plays major role in development of disease. Essential Hypertension is characterized by an increase in sympathetic nervous system activity and reduced vagal modulation of sinoatrial node.³ Previous studies had shown that there is increased sympathetic activity in offspring of hypertensive parents before exercise and a greater response during isometric exercise.⁴ Recently, it has been reported that cardiovascular autonomic responses to whole body isotonic exercise in normotensive healthy adults offspring of hypertensive parents shows signs of sympathetic over activity.⁵ It is also reported that cardiovascular hemodynamic response to repeated mental stress in normotensive offspring of hypertensive parents show enhanced reactivity, blunted adaptations and delayed recovery.⁶ This impaired post stress recovery and enhanced acute stress reactivity indicate disturbances in regulation of

cardiovascular stress responses that contribute to longitudinal changes in blood pressure in middle aged men and women.⁷ Normotensive offspring of hypertensive parents are at increased likelihood to develop hypertension but discernible differences in resting state are unlikely, so we include autonomic challenge i.e. 30% maximal voluntary contraction isometric hand grip in experimental protocol. Spectral analysis of heart rate variability has recently been used as sensitive tool for assessment of autonomic dysfunctions in various clinical disorders⁸. The aim of present study was to unveil malfunctions in autonomic control in subjects genetically predisposed to hypertension. If autonomic differences can be detected before any elevation in blood pressure occurs, elucidation of these differences may lead to design a scheme for the non-invasive early detection of hypertension.

Material and Methods:

Subjects: The present study was carried out in Autonomic function test laboratory of Upgraded Department of Physiology, S M S Medical College Jaipur. The study was conducted on 90 young healthy males (45 case and 45 controls) age 18 to 25 years. The

subjects were of similar nutritional status assessed by body mass index (control group- $20.53 \pm 3.22 \text{ kg/m}^2$ and test group- $21.39 \pm 2.19 \text{ kg/m}^2$). An informed consent was taken from the subjects. A detailed relevant clinical history about the subjects and their parents was obtained from them. This was followed by a brief general physical examination and a complete systemic examination. Healthy, normotensive subjects who were non smokers and non alcoholic were included in the study. Those subjects regularly practicing athletic activities, history of any respiratory, cardiovascular, endocrine and neurological disorders, suffering from Diabetes Mellitus were excluded from the study. The Institutional Review Board of S M S Medical College Jaipur approved this non-invasive study.

Experimental procedure: Subjects were asked to report in autonomic function test laboratory between 9:30am to 12:00 noon after consuming a light standard breakfast 1hr before arrival. Subjects were instructed to abstain from the use of caffeine and other stimulants for 24hr before the study. Temperature of laboratory was controlled at 22-24°C. Subjects were reported to empty their bladder before the experiment. Height was measured using a standard stadiometer. Weight was measured using calibrated weighing machine. Body mass index was calculated as the weight in kilograms divided by the square of height in meters.

Protocol: Autonomic function of subjects by HRV analysis was recorded after making them comfortable by resting them in supine posture for 15 minutes. This recording was considered as basal recording. After baseline HRV, subjects were asked to perform isometric hand grip test. HRV was recorded during the test and at 5 minutes after completion of isometric hand grip test. Subjects was instructed to breath quietly during the entire recording period with closed eyes and to avoid talking, moving hands, legs and body, coughing and sleeping.

Isometric hand grip: The subjects were asked to hold the hand dynamometer in right hand to have a full grip of it. Then the subject was instructed to compress the dynamometer with maximum effort and developed tension was measured. This was maximal isometric tension (T_{\max}). After one minute the subject was asked to maintain a pressure of 30% T_{\max} for 5 minutes⁹.

Heart rate variability: Heart rate variability was recorded by the Medical Analyzer module based on principle of Impedance Plethysmography (NIVOMEN,L&T) and analyses of signal was done in frequency domain measures. The Impedance Peripheral pulse wave signals were continuously amplified, digitized and stored in the computer for offline analysis in frequency domain. The detection of Impedance Peripheral Pulse wave was digitally done by Medical Analyzer, Non-invasive Vascular Monitor, (NIVOMON, and L&T). All recording were visually examined and manually corrected if required. Abnormal beats and area of artefacts were identified and excluded from the study. Power spectral density (PSD) analysis provides analysis of tachogram. The frequency components of HRV were analyzed by using Fast Fourier Transform (FFT).

Statistical analysis of data: Data are presented as Means. Statistical analysis of data was done by students't' test (paired and unpaired) using SPSS version 11.0 software. Paired't' test was applied between baseline indices of HRV and indices of HRV during IHG, and between indices of HRV at baseline and at 5 minutes post IHG. Unpaired't' test was applied for baseline parameters, parameters during IHG and parameters at 5 minutes post IHG of test and control group. Statistical significance was assigned at $P < 0.05$.

Table no 1: Comparison of Mean \pm SD values of Total power and LF/HF of HRV by paired and unpaired't' test at rest, during and after 5 minutes of post IHG in control and test group.

