ORIGINAL ARTICLE

Does masked hypertension exist in healthy volunteers and apparently well-controlled hypertensive patients?

I. Aksoy, J. Deinum, J.W.M. Lenders, Th. Thien[*#]

Department of Medicine, Division of General Internal Medicine, Radboud University Nijmegen Medical Centre, the Netherlands, [*]corresponding author: tel.: +31 (0)24-361 88 19, fax: +31 (0)24-354 17 34, e-mail: T.Thien@aig.umcn.nl

ABSTRACT

Background: Home blood pressure (HBP) measurement is considered to reflect BP during the day better than office BP (OBP). But in some patients HBP is higher than OBP. This is called masked hypertension (MH).
Objective: To examine whether MH occurs in healthy volunteers and apparently well-controlled hypertensives.
Methods: 57 treated hypertensive patients and 31 healthy volunteers (27/22 men) participated. Mean age (± SD) was 61 ± 13 and 29 ± 13 years, respectively. Patients were instructed to measure their BP twice daily for three days (3 readings each) with the Omron 705 CP device after at least 10 minutes rest in a comfortable sitting position. In the outpatient department, OBP was measured four times, in duplicate, every ten minutes by the physician using the same device and under similar conditions.
Results: Mean HBP of the treated hypertensive group was 146/84 ± 18/10 mmHg, significantly higher than OBP 136/79 ± 19/10 (p<0.001). For the healthy volunteer group mean HBP was 123/70 ± 15/8) mmHg and the OBP was 117/69 ± 16/10). Of 57 patients, 16 (28%) were classified as MH. The use of antihypertensive drugs was similar in the MH patients and the uncontrolled hypertensives. Logistic regression analysis showed that age tended to be a weak predictor for MH while gender, BMI and upper arm circumference were not.
Conclusion: This study demonstrates that MH occurs frequently in apparently well-controlled hypertensives, but not in healthy volunteers. However, in healthy volunteers HBP can be relevantly higher than OBP, although both values generally remain within the normotensive range.

KEYWORDS

Home blood pressure measurement, isolated ambulatory hypertension, masked hypertension, reversed white coat hypertension, white coat normotension

INTRODUCTION

It is well known that in many hypertensive patients blood pressure (BP) measured in the office by the physician (OBP) is not always representative for the average BP during the day and thus for cardiovascular risk.[1] This discrepancy has become apparent with the increased availability and use of devices for measurement of the BP at home (HBP) or ambulatory blood pressure monitoring (ABPM). Patients with a normal BP at home but an increased OBP are known as patients with isolated office hypertension, also called white coat hypertension.[2,3]
In 1992, Pickering described the reverse condition: patients who have a normal OBP but are hypertensive at home.[4] The prevalence of this phenomenon may be higher than expected. To date there is no consensus about the nomenclature for this condition. It has been called isolated home hypertension,[3] isolated ambulatory hypertension,[3] reversed white coat hypertension,[5,6] masked hypertension,[7,8] white coat normotension,[9,10] inverse white coat hypertension[11] and inverse white coat response.[12] Although Pickering originally used the term masked hypertension (MH) for untreated subjects, in most later publications[8] the term MH is also used for treated hypertensives. Therefore, in the current study we use the

[#]Th. Thien was not involved in the handling and review process of this paper.

term MH to indicate that a doctor will miss this condition unless HBP or ABPM is performed as well as OBP.

Most previous studies have focused on the prevalence of this condition in the general population or in untreated hypertensive patients. The present study was a pilot study to investigate if MH was, on the basis of OBP, present in healthy volunteers and in apparently well-controlled hypertensive patients.

PATIENTS AND METHODS

The patient group existed of hypertensive subjects who visited the outpatient clinic of our University Medical Centre for regular control. All hypertensive patients had been on antihypertensive drug treatment for at least one year. They were accustomed to the BP measurement procedure. The control group existed of healthy volunteers. Patients with comorbidity such as diabetes mellitus, heart failure, acute/severe diseases or autonomic failure were not included in the study. Patients with an upper-arm circumference (UAC) smaller than 22 cm or larger than 48 cm were also excluded. All patients gave written informed consent after being informed about the study. Body weight and height were measured to calculate body mass index (BMI).

