Slow Breathing Test Increases the Suspicion of White-Coat Hypertension in the Office

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Summary

Background: **It would be useful to have a clinical test that increases the suspicion of white coat hypertension (WCH) during the medical consultation.**

Objective: **To evaluate the Slow Breathing Test (SBT) when differentiating hypertension from WCH.**

Methods: **101 hypertensive patients selected at triage had their medication withdrawn for 2-3 weeks. The blood pressure (BP) was measured before and after the SBT at two consultations at the office. The test consisted in breathing for 1 minute at the frequency of one respiratory cycle every 10 seconds. Two diagnostic criteria were compared: 1 – decrease in diastolic BP ≥10% in at least one visit or 2- decrease in BP to normal levels (<140/90 mm Hg) in at least one visit. The ambulatory blood pressure monitoring (ABPM) was performed while blinded to the clinical measurements.**

Results: **71 women and 30 men, with a mean age of 51±10 years, with mean pre and post-test BP of 152±17/ 99±11 and 140±18/ 91±11 mm Hg were assessed. Nine patients had normal clinical and ambulatory measurements. Of the 92 patients, 28 (30%) were classified as having WCH; 15 had a positive test for Criterion 1 and 21 for the Criterion 2. Among 64 (70%) hypertensive individuals, 14 tested positive for Criterion 1 and 12 for Criterion 2. Sensitivity and specificity (95% CI): 0.54 (0.36-0.71) and 0.78 (0.67-0.87) for Criterion 1; 0.75 (0.57-0.87) and 0.81 (0.70-0.89) for Criterion 2.**

Conclusions: **The SBT showed an increase in the clinical suspicion of WCH in two visits when using the BP normalization criterion. This finding suggests that the test can help in the optimization of ABPM requests for suspected cases. (Arq Bras Cardiol 2008;91(4):243-249)**

Key words: **Hypertension / diagnosis; respiratory function tests; blood pressure monitoring, ambulatory.**

Introduction

White coat hypertension (WCH), the most commonly used designation of isolated office hypertension, is defined as the presence of persistently elevated blood pressure (BP) in the medical environment and normal readings outside of it[1]. It affects 15 to 30% of the presumable hypertensive individuals[2]. This condition can lead to an unnecessary drug treatment, with consequences for patients and health systems[3]. On the other hand, WCH must be considered a pre-hypertensive state[4,5] and not an innocent state[6,7], which needs a more intense follow-up. Diagnosis of WCH requires preferentially, the use of ambulatory blood pressure monitoring (ABPM)[8]. However, since the lack of clinical features is characteristic of WCH, this factor restricts the requisition of ABPM as a diagnostic tool[9].

Slow breathing, at a frequency of 0.1 Hz (6 respiratory cycles per minute, 1 cycle every 10 seconds), showed to be effective in increasing blood oxygenation, exercise tolerance and baroreflex sensitivity[10,11] and decreasing BP in hypertensive individuals[11]. It is presumed that this frequency promotes the synchronization between breathing and innate cardiovascular rhythms (Mayer waves, a 10-second rhythm in humans), with a consequent modulation of the central and peripheral (baroreflex)[12] autonomic activities. At a frequency of 5 cycles per minute, slow breathing produced a small difference in the decrease of diastolic BP between hypertensive individuals and those with WCH, when applied on a single visit[13].

The aim of the present study was to improve the use of the Slow Breathing Test (SBT), which could increase the suspicion of WCH at the office and consequently, optimize the requests for ABPM for the suspected cases.

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Manuscript received December 08, 2007; revised received February 04, 2008; accepted on February 26, 2008..

Methods

Study design and patients

In this cross-sectional accuracy study, 101 patients referred to the Service of Hypertensive Cardiology of the Federal University of Sao Paulo (Unifesp), between March 2003 and March 2005, were assessed through an initial triage. The assessment consisted of a structured questionnaire and interpretation of laboratory and electrocardiogram results, which are part of the routine assessment of the Service.

