Twenty-four Hour Blood Pressure Record for Smokers and Nonsmokers

Marcos Galan Morillo, Marisa Campos Moraes Amato, Sonia Perez Cendon Filha
São Paulo Federal University - UNIFESP, São Paulo, SP - Brazil

Objective: To evaluate the effect of smoking on blood pressure trends during a 24-hour period, by analyzing the parameters of the ambulatory blood pressure monitoring (ABPM).

Methods: The results of 289 ABPM tests conducted on patients classified as smokers or nonsmokers were studied. The parameters analyzed were: mean 24-hour, daytime and nighttime systolic and diastolic blood pressure readings; nocturnal dipping of systolic and diastolic pressures and blood pressure load. The patients were classified in four groups according to whether or not they used antihypertensive medication: 1A – nonsmokers using medication; 1B – smokers using medication; 2A – nonsmokers not using medication; and 2B – smokers not using medication. Variables were expressed as minimum, maximum, median, mean and standard deviation values. Univariate analysis was used for comparing the smoking and nonsmoking groups. The significantly different variables from the groups were selected using multivariate analysis. The significance level adopted was 5%.

Results: Mean daytime systolic and diastolic blood pressures were significantly higher in the smokers, regardless of whether or not they used antihypertensive medication. Mean nocturnal blood pressure readings were similar between smokers and nonsmokers. Mean 24-hour systolic blood pressure readings were significantly higher in the smokers, regardless of whether or not they used antihypertensive medication. Nocturnal dipping was similar for all groups. Blood pressure loads were consistently and significantly higher in the smokers regardless of medication use.

Conclusion: Mean daytime systolic and diastolic blood pressure readings were consistently higher in the smokers when compared to nonsmokers regardless of antihypertension medication use. Nocturnal dipping was similar for smokers and nonsmokers.

Key words: Smoking, blood pressure, blood pressure monitoring, hypertension.

It is known that smoking causes a temporary rise in blood pressure levels for both hypertensive and normotensive individuals. Nevertheless, epidemiological studies evaluating blood pressure levels using casual in-office blood pressure measurements have shown that smokers present blood pressure readings that are less than or equal to those of nonsmokers[1-3]. In these studies, individuals are assessed by an isolated blood pressure measurement according to the recommendations of national and international guidelines (JNC 7, ESH 4, IV DBHA). In contrast, smokers submitted to ambulatory blood pressure monitoring (ABPM) present higher mean blood pressure readings than nonsmokers[4-6].

A better understanding of the 24-hour effect of smoking on blood pressure trends, actual systemic blood pressure and the impact on target organs is required. Ambulatory blood pressure monitoring (ABPM) is the diagnostic tool that enables this analysis, providing a profile of daytime and nighttime blood pressure variations[7]. This test provides a better understanding of hypertension for diagnosis, prognosis or treatment purposes[7-9]. Blood pressure level trends from ABP monitoring as well as measurements taken at home are more reliable in relation to the prognosis of hypertension since they are a better indication of target organ lesions than measurements taken at the doctor's office[10].

The objective of this study is to assess the effect of smoking on blood pressure trends during a 24-hour timeframe using the ambulatory blood pressure monitoring parameters.

Methods

Two hundred and eighty nine ambulatory blood pressure monitoring tests were studied from a population of patients referred by their doctors to a diagnostic testing clinic associated with a teaching institution. Substandard tests were repeated. Seventeen tests were excluded due to

Mailing Address: Marcos Galan Morillo •
Av. Juriti, 144 – 04520-000 – São Paulo, SP - Brazil
E-mail: marcosgmorillo@uol.com.br
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incomplete data, duration of less than 21 hours or automatic exclusions in excess of 20%. The case study included 272 tests with 211 nonsmokers and 61 smokers. The patients were classified as smokers or nonsmokers according to the information given when the device was fitted. Anyone who smoked one or more cigarettes per day was classified as a smoker.

The following ABPM parameters were analyzed: mean 24-hour, daytime and nighttime systolic and diastolic blood pressure readings; Systolic and diastolic nocturnal dip; Daytime, nighttime and 24-hour systolic and diastolic blood pressure loads.

