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Heart rate variability; Comparative study in normotensive subjects with and without parental history of Hypertension

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Abstract:

Objective:
We evaluated the changes in HRV indicesatrest, during exercise, post-exercise period in children with and without parental history of hypertension.

Methods:
The present study was cross sectional in design. Hundred healthy male subjects in the age group of 18-30 years were recruited from the general population of Davangere. They were divided into two groups: with parental history of hypertension and without parental history of hypertension. Digital ECG system with Nivique Software was used for the study. Frequency domainme asurese valuated LF, HF and LF/HF ratio and timed omainmea surese valuated are SDNN, RMSSD andPNN50%toobserve the status of sympathetic and parasympathetic nervous system function. The results were be subjected for appropriate statistical analysis.

Results:
Resting HRVparameters in group with history of parental HTN showed significantly lower values of LF (1496.95 ±336.82 Vs 1670.19 ±350.14, p<0.05), HF(774.45 ±94.23 Vs 895.26 ±96.79,p<0.05) and RMSSD (43.35 ±10.47 Vs 48.85 ±12.33, p<0.05);the changes inresting values of LF/HF ratio, LFnu, HFnu and SDNN were not significant compared to group without history of parental hypertension.

HRV parameters during exercise showed significantly lower values of LF(636.52 ±59.95 Vs 717.91 ±52.28, p<0.001)HF(750.76±111.73 Vs 822.09 ±119.71, p<0.001) and SDNN (67.0 ±10.42 Vs 77.62 ±20.96,p<0.001)];the changes in RMSSD and LF/HF ratio were not significant.

HRV parameters after exercise showed significantly lower values in HF(780.74 ±111.27 Vs 840.47 ±115.65, p<0.05),SDNN (74.3 ±19.26 Vs 111.30 ±14.16, p<0.001)and RMSSD(47.71 ±11.03 Vs 56.14 ±11.97,p<0.001);the changes in LF and LF/HF ratio were not significant. Compared to before and after exercise, time domain parameters like SDNN(95.35 ±14.78 Vs 110.34

±15.44,p<0.001) and RMSSD(46.54 ±11.85 Vs 52.61 ±12.26, p<0.05) increasedsignificantlyandPNN50% increasewerenot significant;LF andLF/HF ratiodecreased significantly.

Conclusion:
Study group with parental history of hypertension showed the increased sympathetic activity and decreased parasympathetic activity. These changes are an early indicator of autonomic impairment in cardiovascular system.

Keywords:
Hypertension;Frequencydomain measures;Timedomain measures; HRV.

Introduction:
Hypertension is an important worldwide public-health challenge because of its high frequency and concomitant risks of cardiovascular and kidney disease (He J etal., 1997,Whelton PK.,1994). It has been identified as the leading risk factor for mortality and is ranked 3rd as a cause of disability-adjusted life-years (Ezzati M et al., 2002). Early detection and appropriate treatment is the solution (Braunwald E et al.,2011). Hereditary play a significant role in development of hypertension(Wang NY et al.,2008). Children with single hypertension parent and both hypertensive parents have 25% and 50 % chance of developing hypertension respectively. Hypertensive parentalhistory hasbeen considered as risk factor for hypertension. Autonomic abnormality has been demonstrated in children with hypertensive parents (Schneider GM et al.,2003).In humans, anticipation of physical activity inhibits the vagal nerve impulses to the heart and increases sympathetic discharge. Increase in heart rate and myocardial contractility is because of the concerted inhibition of parasympathetic areas and activation of sympathetic areas of the medulla on the heart. The tachycardia and enhanced contractility increases cardiac output. As a result, there is an increase in heart rate and blood pressure (Fletcher GF et al.,1992).The rate of post-exercise cardiodecelaration is used as an index of cardiac vagal reactivation(Fletcher GF et al.,1992). It has been demonstrated that children with hypertensive parents have increased sympathetic activity compared with children of normotensive parents. This autonomic abnormality could be the mechanism behind hypertension. Heart rate variability (HRV) is the amount of heart rate fluctuations around the mean heart rate. It is a valuable tool to investigate sympathetic and parasympathetic function of the Autonomic Nervous System (Conny MA et al.,1993).It is an reproducible, accurate reliable, yet simple to measure and to process (Tabassum R et al.,2010).Despite of previous research and reviews on impact of parental history of hypertension in developing hypertension in children, there is still a lack of strong evidence for its clinical application. Hence, current study was designed to evaluate the impact of parental history of hypertension in increasing the risk of hypertension in children.

