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AUTONOMIC IMBALANCE IN PREHYPERTENSIVE YOUNG ADULTS WITH PARENTAL HISTORY OF HYPERTENSION AND IN THOSE WITHOUT IT- A NARRATIVE REVIEW.

General Medicine

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ABSTRACT

The prevalence of prehypertension and its progression to hypertension is high. Till date, the impact of treatment of prehypertension on CVD outcome is still unknown. Altered sympathovagal balance is the early manifestation of the cardiovascular dysregulation. This imbalance is improved with adaptation to a healthier lifestyle which prevents the occurrence of HTN and pre-HTN. This complex phenotype of human hypertension is partly genetically determined, but the mechanism by which these individual genes are responsible for HTN is not clear. This review studied the effects of PHTN on HTN, on heart structure, vascular structure and Sympathovagal imbalance. In conclusion, this review showed that autonomic functions are disturbed in PHTN with family history of hypertension and in those without it. Early detection of altered autonomic states and timely intervention like adoption of healthy lifestyle measures in people with PHTN may reduce the prevalence of HTN.

KEYWORDS

INTRODUCTION-

Prehypertension (PHTN) is a global major health risk that ultimately progresses to overt hypertension. The prevalence rate of PHTN ranges from 21.9% to 52%. The underlying pathophysiology of PHTN involve the renin-angiotensin system (RAS) and vascular endothelium. Additional processes involved are prostaglandins, C-reactive proteins, the inflammatory cytokines, reactive oxygen species and the autonomic and central nervous systems(1).

The prevalence of prehypertension and its progression to hypertension is high. The term prehypertension was introduced because it was seen that blood pressure readings between normal and hypertension is associated with increased risk of cardiovascular disease (CVD). Dyslipidaemia, dysglycaemia and overweight/obesity are commonly associoated with prehypertension. Compared to normotensives, eighty-five percent of prehypertensives have a associated CVD risk factor. Till date, the impact of treatment of prehypertension on CVD outcome is still unknown. Studies have shown results of high CVD risk like diabetes or established CVD associated with prehypertension and reduction in the development of hypertension from prehypertension with angiotensin receptor blocker. However this does not mean nothing can be done for those with prehypertension (2).

Rationale of the Review-

There are many studies on the impact of PHTN on the heart and blood vessels but few systematic summaries of the relationship between PHTN and the cardiovascular system. . The risk of cardiovascular events was reported to be higher in second stage PHTN patients when BP was130–139/85–89 mmHg . Also, as the definition of 'normal BP' and the advantages of more stringent BP control remains unclear, the optimal interventions vary(3).

PHTN has adverse effects on health and is highly prevalent. An effective public health programme is necessary to prevent the progression of PHTN to hypertension. PHTN management aims to lower BP, prevent progression to hypertension and to prevent BP related CVD deaths.

Hypertension is an inherited and life style disease . Hypertension (HTN) and prehypertension (pre-HTN) both have been found to be independent risk factors for adverse cardiovascular events .Various genetic mechanisms have been associated to its causation. The early manifestation of the cardiovascular dysregulation is manifested as altered sympathovagal balance.

As sympathovagal balance maintains the normal regulation of cardiovascular system, any change in this balance can gradually lead to cardiovascular problem mainly hypertension. Sympathovagal imbalance due to sympathetic overactivity and parasympathetic/vagal underactivity has been reported to be the basis of many diseases. Therefore, autonomic function testing can give early insight to the problem. Studies have shown that adaptation to a healthier lifestyle improves sympathovagal homeostasis and prevent the occurrence of HTN and pre-HTN(4).

METHOD

Focussed literature searches were conducted for this study using databases such as Pubmed , Google Scholar and relevant search engines. This is a narrative review so no PRISM (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) or AMSTAR(Assessment of Multiple Systematic Reviews) guidelines were used. Full text article were reviewed for appropriate manuscripts. Terms focused for search were "Autonomic Imbalance , Prehypertension in young adults".

PHTN and HTN-

PHTN patients as compared to subjects with optimal BP, have a higher risk of developing HTN (5,6)[,]A higher baseline BP is also associated with a greater probability of developing HTN. First-stage PHTN subjects have a 2–3-fold and second-stage PHTN subjects have a 5–12-fold increased risk of developing HTN when compared to optimal BP subjects [(5),]It is found that Adolescents with PHTN were also more likely to develop HTN than those with optimal BP (hazard ratio: 2.98; 95% CI: 0.77–11.56) (7).