Devices

HBP was measured by a validated automatic oscillometric blood pressure device, type Omron 705 CP, which is printer-equipped.[13] The inflatable bladder of the cuff had to have a width of at least 40% and a length of at least 80% of the circumference halfway between the olecranon and acromion processes. In patients with an UAC of 22 to 32 cm a normal bladder (24 x 13 cm) was used, whereas in patients with an UAC of 32 to 48 cm a larger bladder (36 x 13 cm) was used.

Study protocol

Patients were carefully instructed to measure BP twice daily (in the morning and in the evening) for three consecutive days and each measurement session consisted of three measurements. Thus in total, 18 HBP measurements were obtained. Each BP measurement was printed out and given to the doctor after the OBP measurement session. Patients were instructed to perform the BP measurements after sitting for ten minutes in a comfortable chair with arms resting on the armrest. The BP was always measured on the nondominant arm. The patients were asked to avoid talking, smoking and watching television. They were also instructed that BP measurements had to be taken after voiding and at least two hours after the meal.

After the last HBP measurements, thus always following the HBP procedure, the patients visited the doctors office and after ten minutes resting in a sitting position with their arm on the armrest, OBP was measured twice on the nondominant arm with the same device that they used at home. OBP measurements were repeated after 20, 30 and 40 minutes, resulting in a total of eight OBP measurements. These BP values were averaged and taken as the OBP for the individual patient.

In addition, auscultatory BP was simultaneously measured by a standard mercury sphygmomanometer using a Y-connector. This procedure was carried out to validate the Omron 705 CP according to the British Hypertension Society (BHS) criteria.[14] Systolic BP (SBP) was taken at phase 1 of the Korotkoff sounds and diastolic BP (DBP) at phase 5 of the Korotkoff sounds. The simultaneous BP measurement (n=528 readings) of the Omron 705 CP and the sphygmomanometer with a Y-connector resulted in grade B for SBP and grade A for DBP (British Hypertension Society protocol).[14]

Data analysis

All results are presented as mean ± SD unless stated otherwise.

Hypertension was defined as a BP of ≥140 and/or ≥90 mmHg and a normal BP as <140 and <90 mmHg. All healthy volunteers and treated hypertensive patients were categorised as follows.

- Category 1: normotensive both in the office and at home (true normotension, TN or controlled hypertension, CH).
- Category 2: hypertensive both in the office and at home (true hypertension, TH or uncontrolled hypertension, UCH).
- Category 3: hypertensive in the office and normotensive at home (isolated office hypertension, IOH, or white coat hypertension).
- Category 4: normotensive in the office and hypertensive at home. This last category was defined as masked hypertension (MH).

Differences between OBP and HBP were tested by the paired Student t-test. The association between BP category and the following factors was analysed by logistic regression analysis: gender, BMI, UAC, age, BP and heart rate.

RESULTS

The characteristics of the two groups are shown in *table 1*. Of the 57 hypertensive patients, 24 had an OBP ≥140 and/or ≥90 mmHg. HBP was stable over the three days of measurement and the evening values were constantly lower than the morning values as shown in *table 2*.

Of the 57 patients, 16 (28%) were classified as having MH as shown in *table 3a*. The OBP and HBP levels in the four groups are shown in *table 4* for the treated hypertensives.

Table 1. *Baseline characteristics of both groups*

	Treated hypertensives	Healthy volunteers
Male/female	27/30	22/9
Body mass index (kg/m²)	28 ± 4.5	24 ± 4.3
Upper arm circumference (cm)	29 ± 2.6	27 ± 3.1
Age (years)	61 ± 13.3	29 ± 13.2
Office blood pressure (mmHg)	136/79 ± 19/10	117/69 ± 16/10
Heart rate (beats/min)	63 ± 10	67 ± 11
Home blood pressure (mmHg)	146/84 ± 18/10	123/70 ± 15/8
Heart rate (beats/min)	65 ± 8	66 ± 10

Mean ± SD are presented.

