Original Article

Circadian Blood Pressure Variability in Normo and Hypertensive Diabetic Patients

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Abstract

Background: Diabetic patients have a higher prevalence of non-dipping pattern in blood pressure (BP) than general population. Non-dipping arterial pressure pattern is associated with increased cardiovascular risk. The objective of this study was to investigate the association between the clinical and paraclinical characteristics of the diabetic patients with circadian BP variability.

Materials and Methods: This cross-sectional study included 114 diabetic patients (more than 18 years old) recruited by consecutive sampling. The patients were divided into two groups according to the results of systolic blood pressure dipping from day to night.

Results: Mean age was 58.3±9.6 years; and 63% of the study population was male. Also, 80.7%, 78.1%, and 78.9% of the patients had non-dipper patterns in systolic, diastolic, and mean BP respectively. The dipping pattern did not have any significant association with baseline or clinical characteristics of the patients ($p>0.05$).

Conclusion: The characteristics of the patients do not assist finding diabetic persons who are more likely to have non-dipping arterial pressure pattern. As such, ABPM is an essential tool for proper risk stratification in diabetic patients.

Keywords: blood pressure, diabetes, dipping pattern, non-dipper pattern

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Introduction

The prevalence of diabetes mellitus is estimated to increase in the future decades. Cardiovascular diseases may be the first cause of mortality in diabetic patients. The prevalence of arterial hypertension in diabetic patients is twice as high as general population[1]. Ambulatory blood pressure (BP), particularly the circadian blood pressure variability (CBPV) is a better predictor of cardiovascular disease than office blood pressure[2].

The primary aim of this study was to determine the CBPV in diabetic patients. The secondary aim of the study was to explore the association between the clinical and paraclinical characteristics of the diabetic patients with CBPV.

Methods

Study Population: This cross-sectional study enrolled 114 diabetic patients including 72 women and 42 men

with age 58.3±9.6 years (mean± SD) from May 2013 to September 2013. Diabetic patients with retinopathy, left ventricular ejection fraction (LVEF) below 40% or nephropathy were excluded. The local ethical committee of Shahid Beheshti University of Medical Sciences approved the study and all the patients gave written informed consent.

Data Collection: The baseline characteristics (such as: age, gender, smoking, hypertension, duration of diabetes mellitus, dyslipidemia, hypothyroidism, body weight, height, body mass index, waist circumference, prior coronary artery disease or cerebrovascular accident), together with the results of paraclinical evaluation (blood chemistry analysis, echocardiography, exercise tolerance test, and 24-hours ambulatory blood pressure monitoring) were recorded.

The Body Mass Index (BMI) was calculated as body weight/height^2 (kg/m^2). Blood chemistry analysis included HbA1c, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglyceride, and creatinine. Individuals, not receiving any antihypertensive medications, were categorized as non-hypertensive patients. Glomerular filtration rate (GFR) was measured using Cockcroft-Gault formula.

Ambulatory Blood Pressure Monitoring: Ambulatory blood pressure monitoring (ABPM) is the method for obtaining automated brachial blood pressure measurements, at fixed time intervals during a 24-hour period away from a medical environment. It provides multiple readings with minimal interference with the patients' activities. The 24-hour ABPM was performed using an automated oscillometric device (ScottCare ABP320), and data were analyzed using SIGMA 2000 software. The device was calibrated before start of the study. Also, for each patient, the same device was used. ABPM was placed on the arm with higher BP value and patients recommended keeping their habitual routine. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean BP, and heart rate (HR) were recorded every 15 minutes throughout the day and every 30 minutes at night. Daytime and nighttime were determined individually, depending upon the patient's sleep-wake times.

SBP, DBP, mean BP, and HR were average for the day and the night. The normal dip was defined as a 10% or more reduction in BP during the night compared with the day. Percent dipping for systolic BP, diastolic BP, and mean BP is calculated from the mean values for daytime and nighttime blood pressure as follows:

[(daytime BP - nighttime BP)/daytime BP] × 100.

Statistical Analysis: Continuous variables were expressed as mean±standard deviation, and dichotomous variables as frequencies. Statistical analysis was performed by using SPSS version 16 (SPSS Inc., Chicago, IL, USA). Differences were examined using Student's t-tests or Mann-Whitney U-test for continuous variables and Chi-Square tests for dichotomous variables (or Fisher's exact test when more than 20% of cells with expected count of less than 5 were observed). A p-value<0.05 was considered statistically significant.