Materials and Methods
The study protocol was approved by ethics committee. A total of hundred normal healthy non-athletic male subjects in the age group 18-30yrs wererecruited for the study.
Control Group; Normotensive subjects without parental history of hypertension.
Study Group; Normotensive subjects with parental history of hypertension.
Inclusion criteria;
1. Males in the age group of 18-30 years.
2. Non-smokers.
3. Normal BMI (18.5-24.9 kgIm2)
Exclusion criteria;
1. Subjects with any acute illness.
2. Females.
3. Subjects with Anti-hypertensive medications, Diabetes Mellitus.
4. History of chest pain, orthopnoea,breathlessness.
5. Subjects with Physical disability

Study Design

The present study was cross sectional in design. Based on parental history of hypertension, they were separated into two groups. – With parental hypertension and without parental hypertension. A pretested structural proforma was used to collect the relevant information and informed consent for the test protocol was obtained from subjects before start of the study. The subjects were explained the purpose and importance of the study, the procedure was explained in detail before starting the recording in their local language. Experiments were conducted in the morning. They were instructed to complete their evening meal by 8 pm., refrain from caffeinated beverages 12 hour prior to the experiment and to avoid strenuous physical activity from the previous evening. Baseline characteristics were noted. Subjects were made to rest in supine position for 15 minutes before the start of procedure. Instructions were given to the subject to sit on the mechanical bicycle ergometer and start pedalling at 60 revolutions per minute. The workload was gradually increased to 50 W. The subject was told to pedal till he reached the target heart rate and the stop watch was started. He was instructed to continue at the same intensity of work for the next 3 minutes. At the end of 3 minutes of exercise, he is instructed to stop. Before stopping, the subject is asked to continue cycling slowly for about 30 seconds before finally getting off the bicycle. Recovery period began from the cessation of exercise and lasted for 10 minutes. Subject then moved to bed, sweat cleaned off and in the supine position systolic blood pressure, diastolic blood pressure with a mercury sphygmomanometer and pulse rate were recorded and continuous standard lead II ECG was recorded for five minutes in eyes closed relaxed state. The data was later computed and analysed automatically using the software ECG V; 52 to acquire the cardiac autonomic activity tone under standard conditions. The subjects were instructed to report immediately if they feel any discomfort, fatigue, heaviness of chest, dizziness, breathing difficulty, nausea and vomiting, burning sensation in chest or restlessness. Simultaneously recording of the blood pressure using mercury sphygmomanometer and heart rate just after the 5th minute when steady state was reached in the sessions of exercise and continuous standard lead II ECG was recorded. Heart rate variability (HRV) at rest, before and after exercise recorded using NIVIQURE computerised ECG.

Heart Rate Variability analysis

Recordings were standardized and instructions followed as per the guidelines of Task Force of the European Society of Cardiology as HRV (Circulation, 1996), Standards of measurement, Physiological interpretation and Clinical Use. The software has an inbuilt analysis and interpretation of five minute uninterrupted recording of standard Lead II recording of ECG for short term HRV analysis using portable ECG acquisition equipment which is a multi-channel digital data acquisition system (NiviqureMeditech Systems, Bangalore, India) which consists of a module with capabilities for real time capture and display of two channels of data. The system can that processes data acquired from a custom-built, portable, and biomedical electronic digital acquisition system. (Battery operated) It is capable of storing digital data sampled between frequencies varying from 100 to 1024 Hz. After examination of ECG waveform for any artifacts or ectopics, a manual computation of successive RR intervals was resorted to. The resulting series of RR intervals was subjected to both time domain and frequency domain analyses. In frequency domain analysis, spectral estimates of RR intervals is done by integrating the power as Total Power (TP) from 0.04 to 0.40 Hz, Low Frequency power(LF) from 0.04 to 0.15 Hz, High Frequency power (HF) from 0.15 to 0.40 Hz . Power contained in VLF band was not calculated because of its dubious physiologic significance. Spectral powers are expressed in absolute units of msec2. Low and high frequency power are expressed in normalized units also. HF reflects parasympathetic nerve activity to the heart, LF mostly reflects sympathetic changes. The ratio of low frequency to high frequency (LF/ HF) which is a mirror of sympathovagal balance was also studied (Pal GK et al.,2011). In time domain analysis, SDNN, (standard deviation of all normal sinus RR) an index of overall Heart Rate Variability, RMSSD (root-mean-square of the successive normal sinus RR interval) and percentage of differences between adjacent normal RR intervals exceeding 50 milliseconds (pNN50%) were studied. RMSSD and pNN50 shows greater correlation with parasympathetic nervous activity (Circulation.,1996).

