Antihypertensive treatment based on home or office blood pressure—the THOP trial

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Objective and methods **In this randomized clinical trial, conducted in 400 hypertensive patients [sitting diastolic blood pressure (DBP) >95 mmHg], blood pressure-lowering therapy was adjusted in a stepwise manner, either on the basis of the self-measured DBP at home or on the basis of conventional DBP measured at the doctor's office.**

Results **Therapy guided by home blood pressure instead of office blood pressure led to less intensive drug treatment and marginally lower costs, but also to less blood pressure control with no differences in left ventricular mass. Self-measurement helped to identify patients with white-coat hypertension.**

Conclusions **The present findings support a stepwise strategy for the evaluation of blood pressure, in which self-measurement and ambulatory monitoring are complementary to conventional office blood pressure measurement.** *Blood Press Monit* **9:311–314 © 2004 Lippincott Williams & Wilkins.**

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Introduction

Our previous research has shown that adjustment of antihypertensive treatment based on ambulatory blood pressure (BP) monitoring instead of conventional office BP measurement over a 6-month period led to less intensive drug treatment and inhibition of left ventricular hypertrophy with preservation of BP control and general well-being [1]. However, this approach did not reduce the overall costs of antihypertensive treatment.

Self-measurement of BP by the patient at home has several of the advantages of ambulatory monitoring, i.e., the greater number of readings, the absence of the white-coat syndrome, and when automated devices are used, the lack of observer bias. Furthermore, self-measurement is less expensive than ambulatory monitoring and may increase compliance to therapy.

The primary objective of the 'Treatment of Hypertension Based on Home or Office Blood Pressure' (THOP) Trial was to compare self-measurement and conventional office measurement of BP as guide to initiate and titrate antihypertensive drug treatment.

Methods

The protocol of the THOP trial was described in detail elsewhere [2,3]. After a 1-month run-in period, hypertensive patients [sitting diastolic blood pressure (DBP) >95 mmHg], were randomized to treatment based either on the self-measured diastolic home BP (HBP group) or on the diastolic office BP (OBP group). In both randomized groups, treatment was adjusted in a stepwise manner to reach the target range of DBP, i.e., 80–89 mmHg. All patients were started on monotherapy with lisinopril 10 mg per day (step I). At each follow-up visit, treatment could be increased stepwise to 20 mg lisinopril per day (step II); addition of 25 mg hydrochlorothiazide or 5 mg amlodipine per day (step III); and addition of 5 mg amlodipine in patients taking the combination of lisinopril and hydrochlorothiazide or 6 mg prazosin per day in the other patients (step IV). In patients with known contra-indications to converting-enzyme inhibitors, lisinopril could be substituted by atenolol (50 or 100 mg/day). Follow-up visits were planned at 1, 2, 4, 6, 8, 10 and 12 months. One physician at the co-ordinating centre, blinded with regard to randomization, made the treatment decisions based either on home BP or office BP. Medical treatment was stepwise intensified, left unchanged or stepwise reduced if the DBP was above target (>89 mmHg), within the target range (80–89 mmHg), or below target (<80 mmHg). Regardless of randomization, both the home and office BPs were measured at each visit. Home BP was the mean of 42 readings, i.e., three readings in the sitting position in the morning and three readings

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in the evening over seven consecutive days taken with an oscillometric Omron (Kyoto, Japan) HEM-705CP device [4]. Office BP was the average of three readings in the sitting position taken by the doctor at the office with a sphygmomanometer. At baseline and after 6 and 12 months, daytime (from 0010 h to 2000 h) ambulatory BP was calculated from recordings obtained with oscillometric SpaceLabs (Redmond, Washington, USA) 90207 recorders [4]. The ambulatory measurements were not considered in any treatment decision.