The questionnaire included: when was hypertension diagnosed, anti-hypertensive medication used (name and dose), other medications being used, smoking and drinking habits, other diseases, hospital admissions (including hypertensive emergency/urgency treatment). At triage, inclusion criteria were: adult patients (age ≥ 18 years) with systolic BP (SBP) ≥140 and <180 mmHg or diastolic BP (DBP) ≥90 and <110 mmHg or those using anti-hypertensive medication and BP <180/110 mmHg. Exclusion criteria were: patients with a history of treatment for hypertensive crises of any origin, secondary hypertension, diabetes mellitus, atrial fibrillation, unstable angina or angina of recent onset, valvulopathies with functional class > 1, moderate to severe chronic obstructive pulmonary disease, serum creatinine ≥1.5 mg/dl, Body Mass Index ≥35, presence of Sokolow-Lyon index (SV 1, + R V 5/V 6 ≥35 mm) at the ECG and alcoholism. All patients gave their free and informed consent to participate in the study and the study protocol was approved by the Ethics Committee in Research of Unifesp.

Slow breathing test and BP measurements

The selected patients were assessed 2 to 3 weeks after the withdrawal of anti-hypertensive medication[14]. The auscultatory measurement of BP (Korotkoff sounds I and V) was obtained through a mercury sphygmomanometer (Wan Med, São Paulo, Brazil) with a 2 mm graduation and cuffs that were adequate to the circumference of the arm. With the patients in the sitting position, the BP was measured in both arms and the arm with the highest BP was chosen. After two minutes, a new measurement in the same arm was performed. In case of differences in DBP > 5 mmHg, the procedure was repeated until a measurement with a lower difference was obtained. With the cuff positioned on the chosen arm, the patient was submitted to the slow breathing test (SBT), which consisted in inducing slow breathing for a minute at the frequency of 0.1 Hz (one respiratory cycle every 10 seconds). The patient was instructed by the doctor to simulate the respiratory pattern based on an analog clock placed on the table. Immediately after that, a single BP measurement was carried out in the previously chosen arm. The pulse frequency was estimated by a 30-second counting, by the radial pulse, immediately after the pre- and post-test measurements.

Subsequently, a monitor was installed to perform the 24-hour ABPM (Dyna-MAPA, Cardios Sistemas, São Paulo, Brazil; equivalent to Mobil-O-Graph, I.E.M., Stolberg, Germany) with an appropriate cuff placed on the non-dominant arm and programmed to measure BP every 15 minutes (while awake) and 30 minutes (during sleep). The sleeping and awake times were established individually and checked with the diary entries. On the following day, after the monitor removal, the same previously described procedures were performed to measure BP before and after the SBT at a new visit. The interpretation of the ABPM results was carried out while blinded to the clinical measurements and according to the Brazilian guidelines[15]. Patients with at least 50 readings while awake were included in the analysis.

Reproducibility

Interobserver reproducibility was verified based on the measurements obtained separately by a second physician who tested 20 patients twice, immediately after the consultations carried out by the first observer. Each doctor performed the assessment in isolation and no observer was allowed during the procedure to prevent the patient's BP elevation[16]. All the clinical measurements were obtained in the morning between 11 AM and 12 PM.

Diagnostic criteria

We considered as WCH the existence of office measurements ≥140 mmHg (SBP) or ≥90 mm Hg (DBP) at the two visits (also at the triage if the patient was not taking medication) and ABPM mean while awake <135 mm Hg (SBP) and <85 mm Hg (DBP).

Two criteria were compared as a positive response to the SBT for the diagnosis of WCH. **Criterion 1**: decrease in DBP ≥10% in at least one of the visits. **Criterion 2**: decrease in BP to normal levels, i.e., SBP <140 and DBP <90mmHg in at least one of the two visits.

Statistical analysis

Considering a mean prevalence of 20% of WCH, alpha error of 5% and statistical power of the sample of 90%, we estimated as necessary to have 92 individuals with a presumable diagnosis of sustained hypertension. The results were expressed as means and standard deviations (SD). The paired Student's *t* test and the Chi-square test were used to analyze the results. The performance of the SBT was evaluated by the determination of sensitivity, specificity, predictive values and likelihood ratio, with the respective 95% confidence intervals. To evaluate the interobserver reproducibility of the SBT, Kappa test was used. The statistical analyses were carried out with the programs Microsoft Excel and Confidence Interval Analysis, version 2.