Bicycle Ergometer

A Bicycle frame is supported withwooden stand, from front of which two uprights ascend and carry a cross piece anddesk, which provide for the attachment directly in front of the subject of the tension balances and other piece of apparatus. A cast iron wheel measuring five and half feet (165cm/1.65m) in circumference, weighing 22kilo and mounted on ball bearing is substituted for the back wheel. This wheel has slightly bevelled edges and is turned true. The circumference of this, a stout calico is applied and the two ends of the band are attached to the spring balances of six lbs. range attached to a board at the top of the uprights. The cords from calico band to the balance pass round adjustable pulley in order to give them the right deviation. An adjustable record counter records the revolution of the wheel.

Statistical analysis:

The data were expressed as Mean ±SD. The student Independent t test has been used to find significance between subjects with and without parental history of hypertension. Analysis of variance and Post-hoc Tukey's test were used to compare the change in parameters at rest, during exercise and after exercise. The null hypothesis was rejected at P<0.05. The p value less than 0.05 was considered as statistical significance and the p value less than 0.001 was considered as high statistical significance. SPSS version 16.0 software was used for analysis of data.

Results:

The present study recruited hundred healthy non athletic subjects. All the subjects were in age group of 18-30 years. Out of which 42 were found to be having positive parental history of hypertension and 58 were with negative parental history of hypertension.

Heart rate was significant increasedduring exercise and significant decrease after exercise in both the groups with and without h/o parental HTN was observed.

Heart rate	At rest (Mean ±SD)	During exercise (Mean ±SD)	After exercise (Mean ±SD)	Comparison between groups p value
With h/o parental hypertension	75.5 ±4.54	134.05 ±5.06	93.79 ±10.75	<0.001, HS
Without h/o parental hypertension	76.88 ±5.18	125.10 ±5.25	94.22 ±8.45	<0.001, HS

ANOVA test, HS– Highlysignificant (<0.001)

Table1:Comparisonofheartrateinsubjectswithandwithouth/oparental HTN, at rest, during andafter exercise.

There was no significant difference in the heart rate recovery between the two groups with and without h/o parental HTN.

With parental h/o hypertension (Mean ±SD)	Without h/o parental hypertension (Mean ±SD)	p value
68.58 ±19.01	65.15 ±19.68	>0.05 , NS

Student t test, NS– Not significant(>0.05)

Table2:ComparisonofHeartRateRecoverywithandwithouth/oparentalHTN.

When compared to the subjects without h/o parental HTN, in the subjects with h/o parental HTN the parameters LF, HF and RMSSD were significantly low, and HF nu and SDNN were lower but not significant and the LF nu and LF/HF ratio were non-significantly higher.

HRV	Withparental h/o hypertension (N-42) (Mean ±SD)	Without parental h/o hypertension (N-58) (Mean ±SD)	Comparison between with and without parental h/o HTN	
			p value	Remarks
LF	1496.95 ±336.82	1670.19 ±350.14	<0.05	S
HF	774.45 ±94.23	895.26 ±96.79	<0.001	HS
LF/HF	1.96 ±0.51	1.88 ±0.45	>0.05	NS
LFnu	65.29 ±5.64	64.49 ±5.87	>0.05	NS
HFnu	34.7 ±5.64	35.5 ±5.87	>0.05	NS
SDNN	92.97 ±14.39	96.77 ±14.81	>0.05	NS
RMSSD	43.35 ±10.47	48.85 ±12.33	<0.05	S

Unpaired t-test, S-Significant (<0.05),HS – Highlysignificant (<0.001), NS– Not significant (>0.05)

Table3: HRV Parameters with and without history of parental HTN at rest.

When compared to the subjects without h/o parental HTN, the subjects with h/o parental HTN showed significantly lower values of LF, HF and SDNN. The LF/HF ratio non-significantly was lower. The RMSSD was higher but not significant.

