ORIGINAL RESEARCH PAPER

Cardiology

A STUDY OF ASSOCIATION OF TMT PARAMETERS WITH 24-HOUR AMBULATORY BLOOD PRESSURE FINDINGS IN NEWLY DIAGNOSED HYPERTENSIVE PATIENTS

KEY WORDS: Ambulatory, blood pressure, hypertensive, Treadmill Stress Test

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ABSTRACT

Introduction: It has been reported that the lack of nocturnal BP fall which is called nondipping is associated with more serious end organ damages when compared to hypertensives with a dipping pattern. This study was done to evaluate associations between the extent of nocturnal dipping in blood pressure and physical capacity parameters like Exercise capacity (METs), Maximal heart rate (MHR), Heart Rate Recovery in 1st min post exercise (HRR-1), Heart Rate Reserve(HR) assessed through a standard cardiovascular treadmill stress test.

Methods: This is a hospital based observational study. 140 Men and non- pregnant women with newly diagnosed were recruited. All the subjects underwent the 24-h ambulatory blood pressure (BP) assessment. The patient population was then divided into two groups based on their results of ABPM i.e Dippers and Non Dippers. All the individuals of both the groups underwent Treadmill Stress Test. Comparison of parameters of treadmill test (METs, HRR-1, MHR, HR) were made using appropriate statistical tests between the two groups.

Results: On the basis of ABPM the study population was divided into two groups i.e. Dipper (n=66) and Non Dippers (n=74). The Dipper and Non Dipper groups were similar to each other with respect to age, gender distribution, smoking status, LVEF and s.creatinine levels. Non –Dippers (n=74) had a significantly higher Maximal Heart Rate on exercise (156.8 vs 146.4, p <0.05) and Heart Rate Reserve (74.01 vs 67.7 p<0.05) which is the difference of maximal heart rate (MHR) and baseline heart rate (BHR). Mean HRR-1 values (28.64 vs 22.84 bpm, P=.007) were significantly higher in dipper group than the hypertensive nondipper group.

Conclusion: Blunting of the nocturnal fall of BP in hypertensives associates with a delayed recovery of heart rate after graded maximal exercise suggesting that a general decrease of vagal modulation within an abnormal sympathovagal response is present. That may indicate that in hypertensives without signs of coronary disease the decrease of vagal activity is linked to the failure of nighttime fall of BP that might represent an alteration of the autonomic nervous drive with possible deleterious consequences of a greater deterioration of target organs.

INTRODUCTION:

Arterial blood pressure (BP) follows a circadian type rhythm. Ambulatory blood pressure monitoring (ABPM) is the recommended standard method in accurate diagnosis of true high blood pressure (BP), systolic and diastolic values along with all particular aspects of the circadian BP variation.[1] Most people have a decline in arterial BP between 10%–20% during nighttime intervals known as a dipper pattern.[2] It has been reported that the lack of nocturnal dipping which is called nondipping is associated with more serious end organ damages when compared to hypertensives with a dipping pattern.[3]

Although exact etiology responsible for non-dipping pattern in BP are still unclear, it has been suggested complex mechanisms originating in endocrine, renal, neural, and vascular systems are involved in the pathogenesis of arterial hypertension and its circadian variability. Poor sleep quality and the absence of physical exercise during the day, likely affect the abnormal night-to-day BP ratio.[4,5] Since a decrease in vagal activity has been known as a powerful independent predictor of overall mortality, the decline in vagal tone might explain the increase in cardiovascular risk in nondipper subjects.[6]

Exercise capacity and the cardiovascular response to exercise using treadmill test are routinely assessed for both diagnostic (e.g. identifying myocardial ischemia) and prognostic (e.g. risk stratification) purposes because reduced exercise capacity, suboptimal heart rate response to exercise, inadequate increase in heart rate during exercise, abnormal heart rate recovery after exercise and ST-T changes are strong predictors of mortality and disease severity.