Figure 1 summarizes the present study method:

Results

Some characteristics of the sample

The sample consisted of 71 women and 30 men, with a mean age of 51±10 years. Of the 101 patients, 57 were Caucasians, 40 were Black and 4 were Asians. Ten patients were aged ≥ 65 years (7 women). Ninety-four patients used anti-hypertensive medication. Of these, 17 used monotherapy, 74 used 2 medications and 3 patients

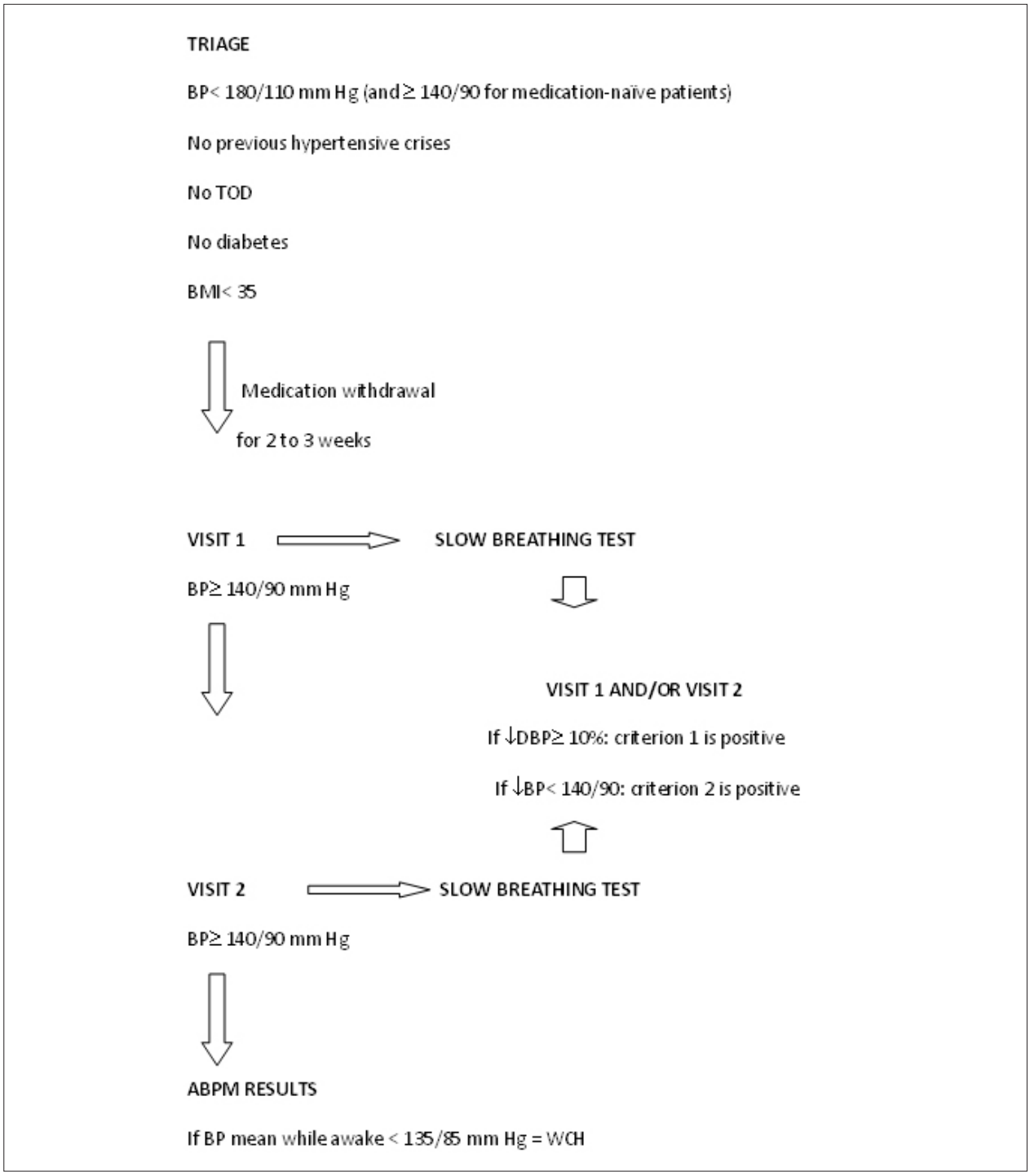


Figure 1 - Diagnostic Algorithm of the Study; BP - blood pressure; TOD – target-organ damage; BMI - body mass index; ↓DBP - decrease in diastolic blood pressure; ↓BP - decrease in blood pressure; ABPM - ambulatory blood pressure monitoring; WCH - white coat hypertension.

used 3 medications (the latter used suboptimal doses). The drugs used belonged to the following categories: thiazide diuretics, betablockers, dihydropiridinic calcium channel blockers and angiotensin-converting enzyme inhibitors (ACEI).