The Dyna-MAPA 24-hour oscillometric ABP-Monitor that has been validated by the American Association for the Advancement of Medical Instrumentation (AAMI) and the British Hypertension Society (BHS) was used. The programming and report generation software was also Dyna-MAPA. The program automatically produces the statistical report without interpretation by any professional.

The patients were fitted with the device during normal daytime working hours by a trained technician. Each patient wore the device for 24-hours and returned to the clinic the following day for removal. The monitoring was performed on a weekday that reflected the patient's normal activities. No patient was monitored on a Saturday, Sunday or holiday. The cuff was placed on the non-dominant arm two fingers above the elbow crease. Adequate size cuffs according to arm circumference were used. A previously established set of instructions was given to the patients when the device was fitted.

The device's program registered measurements every 15 minutes during the day and every 20 minutes during the night. The patients were instructed to keep a diary of their activities that was to include lunch and dinner times and the time they went to bed and woke up. They were also to record the names of any medications they were taking, the dosage and the times they were taken. If they had any symptoms they were to record them with the hour of onset and conclusion. Daytime was considered as the period between 7a.m. and 11p.m. and nighttime between 11p.m. and 7a.m. as outlined in the recommendations of the 2nd Brazilian Consensus for ABPM[11]. Initially the test sample was divided into two groups based on whether or not the patients used antihypertensive medication. These two groups were then further subdivided into smokers and nonsmokers as follows: *Group 1A* – Nonsmokers using antihypertensive medication; *Group 1B* – Smokers using antihypertensive medication; *Group 2A* – Nonsmokers not using antihypertensive medication; *Group 2B* – Smokers not using antihypertensive medication.

No distinction was made among the groups in relation to normotensive patients or hypertensive patients with or without satisfactory control. Variables were expressed as minimum, maximum, median, mean and standard deviation values.

The Student's t-test was used in the univariate analysis to compare the ABPM variables with normal distribution for the groups of smokers and nonsmokers[12]. The variables that did not have normal distribution were analyzed using the Wilcoxon test for two independent samples. The gender variable distribution was compared between the groups of smokers and nonsmokers using the Pearson chi-square test[12].

The variables that presented a significant difference in the univariate analysis between the groups of smokers and nonsmokers were used in the multivariate analysis. The logistic regression model was adopted in this phase in order to determine the most important variables in the differentiation between the two groups. The stepwise method[13] was used to select the variables with equal input (0.10) and output (0.05) significance levels.

Separate analyses were conducted for the groups of patients who used or did not use medication. The significance level adopted was 5%. This study was approved by the institution's research and ethics commission.

Results

The descriptive analysis of the sample in relation to gender and age presented the following results (Tab.1) (Fig. 1).

Smoking and antihypertensive medication - Univariate analysis - The ABPM parameters were expressed as minimum, maximum, median, mean and standard deviation values. Univariate analysis was conducted using the smoking variable for the groups that used and did not use antihypertensive medication. The data with a statistical significance of p less than 0.05 ($p < 0.05$) were selected.

Mean systolic and diastolic blood pressure measurements - The mean daytime systolic and diastolic blood pressure measurements (Figs.2B and 3B) were significantly higher for the smokers in both Group 1 that used antihypertensive medication and Group 2 that did not use medication. There was no difference in the mean nocturnal (Fig. 2C) or 24-hour (Fig. 2A) systolic blood pressures between the smokers and nonsmokers who used antihypertensive medication. The mean nocturnal and 24-hour systolic blood pressure (Figs.2C and 2A) were significantly higher in the smokers that did not use antihypertensive medication. The mean 24-hour diastolic blood pressure (Fig.3A) was significantly higher for smokers regardless of whether or not they used antihypertensive medication.

Systolic and diastolic nocturnal dip - There was no significant statistical difference for systolic nocturnal dipping related to smoking between Group 1 that did not use antihypertensive medication and Group 2 that used antihypertensive medication. There was also no statistical significance between the groups in the univariate analysis of diastolic nocturnal dipping.

Systolic and diastolic blood pressure loads - Systolic blood pressure loads (SBPL) were consistently and significantly higher for all periods for the smokers that used antihypertensive medication (SBPLday $p = 0.0225$ / SBPL24h $p = 0.03$ / SBPLnight $p = 0.0225$), and did not use antihypertensive medication (SBPLday $p < 0.0001$/ SBPL24h $p< 0.001$/ SBPLnight $p < 0.005$).