There are no evaluations of various TMT parameters non-dipping hypertensives in our population. This study was done to evaluate associations between the extent of nocturnal dipping in blood pressure and physical capacity parameters like Exercise capacity (METs), Maximal heart rate (MHR), Heart Rate Recovery in 1st min post exercise (HRR-1), Heart Rate Reserve(HR) assessed through a standard cardiovascular treadmill stress test.

METHODS :

This is an hospital based observational study conducted at Department of Cardiology ,SMS Medical College , Jaipur from May 2017 to Feb 2019. Ethical clearance was taken from Institutional Ethics Committee (ref no. 3823/MC/EC/2018). 140 Men and non- pregnant women with newly diagnosed hypertension between age 18-60yrs and giving an informed consent were recruited from the OPD.

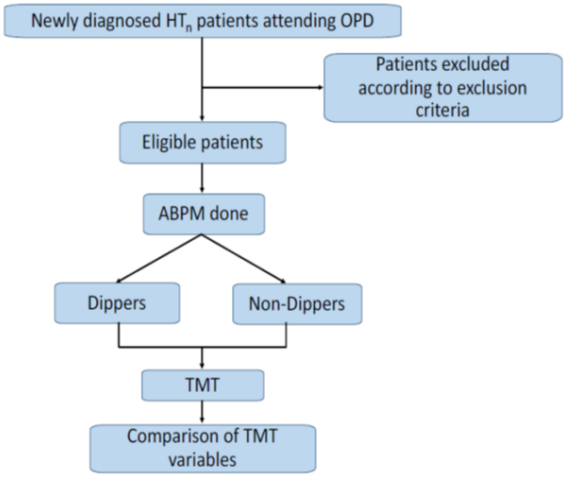
Hypertension was defined as abnormally high arterial BP that is usually indicated by in adults average SBP of 140 mmHg or greater a diastolic BP of 90 mmHg or greater at rest. Diabetes mellitus was defined as fasting plasma glucose levels above 126 mg/dL, HbA1c > 6.5 in at least two different measurements or active use of anti-diabetic drugs. Patients with chronic kidney disease, peripheral artery disease, coronary artery disease, stroke, valvular heart diseases, arrhythmias, chronic liver diseases, diabetes mellitus, pre existing ST-T changes in ECG not allowing interpretation of TMT were excluded from the study

All the subjects underwent the 24-h ambulatory blood pressure (BP) assessment using a Tracker NIBP2 (Del Mar Reynolds Medical Ltd, UK) monitoring device. The first hour was discarded from analysis. BP readings were obtained by the recorder at 20-minute intervals during the day and nighttime. Recordings were accepted only if more than 85% of

the raw data were valid. The absolute and the percentage of the decrease of nighttime systolic BP as compared to daytime systolic BP were calculated in all subjects.

Night time was defined based on the patient-kept diary that documented the exact time of getting into and arising from bed. The average BP for this time in bed was calculated from the ambulatory monitoring data (termed nighttime BP). Daytime BP was defined as the average BP during the 24-hour period minus the night time. Mean BP was calculated by adding one-third of pulse pressure to diastolic pressure. The percentage decline (dipping) in nighttime BP was calculated as follows: (mean daytime BP – mean nighttime BP mean daytime BP *100). Patients with a decline in mean nighttime BP of less than 10% were grouped as nondippers.

The patient population was then divided into two groups based on their results of ABPM i.e. Dippers and Non Dippers. A treadmill exercise testing was conducted in all patients using modified Bruce protocol. Patients were continuously monitored by simultaneous 12- lead electrocardiography (Mason-Liker modification) before and during exercise and until the end of recovery. On achieving peak workload, all patients spent at least 3 minutes recovery. Exercise capacity was measured in metabolic equivalent levels (METs) at peak exercise. HRR indices were calculated by subtracting first, second, and third minute heart rates from the maximal heart rate(MHR) achieved during stress testing as HRR1, HRR2, and HRR3.Comparison of parameters of treadmill test (METs , HRR-1 ,MHR, HR) were made using appropriate statistical tests.