Para meters	Control Group			Test Group		
	At rest	During IHG	At 5 Minutes post IHG	At rest	During IHG	At 5 minutes post IHG
Total power	2060.2 \pm 2905.8	2154.61 \pm 2336.48	2796.33 \pm 3788.62	1742.88 \pm 1472.17	1832.92 \pm 1307.56	2108.29 \pm 2017.23
LF/HF	0.93 \pm 0.79	0.97 \pm 0.98	0.88 \pm 0.64	1.09 \pm 0.91	1.33 \pm 0.93**	1.29 \pm 1.71

Data presented as Mean \pm SD

*Depicts comparison by paired't' test with Parameters at rest

^o Depicts comparison by unpaired't' test with Control group * $P < 0.05$, ^o $P < 0.05$, ** $P < 0.01$, ^{oo} $P < 0.01$

Table no 2: Comparison of Mean±SD values of LFnu and HFnu of HRV by paired and unpaired 't' test at rest, during and after 5 minutes of post IHG in Control and test group.

Parameters	Control Group			Test Group		
	At rest	During IHG	At 5 minutes post IHG	At rest	During IHG	At 5 minutes post IHG
LFnu	41.59±18.03	42.19±18.33	40.47±16.11	44.85±16.44	51.52±14.48**°	47.57±17.91
HFnu	56.22±16.98	55.03±17.45	57.17±16.56	55.03±16.45	48.39±14.44**°	50.91±14.60*

Data presented as Mean±SD

*Depicts comparison by paired't' test with parameters at rest

° Depicts comparison by unpaired't' test with control group

*P<0.05, °P<0.05, **P<0.01, °°P<0.01

Table no 3: Comparison of Mean±SD values of LFpower And HF power of HRV by paired and unpaired't' test at Rest, during and after 5 minutes of post IHG in control and test group

Parameters	Control Group			Test Group		
	At rest	During IHG	At 5 minutes post IHG	At rest	During IHG	At 5 minutes post IHG
LFpower	373.8±308.1	413.1±283.5	455.4±313.2	418.3±418.3	507.2±404.8	747.5±850.4*
HFpower	772.7±1050.4	787±859.2	777.1±879.8	633.1±594.8	591.4±618.5	24.81±695.1

Result:

HRV parameters at rest do not differ between test and control group. There is no significant effect of IHG on Total power in test and control group. LFnu is significantly increased when comparison is done between mean value at rest and during IHG in test group (paired't' test). This finding is further strengthened by significant difference of values during IHG between control and test group (unpaired't' test). HFnu is significantly decreased during IHG in test group. (paired 't'test). This decrease in HFnu during IHG is further strengthened by significant decrease in HFnu during IHG in test group in comparison to

control group (unpaired't' test). HFnu at 5 minute post IHG is significantly decreased in test group as compared to HFnu at rest (paired't' test). There is significant increase in LF power at 5 minutes post IHG as compared to LF power at rest (paired't' test). There is no significant effect of IHG on HF power in both group. There is significant increase in mean values of LF/HF ratio during IHG in test group.

Discussion:

In present study it is found that values of HRV parameters at rest do not differ between two groups. LFnu, LF/HF ratio are significantly increased and HFnu is significantly decreased during IHG in test group in comparison to control group indicating hyper responsiveness of sympathetic nervous system to stress in test group in comparison to control group. Decreased HFnu during recovery indicates reduced vagal reactivation on recovery from IHG in test group as compared to control group. In present study it is found that HRV parameters at rest do not differ between two groups. This is in accordance of previous studies^{9,10} that no signs of difference in sympathetic nervous system activity measured by 24 hours urinary catecholamine excretion or venous plasma concentrations of norepinephrine and epinephrine was observed in offspring of hypertensive parents. In present study there is increased sympathetic activity during IHG. This is in accordance of Grassi G (1988)¹¹, Noll G (1996)¹² and Davrath LR (2003)¹³. Grassi G et al. observed that adrenergic activation in hypertension is not a consequence of high BP state but rather plays a pathogenic role in its occurrence. It triggers the elevation in BP and favours the maintenance of hypertensive state. Noll G et al did not find differences in sympathetic activity before exercise in offspring of hypertensive parents but found a greater increase in sympathetic activity during mental stress. Davarath LR also suggested that normotensive individuals with a genetic predisposition for hypertension showed increased sympathetic activity only in response to autonomic perturbations like IHG. Davrath LR found increased LF/HF ratio during IHG which is in accordance of present study. In present study it is observed that there is decreased parasympathetic tone during recovery in test group. This is in accordance of Eckoldt K et al (1976)¹⁴, Grossman P et al (1992)¹⁵, Mezzacappa (2007)¹⁶ and Sheila R Pai et al (2013)¹⁷. Eckoldt K et al. and Grossman P et al suggested that parasympathetic tone decreases as

hypertension progress. Mezzacappa et al and Sheila R Pai found that vagal rebound after cold pressor and mental arithmetic task was poorer in test group than in control group.

Conclusion:

It can be deduced from present study that there is enhanced sympathetic activity during IHG and reduced vagal reactivation during recovery from IHG in test group. This indicates an early existence of malfunctions in both branches of autonomic nervous system in individuals at increased risk of hypertension. The limitations of present study are that we could not be able to record the beat to beat blood pressure variability during whole procedure. If this can possible then we would be able to yield valuable data and conclusive results.

Potential implications of the study: Identification of individuals prone to hypertension may be possible with the use of these non-invasive techniques. By establishing a set of threshold values for autonomic responses to challenges such as IHG, individual prone to hypertension can be identified. By identifying elevated sympathetic activation at early stage, and then methods can be devised such as lifestyle modification for prevention and treatment of hypertension. Further longitudinal study can be done on same subjects and effect of life style modifications can be studied. Hence finding of our study suggest that there is increased sympathetic activity and reduced vagal tone in offspring of hypertensive parents. Early detection in autonomic abnormality can lead to precautionary methods like life style modification at early age.

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