PHTN was diagnosed in adolescents when their BP at lowest follow-up was at the ≥90th percentile (or 120/80 mmHg) to the <95th percentile(7).

Studies have identified some clinical variables like , black ethnicity, older age, higher body mass index (BMI), and the presence of diabetes or chronic kidney disease to predict the probability of PHTN subjects who are most likely to develop HTN(8).

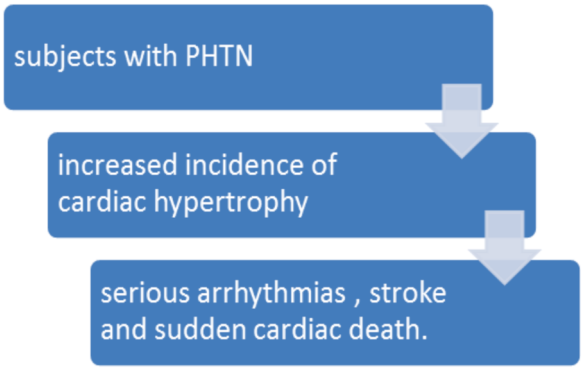

Figure-1-PHTN and Heart

PHTN and Sympathovagal imbalance-

Cardiovascular dysfunction in PHTN is caused by sympathovagal imbalance (SVI , where sympathetic overactivity is related to vagal withdrawal . Vagal withdrawal increases heart rate and causes a decrease in heart rate variability (HRV), which is a sensitive marker of SVI. Decreased HRV is known to cause CV morbidity and mortality (9).Studies have shown that the vagal tone of patients with PHTN needs to be set at a higher level to decrease the future risk of BP rise

(10).Sympathetic activation leads to vasoconstriction which increases cardiac afterload.

Vasoconstriction also increases vascular resistance and systemic arterial pressure. Increased BP occurs due to sympathetic overactivity for a longer duration due to vascular damage. Vascular hypertrophy leads to decreased blood flow to end organs due to consequent atherosclerosis which predisposes to ischemic heart disease such as CHD. Cardiac afterload causes ventricular hypertrophy and an increase in the myocardial demand for oxygen and nutrition. Shin K et al 2015 reported significantly lower Heart rate recovery in PHTN patients when compared to optimal BP group (P<0.05) indicating ANS dysfunction in PHTN patients(11) .Pal GK et al 2013, in their study found sex-related difference in the SVI. HRV finding showed significantly higher ratio of the low-frequency to high-frequency powers in men with PHTN when compared to women (P<0.001) . They suggested consider lifestyle modifications to achieve effective sympathovagal homeostasis(10).

Autonomic Function Tests-

Resting BP Measurement

SBP and DBP (in mm of mercury) measured with the help of a mercury sphygmomanometer after rest of 5 minutes.An average of three such measurements is taken as the resting BP(12).

Resting Heart Rate

After rest of 15–20 min electrocardiography (ECG) was recorded from standard limb leads for complete 1 min and the total number of R waves on the recordings in 1 min is counted and taken as resting heart rate.

Mean BP (MBP)

It is derived from the following formula: MBP Diastolic BP + 1/3 Pulse Pressure.

Parasympathetic Reactivity Tests

1. Expiration/ Inspiration ratio [E/I]) - Heart rate variation with deep breathing-

It is calculated as- E/I Ratio = Longest R-R interval while Expiration/Shortest R-R interval while Inspiration.

2. 30:15 ratio - Heart rate variation during supine to standing position

It is calculated as- 30:15 Ratio = maximum R-R interval about 30th beat during standing/minimum R-R interval about 15th beat during standing.

***3.* IV/II ratio - Valsalva ratio**

The Valsalva maneuver is calculated as- Valsalva Ratio = Longest R-R interval post strain (up to 20 beats)/shortest R-R interval during strain.