HRV	Withparental h/o hypertension (N-42) (Mean ±SD)	Without parental h/o hypertension (N-58) (Mean ±SD)	Comparison between with and without parental history of hypertension	
			p value	Remarks
LF	636.52 ±59.95	717.91 ±52.28	<0.001	S
HF	750.76 ±111.73	822.09 ±119.71	<0.001	HS
LF/HF	0.86 ±0.15	0.89 ±0.16	>0.05	NS
SDNN	67.0 ±10.42	77.62 ±20.96	0.001	HS
RMSSD	85.38 ±9.86	84.28 ±14.8	>0.05	NS

Unpaired t-test, S– Significant (<0.05), HS– Highlysignificant (<0.001),NS– Not significant (>0.05)

Table4: HRV Parameters with and withouth/o parental HTN during exercise

In comparison with the subjects without h/o parental HTN, the subjects with h/o parental HTN showed significantly lower HF, SDNN and RMSSD. And higher LF and LF/HF ratio were not significant.

HRV	With parental h/o hypertension (N-42) (Mean ±SD)	Without parental h/o hypertension (N-58) (Mean ±SD)	Comparison betweenwith and without parental history of hypertension	
			p value	Remarks
LF	858.31 ±118.84	855.1 ±77.17	>0.05	NS
HF	780.74 ±111.27	840.47 ±115.65	<0.05	S
LF/HF	1.13 ±0.29	1.03 ±0.18	>0.05	NS
SDNN	74.3 ±19.26	111.30 ±14.16	0.001	HS
RMSSD	47.71 ±11.03	56.14 ±11.97	<0.001	HS

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Unpaired t-test, S– Significant (<0.05), HS– Highlysignificant (<0.01), NS– Not significant (>0.05)

Table5:HRV Parameters withandwithout h/o parental HTN afterexercise

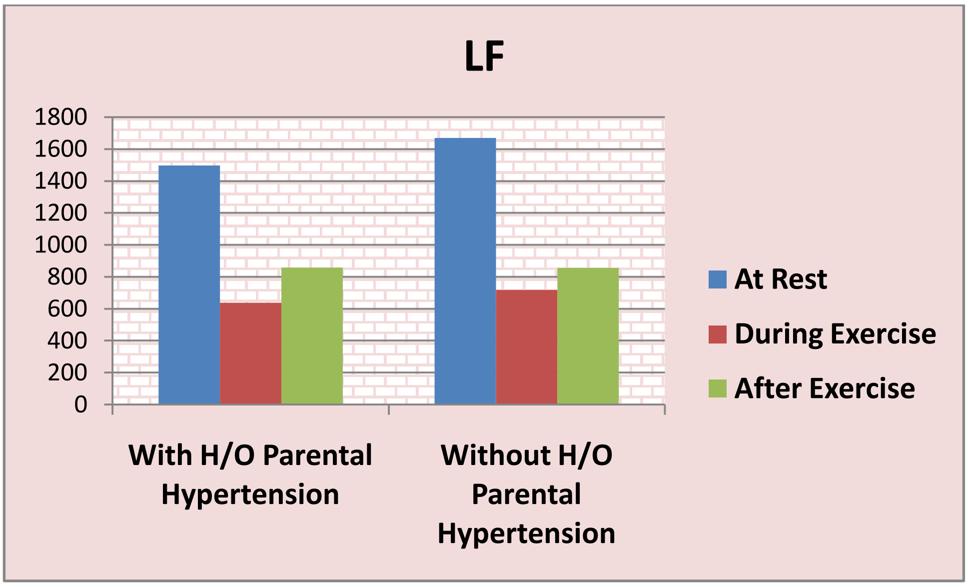

Figure 1. Comparison of LF with and without parental h/o HTN at rest, during and after exercise.

