ABPM in COPD Patients with Sleep Desaturation

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Summary

Background: Sleep hypoxemia may change blood pressure by sympathetic activation. Few studies have analyzed blood pressure parameters in COPD patients who do not present sleep apnea, but do present sleep desaturation.

Objectives: To analyze blood pressure parameters in COPD patients with sleep desaturation not caused by apnea.

Methods: Thirteen patients with COPD underwent spirometry, blood gas, polysomnography and ABPM for blood pressure evaluation. Fourteen patients without COPD underwent spirometry, oximetry and ABPM. Blood pressure analyses were carried out both during wakefulness and sleep. Both groups were comprised of patients with no history of hypertension.

Results: The two groups were similar as regards age, height, weight, and body mass index. A significant difference (p<0.05) was found between blood pressure levels during the wakefulness, sleep, 24-hour and sleep dip periods. Higher blood pressure levels were observed in patients with COPD, except for diastolic levels during wakefulness and maximum values during sleep and in the 24 hours. Sleep dip in the COPD group was attenuated, whereas physiological dip was observed in the control group, with lower blood pressure levels.

Conclusions: Systolic and diastolic blood pressure levels in the COPD group were higher than those of the control group, with a significant difference found for all periods studied, except for diastolic levels during wakefulness and in the 24 hours. We can conclude that the group of COPD patients with sleep desaturation has significantly higher blood pressure levels than the control group. (Arq Bras Cardiol 2009; 93(3):255-261)

Key Words: Blood Pressure Monitoring, Ambulatory; Sleep; Pulmonary Disease, Chronic Obstructive; Polysomnography.

Introduction

Chronic obstructive pulmonary disease (COPD) is currently the fourth leading cause of death, and its main complication is related to cardiovascular events1-3. The literature shows that in a five-year period 48% of all hospitalizations of patients with COPD were due to cardiovascular complications and that, independent of gender, age, and smoking, COPD increases the cardiovascular risk twofold1-2. The factors that correlate COPD with cardiovascular events are not fully understood. Studies demonstrate that chronic systemic inflammation and disorders of the neurohumoral regulation may be involved3-7, and suggest that patients with COPD develop sympathetic hyperactivity, decreased vagal tonus and dysautonomia.

The prevalence of hypertension is high among the world population8-10, and increases with the age range11; between 60 and 69 years of age, more than 50% of the individuals are affected by hypertension. Above 70 years of age, in turn, the prevalence of hypertension reaches 75%. Mortality for cardiovascular diseases increases with blood pressure (BP) elevation9-10.

In addition to showing scarce and conflicting data on blood pressure in patients with COPD, the literature also points out the need for further studies to explain the behavior of blood pressure during sleep desaturation and, most importantly, its effects on target organs. Ambulatory blood pressure monitoring (ABPM) is the diagnostic tool that provides this analysis, thus permitting the knowledge of the pattern of blood pressure variations during wakefulness and sleep11,12.

The objective of this study was to evaluate the behavior of blood pressure in the 24 hours, in COPD patients with sleep desaturation not caused by apnea, using ABPM parameters.

Methodology

This is a descriptive, cross-sectional study of patients with COPD referred to the pulmonary rehabilitation program of the Pneumology outpatient clinic of Hospital Universitário de Brasília (HUB).

Inclusion criteria

A total of 13 patients clinically and functionally (spirometry: FEV1/FVC lower than 0.70 post bronchodilator) diagnosed
with COPD and enrolled in the previously mentioned program were included. The control group was comprised of 14 volunteers without COPD (clinical and spirometric diagnosis). The patients of both groups had a negative history of hypertension, did not use any antihypertensive medication and did not present white-coat hypertension. Those who agreed to participate in the study gave their written informed consent.

Exclusion criteria

After thorough history taking, physical examination and 12-lead echocardiogram, the presence of the following conditions was used as the exclusion criterion: other clinically detectable pulmonary disorder; obstructive sleep apnea syndrome (as detected by polysomnography); other system or organ failure (renal failure, heart failure and hepatic failure); systemic hypertension; technically unfeasible 24-h ABPM; and conditions affecting the autonomic nervous function (neuropathies, psychiatric disorders, diabetes mellitus, autoimmune diseases, Parkinson’s disease).

Criteria from the IV ABPM Guidelines were used for the definition of hypertension. The following ABPM parameters are considered normal: 24-hour BP < 130/80 mmHg; daytime BP < 135/85 mmHg; and night-time BP < 120/70 mmHg.

Patients with COPD who participated in the study underwent thorough clinical assessment. Next, spirometry, blood gas, polysomnography (PSG) and 24-hour ABPM were performed. Control group patients also underwent thorough clinical assessment, followed by spirometry, pulse oximetry during sleep and 24-hour ABPM.

