ORIGINAL RESEARCH PAPER

VOLUME-6 | ISSUE-5 | MAY - 2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

STUDY OF AUTONOMIC FUNCTIONS- HERT RATE VARIABILITY AND ASSOCIATED PARAMETERS -IN NORMOTENSIVE, YOUNG HEALTHY OFFSPRING OF HYPERTENSIVE PARENTS AND NORMOTENSIVE PARENTS.

Physiology

DR. BHUVANESH CHAMPAWAT Resident doctor, Physiology Department, JLN Medical College, Ajmer, Rajasthan.

DR. RAJESH PATHAK Professor & Head, Physiology Department, JLN Medical College, Ajmer, Rajasthan.

DR. GARIMA BAFNA Professor, Physiology Department, JLN Medical College, Ajmer, Rajasthan.

ABSTRACT

Introduction: Essential hypertension is a 'silent killer' and a major health challenge in all countries of the World. The purpose of study was undertaken to identify early autonomic dysfunction in individuals with parental history of essential hypertension.

Methodology: Present study was conducted to determine differences in cardiovascular reactivity and recovery. Comparison was done between normotensive, young healthy offspring of hypertensive parents (40 cases) and normotensive parents (40 controls). Autonomic functions were assessed by RMS Digitized Polygraph Polyrite D Version 2.4 and analysis of signal was done in time and frequency domain measures. After recording baseline HRV (heart rate variability), subjects were asked to do isometric hand grip (IHG) test. HRV was recorded during the test and 5 minutes after completion of IHG. Comparison was done by paired and unpaired t test.

Results: Baseline HRV parameters were not different between control test group. There was increased LF/HF ratio, LFnu and decreased HFnu during IHG in test group versus control group. This is a measure of greater sympathetic activation in test group. Increased LFnu, LF/HFratio and decreased HFnu during recovery displayed reduced vagal reactivation on recovery from IHG in test group. There was no effect of IHG on Total power, LFpower, HFpower and time domain indices i.e. SDNN, pNN50, and RMSDD.

Conclusion: The study indicates the early existence of malfunctions in autonomic nervous system associated with increased risk of hypertension.

KEYWORDS:

INTRODUCTION

Essential hypertension1 affecting 95% of hypertensive patients has no identifiable cause[2,3,4] According to Joint National Committee report (JNC 8), blood pressure ≥140/90 mmHg is hypertension.[5] Various risk factors associated with hypertension are obesity,[6] salt sensitivity,[7] genetics[8] obstructive sleep apnea,[9] insulin resistance,[10] sympathetic over activity,[11] and [12] etc. Despite awareness of multiple risk factors, pathophysiology of hypertension remains ambiguous.

Autonomic functions can be assessed by heart rate variability (HRV)3 which is beat to beat variation in heart rate (ie in R-R intervals), due to continuous changes in the sympathetic and parasympathetic outflow. The beat to beat variation occurs predominantly due to respiratory sinus arrhythmia (RSA).[9] HRV has been associated with predictive value in many diseases[10] e.g. Bronchial Asthma[11], MyocardialInfraction[12,13,] Diabetic Neuropathy[5,14,] Myocardial Dysfunction[12], Post cardiac Transp lantation[15] and Tetraplegic patients[16] Present study was planned to use non invasive techniques of HRV analysis to detect any early autonomic dysfunction between normotensive offsprings of normotensive and hypertensive parents.