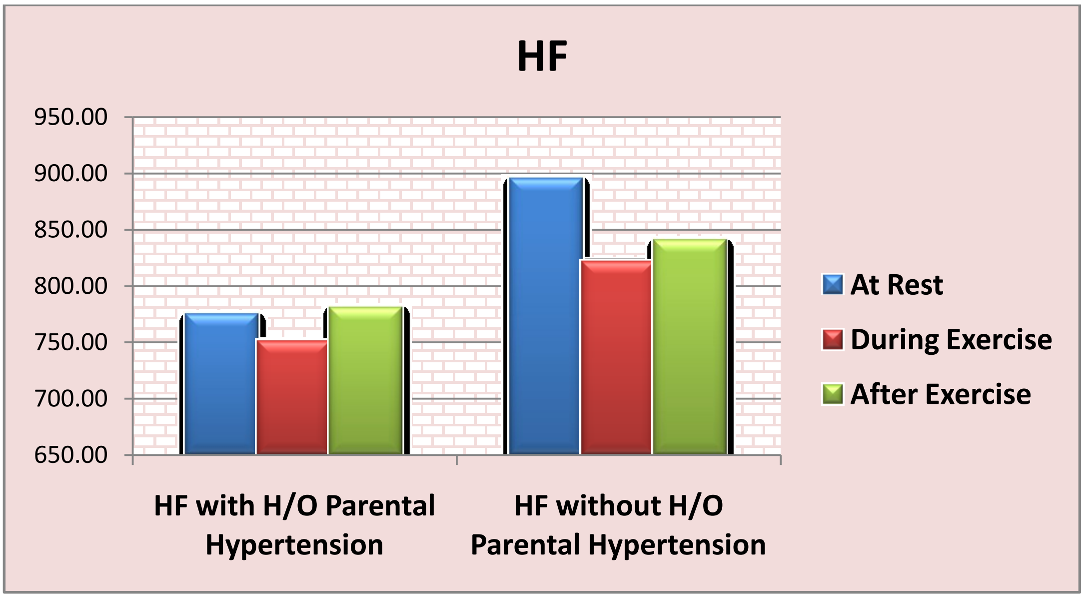

Figure 2. **Comparison of LF with and without parental h/o HTN at rest, during and after exercise.**

Table 6. Shows the comparison of HRV parameters at rest and during exercise. The LF, HF, LF/HF ratio, SDNN and PNN50% were significantly reduced during exercise. The RMSSD showed a significant increase during exercise.

HRV	At rest (Mean ±SD)	During exercise (Mean ±SD)	Comparison between atrest and duringexercise	
				Remarks
LF	1597.43 ±353.49	683.73 ±65.74	<0.001	HS
HF	844.54 ±112.51	792.13 ±121.13	0.05	S
LF/HF	1.92 ±0.47	0.88 ±0.15	<0.001	HS
RMSSD	46.54 ±11.85	84.75 ±12.91	<0.001	HS
SDNN	95.35 ±14.78	66.71 ±11.94	<0.001	HS
PNN50%	15.68 ±1.82	11.91 ±1.93	<0.001	HS

Unpaired t-test, S– Significant (<0.05), HS– Highlysignificant (<0.001)

Table6:ComparisonofHRV parameters atrestand during exercise.

Table 7. Shows the comparison of HRV parameters during and after exercise. LF, LF/HF ratio, SDNN and PNN50% showed a significant increase, RMSSD showed significant decrease and HF increase was not significant after exercise when compared to during exercise levels.

HRV	During exercise (Mean ±SD)	After exercise (Mean ±SD)	Comparison between duringand After exercise	
			p value	Remarks
LF	683.73 ±65.74	866.54 ±96.33	<0.001	HS
HF	792.13 ±121.13	815.38 ±117.07	>0.05	NS
LF/HF	0.88 ±0.15	1.08 ±0.23	<0.001	HS
RMSSD	84.75 ±12.91	52.61 ±12.26	<0.001	HS
SDNN	66.71 ±11.94	110.34 ±15.44	<0.001	HS
PNN50%	11.91 ±1.93	16.01 ±1.95	<0.001	HS

Unpaired t-test, HS–Highlysignificant (<0.001),NS– Not significant (>0.05)

Table7:ComparisonofHRV parameters during andafter exercise.

Table 8. Shows the comparison of HRV parameters at rest and after exercise. When compared to the resting HRV parameters, after exercise the LF and LF/HF ratio decreased significantly; HF decrease was not significant; RMSSD and SDNN were significantly increased.

HRV	Atrest (Mean +SD)	After exercise (Mean +SD)	Comparison between atrest and afterexercise	
			p value	Remarks
LF	1597.43 +353.49	866.54 +96.33	<0.001	HS
HF	844.54 +112.51	815.38 +117.07	>0.05	NS
LF/HF	1.92 +0.47	1.08 +0.23	<0.001	HS
RMSSD	46.54 +11.85	52.61 +12.26	<0.05	S
SDNN	95.35 +14.78	110.34 +15.44	<0.001	HS
PNN50%	15.68 +1.82	16.01 +1.95	>0.05	NS

Unpaired t-test, S-Significant (<0.05),HS– Highlysignificant (<0.001), NS– Not significant (>0.05)

Table8:ComparisonofHRV parameters atrestandafter exercise.