Results

At the time of study, 49 (43%) patients had diagnosed hypertension and were under treatment with hypertension medications; and 92 (80.7%) patients had non- dipper patterns.

Table 1 displays baseline and clinical characteristics of the patients stratified in two groups (the dipper and non-dipper pattern). There was not any significant difference between the two groups regarding age, gender, duration of diabetes mellitus, smoking, presence of hypertension or dyslipidemia or hypothyroidism, body weight, height, body mass index; and waist circumference (p-values>0.05).

Table 2 shows paraclinical characteristics and drug history of the patients stratified by dipping pattern. There was not any significant difference between the two groups according to HbA1c, lipid profile, GFR, results of exercise tolerance test including heart rate recovery; and drug usage (p-values>0.05).

Table 3 presents ambulatory blood pressure monitoring results of the patients. The two groups (the dipper and non-dipper pattern) had significant difference in the average of SBP, DBP, and mean BP in all day as well as nighttime (p-values<0.05). However, the two aforementioned groups did not reveal any significant difference in the average of SBP, DBP, and mean BP in wake time (p-values>0.05).

Also, there was not any significant difference in the

Table 1: Baseline characteristics of the enrolled diabetic patients stratified by dipping pattern in systolic blood pressure.

Characteristics	dipping pattern	Non-dipping pattern	p-value
Number of patients	22	92	-
Age, yrs. (mean±SD)	59.3±9.9	58.1±9.5	0.608
Age≥70 yrs.	2 (9.1%)	9 (9.8%)	0.921
Gender, male	10 (45.5%)	32 (34.8%)	0.351
Current Smoking	1 (4.5%)	9 (9.8%)	0.435
Hypertension	7(31.8%)	42 (45.7%)	0.239
Duration of DM, yrs. (mean±SD)	7.3±6.7	10.1±7.7	0.297
Dyslipidemia	9 (40.9%)	45 (48.9%)	0.499
Hypothyroidism	2 (9.1%)	4 (4.3%)	0.371
Body weight (Kg) (mean±SD)	73.0±9.6	74.4±13.2	0.564
Height (m) (mean±SD)	161.9±7.3	159.4±10.8	0.211
Body mass index (Kg/ m2) (mean ± SD)	28.0±4.3	29.5±5.7	0.186
Waist circumference(mean±SD)	97.1±9.2	95.3±10.9	0.443
Prior CAD	3 (13.6%)	9 (9.8%)	0.597
Prior CVA	1 (4.5%)	2 (2.2%)	0.532

Values are presented as n (%) unless otherwise expressed.
DM=Diabetes mellitus, CAD=Coronary artery disease, CVA=Cerebrovascular Accident

average of heart rate among the two groups according to heart rate in all times (all p-values>0.05).

Discussion

In patients with diabetes, a non-dipping pattern is frequently observed.[3]This pattern is associated with fatal and non-fatal cardiovascular events[4- 6].

The incidence of non-dipping pattern in elderly patients is high and it may be reached to more than 2/3 of patients in some studies similar to present data[7,8]. However, in contrast to some reports there was not a meaningful relationship between age and presence of dipping pattern; which may be due to larger our study population[9].

There is conflicting evidence that obesity is associated with abnormal circadian rhythm. Some previous studies reported higher prevalence of non-dipping pattern in obese patients than in the normal weight groups (71.4% versus 41.1% in the normotensive, and 72.7%, versus 61.5% in the hypertensive subjects) [10].

Moreover, the association between dysglycemia, HbA1c, and GFR with CBPV had seen in some studies, but not in this study[11, 12].

In contrast to some previous studies, there was not any meaningful relationship between CBPV and heart rate recovery[13].

Diuretics, beta blockers, and calcium channel blockers are able to normalize non-dipper pattern of BP in some reports, but there was not a significant relationship

Table 2: Paraclinical characteristics and drug history of the enrolled diabetic patients stratified by dipping pattern in systolic blood pressure.