Classification after the ABPM

The pre- and post-test BP means were 152±17 / 99±11 and 140±18 / 91±11 mm Hg, respectively.

Nine patients presented normal clinical and ambulatory measurements after medication withdrawal. Of the remaining

92, 28 (30%) were classified as having WCH (35% of the women and 20% of the men) and 64 (70%) as hypertensive (HT).

Table 1 shows the BP means (±SD) at the first and second visits before and after the SBT was applied and the ABPM means (±SD) while awake in relation to the WCH and HT groups. As expected, the pre-test means in the WCH group were lower than those in the HT group.

A spontaneous pre-test decrease in BP was observed between visits 1 and 2 in both groups. A significant decrease in systolic and diastolic BP after the test in both groups was also observed.

The highest decrease was observed at visit 2 in the WCH group; the lowest decrease was observed at visit 1 in the HT group. There was no significant difference between the pre- and post-test means of pulse frequency for both groups.

For the WCH group and according to criterion 1, 8 patients were identified at visit 1 and 7 at visit 2; 4 patients responded positively to the SBT at the two visits. Regarding criterion 2, 12 patients were identified at visit 1 and 9 at visit 2; 9 patients responded positively to the SBT at both visits.

Positive responses to both criteria were observed in 12 patients and 5 were not identified by either of the criteria.

Tables 3 and 4 show the responses to the SBT (positive or negative) by criteria 1 and 2, according to the stages of hypertension defined by the V Brazilian Guidelines[17] and by the measurements registered at visit 2. In the WCH group, 25 individuals had clinical measurements compatible with stage 1 arterial hypertension; the other 3, with stage 2. In the HT group, 35 individuals had clinical measurements compatible with stage 1 arterial hypertension, 24 with stage 2 and 5 with stage 3.

For the patients with BP compatible with stage 1, there was a significant difference between HT and WCH in response to the test for the criterion 2 ($p<0.003$), but not for criterion 1 ($p<0.26$).

Table 1 – Blood pressure responses (systolic/diastolic ± SD), respective percentage variations and significance at the clinical visits before and after the SBT and means of ABPM while awake (±SD)

	HT (n=64)	WCH (n=28)
BP1 pre	158 ± 18 / 101 ± 10	150 ± 13 / 92 ± 8
BP1 post	149 ± 17 / 97 ± 10	140 ± 12 / 87 ± 8
Δ%(p)	-6 * / -4 **	-7 * / -6 **
BP2 pre	154 ± 16 / 99 ± 10	146 ± 11 / 89 ± 9
BP2 post	142 ± 15 / 95 ± 10	132 ± 12 / 84 ± 9
Δ%(p)	-8 * / -4 **	-11 * / -6 **
ABPM (awake)	144± 10 / 91± 8	125± 6 / 77± 6

*SBT - slow breathing test, BP1, BP2 - BP means at the 1st and 2nd visits, pre- and post-SBT; Δ% (p) - percentage variation (p value); * = p<0.0001 ** = p<0.003*

Table 2 – Patient distribution according to criteria 1 and 2.

	WCH (n=28)	HT (n=64)
Criterion 1: ↓DBP≥10%	15	14
↓DBP<10%	13	50
Criterion 2: ↓ BP<140/90	21	12
↓BP≥140/90	7	52

WCH - white coat hypertension; HT - hypertension; ↓DBP≥10% - decrease in diastolic BP ≥10% after the SBT in at least one of the two visits; ↓ DBP<10% - decrease in diastolic BP <10% after the SBT in both visits; ↓ BP<140/90 - BP decrease to a value <140/90 mm Hg after SBT in at least one of the two visits; ↓BP≥140/90 - BP decrease to a value ≥140/90 mm Hg after SBT in both visits.