Diastolic blood pressure loads (DBPL) registered

Group 1 – with medication				Group 2 – without medication			
Smoker	Gender		Total	Smoker	Gender		Total
	Male	Female			Male	Female	
1A nonsmoker	53 (40.15%)	79 (59.85%)	132	2A nonsmoker	35 (44.3%)	44 (55.7%)	79
1B smoker	15 (53.57%)	13 (46.43%)	29	2B smoker	10 (30.3%)	23 (69.2%)	33
TOTAL	68	92		TOTAL	45	67	
Chi-square p = *0.192*				*Chi-square* p = *0.1683*			

Table 1 - Sample distribution in relation to gender (Group 1 – with medication and Group 2 – without medication)

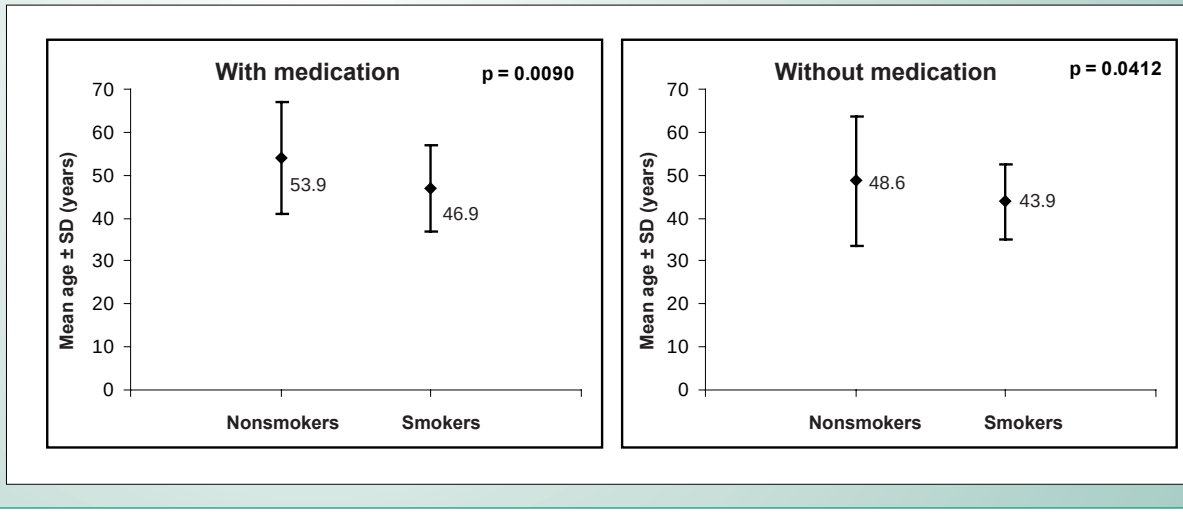


Fig. 1 - *Graphic demonstration of the sample distribution (with and without medication) in relation to age.*

similar results for those using antihypertensive medication (DBPLday p = 0.0225/ DBPL24h p = 0.0044/ DBPLnight p = 0.0404), and those that did not use antihypertensive medication (DBPLday p = 0.0297/ DBPL24h p = 0.0083/ DBPLnight p = 0.042).

Multivariate analysis - The significantly different variables from the univariate analysis of smokers and nonsmokers were selected according to their ability to demonstrate the greatest differentiation between the groups.

In the group of patients that used antihypertensive medication, the daytime diastolic blood pressure load was significantly higher (p = 0.0107) in the smokers. In the group of patients that did not use antihypertensive medication, the daytime systolic blood pressure load was significantly higher (p < 0.0001) in the smokers.

Discussion

During regular blood pressure assessments the absence of the adrenergic effect caused by smoking probably produces a transitory decrease[3]. It was not possible to distinguish which normotensive and hypertensive patients controlled their blood pressure satisfactorily.