Discussion:

Hypertensionisanimportantworldwide public-healthchallenge. Positive family history isanacceptedriskfactorforfuturedevelopmentofcardiovascular disease (AHA, 2006),thereisincreasedriskofhypertensioninthe offspring (Dallas TX et al., 2002, Harlan WR et al., 1962)andthe relationshipisstrongerifbothparentsarehypertensive. Thenormotensiveprogeny of hypertensive parentsmightdevelop hypertension in future due to imbalance in sympatheticand parasympathetic activity. Autonomicabnormality intheformofincreasedsympathetictonehasbeen demonstratedinyoungnormotensive offspringof hypertensive parents (Lopes HF et al., 2000).There are variousmethodstoassessthe effectsofautonomic nervoussystemonthe cardiovascularsystem inhumans. Exercise stresstestisone of themostusefultestsavailable toevaluate cardio- respiratory fitness, by assessmentofendorganresponsessuchasbloodpressureand heart rate.Inthisstudyweevaluatechangesintheheartratevariability,atrest,duringexerciseandimmediatelyafterexercise

At Rest

Inour study,the normotensive subjectswithhypertensive parentsshowedthe followingchanges:

Frequency domain parameters

LowbasalHFpower,thismightbeduetoalteredsympathovagalbalance withdecreasedparasympatheticactivity atthecardiaclevel.LF/HFratiowas significantly higher,LF/HFratioisconsideredbysometomirror thesympathovagal balance,andtheratioofsympathetictovagalactivity was higher in this group. LF nu was significantly higher which represented the sympathetic activity and the HF nu was significantlylowerwhich represented parasympathetic activity.

Timedomain parameters

DecreasedSDNNandRMSSD,whichwasnotstatistically significant.SDNN representsthelong termvagalmodulationofcardiacfunctions.Comparatively decreasedSDNNindicatesdiminishedbaroreflexmodulationof RRintervals. Decreased SDNNinadditiontothe decreasedHF wouldindicate poor vagalcontrol. RMSSDreflectsvagalmodulationofheartrate,andthereforeRMSSDisconsidered as asignificant short term indicatorofparasympatheticdrive (Circulation.,1996). Other studies supporting these results are Krishnan et al.,2011,Pal et al., 2011, Surekharaniet al.,2013.

DURINGEXERCISE

Frequency domainanalysis

Inourstudy bothLFandHFcomponentofHRVweredecreased during exercise.EventheLF/HFratiowasdecreased.Similarfindingsareseeninthestudy bySarmiento Samuel etal.,2013. Thisresponseinitiallyinvolvesparasympathetic withdrawalandaugmented sympatheticactivity (Bernardi et al.,2001).Theexplanationfortheincreasedsympatheticactivityatthestartofexercise is not fully understood at present. Some of the studies like Victoret al.,1988,Rotto DM et al.,1989, and Sinoway, et al.,1989,Vissing J et al.,1998 link metabolic acidosis to increased sympathetic activity. The decrease in LF is also seen in studies by Perini R et al.,2000 and Cottin F et al., 2006.In onestudytheyshowincreaseinLFvaluesaswellastheLF/HFratioduring a ramptest(YamamotoY et al.,1992).Howeveritmustbenotedthattheyincluded VLF(0.00- 0.004Hz)values within the LFband.

Timedomainanalysis

In our study the timed main parameters like SDNN and PNN 50% were significantly reduced and RMSSD was significantly increased during exercise. In the studies by Javorka M et al.,2002 and Kluess HAet al.,2000 similar results werefound.In our study, the subjects with hypertensive parents showed significantly lower values of LF, HF and SDNN; and the changes in LF/HF ratio and RMSSD is not significant when compared with subjects having normotensive parents. There as on for this might be the increased sympathetic drive and decreased parasympathetic drive which is more in the offspringofhypertensiveparentsthanintheoffspringof normotensiveparents (Surekharani et al.,2013)

AFTER EXERCISE

Inourstudy theheartraterecovery inbetweenthetwogroupsshowedno significantchanges. Similar findingswereseen inthestudies bySoumyaetal.,2009.