MATERIAL AND METHOD

The prospective study was carried out in the Department of Physiology, J. L. N. Medical College, Ajmer, from 2015 to 2016 study A total of 80 subjects (age 17 to 25 years) were included (40 cases and control each. The subjects were classified into four groups: group A (n=20) Male subjects without family history of hypertension. Group B (n=20) Female subjects without family history of hypertension. Group C (n=20) Male subjects with family history of hypertension. Group D (n=20) Female subjects with family history of hypertension. The subjects were of similar nutritional status assessed by body mass index. Subjects taking any type of medications especially those affecting autonomic activity, Cardiorespiratory disease, Thyroid disease, Diabetes Mellitus, Smokers and Alcoholic were excluded from. The study protocol was explained to subjects after obtaining informed written consent to participate in the study. A detailed history and clinical examination was done. The study was carried out between 9:30 am-12:00 pm after emptying bladder, consuming a light standard breakfast 1½ to 2 hrs before arrival. Subjects were asked to abstain from the use of caffeine and other stimulants 12 hrs before the study and strenous exercise 24 hrs before the study. Room ambient temperature was maintained between 24-25°C. Subject was instructed to breathe quietly during the entire recording period with closed eyes Basal Heart Rate, Blood Pressure and Autonomic function of subjects by HRV analysis was recorded after making them comfortable by resting in supine posture for 15 minutes. Blood Pressure and Heart Rate Variability was recorded by RMS Digitized Polygraph Polyrite D; Version 2.4 and analysis of signal was done in time and frequency domain measures. After baseline HRV, subjects were asked to do Isometric Hand Grip test. HRV was recorded during the test and 5 minutes after completion of Isometric Hand Grip test. BP and Heart Rate was recorded at rest (Baseline), 4 minutes after initiation of IHG and 5 minutes after completion of IHG. The subject was instructed to compress the hand dynamometer (right hand) with maximum effort and developed tension was measured. This was maximal isometric tension (Tmax). After one minute the subject was asked to maintain a pressure of 30% of Tmax. The Impedance Peripheral Pulse wave signals were continuously amplified, digitized, and stored in the computer for offline analysis in Frequency domain and Time domain.

Measurement of HRV

The measurement and analysis of HRV is done by three methods- Time domain, Frequency domain and Non-linear methods

Table: 1 Selected Time Domain Measures of HRV

Variable	Units	Description
Statistical Measures		
SDNN	ms	Standard deviation of all NN intervals

SDANN	ms	Standard deviation of the averages of NN intervals in all 5-minute segments of the entire recording
RMSSD	ms	The square root of the mean of the sum of the squares of differences between adjacent NN intervals
SDNN index	ms	Mean of the standard deviations of all NN intervals for all 5-minute segments of the entire recording
SDSD	ms	Standard deviation of differences between adjacent NN intervals
NN50 count		Number of pairs of adjacent NN intervals differing by more than 50 ms in the entire recording; three variants are possible counting all such NN intervals pairs or only pairs in which the first or the second interval is longer
pNN50	%	Nn50 count divided by the total number of all NN intervals
Geometric Measures		
HRV triangular index		Total number of all NN intervals divided by the height of the histogram of all NN intervals measured on a discrete scale with bins of 7.8125 ms (1/128 seconds)
TINN	Ms	Baseline width of the minimum square difference triangular interpolation of the highest peak of the histogram of all NN intervals
Differential index	Ms	Difference between the widths of the histogram of differences between adjacent NN intervals measured at selected heights (eg, at the levels of 1000 and 10 000 samples)
Logarithmic index		Coefficient of the negative exponential curve k e-t, which is the best approximation of the histogram of absolute differences between adjacent NN intervals

Table: 2 Selected Frequency Domain Measures of HRV[17]

Variable	Units	Description	Frequency Range
Analysis of Short-term Recordings (5 min)			
5-min total power	ms^2	The variance of NN intervals over the temporal segment	0.4 Hz
VLF	ms^2	Power in VLF range	0.04 Hz
LF	ms^2	Power in LF range	0.04-0.15 Hz
LF norm	Nu	LF power in normalized units LF/(total power-VLF)x100	
HF	ms^2	Power in HF range	0.15-0.4 Hz
HF norm	Nu	HF power in normalized units HF/(total power-VLF)x100	
LF/HF		Ratio LF (ms2)/HF(ms2)	
Analysis of Entire 24 Hours			
Total power	ms^2	Variance of all NN intervals	0.4 Hz
ULF	ms^2	Power in the ULF range	0.003 Hz
VLF	ms^2	Power in the VLF range	0.003-0.04 Hz
LF	ms^2	Power in the LF range	0.04-0.15 Hz
HF	ms^2	Power in the HF range	0.15-0.4 Hz

Quantification of HRV Various spectral methods for the analysis of the tachogram have been applied since the late 1960s. Power spectral density (PSD) analysis provides the basic information of how power (variance) distributes as a function of frequency.