STASTICAL ANALYSIS:
Categorical data were expressed as numbers (percentages), continuous variables as means ± 2SD. For group comparisons, Student T-test was used for continuous variables and the Chi-square test for categorical variables. Statistical analyses were performed using SPSS for Windows, release 17.0 (SPSS Inc., Chicago, IL). All P-values refer to two-tailed tests of significance; P≤ 0.05 was considered significant.

RESULTS:
On the basis of ABPM the study population was divided into two groups i.e. Dipper (n=66) and Non Dippers (n=74). The baseline characteristics of the patients in both groups are shown in table 1.

Table 1: Baseline characteristics of patients in both groups

	Non-Dippers (n= 66)	Dippers (n= 74)	P value
Sex (female)	37 (56%)	39(53%)	0.721
Age	52.0±6.8	52.4±8.7	0.882
BMI	24.5±5.2	24.6±4.8	0.48
Smoker	28 (41.5%)	23 (45%)	0.80
Total cholesterol	186.5±41.8	190.8±37.3	0.63
HDL	45.4±9.5	42.5±10.4	0.170
LDL	113.0±36.3	112.4±42.8	0.926
TG	159.9±64.3	146.2±50.2	0.324
FBS	91.1±19.7	88.4±20.1	0.124
LVEF (%)	60.5±2.6%	60±2.5%	0.23
s.creatinine	0.9±0.05	1.03±0.1	0.09

Ambulatory BP recordings of patients of both groups are shown in table2.

Table 2: Ambulatory BP recordings of both groups

	Dippers (n=66)	Non-Dippers (n=74)	P value
Average 24 hr SBP (mmHg)	145.6±12.2	144.6±13.4	0.413
Average 24 hr DBP (mmHg)	84.2±9.8	99.5±8.0	<0.001
Decline in Night Time BP (%)	13.4	4.5	<0.05

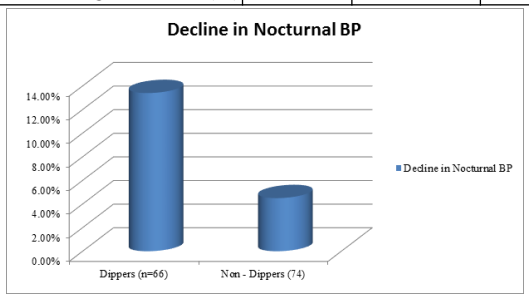


Fig 1: % Dipping in both Groups

The baseline demographic characteristics were comparable in two groups. The Dipper and Non Dipper groups were similar to each other with respect to age, gender distribution, smoking status, LVEF and s.creatinine levels. Non Dippers had a significantly higher Average 24 hr DBP (84.2±9.8 vs 99.5±8.0 vs. 84.2±9.8 p <0.001).The results of the TMT parameters are shown in Table 3. Both the groups had a similar Exercise duration (9.3±2.1 vs 9.1±2.4, p = 0.23), peak exercise capacity (13.0±2.1 vs 12.9±1.9, p= 0.34) and baseline heart rate (77.3 vs 79.2, p = 0.19).

Table 3 : Treadmill Parameters of Dippers(n=66) and Non Dippers (n=74)

	Dippers (n= 66)	Non Dippers (n=74)	P value
Duration of Exercise(min)	9.3±2.1	9.1±2.4	0.23
Peak Exercise capacity (METs)	13.0±2.1	12.9±1.9	0.34
MHR (bpm)	146.4±10.4	156.8±11.7	<0.05
BHR(bpm)	77.3±5.8	79.2±6.4	0.19
HR (bpm)	67.7±6.7	74.01±5.8	<0.05
HRR-1(bpm)	28.6±4.0	22.8±4.6	<0.05