Table 2. *The mean home systolic (SBP) and diastolic (DBP) blood pressure values in mmHg on the three measurement days*

	Day 1		Day 2		Day 3	
	SBP	DBP	SBP	DBP	SBP	DBP
Treated hypertensives (n=57)						
Morning	145	88	151	88	148	85
Evening	144	81	144	82	141	80
Healthy volunteers (n=31)						
Morning	122	71	120	70	121	71
Evening	124	70	124	70	125	70

Each value is the mean of all blood pressure values that were measured at that time point.

Table 3a. *Number of patients in each blood pressure (mmHg) category for the treated hypertensive group*

	OBP <140 and <90	OBP ≥140 and/or ≥90
HBP <140 and <90	n=17 (controlled hypertension)	n=4 (isolated office hypertension)
HBP ≥140 and/or ≥90	n=16 (masked hypertension)	n=20 (uncontrolled hypertension)

OBP = office blood pressure; HBP = home blood pressure.

Table 3b. *Number of patients in each blood pressure (mmHg) category for the normotensive group*

	OBP <140 and <90	OBP ≥140 and/or ≥90
HBP <140 and <90	n=28 (true normotension)	n=1 (isolated office hypertension)
HBP ≥140 and/or ≥90	n=0 (masked hypertension)	n=2 (true hypertension)

OBP = office blood pressure; HBP = home blood pressure.

In the MH group, systolic HBP was 23.6 ± 13.6 mmHg and diastolic HBP was 14.5 ± 9.1 mmHg higher than the corresponding OBP. In 11 of these 16 patients systolic HBP was even >20 mmHg higher than systolic OBP (*figure 1*), while this was the case in four patients for diastolic HBP (*figure 1*). Using the official BP thresholds for definition of hypertension diagnosis based on home BP measurement of the guidelines committee of the 2003 European Society of Hypertension-European Society of Cardiology (ESH/ESC):[15] OBP <140 and <90 mmHg together with an HBP ≥135 and/or ≥85 mmHg, as many as 21 (37%) of the patients were classified as MH. In contrast, 20 patients (35%) were uncontrolled hypertensives since they were still hypertensive both at home and in the doctors office. Obviously, the differences between HBP and OBP were smaller in this group, with systolic HBP being 4.9 ± 13.5 and diastolic HBP 2.1 ± 7.1 mmHg higher than the corresponding OBP. In only three of these 20 patients was the systolic HBP >20 mmHg higher than systolic OBP, and this was not seen at all in the diastolic HBP. In four patients both systolic and diastolic HBP were lower than the corresponding OBP and these subjects were classified as IOH. Seventeen of the 57 patients were normotensive both at home and in the office, thus called controlled hypertensives. Even in this subgroup mean HBP was higher than mean OBP (8.3 ± 9.0 and 2.8 ± 5.0 mmHg for systolic and diastolic BP, respectively).

The average number of antihypertensive drugs used in the treated hypertensive group was very similar for the four groups, as shown in *table 5*. The subgroups are small and despite this there were no relevant differences in the pharmacotherapeutic regimens between the MH and the UCH groups, but the CH group were on diuretics more often and ACE inhibitors less frequently than the UCH group.

Logistic regression analysis showed that in this study age tended to be a weak predictor (B=0.07; p=0.06) for MH in treated hypertensives while gender, BMI and UAC were not. The mean age in the MH subgroup was nearly 17 years higher than that in the CH subgroup.