The frequency components of HRV were analyzed by using Fast Fourier Transform (FFT).The power spectrum was subsequently divided into three frequency bands; VLF-(0.001 to 0.04) Hz, LF-(0.04 to 0.15)Hz and HF –(0.15 to 0.4) Hz. Power of the spectral bands were calculated in normalized units(nu).

The normalized units were calculated as

HF (nu) =	HF (absolute units)	x100
	Total Power (absolute units) - VLF (absolute units)	

LF (nu) =	LF (absolute units)	x100
	Total Power (absolute units) - VLF (absolute units)	

The LF(nu)/HF(nu) ratios were calculated to assess sympathetic/parasympathetic modulation.

RMSDD and pNN50 were used as analysis of time domain measures of short term HRV.

Analysis of data Collected data were entered in computer based Microsoft Excel sheet. Comparisons were done by applying Student's 't' test (paired and unpaired), using PRIMER software.

OBSERVATIONS

In present study indices of Heart Rate Variability (HRV) were measured at rest (Basal), during (i.e. with the initiation of IHG for 5 minutes) and after 5 minutes of IHG (Table 3)

Table 3. heart rate variability and associated parmeter in mean (SD)

	A			B			C			D		
HRV	Resting	During IHG	After 5 min	Resting	During IHG	After 5 min	Resting	During IHG	After 5 min	Resting	During IHG	After 5 min
Total power	759.732 ± 751.886	621.02 ± 444.23	693.15 ± 555.79	726.094 ± 418.612	436.39 ± 425.93	681.56 ± 302.26	706.2 ± 540.5	538.1 ± 492.5	674.5 ± 382.5	556.3 ± 549.3	634.2 ± 559.8	572.4 ± 512.8
Lf_{nu}	58.137 ± 15.897	63.798 ± 15.556	66.816 ± 9.456	54.735 ± 18.124	53.16 ± 23.751	65.193 ± 8.731	67.28 ± 0.731	59.8 ± 10.63	66.2 ± 11.4	53.42 ± 18.92	57.05 ± 20.07	63.57 ± 11.46
Hf_{nu}	41.309 ± 15.842	36.202 ± 15.556	33.186 ± 9.456	45.165 ± 18.192	46.855 ± 23.767	34.84 ± 13.456	32.73 ± 9.032	40.61 ± 10.66	33.79 ± 11.44	46.6 ± 18.94	42.97 ± 20.06	36.68 ± 11
Lf Power	223.83 ± 185.43	150.77 ± 113.31	222.15 ± 187.56	222.34 ± 158.18	105.24 ± 97.986	264.19 ± 119.17	199.8 ± 182	163.4 ± 136	246.5 ± 172.8	160.5 ± 174.7	158.4 ± 111.3	244.6 ± 224.3
Hf power	15.15 ± 119.95	99.247 ± 135.69	108.84 ± 92.415	187.64 ± 165.89	69.109 ± 80.026	141.71 ± 92.593	104.9 ± 99.37	120.4 ± 111.4	140.8 ± 140.2	148.7 ± 164.4	128.3 ± 164	155.8 ± 162.7
Lf/Hf ratio	1.7709 ± 1.0026	2.1151 ± 0.9933	2.2321 ± 0.859	1.5445 ± 0.9273	1.7004 ± 1.2208	2.1282 ± 0.9951	2.275 ± 0.899	1.637 ± 0.611	2.213 ± 0.836	1.566 ± 1.007	1.797 ± 1.144	1.969 ± 0.779
RMSDD	38.024 ± 18.225	39.38 ± 23.44	33.86 ± 19.474	37.04 ± 13.63	50.081 ± 40.151	48.053 ± 41.476	30.02 ± 10.23	50.54 ± 30.8	34.24 ± 20	48.15 ± 41.33	58.23 ± 53.44	37.28 ± 23.55
SDNN	49.801 ± 13.49	51.846 ± 17.184	50.255 ± 18.261	45.84 ± 9.222	56.161 ± 27.881	53.778 ± 14.37	51.85 ± 16.26	57.67 ± 32.95	47.74 ± 15.46	55.27 ± 34.39	68.64 ± 38.61	49.01 ± 17.56

pNN50	18.835 ± 16.05	14.69 ± 17.073	13.28 ± 15.166	17.89 ± 14.729	18.965 ± 21.843	14.31 ± 13.376	9.24 ± 7.359	18.79 ± 16.422	13.525 ± 15.793	21.06 ± 19.54	22.785 ± 23.309	15.115 ± 18.452