DISCUSSION-

Table -1-Clinical Studies

Title of study	Authors	Year	Method	Outcome
Assessment of frequency of progression to hypertension in non-hypertensive participants in the Framingham Heart Study: a cohort study.	R S Vasan, M G Larson, E P Leip, et al	assessed repeated BP measurements in individuals without hypertension (BP<140/90 mm Hg) from the Framingham Study (4200 men, 5645 women; mean age 52 years) who attended clinic examinations during 1978-94.	A stepwise increase in hypertension incidence occurred across the three non-hypertensive BP categories; 5.3% (95% CI 4.4-6.3%) of participants with optimum BP, 17.6% (15.2-20.3%) with normal, and 37.3% (33.3-41.5%) with high normal BP aged below age 65 years progressed to hypertension over 4 years.	A stepwise increase in hypertension incidence occurred across the three non-hypertensive BP categories; 5.3% (95% CI 4.4-6.3%) of participants with optimum BP, 17.6% (15.2-20.3%) with normal, and 37.3% (33.3-41.5%) with high normal BP aged below age 65 years progressed to hypertension over 4 years.
Progression to hypertension in the non-hypertensive participants in the Flemish Study on Environment, Genes and Health Outcomes.	Haifeng Zhang , Lutgarde Thijs, Tatiana Kuznetsova, et al	2006	781 women and 675 men (age range 10-77 years) who were followed up for a median of 4.6 years .Statistical methods Included Kaplan-Meier survival function estimates, the log-rank test and multiple Cox regression.	stepwise increase in incidence of hypertension across the three non-hypertensive blood pressure categories .
Risk of progression to hypertension across baseline blood pressure in nonhypertensive participants among rural Chinese adults: a prospective study	Liqiang Zheng 1, Zhaoqing Sun, Xingang Zhang, et al	2010	A population-based 24 052 rural chinese adults aged at least 35 years .	stepwise increase in risk of progression to hypertension across baseline BP level. The adjusted hazard ratios of participants with normal and high-normal BP for incident hypertension were 1.16 (95% confidence interval 1.08-1.24) and 1.28 (95% confidence interval 1.20-1.36), respectively
Association of Sympathovagal Imbalance with Cardiovascular risks in Young Prehypertensives.	Gopal Krushna Pal et al.	2013	young normotensives (n = 118) and prehypertensives (n = 58).	BP variability, HRV, and autonomic function test parameters were significantly altered in prehypertensives and these parameters were correlated with LF/HF.
Sympathovagal imbalance in Young Pre-Hyperternsives-Importance of Male-Female Difference.	G.K.Pal et al	2013	young normotensive (n=344) and prehypertensive (n=69) subjects. Pearson correlation analysis. and multiple regression analysis.	Ratio of low-frequency to high-frequency powers (LF-HF ratio) of heart rate variability spectrum, the sensitive marker of sympathovagal imbalance (SVI), in males was significantly more increased.
Assessment of Autonomic Functions in the NormotensiveOffspring of Hypertensive Parents	K Tamilselvan, N Nirmala, R Latha, S G Vijayasri	2018	50 healthy normotensive volunteers without parental historyof hypertension.	impaired sympathovagal balance.

A comparative study of autonomic reactivity in normotensive and pre-hypertensive young adult Indian males .	Pratik N Akhani, Vijay Nayak, Rajeev V Joshi, Jaman M Harsoda	2020	60 (30 normotensives and 30 pre-hypertensive) young adult males	statistically significant increase in sympathetic reactivity by handgrip dynamometry test in pre-hypertensive .
Comparative study of heart rate variability in normotensive young adults with family history of hypertension	Ovais K. Wadoo, Sheikh . Sayeed, Mariya R. Tramboo.	2021	test group consisted of 30 healthy normotensive subjects studying in 1st year of MBBS with hypertensive parents ..	SDNN & RMSSD was reduced in cases. LFnu was found to be significantly higher in cases. The HFnu was significantly reduced in cases.

Sympathetic Reactivity Tests

1. Hand grip test - BP changes to isometric exercise

Isometric exercise is performed using hand grip dynamometer. At the end of exercise, the BP is recorded till it reaches the normal level.

***2.* Cold pressor test [CPT])- BP changes to cold stimulation-**

Subject is instructed to submerge his/her hand in a vessel with ice-cold water at 4–6°C. The SBP and DBP are measured in other arm for 2 min period at 30 s intervals. Subject is instructed to remove his hand after 2 min. The maximum increases in the SBP and DBP indicates response to cold stimulation.

CONCLUSION-

This review studied the relationship between PHTN and the cardiovascular system. In conclusion, it can be stated that autonomic functions are disturbed in PHTN with family history of hypertension and in those without it. Early detection of altered autonomic states and timely intervention like adoption of healthy lifestyle measures in people with PHTN may reduce the prevalence of HTN. Llifestyle modifications include changes in diet pattern, physical activity and simple breathing exercises . Though these measures can effectively lower BP and also have favorable effects on reducing cardiovascular-related morbidity, but it is difficult to continue and maintain for a long term.

Hence, future research should address non-pharmacological therapies including cost effective , low potency drugs which can improve SVI for the management of PHTN. Exercise recommendations should be tailor made to suit patient's medical history, ability to exercise and other risk factors.

Conflict of interest- Nil

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