Mean systolic and diastolic blood pressure measurements are essential data for ABPM analysis for diagnostic purposes as well as therapeutic and prognostic evaluation[14]. Currently, mean pressure measurements are considered the most important parameter to analyze the 24-hour pressure curve since they are positively related to target organ alterations such as the left ventricular mass index, encephalic ischemic lesions and microalbuminuria[14]. The Syst–Eur[15] and Ohasama16 studies demonstrated that the variables that are more closely related to cardiovascular events such as acute myocardial infarction and encephalic stroke were the mean nighttime systolic blood pressure followed by the mean 24-hour systolic blood pressure and the mean daytime blood pressure measurements.

The results showing that the mean daytime systolic and diastolic blood pressure measurements were significantly

	Group 1 with medication	Group 2 without medication
A nonsmokers	132	79
B smokers	28	33

Table 2 - Sample distribution in relation to smoking in Groups 1 and 2

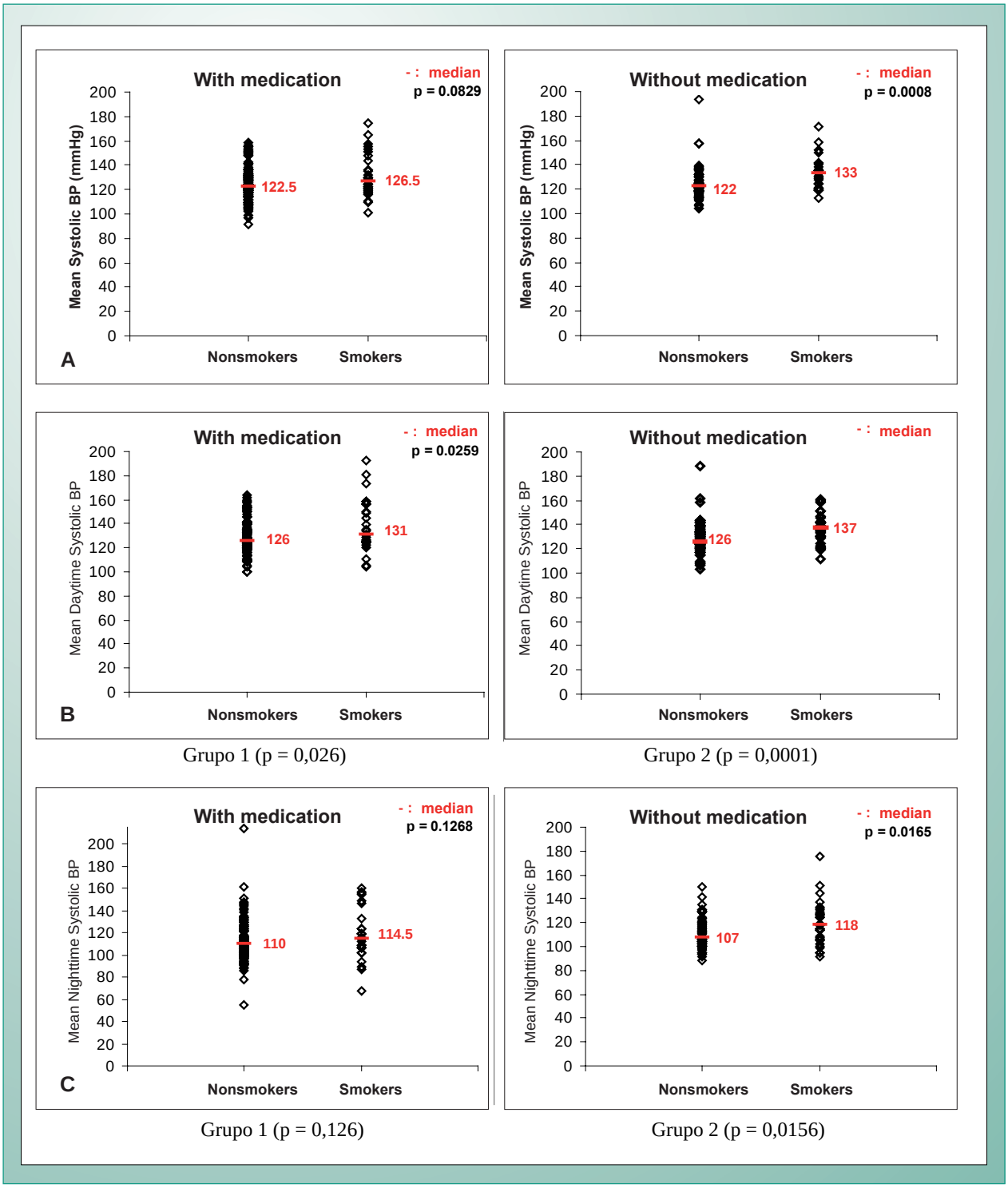
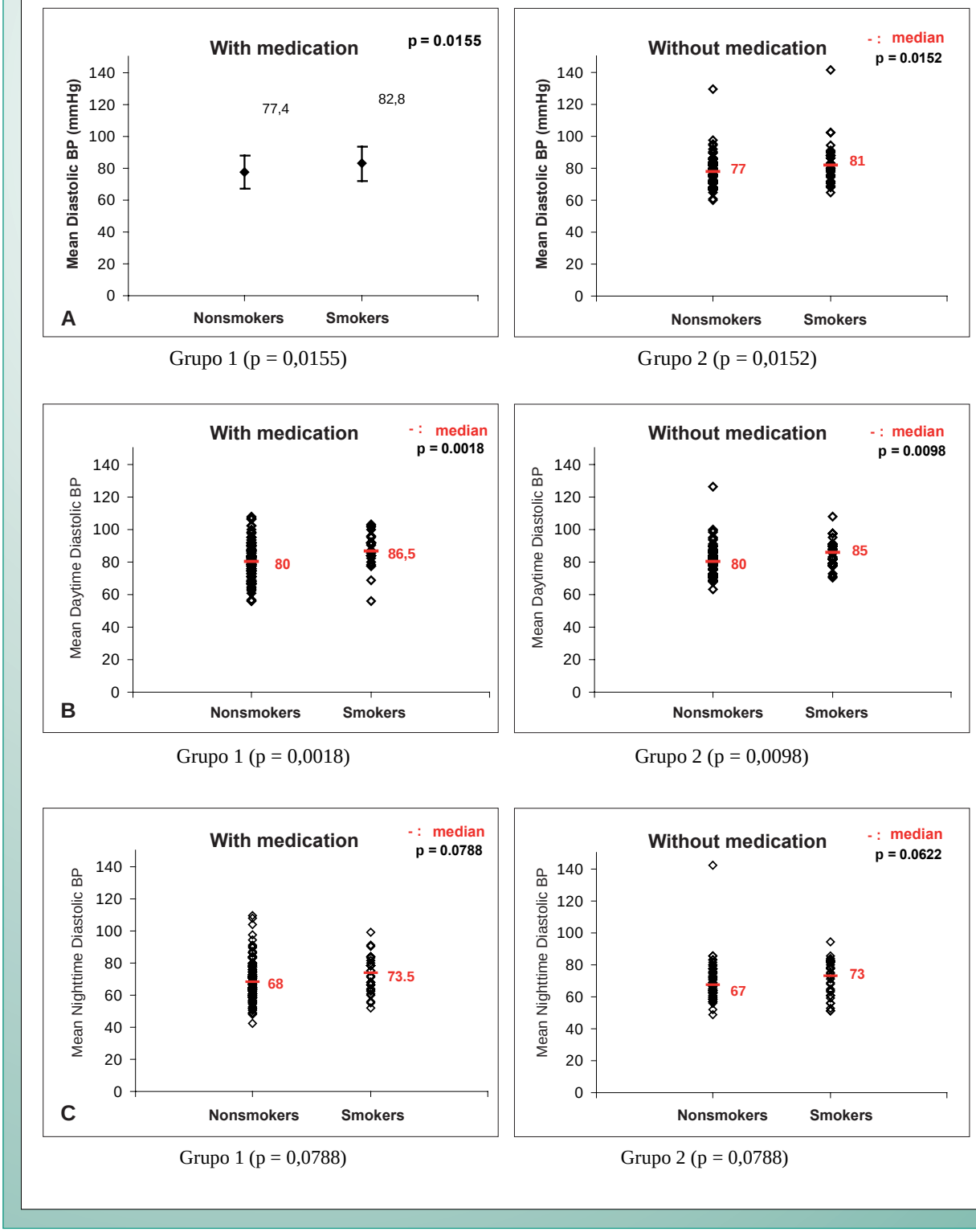


Fig. 2 - *Graphic demonstration of univariate analysis for mean 24-hour (A), daytime (B) and nighttime (C) systolic blood pressure.*

higher in smokers regardless of whether or not they used antihypertensive medication agree with the majority of studies conducted in other countries with normotensive[17-19] and hypertensive patients[20-23].