Table 4: p value Unpaired t test

Group / Study Parameter		At rest	During IHG	Post IHG
Total power	Group A and C	0.797	0.579	0.902
	Group B and D	0.278	0.216	0.417
Lf_{nu}	Group A and C	0.030	0.349	0.853
	Group B and D	0.829	0.579	0.683
Hf_{nu}	Group A and C	0.42	0.302	0.857
	Group B and D	0.808	0.05	0.639
Lf Power	Group A and C	0.681	0.99	0.672
	Group B and D	0.248	0.338	0.732
Hf power	Group A and C	0.178	0.593	0.400
	Group B and D	0.460	0.155	0.738
Lf/Hf ratio	Group A and C	0.102	0.075	0.944
	Group B and D	0.944	0.853	0.576
RMSDD	Group A and C	0.095	0.277	0.952
	Group B and D	0.261	0.589	0.319
SDNN	Group A and C	0.667	0.488	0.641
	Group B and D	0.244	0.249	0.353
pNN50	Group A and C	0.620	0.444	0.960
	Group B and D	0.566	0.596	0.875

DISCUSSION

There is a controversy about whether normotensive children of hypertensive parents have an increased sympathetic response to stress. Such a response could produce a hyperactive sympathetic response which in turn may lead to the development of hypertension. Present study was conducted to determine if there were differences in cardiovascular reactivity (initial stress response) or recovery (time required to return to baseline) between normotensive, young offspring of hypertensive parents and normotensive offspring of normotensive parents.

Effect of IHG on Heart Rate Variability

There was no significant effect of IHG on Total Power in all four groups. Although total power was significantly increased at 5 minutes post IHG in group C but there was no significant difference between mean values of total power at 5 minutes post IHG when comparison was done between A and C, and B and D group (Table 4).

$Lf_{nu}$was significantly increased during when comparisons were done between mean values at rest and during IHG, and at rest and at 5 minutes post IHG in group C and D. This finding was further strengthened by significant difference of mean values during IHG between group A and C, and of mean values at 5 minutes post IHG between group B and D (Table 4).

$Hf_{nu}$was significantly decreased IHG in test group. Furthermore there was significant decrease in mean values of HF_{nu}at 5 minutes post IHG in group D. This decrease in HF_{nu}during IHG and at 5 minutes post IHG was further strengthened by significant decrease in HF_{nu}duringIHG in group C in comparison to group A and significant decrease inHF_{nu}, at 5 minutes post IHG in group D in comparison to group B (Table 4).

There was no significant effect of IHG on LF_{power} and HF_{power} in all four groups (Table No. 4).

There was significant increase in mean values of LF/HF ratio during IHG in test group. This finding was further strengthened by significant increase of LF/HF ratio during IHG in group D in comparison to group B (Table 4).

There was no significant effect of IHG on mean values of RMSDD, SDNN and pNN50 in all four groups (Table 4).

As evident from Table No. 14 to 40 HRV parameters at rest did not differ between test and control group.LFnu, LF/HF ratio were significantly increased and HFnuwas 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.

Increased LF_{nu}, LF/HF ratio and decreased HF_{nu} during recovery indicate reduced vagal reactivation on recovery from IHG in test group as compared to control group.

In present study values of HRV parameters at rest did not differ between two groups. This is in accordance of previous studies[21-23] that no signs of difference in sympathetic nervous system activity measured by 24 hour urinary catecholamine excretion or venous plasma concentrations of norepinephrine and epinepherine was observed in offspring of hypertensive parents.