Slow breathing test performance

Table 5 summarizes the SBT performance for the two criteria. The sensitivity, specificity, predictive values, likelihood ratios and Kappa test for the analysis of interobserver reproducibility were calculated, with the respective confidence intervals (Wilson's method).

Graph 1 shows the improvement in the performance of the SBT in terms of sensitivity, specificity and predictive values when the same cut-off value used in the clinical diagnosis (140/90 mm Hg for criterion 2) was applied.

Discussion

The SBT showed sensitivity of 75% and specificity of 81% for the BP normalization criterion in the identification of WCH in two visits, when non-medicated hypertensive patients, with no target-organ damages and no important comorbidities were assessed. The positive likelihood ratio obtained by the test points to an up to four-fold increase in the chance of WCH. These results suggest that this is a simple, easy-to-apply test by the clinician at the office, which allows a considerable increase in the suspicion of this diagnosis.

We performed a concordance analysis between two observers and found a Kappa test of 0.42 for the BP normalization criterion, completely acceptable for a clinical maneuver in a situation that presents great variability.

The variations in BP represent a problem for the diagnosis and control of hypertension. The spontaneous pre-test decrease in BP between visits 1 and 2 (Table 1) confirms the necessity of having at least 2 visits after triage to attenuate the patient's alert reaction to a medical environment[18,19]. Through this procedure, we found 9 normotensive patients (9% of the initial sample) all of them previously taking antihypertensive drugs. On the other hand, WCH seems to be a conditioned response that does not disappear with time[20] and of which diagnosis depends on the level of the suspicion by the physician.

Table 3 – Response to SBT according to the stages of hypertension (clinical measurements after consultation 2) using criterion 1

	WCH+ (n=15)	WCH–(n=13)	HT+ (n=15)	HT– (n=49)	Total (n=92)
Stage 1	13	12	12	23	60
Stages 2 and 3	2	1	3	26	32

SBT - slow breathing test, WCH: white coat hypertension, HT - hypertensive; criterion 1: decrease in DBP ≥10% after SBT in at least one of the two visits, +: positive response to the test; -: negative response to the test; tage 1: BP entre 140 and 159 (systolic) and 90 and 99 mm Hg (diastolic); Stages 2 and 3: BP ≥160/100 mmHg

Table 4 – Response to SBT according to the stages of hypertension (clinical measurements after visit 2) using criterion 2

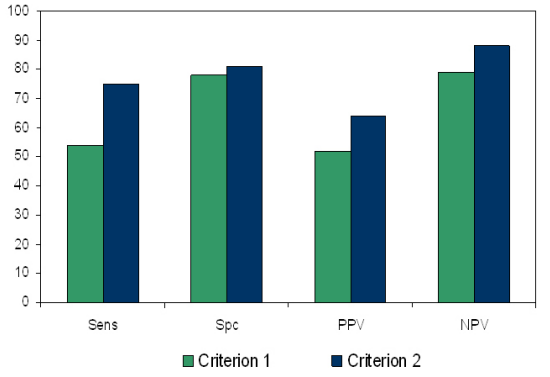
	WCH+ (n=21)	WCH– (n=7)	HT+ (n=12)	HT– (n=52)	Total (n=92)
Stage 1	19	6	12	23	60
Stages 2 and 3	2	1	0	29	32

SBT - slow breathing test, WCH - white coat hypertension, HT- hypertensive; criterion 2: decrease in DBP to < 140/90 mm Hg after SBT in at least one of the two visits; + - positive response to the test; -: negative response to the test; Stage 1: BP between 140 and 159 (systolic) and 90 and 99 mmHg (diastolic); Stages 2 and 3: BP ≥160/100 mmHg

Table 5 – Analysis of the SBT performance in WCH identification.