It is a known fact that smoking one cigarette increases the heart rate by 14% and blood pressure by 6%24. This reaction is probably caused by the increased plasmatic concentrations of adrenaline and noradrenaline while smoking[25]. Norepinephrine levels increase within 12.5 minutes and peak after 15 minutes before returning to initial levels after 30 minutes. This alteration causes a maximum blood pressure increase which reduces after 30 minutes, however, the level



Grupo 1 (p = 0,0155) Grupo 2 (p = 0,0152)

Grupo 1 (p = 0,0018) Grupo 2 (p = 0,0098)

Grupo 1 (p = 0,0788) Grupo 2 (p = 0,0788)

Fig. 3 - *Graphic demonstration of univariate analysis for mean 24-hour (A), daytime (B) and nighttime (C) diastolic blood pressure.*

remains higher than the values registered before smoking[25].

Ward et al[26] studied blood pressure and heart rate trends in patients during the first week after they had quit smoking and observed a significant decrease in these variables. These patients also demonstrated a significant decrease in the plasmatic and urinary levels of norepinephrine and epinephrine after one week of no smoking.

Groppelli et al[27], evaluated ten normotensive smokers who smoked one cigarette every fifteen minutes during an hour and demonstrated that blood pressure and heart rate increased immediately after smoking the first cigarette and remained at that level while the other three cigarettes were smoked. The initial blood pressure increase was approximately 12 mmHg for the systolic reading and 15 mmHg for the diastolic reading. The pressor effect caused by smoking decreased during the first hour after smoking probably due to an unknown compensatory mechanism. In this same study, six other normotensive smokers smoked one cigarette every thirty minutes during eight hours and once again there was an increase in blood pressure and heart rate soon after smoking the first cigarette and they remained elevated during the entire period of exposition to tobacco. The greatest blood pressure variations for both groups occurred while they smoked.

Chronically, nicotine diminishes baroreceptor sensitivity and increases the production of thromboxane A2, a powerful vasoconstritor[28]. High levels of thromboxane B have been found in hypertensive smokers[29]. The synthesis of nitric oxide and endothelin is reduced in smokers regardless of the number of cigarettes smoked daily[30]. It has also been demonstrated that smoking increases angiotensin II production[31].

Contrary to the results of this study, Mikkelsen et al[32], studying normotensive patients submitted to ABPM, demonstrated that the smokers presented lower mean daytime systolic BP readings while Green et al[2] also observed lower mean daytime diastolic BP readings. Mikkelsen et al[32] suggest that this outcome is caused by an adaptive effect in the sympathetic nervous system after numerous years of exposure to nicotine. They also report that smokers are less affected by "white coat" hypertension and confirm that the chronic stimulation by nicotine and its metabolites eliminate the power of any other stimuli to provoke further reaction. The authors emphasize that smoking also helps to reduce stress, which could be associated with the lowering of blood pressure.

Mean nighttime blood pressure did not present a significant difference between the groups in relation to smoking, as seen previously in other studies with normotensive[33,34] and hypertensive patients[22,23]. Only the mean nighttime systolic blood pressure was significantly higher in the smokers that did not use antihypertensive medication.

It is believed that the acute pressor effect caused by smoking does not exist during the night when most individuals are sleeping and therefore justifies the similar blood pressure measurements of smokers and nonsmokers. For both normotensive and hypertensive patients, the physiological blood pressure trend has a circadian rhythm, which reaches lower levels when the person is sleeping and returns to higher levels when the person wakes up. In this study there was no significant statistical difference in the systolic and diastolic nocturnal dip associated with smoking in either group.