In present study there was increased sympathetic activity during IHG. This is in accordance of Grassi (1988[24], Noll et al (1996)[7] and Davrath (2003)[25].

In present study there was decreased HFnu during IHG and in recovery suggesting decreased parasympathetic tone in test group[26-28]. This is in accordance of Eckoldt et al (1976)[26], Grossman et al (1992)[27], Mezzacappa (2007)[28].

Thus it can be deduced from present study that heart rate at rest was significantly greater in group A than group C. Heart rate showed greater increase during IHG and delayed recovery at 5 minutes post IHG in test group. Baseline SBP and DBP was not different between test group and control group. SBP and DBP was increased significantly during IHG with greater increase of SBP in C group as compared to A group. SBP and DBP showed delayed recovery in test group.

HRV parameters at rest did not differ between two groups. LFnu was increased significantly during IHG and at 5 minutes post IHG in test group. Furthermore LF/HF ratio was increased during IHG in test group. This indicates hyperactive sympathetic nervous system in test group. HFnu decreased during IHG in test group and at 5 minutes post IHG indicating reduced vagal tone. There was no effect of IHG on Total Power, LFpower, HFpower, RMSDD, SDNN and pNN50.

Hence it can be deduced from present study that there is enhanced sympathetic activity during IHG and on recovery from IHG vagal reactivation is sluggish in test group, indicating an early existence of malfunctions in both branches of autonomic nervous system in individuals at increased risk of hypertension.

Limitation of present study is that we could not record the beat to beat blood pressure during whole procedure. This may have resulted in missing out valuable data that could have yielded conclusive results.

There was increased LF/HF ratio, LFnu and decreased HFnu during IHG in test group versus control group. This is a measure of greater sympathetic activation in test group. Increased LFnu, LF/H Fratio and decreased HFnu during recovery displayed reduced vagal reactivation on recovery from IHG in test group. There was no effect of IHG on Total power, LFpower, HFpower and time domain indices i.e. SDNN, pNN50, and RMSDD.

Potential Implications of the Study

Identification of individuals prone to hypertension may be possible with the use of these noninvasive techniques, by establishing a set of threshold values for autonomic responses to challenges, such as change in posture and IHG. Evidence of elevated sympathetic29 activation can be targeted as primary goal in the prevention and treatment of HT.

CONCLUSION

It can be deduced from present study that there is enhanced sympathetic activity during IHG in test group and on recovery from IHG, vagal reactivation is more sluggish in test group. Current study indicates that early existence of malfunctions29 in both branches of autonomic nervous system in individuals at increased risk of hypertension.