During recovery there was no difference in the heart rate variability parametersbetweensubjectswithhypertensive parentsandsubjectswithout hypertensiveparents in ourstudy.In our study, when compared to the subjects without h/o parental HTN, the subjects with h/o parental HTN showed significantly lower values of HF, SDNN and RMSSD; the changes in LF and LF/HF ratio were not significant. HF represents theparasympatheticcomponent. Withthe commencementofexercise there is parasympatheticwithdrawalandsympatheticactivation.Oncessationofexercise, there isparasympatheticreactivationwhichshouldlead togradualincrease in the HF component (Javorka M et al., 2002).Ourresultsinthisstudy withsignificantlylowerHFinsubjectswithh/o parentalHTNmightbedue topoorparasympathetic reactivationinthegroupwith parental historyofhypertension (Sowmya et al 2009).Inastudy conducted byMezzacappaetal.wheresubjectshadtoperformcold pressor testandmentalarithmetic tasks,resultsshowedthatvagal reboundafter the testswaspoorinthegroupwithparentalhistoryofhypertension.Mostlikely,a similar mechanism is operating in our subjects with parental history of hypertension (MezzacappaES et al.. 2001)Comparedtobeforeexercise,changesinthe afterexercisevaluesoftime domainparameterslikeSDNNandRMSSD increasedsignificantlyandPNN50% increase wasnotsignificantinourstudy.Andalsotherewas asignificantdecreasein theLFcomponent of HRVandLF/HFratio;thechangesinHFcomponentwerenot significant.They werepredominantly influencedby thechangesofparasympathetic activity. Similarresultswereseeninthestudiesby Javorka Metal.,2002andBreuerHWet al.,1993.

In conclusion: Sympathetic activity was increased in study group. This finding is an early indicator of cardiovascular autonomic abnormality.

References:

[1.] HeJ, WheltonPK. (1997).Epidemiologyandpreventionofhypertension.MedClinNorth Am, 81(5), 1077-97.

[2.] WheltonPK. (1994). Epidemiologyofhypertension.Lancet, 344,101-6.

[3.] EzzatiM,Lopez.AD,RodgersA,VanderHSandMurrayCJ. (2002).Selectedmajorrisk factors andglobal and regional burden ofdisease.Lancet, 360,1347-60.

[4.] BraunwaldE, FauciAS, Kasper DL, Hauser SL, Longo DL, Jameson JL.(2011).HarrisonsPrinciplesofInternalMedicine,18thEdition,NewYork,McGraw- Hill.

[5.] Wang NY, Young JH, Meoni LA, Ford DE, Erlinger TP, Klag MJ. (2008).Blood pressure change and risk of hypertension associated with parental hypertension: the john's Hopkins precursor study. Archieves of Internal Medicine,168(6), 643-648.

[6.] Schneider GM, Jacobs DW, Gevirtz RN and O'Connor DT.(2003). Cardiovascular hemodynamic responseto repeated mental stress in normotensive subjects at genetic risk of hypertension: evidence of enhanced reactivity,blunted adaptation, and delayed recovery.Journal of human hypertension ,17, 829-840.

[7.] FletcherGF,BaladyG,FroelicherVF,HartleyLH,HaskellWL,PollockML,et al. (1992). Exercisestandards. Circulation,86,340-4.

[8.] ConnyMA,RavenswaaijV,LouisAA,HopmanCWJ, StoelingaBAG, VanGeijn HPet al. (1993) . Heart ratevariability. AnnIntern Med ,118,436-47.

[9.] TabassumR,BegumN,FerdousiS.Begum S,AliT.(2010).Heartratevariabilityin patientswithessentialhypertension.JBangladeshSocPhysiol,5(1),1-7.

[10.] TaskforceoftheEuropeanSocietyofCardiologytheNorthAmericanSocietyof Pacing Electrophysiology. (1996). Heart RateVariability:Standards ofMeasurement, PhysiologicalInterpretation, and Clinical Use. Circulation,93,1043-65.

[11.] Pal GK, Pal P, Nanda N, LalitaV, DattaTK, AdithanC. (2011).Sympathovagal imbalanceinpre-hypertensiveoffspring oftwoparentsversusoneparent hypertensive.InternationalJournal ofHypertension,2011,263170;doi:10.4061/2011/263170.

[12.] American HeartAssociation. (2006). Heartdisease and stroke statistics update.

[13.] Dallas,TX. (2002). AmericanHeartAssociation.StolrazK,GrodzickiT,LubaszawskiW.Heartratevariabilityinoffspringofhypertensiveparents.PrzeglLek.,59,892-94.