Clinical assessment

The COPD group comprised 13 patients, of whom eight (61%) were males. All had been smokers and were receiving inhaled beta 2-adrenergic receptor agonists, selective for these receptors, with direct delivery at the site of action in the airways; these features provide a reduction of extrapulmonary side effects, particularly of cardiac effects, and thus blood pressure readings were less likely to be influenced. In the control group, 14 patients, six (42%) were males with no history of smoking.

Body mass index (BMI) was calculated by dividing weight (kg) by the square height (m). Values were classified as: < 18.5 kg/m² (underweight); 18.5 to 24.9 kg/m² (normal weight); 25 to 29.9 kg/m² (overweight) and ≥ 30 kg/m² (overall obesity).

In order to compare the COPD and control groups, the mean anthropometric measurements were tested to control the factors that could interfere with blood pressure and oximetry parameters.

Spirometry – Both groups underwent spirometry with the patients in the sitting position and using an adaptor to prevent breathing through the nares. Ventilation was fully oral, with the circuit closed and the anatomical adaptor connected to the oral cavity; the circuit was coupled to the device, according to the guidelines of the American Thoracic Society. The Vmax®-22 device (spirometer series, SensorMedics, Yorba Linda, California, USA, 2004) was used for the procedure.

Blood gas – Blood was drawn from the radial artery only in the COPD group, for comparison with sleep desaturation levels. The Ciba Corning 278 Gas System® blood gas analyzer (Ciba Corning, Diagnostics Corp, Medfield, USA, 2004) was used.

Polysomnography – Polysomnography (PSG) was performed over only one night’s sleep, exclusively in the COPD group, during the whole night, at the Sleep Laboratory of Hospital Universitário de Brasília. PSG was performed in this group to rule out other sleep disorders, among which is the obstructive sleep apnea syndrome (OSAS), a condition that is distinct from COPD, but also causes nocturnal hypoxemia. Polysomnography was performed according to criteria established by Rechtschaffen and Kales and revised by Carskadon et al. The Alice 3® device (Infant and Adult Computerized Polysomnographic System, Georgia, USA) was used.

Oximetry analysis in the real sleep time of the control group – The Nonin 3100 WristOx device was used. The parameters analyzed on nocturnal oximetry were: episodes of desaturation (considering a SpO₂ fall of at least 4% for at least 10 seconds) and episodes of pulse rate change (at least 4 bpm for at least 10 seconds). Oximetry analysis was chosen as the assessment method in the control group, based on data from the literature showing that it is possible to compare these two groups even if they had not undergone the same assessment procedures. This statement is supported by the fact that oximetry is proven to be an efficient technique for this purpose, and several studies have demonstrated its effectiveness for the diagnosis of other sleep disorders, including OSAS. This was important in our study in relation to cost reduction. It is important to underscore that the oximetric control in polysomnography (COPD group) was made with the same oximeter used in the control group. The apnea-hypopnea indexes (AHI) in COPD patients were not > 5, therefore they did not present OSAS. On the other hand, no individuals in the control group had complaints suggestive of OSAS (snoring, respiratory arrests witnessed during sleep, and daily sleepiness). Polysomnography was considered unnecessary for the control group and was replaced by overnight oximetry to rule out the remote possibility of sleep hypoxemia.

24-h ABPM – 24-h ABPM was used to evaluate blood pressure variables in the two groups studied using the oscillometric method, with a portable Dyna-MAPA ABP-Monitor (Cardio Sistemas Comercial e Industrial Ltda., Sao Paulo, Brazil) validated both by the American Association for the Advancement of Medical Instrumentation (AAMI) and by the British Hypertension Society (BHS). The sleep period was considered the real period and not the fixed time. Variables were described as minimum, maximum and mean values, and standard-deviation.

Ethical Aspects – This study was approved by the Adjunct Learning and Research Board of Hospital Universitário de Brasília (HUB).

Statistical analysis – The Shapiro-Wilk test was used to analyze the data collected in order to test normality of quantitative variables, aiming to compare the mean values of variables in the COPD and control groups. The Student’s
Results

The main results of this study were:

The mean age was 70 ± 11 years and 70 ± 8 years for the COPD and control groups, respectively, with no difference between the groups in relation to the age range.

The mean BMI was 24 ± 4 kg/m² and 24 ± 2 kg/m² for the COPD and control groups, respectively, and both were within normal limits\(^{13}\).

No difference was found between the two groups as regards the anthropometric measurements, as shown in Table 1.

On spirometry, the mean FEV\(_1\)/FVC% ratio was 44 ± 5% and 74 ± 2% in the COPD and in the control group, respectively. Considering the GOLD classification\(^{22}\), based on spirometric criteria, in the COPD group the disease was characterized as severe (stage III) whereas the control group showed normal parameters.