REFERENCES

1. Akselord S, OzO, Greenberg M, and Keselbrener L. Haemodynamic regulation: Investigation by spectral analysis. Am J Physiol. 1985; 249: H867-H875.
2. Akselrod S Gordon D, Ubel FA, Shannon DC, Berger AC, and Cohen RJ Power spectrum analysis of heart rate fluctuation. A quantitative probe of beat to beat cardiovascular control. Science 1981; 213: 220-222.
3. Ambarish V,Barde P, Vyas A, Deepak KK. Comparison between prepradial and post-prandial heart rate variability. Indian J PhysiolPharmacol 2005; 49(4): 436-442.
4. Bannister R. Autonomic failure – A textbook of clinical disorders of the autonomic nervous system. Oxford University Press, 1983.
5. Benett T, Farquhar IK, Hosking DJ. Assessment of methods for estimating autonomic nervous control of the health in patients with Diabetes Mellitus 1978; 27: 1167-1174.
6. Biagini M et al. Blood pressure response to excercise in young subject with and without parental history of hypertension. J Hum Hypertension 1996; 10(Suppl 3): 81-83.
7. Noll G, Wenzel RR, Schnieder M, Oesch V, Binggeli C, Shaw S, WiedmannPand Luscher TF. Increased activation of sympathetic nervous system and endothelium by mental stress in normotensive offspring of hypertensive parents. Circulation 1996; 93: 866-869.
8. Ferrier C, Cox H and Esler M. Elevated total body nonadrenaline spillover in norm otensive members of hypertensive families. ClinSci (Lond) 1993; 84: 225-230.
9. John D, Catherine T. Heart Rate Variability: wwwmascesuccf.edu/Researc/ Allostatic/ notebook/heart.rate.html; last revised 1997; search engine Google.
10. Watt G. Design and interpretation of studies comparing individuals with or without a family history of hypertension. J Hypertens 1986; 4: 1-7.
11. Tuomas J, Timo K. Tom K. The acute effects of inhaled salbutamol on the beat to beat variability of heart rate and blood pressure assessed by spectral analysis. Bri J ClinPharmacol 2003; 43(4): 421-428.
12. Cosolo G, Balli E, Toddei T, Gori C. Decreased spontaneous heart rate variability on congestive heart failure. Am J Cardiol 1992; 69: 482-485.
13. Malik M, Fareell T, Cripps T, Camm AJ. Heart rate variability in relation to prognosis after myocardial infarction: Selection of optimal processing technique. Euro Heart J 1989; 10: 1060-1074.
14. Ewing DJ, Martin CN, Young RJ, Clarke BF.The value of cardiovascular autonomic functions 10 years experience in Diabetes. Diabetes Care 1985; 8: 491-498.
15. Fallen EL, Kamath MV, Ghista DN. Spectral analysis of heart rate variability following human heart transplantations: Evidence for functional reinnervation. J Anton NeurolSyst1988;23:199-206.
16. Oh J, Brown TE, Hay CY. Human autonomic rhythms: Vagal cardiac rhythms in tetraplegic patients. J Physiol 1994; 474(3): 483-495.
17. Task force of European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability standards of measurement, physiological interpretation and clinical circulation 1996; 38: 133-137.
18. Kobayasbi M, MushaT. I/F fluctuation of heart beat period. Trans Biomed Eng 1982; 29: 457.
19. Saul JP, Albrecht, Breger RD, Cohen RJ. Analysis of long terms heart rate variability: methods, I/F scaling and implications in: Computers in Cardiology 1987. Washington DC: IEEE Computer Society Press; 1988.
20. Yamamoto Y, Hughson RL. Coarse graining spectral analysis; new method for studying heart rate variability. JApplPhysiol 1991; 71: 1143-1150.
21. Hausberg M, Sinkey CA, Mark AL, Hoffman RP, Anderson EA, Sympathetic nerve activity and insulin sensitivity in normotensive offspring of hypertensive parents. Am J Hypertens 1998; 11: 1312-1320.
22. Wedgren B R, Herlitz H, Berglund D, Wikstrand J, Normotensive young men with family histories of hypertension gain weight and decrease their intra-erythrocyte sodium content during a 5 year follow up. J Intern Med 1991; 229: 217-223.
23. Yamada Y, Miyajima E, Tochikubo O, Matsukawa T,Shionoiri H, Ishii M, Impaired baroreflex changes in musclesympathetic nerve activity in adolescents. Who have a familyhistory of essential hypertension. J HypertensSuppl 1988; 6: S525-S528.
24. Grassi G. Role of Sympathetic nervous system in human hypertension. J Hyperten 1998; 16: 1979-1987.
25. Davrath LR, Goren, Y Pinhas I. Early autonomic malfunction in normotensive individuals witha genetic predisposition toessential hypertension. Am J Physiol Heart Cir Physiol 2003; 285: H1697-H1704.
26. Eckoldt K et al. Sinus arrhythmia and heart rate in hypertonic disease. AdvCardiol 1976; 16: 366-369.
27. Grossman P, Brinkman A, De Vries J Cardiac autonomic mechanisms associated with borderline hypertension under varyingbehavioral demands: evidence for attenuated parasympathetic tone but not for enhanced beta adrenergic activity. Psychophysiology 1992; 29: 698-711.
28. Mezzacappa ES Kelsey RM, Katkin ES, Sloan RP. Vagal rebound and recovery from psychological stress. Psychosom Med 2007; 63: 650-657.
29. Saxena T, Patidar S,Saxena M. Assessment of left ventricular ejection force and sympathetic skin response in normotensive and hypertensive subjects: A double-blind observational comparative case–control study. Indian Heart J 2016;68:685–92.