Characteristics	dipping pattern	Non-dipping pattern	p-value
Number of patients	22	92	-
HbA1c (mg/dl)	8.8±1.6	8.3±2.1	0.495
LDL (mg/dl)	110.7±29.4	107.2±33.8	0.719
HDL (mg/dl)	34.9±6.2	38.1±9.4	0.160
TG (mg/dl)	168.9±60.1	161.4±57.7	0.700
Hb (mg/dl)	13.4±0.9	13.0±1.2	0.050
GFR	79.0±23.0	83.9±25.3	0.404
Positive ETT for CAD [n (%)]	3 (13.6%)	13 (14.1%)	0.952
METs	7.0±2.2	6.8±2.2	0.594
HRR	36.7±18.6	33.4±15.7	0.473
LVEF	56.4±7.6	56.4±6.2	0.961
Beta blocker usage [n (%)]	7 (31.8%)	20 (21.7%)	0.318
Calcium blocker usage [n (%)]	0 (0.0%)	8 (8.7%)	0.151
ACE inhibitor or ARB usage [n (%)]	5 (22.7%)	31 (33.7%)	0.320
Diuretic usage [n (%)]	1 (4.5%)	3 (3.3%)	0.769
Insulin usage [n (%)]	5 (22.7%)	13 (14.1%)	0.321
Statin usage [n (%)]	7 (31.8%)	42 (45.7%)	0.239

Values are presented as (mean±SD) unless otherwise expressed.
LDL=Low density lipoprotein, HDL=High density lipoprotein, TG=Triglyceride, Hb=Hemoglobin, GFR=Glomerular filtration rate, ETT=exercise tolerance test, CAD=Coronary artery disease, METs=Metabolic Equivalent, HRR= Heart Rate Recovery, LVEF=Left Ventricular Ejection Fraction, ACE=Angiotensin Converting Enzyme, ARB= Angiotensin Receptor Blocker.

between drug usage and dipping pattern in this study which is probably related to small percent of drug usage[14,15].

However, similar to our study the definite relationship between patients' characteristics with CBPV is not confirmed and ABPM is needed to evaluate the dipping pattern particularly in diabetic patients.

In this study, the average of SBP, DBP, and mean BP showed significant difference between the two groups (the dipping and non-dipping pattern) in all day, and also in nighttime. But these averages did not have any meaningful difference between the two groups in wake time. The issue has a practical importance because nighttime BP and dipping can only be detected by 24-hours ABPM. So, in diabetic patients ABPM can provide valuable data for risk stratification.

Study Limitations: Reproducibility of 24-hours ambulatory BP measurements has been demonstrated, but reproducibility of non-dipping pattern did not approve and as such it is not reliable[16]. The nighttime

Table 3: Ambulatory blood pressure monitoring results of the enrolled diabetic patients stratified by dipping pattern in systolic blood pressure.

Characteristics	dipping pattern	Non-dipping pattern	p-value
Number of patients	22	92	-
SBP in all day, mmHg	116.0±14.8	125.0±16.5	0.017
DBP in all day, mmHg	69.1±7.7	75.1±8.7	0.003
Mean BP in all day, mmHg	89.2±8.8	96.3±10.4	0.002
HR in all day, mmHg	75.6±11.6	75.4±9.8	0.943
SBP in wake time, mmHg	120.7±15.1	123.5±15.2	0.446
DBP in wake time, mmHg	71.9±7.7	75.2±8.8	0.088
Mean BP in wake time, mmHg	92.8±8.7	95.6±10.1	0.084
HR in wake time, mmHg	76.1±12.3	77.6±10.3	0.608
SBP in night, mmHg	102.3±14.3	124.2±19.3	0.000
DBP in night, mmHg	62.3±5.0	74.7±10.6	0.000
Mean BP in night, mmHg	79.3±7.9	95.9±13.2	0.000
HR in night, mmHg	69.9±10.9	71.7±10.2	0.493
Percent dipping for SBP	15.3±5.1	-0.45±7.5	0.000
Percent dipping for DBP	12.8±6.9	0.52±9.1	0.000
Percent dipping for mean BP	14.5±4.8	0.8±7.8	0.000

Values are presented as (mean±SD).
SBP=Systolic blood pressure, DBP=Diastolic blood pressure, BP=Blood pressure, HR=Heart rate.

BP is influenced by two factors: assuming the supine position, and sleeping. Thus, wake time BP maybe depends on posture and activity which has been studied in a two-days BP monitoring when subjects were active during one day and inactive during the second day. The recorded blood pressures in wake time were higher on the active days, and so patients were more likely to be classified as dipper in these days than on the inactive days[17]. In this study, all ABPMs were done in active days. Further studies may be needed for the proper application of ABPM in diabetic patients.

Conclusion

ABPM in diabetic patients is superior to clinic BP in predicting cardiovascular prognosis[4]. ABPM should be recommended at least once for detection of nocturnal hypertension and non- dipping pattern of BPin diabetic patients.

ABPM emerges as a useful tool in the evaluation of dipping pattern in diabetic patients.

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