Blood gas showed mean PaO\(_2\) of 60.6 ± 6.1 mmHg and mean PaCO\(_2\) of 36.7 ± 6.9 mmHg in the COPD group. These values are consistent with stage III COPD, according to the literature\(^{22}\).

Polysomnography of the COPD group showed a total sleep time of 326.7 ± 70 minutes, which is lower than desired, but consistent with values found in the review of the literature\(^{26}\). The mean sleep efficacy was 74.8%, slightly lower than the value considered as ideal for individuals in this age range, which is of approximately 80%. The mean sleep latency was 29.7 ± 30 minutes, slightly above the expected. The mean REM sleep latency (LatREM) was 151 ± 84 minutes, above the expected time of 150 minutes. No patient experienced REM sleep deprivation. The absence of apnea-hypopnea index was ≥ 5.

Blood pressure and oximetry parameters are shown in Table 2 and are described below.

In relation to sleep dip, significant differences were observed both for systolic and diastolic blood pressure parameters during wakefulness, with attenuated dip in the COPD group and physiological dip in the control group, as shown in Graph 1.

As regards systolic blood pressure parameters during wakefulness (mmHg), the mean, minimum and maximum values were statistically higher in the COPD group than in the control group, with p values of 0.009, 0.018 and 0.032, respectively. In turn, no significant difference was found between the groups in relation to diastolic blood pressure parameters during wakefulness.

Blood pressure measurements during sleep (mmHg) were statistically higher among individuals of the COPD group than among those of the control group, except for the maximum diastolic blood pressure level, for which no significant difference was found between the groups.

As regards the mean 24-hour blood pressure parameter, statistically higher values were found in the COPD group for systolic blood pressure (p=0.002). No significant difference was found between the groups for the diastolic measurements. The mean systolic and diastolic blood pressure readings taken in the morning were statistically higher in the COPD group.

Minimum saturation values achieved during sleep (minimum % SpO\(_2\)) were not significantly different between the two groups, as shown in Graph 2. The parameter for which a significant difference was found was desaturation time in the COPD group (T90 > 30%), whereas this value was close to zero in the control group, as shown in Graph 3.

Discussion

COPD is a complex disorder characterized by airflow obstruction, which is partially reversible with the use of bronchodilator drugs\(^{3,5-7}\), and is accompanied by cardiovascular comorbidities\(^{1,2}\).

In the present study, blood pressure and oximetry variables were analyzed in patients with COPD. The results were compared with those of the control group, which had similar anthropometric characteristics.

### Table 1 – Anthropometric measurements in the COPD and control groups

<table>
<thead>
<tr>
<th>Parameter measured</th>
<th>COPD</th>
<th>Control</th>
<th>Difference between means</th>
<th>p value</th>
<th>Sig.(^{(3)})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>70.00(11.90)</td>
<td>70.14(8.89)</td>
<td>-0.14</td>
<td>0.972</td>
<td>(\text{(1)})</td>
</tr>
<tr>
<td>Weight</td>
<td>67.43(13.73)</td>
<td>68.0(16.41)</td>
<td>-0.57</td>
<td>0.756</td>
<td>(\text{(2)})</td>
</tr>
<tr>
<td>Height</td>
<td>1.640(0.07)</td>
<td>1.67(0.14)</td>
<td>-0.03</td>
<td>0.562</td>
<td>(\text{(3)})</td>
</tr>
<tr>
<td>BMI</td>
<td>24.41(04.61)</td>
<td>24.64(2.94)</td>
<td>-0.22</td>
<td>0.881</td>
<td>(\text{(3)})</td>
</tr>
</tbody>
</table>

\(^{(1)}\) Student’s t test

\(^{(2)}\) Mann-Whitney test

\(^{(3)}\) Statistical significance (p<0.05)
All individuals in the COPD group were hypoxemic during sleep (mean T90 of 42 ±36) and their sleep quality was affected, with sleep efficiency slightly lower than optimum in comparison to healthy individuals of the same age range (80%), and sleep latency and LatREM above the expected. No patient presented with sleep apnea.

*BP dip during sleep* – Patients with COPD showed attenuated mean sleep dip (systolic and diastolic), whereas those without COPD showed physiological mean sleep dip (systolic and diastolic)23. Tanigawa et al24 studies correlated the severity of respiratory disorders with increased diastolic blood pressure levels during sleep, thus hindering the physiological dip in this period. Our data are consistent with those of the literature24 with regard to the mean reduction of oxygen saturation during sleep and sleep dip. This may occur because the sympathetic activity is triggered by nocturnal hypoxia, thus releasing catecholamines in blood circulation, and consequently elevating blood pressure25.