Abbreviations: bpm, beats per minute; HRR-1, heart rate recovery in 1st min post exercise ; MHR : maximal heart rate indices ; METs, metabolic equivalent levels; NS, not significant; BHR : Basal heart rate ; HR : Heart rate reserve

Non –Dippers (n=74) had a significantly higher Maximal Heart Rate on exercise (156.8 vs 146.4, p <0.05) and Heart Rate Reserve (74.01 vs 67.7 p<0.05) which is the difference of maximal heart rate (MHR) and baseline heart rate (BHR).Mean HRR-1 values (28.64 vs 22.84 bpm, P=.007) were significantly higher in dipper group than the hypertensive nondipper group. (Table 3).

DISCUSSION:
It has been shown that some cardiovascular complications of essential hypertension such as left ventricular hypertrophy microalbuminuria and cerebrovascular damage tend to be more common in patients with a non-dipping pattern of BP.[7,8,9]

Although the underlying mechanisms of nocturnal decrease

of BP are not yet fully understood, withdrawal of sympathetic activity during sleep probably plays an important role.[10,11]

Abnormalities on autonomic nervous activity, particularly of the sympathovagal balance as seen in patients with autonomic neuropathy are thought to explain the blunting of the normal nighttime BP decline.[12,13]

Heart rate recovery after graded exercise is a commonly used tool that reflects autonomic activity. An attenuated HRR, which is defined as the decrease in heart rate immediately after exercise, ia a reflection of reduced parasympathetic nervous system (PNS) activity.[14,15]

In the present study we have shown in hypertensives that the percentage of the fall of nighttime BP is positively related to the decrease in the heart rate during the first minute after graded exercise, which has been shown to reflect the capacity of activation of the parasympathetic nervous system and to represent an important marker of cardiovascular prognosis .Non-Dippers also had a significantly higher average 24 hour diastolic blood pressure and a maximal heart rate during exercise also suggesting an increased sympathetic activity.

Chaitman et al showed that, the finding of an abnormal HRR response was a surrogate for underlying autonomic dysfunction and that the mechanism of increased mortality associated with this finding might be more related to autonomic dysfunction than to the presence or extent of coronary artery disease. HRR indices immediately after the completion of an exercise stress test were found as predictors of all cause mortality.[16]

Schwartz et al reported that increased PNS activity had been associated with a decrease in the risk of death by protecting the heart against lethal arrhythmias.[17]

Studies have also shown that abnormal HRR, defined as failure of heart rate to decrease 12 beats or more during the first minute after peak exercise, independently predicts an increased mortality.[18]

A delayed recovery of heart rate after exercise has been considered to be a consequence of the blunting of a vagus nerve-mediated response after exercise. In other words, in the present study we have found in hypertensives that the lack of the nocturnal decline of BP is associated with a delayed heart rate recovery immediately after exercise suggesting that a decreased vagal activity is present in patients with a nondipper circadian BP rhythm.

Morshedi-Meibodi et al demonstrated that the greater HRR in the first minute of recovery the lower the subsequent mortality. [19] Polonia et al have also reported an association between the blunting of the nocturnal fall of BP and delayed HRR after graded maximal exercise, but different from our study as normotensive individuals were not involved in our study.[20]

Conclusion:

Blunting of the nocturnal fall of BP in hypertensives associates with a delayed recovery of heart rate after graded maximal exercise suggesting that a general decrease of vagal modulation within an abnormal sympathovagal response is present. That may indicate that in hypertensives without signs of coronary disease the decrease of vagal activity is linked to the failure of nighttime fall of BP that might represent an alteration of the autonomic nervous drive with possible deleterious consequences of a greater deterioration of target organs. The main strength of the present study was the selection of patients from the most frequently encountered patients in the daily practice of cardiology. The major limitations of the study are that there were small number of patients and results are based on a single center.

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