	Criterion 1	Criterion 2
Sensitivity	0.54 (0.36 to 0.71)	0.75 (0.57 to 0.87)
Specificity	0.78 (0.67 to 0.87)	0.81 (0.70 to 0.89)
PPV	0.52 (0.34 to 0.69)	0.64 (0.47 to 0.78)
NPV	0.79 (0.68 to 0.88)	0.88 (0.78 to 0.94)
PLR	2.5 (1.4 to 4.4)	4.0 (2.3 to 7.0)
NLR	0.6 (0.40 to 0.90)	0.3 (0.16 to 0.59)
Kappa Test	-0.12 (-0.67 to 0.42)	0.42 (0.02 to 0.86)

SBT - slow breathing test; WCH - white coat hypertension; criterion 1: decrease in DBP ≥10% after SBT in at least one of the two visits; criterion 2: decrease in BP to < 140/90 mm Hg after SBT in at least one of the two visits; PPV - positive predictive value; NVP - negative predictive value ;PLR - positive likelihood ratio; NLR: negative likelihood ratio.



Graph 1 - Comparison of the performance between criterion 1 and criterion 2; Sens - Sensitivity; Spc - specificity; PPV - positive predictive value; NPV - negative predictive value; Criterion 1: decrease in DBP ≥10% after SBT in at least one of the two visits; Criterion 2: decrease in BP to < 140/90 mm Hg after SBT in at least one of the two visits;

The present study suggests that the SBT is more effective as proposed here than as proposed by Yoshihara et al[13]. These authors reported better differentiation of the test effect between the groups when using the percentage decrease in diastolic BP on the first of three visits. In our study, the test was performed on two visits after triage, when the habituation effect that occurs along the repetition of the visits may enhance the effect of slow breathing. This is a probable cause of the more intense decrease in post-test systolic BP on the second visit in comparison to the first, for both WCH and HT groups (Table 1).

Additionally, the criterion of BP normalization is easily interpreted by the physician. These criteria were derived from the literature (criterion 1)[13] and from our own observation (criterion 2).

We also evaluated two other alternative criteria: decrease in diastolic BP ≥5% and decrease in systolic BP ≥10%. For these criteria, we obtained sensitivity of 68% and 54% and specificity of 36% and 55% for these cutoffs, respectively.

The prevalence of WCH is inversely proportional to the severity of hypertension in the office[21]. The responses to the SBT according to the stages of hypertension (Tables 4 and 5) indicated that the results using the criterion 2 (Table 5) respected the same determinants for the ABPM in the diagnosis of WCH: the lower the stage of clinical hypertension, the higher the chance of positivity for WCH when applying the SBT.

The larger number of women in our series reflects the frequency of users in this Service (7 women: 3 men). This fact is not surprising, as it is known in Brazil that women seek health services more often than men[22]. It is very important to attain the diagnosis of WCH in women, as they are more susceptible to this

condition[21]. WCH was found in 35% of the women and 20% of the men in our series.

The BP decrease after the test was more marked in the WCH group when compared to the HT group, in both consultations (Table 1). One can question whether these results could be influenced by any possible physiological difference in the mechanisms of rapid BP change between hypertensive individuals and those with WCH. Concerning that, a study[23] using direct ABPM (intra-arterial) in individuals with clinical hypertension detected higher baroreflex sensitivity in those with lower ambulatory means when compared to those that had higher means. No significant difference in the mean BP at the office was observed between the groups.

As previously observed, slow breathing increases baroreflex sensitivity and decreases BP in hypertensive individuals[11]. Would this stimulus be more effective in decreasing elevated BP levels in individuals with a higher sensitivity of this reflex? Further studies will be necessary to investigate possible physiological differences.

Limitations

We did not determine the reproducibility of the SBT in the same individuals throughout time. We took into consideration the recommendation made by the Ethics Committee, which considered the viability of maintaining previously treated hypertensive individuals (now after ABPM) without medication for longer. Medication withdrawal had an ansiogenic effect on some patients, which required support by telephone during the withdrawal period (we had two telephone consultations and one patient withdrew from the study during the period). Finally, it would be advantageous to increase the sample with newly-diagnosed and medication-naïve patients.

Conclusion

The present study showed that the SBT increased the clinical suspicion of WCH in two visits when using the BP normalization criterion. This suggests that this simple and easy-to-apply test can help in the optimization of requests for ABPM for the suspected cases.

Potential Conflict of Interest

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

Sources of Funding

This study was funded by Fundação de Auxílio à Pesquisa do Estado de São Paulo (FAPESP).

Study Association

This article is part of the Doctoral thesis submitted by José Marcos Thalenberg, from Universidade Federal de São Paulo.

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