The role of the autonomous nervous system on sleep dip remains controversial, but there are evidences of sympathetic participation on blood pressure regulation in patients with OSAS25, in whom hypoxia and hypercapnia, acting via the
chemoreceptors, elicit increases in sympathetic activity. The sympathetic vasoconstrictor response to apneic events leads to increases in blood pressure during sleep, especially at the end of apnea. Oliveira et al. reported that the absence of blood pressure dip during sleep has been attributed to an autonomic nervous dysfunction and is related to increased cardiovascular risk and target-organ damage, particularly in the left ventricular mass, silent cerebrovascular disease and microalbuminuria.

During wakefulness – Higher mean, minimum and maximum systolic blood pressure levels were observed in the COPD group. In agreement with the literature, the Syst-Eur substudy demonstrated that isolated systolic hypertension in older patients is associated with attenuated sleep dip, with an inverse association between blood pressure dip and cardiovascular risk. No significant differences in diastolic blood pressure levels (mean, minimum and maximum values) were observed between the groups during wakefulness.

During sleep – Mean, minimum and maximum systolic blood pressure (SBP) levels, as well as mean and minimum diastolic blood pressure (DBP) levels during sleep were higher in the COPD group. No difference was found in maximum DBP levels between the COPD and control groups. During sleep, although blood pressure mediators are not fully understood, blood pressure and heart rate correlate with the sympathetic nervous system activity.

24-hour means – Mean 24-hour SBP values were higher in the COPD group, but with no significant difference in relation to mean DBP in this period. According to data from the literature, mean 24-hour blood pressure levels are the gold-standard parameter among those obtained by ABPM, because they are more accurately correlated with target-organ damage, morbidity and mortality.

Morning period – Mean SBP and DBP values were statistically higher in the COPD group in comparison to the control group. Corroborating these findings, studies have demonstrated that attenuated or absent sleep dip predisposes to sustained high blood pressure in the first few hours of the morning. Eguchi et al, Kario et al. showed that increased blood pressure levels in the first two hours after waking up were significantly correlated with a higher prevalence of cerebral infarcts. Morning blood pressure elevation is correlated with increased risk of target-organ damage and cardiovascular events, as well as with increased risk of coronary ischemia and stroke. In corroboration
with our findings, Kishimoto et al\textsuperscript{13} demonstrated that the reduction in sleep oxygen saturation was significantly correlated with morning blood pressure elevation. Elliot\textsuperscript{13} and Cohen et al\textsuperscript{14} correlated morning hypertension with higher cardiovascular mortality.

Oxygen saturation (minimum % SpO\textsubscript{2} and T90(\%)) - The COPD group showed more prolonged desaturation during sleep. In the control group, the assessment was made using digital oximetry, whose diagnostic accuracy has been proven in several studies of the literature\textsuperscript{17-19}. Oximetry in the control group showed episodes of minimal desaturation with no statistical difference in relation to the COPD group; however, the duration of desaturation was negligible (close to zero / punctual events), whereas it lasted longer in the COPD group. Consistent with the literature, Tanigawa et al\textsuperscript{14} studies correlated oxygen desaturation index on pulse oximetry with blood pressure levels. Oxygen desaturation index (3\%) was associated with SBP elevation by 0.8 mmHg (p=0.05) and increased DBP by 0.7 mmHg (p=0.05).

\textit{Study limitations} – The small sample size was a limitation of the present study, and resulted from the severity of the disease in COPD group patients with nocturnal desaturation; the majority of these individuals was elderly, with physical difficulties to undergo ancillary tests. In public and private hospitals there are few beds available for the study of sleep, and this justifies the use of oximetry as an assessment method in patients without COPD and with no complaints suggestive of sleep disorders, based on the studies previously mentioned\textsuperscript{17-19}, which demonstrated that these methods are comparable. Oximetry is the easiest test to perform given its lower cost in relation to polysomnography. Polysomnography is costly and difficult to perform, and this limits its indication in patients without sleep complaints.

Polysomnography was used in the present study to differentiate sleep variables and, particularly, to identify individuals with or without obstructive sleep apnea syndrome. The test was performed over a single night’s sleep.

Despite its limitation, we think that our study is valid for the correlation between severe chronic pulmonary disease and old age, blood pressure and oximetry levels.

Conclusions

Our study suggests that sleep dip is attenuated or absent in COPD patients with sleep desaturation. Systolic and diastolic blood pressure levels were higher in the COPD group than in the control group. A significant difference was observed in all periods studied, except for diastolic blood pressure during wakefulness, in the 24-hour period, and maximum values during sleep. Therefore we can conclude that the COPD group had higher blood pressure levels than the control group, and this can be the result of increased sympathetic activity elicited by sleep desaturation.

Potential Conflict of Interest

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

Sources of Funding

There were no external funding sources for this study.

Study Association

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