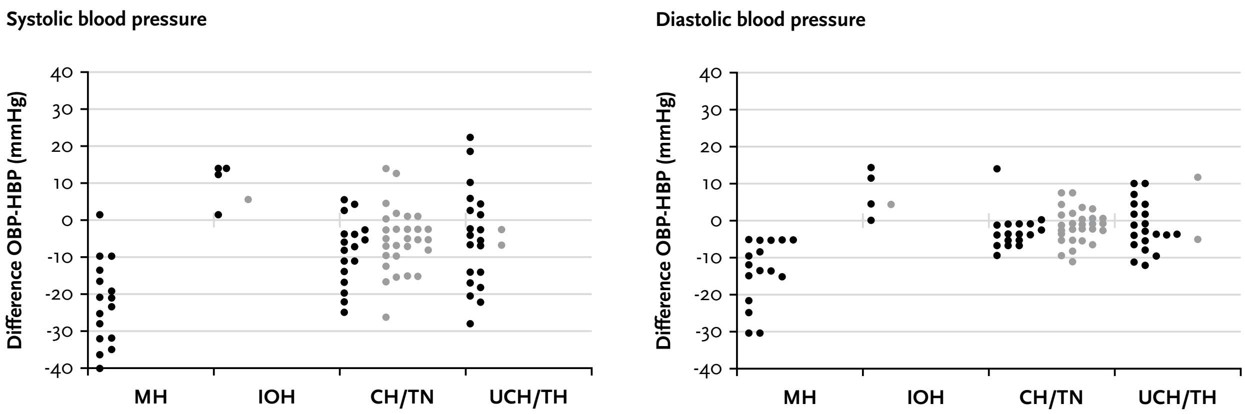
The healthy volunteers group was classified as follows: no MH (by study definition), one IOH, two TH, whereas the remaining 28 subjects were TN, as shown in *table 3b*.

Table 4. *Blood pressure (mmHg) and heart rate (beats/min) in the four groups of treated hypertensives (mean ± SD)*

	Systolic		Diastolic		Heart rate	
	OBP	HBP	OBP	HBP	OBP	HBP
Controlled hypertension	117 ± 11	126 ± 9	72 ± 7	75 ± 7	63 ± 7	65 ± 6
Uncontrolled hypertension	154 ± 15	159 ± 14	87 ± 9	89 ± 8	63 ± 11	65 ± 9
Isolated office hypertension	145 ± 4	134 ± 4	87 ± 10	79 ± 6	62 ± 4	63 ± 5
Masked hypertension	129 ± 9	153 ± 10	74 ± 7	89 ± 9	65 ± 13	65 ± 10

OBP = office blood pressure; HBP = home blood pressure.

Figure 1. *Individual data of the differences between office (OBP) and home (HBP) systolic (left panel) and diastolic (right panel) blood pressure of treated hypertensives (black dot) and healthy volunteers (grey dot)*



MH = masked hypertension; IOH = isolated office hypertension (white coat); CH = controlled hypertension; TN = true normotension; UCH = uncontrolled hypertension; TH = true hypertension.

Table 5. *Classes of antihypertensive drugs used by the patients of the four groups of treated hypertensives*

	Beta-receptor antagonists (%)	Calcium antagonists (%)	Diuretics (%)	ACE inhibitors and angiotensin-II receptor antagonists (%)	Average numbers of antihypertensive drugs
Controlled hypertension	59	41	71	29	2.0
Uncontrolled hypertension	65	30	55	55	2.1
Isolated office hypertension	75	25	75	50	2.3
Masked hypertension	63	31	56	69	2.2

ACE = angiotensin converting enzyme inhibitors.

Using the above-mentioned ESH criteria two subjects in the healthy volunteers group were classified as MH. None of the normotensive subjects were taking antihypertensive drugs. Within the healthy volunteers, there were striking differences between HBP and OBP although mostly within the normotensive range (*figure 1*).

DISCUSSION

The present study demonstrates that in this small group of apparently well-controlled outpatient clinic hypertensives a relevant percentage (28%) turned out to have hypertension at home and normotension in the office. Applying the official ESH/ESC definition[15] for the diagnosis hypertension based on home BP measurement, as many as 37% had MH.