Other studies[20,35] have observed that the nocturnal dip of smokers is more pronounced than that of nonsmokers. This alteration can be explained as a result of the elimination of the acute pressor effect during the night in smokers. To date, the actual cause of nocturnal blood pressure dipping is unknown. This fact could be related to an intrinsic biological rhythm or the lack of external stimuli or even an association of the two factors[36]. The determination of nighttime and daytime periods with preset hours and the accuracy of the patient's diary of exact hours[37] are questionable.

Most of the devices, including those used in this study, register nighttime hours as the period between 11p.m. and 7 a.m. that obviously could lead to inaccurate results for any patients that do not strictly abide by these hours for going to sleep and waking up. Encouraging the patients to use the sleep/activity button could result in more accurate data for hours of sleep. However, we have observed that some patients become confused when they have to adjust the device distorting the registers. Sleep quality could interfere in the physiological decrease and this information should also be recorded on the test report.

The evaluation of the nocturnal dip enables better risk stratification for hypertensive patients[38]. It has been well established that the lack of an adequate nighttime blood pressure dip (less than 10%)[39-41] in these patients, as well as an accentuated dip (higher than 20%) in elderly hypertensive patients[42] is associated with a more severe risk to the target organ.

Blood pressure loads represent a percentage of measurements that are considered higher than normal by the ABPM and reflect a greater fluctuation in the pressure levels. In the latest version of the Brazilian ABPM Guidelines (2001), blood pressure loads were given a secondary importance and the clinical interpretation of this method was limited. In this study the parameter was analyzed however we are aware that its use in the monitoring evaluation is subject to much criticism. There was a great variation in the daytime, nighttime and total systolic and diastolic blood pressure load values obtained for Groups 1 and 2 since the standard deviation value was very close to the mean value. The median values were similar for both groups.

The most interesting and evident fact of this study is that blood pressure levels for smokers increase during the day. If we continue to exclusively use in-office blood pressure measurements for smokers it is possible that regular evaluations could be made that do not reflect the actual systemic blood pressure and inadequately estimate the hemodynamic effect of target organ lesions. Some theories try to explain the epidemiological findings of blood pressure levels in smokers that are less than or equal to the casual blood pressure measurement. The theory with the highest acceptance rate is the reduction of the acute pressor effect caused by smoking due to tobacco abstinence for a few minutes or hours before the office measurement. Another attempt to explain this phenomenon is that the prolonged and chronic use of tobacco increases heart rate that would lead to a decrease in left ventricular end-systolic volume and consequently lower blood pressure. The use of ABPM exclusively during the daytime can

be a valid consideration of future studies for both diagnostic purposes and the assessment of antihypertensive treatment in smokers.

Repetitive in-home blood pressure measurements taken over a period of a few days using validated equipment can become an alternative to ABPM to evaluate smokers. This method has been recommended[3], since it helps in treatment adhesion and is superior to the casual measurements taken at the doctor's office in regard to target organ lesions[43,44]. In comparison to in-office measurements the in-home blood pressure measurements offer a greater number of readings, better reproducibility and data storage in the unit's memory chip. However, a greater number of more economical units need to be validated and specific diaries should be created for these patients[45]. A series of in-home readings recording the times of cigarette smoking can be useful for these patients, avoiding interpretations based on unreal situations like a programmed abstinence from smoking.

All hypertensive patients are advised to quit smoking as a control measure for cardiovascular risk factors. This advice is part of the non-medicinal hypertension treatment that is being incorporated which also includes a low sodium diet, moderate alcohol consumption, weight loss and periodic physical activity[10,46,47].

Short-term longitudinal studies using ABPM to evaluate patients that have quit smoking reveal that the blood pressure measurements of these patients are substantially lower than when they were smoking[34,48]. These observations suggest a possible etiopathogenic link between the effect of smoking and hypertension. Prospective studies with long-term follow-up and the control of variables such as weight gain can confirm and quantify this effect.

It appears that the smoking population is a special group in which ABPM is the most adequate method for blood pressure assessment, avoiding the isolated measurement at the doctor's office, a procedure which could incorrectly diagnose hypertensive patients or undermedicate patients using antihypertensive treatments.

Limitations - The univariate analysis was adjusted for age and gender variables, however, it was not possible to analyze data such as body mass index, sedentary lifestyle, type of medication used or co-morbidities.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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