[14.] Harlan,W.R.,Osborne,R.K.,&Graybiel, A.(1962).Alongitudinalstudyof blood pressure.Circulation, 26, 530-543.

[15.] . Lopes HF,Silva HBConsolim FM, Colombo et al. (2000). "Autonomic abnormalitiesdemonstrableinyoung normotensivesubjectswhoarechildren of hypertensiveparents, BrazilianJournalofMedicalandBiologicalResearch,vol.33, no. 1, pp. 51 54,

[16.] Krishnan Muralikrishnan, KabaliBalasubramanianand BadanidiyurVishwanathaRao. (2011).HeartRateVariability inNormotensiveSubjects with FamilyHistory of Hypertension. Indian JPhysiolPharmacol, 55(3),253-261.

[17.] SurekharaniChinagudi,AnitaHerur,ShailajaPatiletal.(2013).Comparativestudy of HeartRateVariability innormotensiveoffspringsofhypertensiveparents. Biomedical Research,24 (1), 123-126.

[18.] SarmientoSamuel,Garc´Ia-MansoJuanManuel,Mart´In-Gonz´Alezetal., (2013).Heart Rate Variability during High-Intensity Exercise. J SystSci Complex, 26, 104 -116.

[19.] Bernardi L and Piepoli M F (2001). Autonomic nervous system adaptation during exercise .Ital. Hearth J,2(8), 831-9

[20.] Victor R G, Bertocci L A, Pryor S L, and Nunnally R L, Sympathetic nerve discharge is coupled to muscle cell pH during exercise in humans, J. Clin. Invest.,1988, 82(4): 1301-05.

[21.] Rotto D M, Stebbins C L, and Kaufman M P. (1989).Reflex cardiovascular and ventilatory responses to increasing H+ activity in cat hindlimbmuscle.J. Appl. Physiol, 67(1), 256 -63.

[22.] SinowayL,PhophetS,GormanI,MosherT,ShenbergerJ,DoleckiM,Briggs R,andZelisR. (1989).Muscleacidosisduring staticexerciseisassociatedwithcalf vasoconstriction.J. Appl.Physiol, 66(1), 429-6.

[23.] VissingJ,VissingSF,MacLeanDA,Saltin B,QuistorffB,andHallerRG. (1998). Sympatheticactivationinexerciseisnotdependentonmuscleacidosis:Direct evidencefromstudiesinmetabolicmyopathies.J. Clin.Invest,101(8),1654-60.

[24.] PeriniR,MilesiS,FisherNM,PendergastD RandVeicsteinasA. (2000). Heartrate variability duringdynamicexerciseinelderlymalesandfemales.Eur.J.Appl. Physiol, 82(12),8 -15.

[25.] CottinF,LepretrePM,LopesP,PapelierY, MedigueC,BillatV. (2006).Assessmentof ventilatory thresholdsfromheartratevariabilityinwell-trainedsubjectsduring cycling.Int JSports Med,(12),959-67.

[26.] Yamamoto Y, Hughson R L, and Nakamura Y.(1992). Autonomic nervous system responses to exercise in relation to ventilatory threshold. Chest,101(5),206S.

[27.] Javorka M, Zila I, Balharek T, Javorka K. (2002). Heart rate recovery after exercise: Relations to heart rate variability and 1. complexity. Braz J Med BiolRes ,35 (8),991-1000.

[28.] KluessHA,WoodRH&WelschMA.(2000).Vagalmodulationsoftheheart andcentralhemodynamicsduring handgripexercise.American Journalof Physiology, 279, H1648-H1652.

[29.] SowmyaR, MaruthyK. N. andRani Gupta. (2009). CardiovascularAutonomic ResponsestoWholeBody IsotonicExerciseinNormotensiveHealthy Young AdultMaleswithParentalHistoryofHypertension.IndianJPhysiolPharmacol,54 (1) , 37- 44.

[30.] MezzacappaES, Kelsey RM, KatkinES, Sloan RP. (2001).Vagal reboundand recoveryfrom Psychological Stress. PsychosomaticMedicine,63,650-7.

[31.] BreuerHW,SkyschallyA,SchulzR,MartinC,WehrM,HeuschG. (1993).Heartrate variability andcirculatingcatecholamineconcentrationsduringsteadystate exercisein healthyvolunteers. BrHeart J,70, 144-9.