It is difficult to compare our study with the literature because of inconsistencies in nomenclature and definitions. In addition, differences in methodology may account for disparity in results. BP was measured with the same device (tested according to the criteria of the BHS) both in the office and at home whereas in previous reports a conventional sphygmomanometer was used for the OBP measurement while in most studies another device was used for ABPM or HBP (self) measurement.[3,6,8,10,11,16]

Some but not all of the previous studies have reported that untreated patients with MH were older, more likely male, smokers, used alcohol and had higher BMI.[6,9-11,17] In our study the MH patients were older but there were no differences in BMI, BP levels and heart rate. There were no differences in the average number of antihypertensive drugs used either.

Since 1992, when Pickering *et al.*[4] described MH for the first time, several studies have reported the existence of this phenomenon,[3,5,7,9,10] and it has been suggested that the increased HBP values are due to an alerting response to the self-measurement procedure.[12] Several arguments can be raised against this suggestion. First, in the present study the same device was used both in the office and at home and the HBP levels on the three measurement days did not show any decrease as a consequence of habituation to the measurement procedure. Secondly, heart rate levels in all four groups were similar in the office and at home. Finally Parati *et al.* showed that there was no alarm reaction with the use of noninvasive BP monitoring devices.[18]

What are the possible explanations for the rather high percentage of MH? In the first place there may be a pharmacological explanation consisting of two factors: poor medication compliance at home and medication intake just before visiting the outpatient clinic so that the peak effect is observed. Although we always use long-acting medication to prevent compliance problems and we always carefully instruct and motivate our patients, we can not rule out this possibility. A second explanation is the possibility of differences in measurement conditions between office and home. Although the device was the same, BP was measured in the office four times, in duplicate, in the presence of the physician and the average was compared with the average of all home sessions on three consecutive days. However, if one looks at the four separate measurement sessions in the protocol, MH was present in 11 to 16 patients (19 to 28%), although not in the same patients in every session. As could be expected the frequency of MH was lowest in the first session, although still 19%. On the other hand the presence of the physician increases rather than decreases BP. A third explanation may be that nervous and/or older patients are less familiar with this type of technical procedure and measure a higher HBP due to a kind of stress.

In contrast to previous studies, this is one of the few reports that studied MH in treated hypertensives. In a recent retrospective study, Bobrie *et al.*[19] reported that in his study group of treated elderly hypertensives the prevalence of MH was 10.8%. In a prospective follow-up study[8] of 3.2 years they show that the MH group had the same risk for cardiovascular events as treated but insufficiently controlled hypertensives. A pivotal question pertains to whether MH carries a worse prognosis in terms of target organ damage than the patients whose BP is in the normotensive range both in the office and at home. It is generally accepted that HBP values measured by ABPM are superior to OBP values in predicting target organ damage.[5,11,20,21] If risk assessment is only based on OBP values in MH patients, the real risk is underestimated, as shown by the recent study of Bobrie *et al.*[8] In that study the cardiovascular mortality in the MH group was similar to that in the uncontrolled hypertensives and much higher than both in the isolated office or white coat hypertension group and in the controlled hypertension group. In earlier studies Liu *et al.*[10] and Sega *et al.*[3] showed that left ventricular mass index and wall thickness in patients with MH were close to that in the uncontrolled hypertension group and differed significantly from that in controlled hypertension group. Björklund *et al.*[16] showed in a longitudinal study that the multivariate hazard ratio for cardiovascular morbidity in the MH group was 2.74, while this was 3.14 in the uncontrolled hypertension group and 0.99 per 100 person-years at risk in the controlled hypertensives. So at this stage, it cannot be stated that MH is harmless. However, there are no studies about the reproducibility of MH, yet.

Of course our small study also has limitations. The protocol with the BP measurement procedure with four sessions of two readings, each time after a ten-minute rest period, is unusual in daily practice. The fixed sequence i.e. always the HBP first followed by the OBP may be considered a limitation. On the other hand, the whole protocol in all 88 subjects was performed by only one trained observer (I.A.), using the same automatic device for the OBP as used by the subjects for the HBP, thus without observer bias.

In conclusion, according to this pilot study, one should be aware that a substantial number of the apparently well-controlled hypertensives are still hypertensive at home. Therefore, without HBP measurements this condition may escape the physician's attention. However, data about reproducibility and about the prognostic significance of MH are still needed.

REFERENCES

1. Ayman D, Goldshine AD. Blood pressure determinations by patients with essential hypertension: the difference between clinic and home readings before treatment. Am J Med Sci 1940;200:465-74.
2. Bidlingmeyer I, Burnier M, Bidlingmeyer M, Waeber B, Brunner H. Isolated office hypertension: a prehypertensive state? J Hypertens 1996;14:327-32.
3. Sega R, Trocino G, Lanzarotti A, et al. Alterations of cardiac structure in patients with isolated office, ambulatory or home hypertension. Data from the general Pamela population. Circulation 2001;104:1385-92.
4. Pickering TG. The ninth Sir George Pickering memorial lecture: Ambulatory monitoring and the definition of hypertension. J Hypertens 1992;10:401-9.
5. Imai Y. Prognostic significance of ambulatory blood pressure. Blood Press Monit 1999;4:249-56.
6. Wing LMH, Brown MA, Beilin LJ, Ryan P, Reid CM. 'Reverse white coat hypertension' in older hypertensives. J Hypertens 2002;20:639-44.
7. Pickering G, Davidson K, Gerin W, Schwartz E. Masked Hypertension. Hypertension 2002;40:795-6.
8. Bobrie G, Chatellier G, Genes N, et al. Cardiovascular prognosis of 'Masked Hypertension' detected by blood pressure self-measurement in elderly treated hypertensive patients. JAMA 2004;291:1342-9.
9. Selenta C, Hogan BE, Linden W. How often do office blood pressure measurements fail to identify uncontrolled hypertension? An exploration of white coat normotension. Arch Fam Med 2000;9:533-40.
10. Liu J, Roman M, Pini R, Schwartz E, Pickering TG, Devereux RB. Cardiac and arterial target organ damage in adults with elevated ambulatory and normal office blood pressure. Ann Intern Med 1999;131:564-72.
11. Hernandez del Rey R, Armario P, Martin-Berberana M, Sanchez P. Cardiac damage in hypertensive patients with inverse white coat hypertension. Blood Press 2003;12:89-96.
12. Donner-Banzoff N, Chan Y, Szalai J, Hilditch J. 'Home hypertension': exploring the inverse white coat response. Br J Gen Pract 1998;48:1491-5.
13. O'Brien E, Mee F, Atkins N, Thomas M. Evaluation of three devices for self-measurement of blood pressure according to the revised British Hypertension Society Protocol: the Omron HEM-705CP, Philips HP5332 and Nissei DS-175. Blood Press Monit 1996;1:55-61.
14. O'Brien E, Petrie J, Littler W, de Swiet M, Padfield PL, Altman DG. The British Hypertension Society Protocol for the evaluation of blood pressure measuring devices. J Hypertens 1993;11(suppl 2):S43-62.
15. Guidelines Committee. 2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens 2003;21:1011-53.

16. Björklund K, Lind L, Zethelius B, Andrén B. Isolated ambulatory hypertension predicts cardiovascular morbidity in elderly men. Circulation 2003;107(9):1297-302.

17. Palatini P, et al. Masked hypertension: how can the condition be detected? Blood Press Monit 2004;9:297-9.

18. Parati G, Pomidossi G, Casadei R, Mancia G. Absence of alarm reactions with use of non-invasive blood pressure monitoring devices. Clin Exp Hypertens 1985;7:429-36.

19. Bobrie G, Genes N, Vaur L, Clerson P, Vaisse B, Mallion J. Is "isolated home" hypertension as opposed to "isolated office" hypertension a sign of greater cardiovascular risk? Arch Intern Med 2001;161:2205-11.

20. White WB. Ambulatory blood pressure as a predictor of target organ disease and outcome in the hypertensive patient. Blood Press Monit 1999;4:181-4.

21. Mansoor GA, White WB. Ambulatory blood pressure monitoring is a useful clinical tool in nephrology. Am J Kidney Dis 1997;30:591-605.