The main endpoints of the study were changes in blood pressure (home, office and daytime ambulatory BP) and intensity of antihypertensive drug treatment. The latter was evaluated by assigning a score proportional to the dose of each of the study medications with values set at 1 for the maximal daily dose (20 mg lisinopril, 100 mg atenolol, 25 mg hydrochlorothiazide, 5 mg amlodipine, or 6 mg prazosin) and at 0 in untreated patients. For each patient and at each visit the scores of all medications were summed. Electrocardiographic indexes of left ventricular mass (the *R*-wave in lead aVl, the Sokolow–Lyon index [5], and the Cornell product [6]) were measured at baseline, after 6 months and at the end of the trial. Cost–benefit analyses accounted for the doctors' fee, the costs for antihypertensive treatment based on the rates of the Belgian health insurance system and the costs for home BP measurement.

Database management and statistical analyses were performed with SAS software, version 8.1 (SAS Institute Inc, Cary, North Carolina, USA). Between-group comparisons involved Mann–Whitney's rank-sum test and Student's *t*-test. Proportions were compared by the χ^2-statistic and longitudinal changes in treatment by Kaplan–Meier survival function estimates.

Results

Of 606 selected patients, 400 (66.0%) met the entry criteria and were randomized either to the OBP group ($n = 197$) or the HBP group ($n = 203$). Baseline characteristics, median follow-up and withdrawal rates from the trial were similar in both randomization groups. Overall, the study group included 209 (52.2%) women, 182 (45.5%) previously treated patients, 307 (76.7%) patients enrolled at family practices and 87 (21.7%) smokers. Patients had a mean (SD) age of 54.3 (12.0) years and a body-mass index of 28.1 (4.6) kg/m^2. The median (25th–75th percentiles) follow-up was 350 (323–411) days and 347 (86.7%) patients completed the trial.

At randomization, there were no significant differences in BP between the OBP and HBP group (Table 1). In both groups, BP decreased significantly on treatment. Until 6 months, these decreases remained of similar magnitude in the two randomized groups, but thereafter, the reductions became significantly greater in OBP than HBP patients. The final differences in BP reduction between the two treatment groups were 6.8 mmHg systolic ($P < 0.001$) and 3.5 mmHg diastolic ($P < 0.001$) for office pressure. Respective between-group differences were 4.9 and 2.9 mmHg for home pressure and 5.3 and 3.2 mmHg for daytime ABP (all $P < 0.001$) (Table 1).

Table 1 Blood pressure at randomization and end of follow-up in patients randomized to treatment based on blood pressure measurement at the office (OBP group) or at home (HBP group)

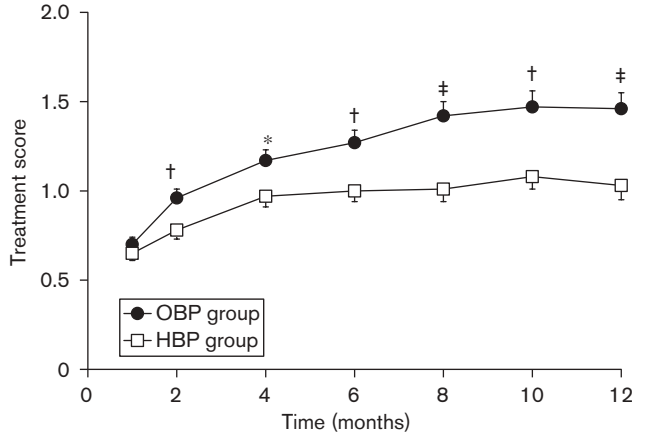
Blood pressure (mmHg)	OBP group ($n = 197$)	HBP group ($n = 203$)	*P*
Office BP			
Systolic			
Randomization	159.1 (19.3)	160.8 (18.6)	0.37
Adjusted change	−22.0 (1.1)	−15.3 (1.1)	<0.001
Diastolic			
Randomization	101.5 (6.5)	101.8 (7.4)	0.66
Adjusted change	−14.0 (0.6)	−10.5 (0.6)	<0.001
Home BP			
Systolic			
Randomization	146.4 (17.1)	146.8 (17.2)	0.82
Adjusted change	−16.0 (0.9)	−11.1 (0.9)	<0.001
Diastolic			
Randomization	92.2 (10.2)	92.0 (9.2)	0.85
Adjusted change	−10.2 (0.5)	−7.3 (0.5)	<0.001
Daytime ambulatory BP			
Systolic			
Randomization	148.2 (15.0)	148.9 (15.0)	0.65
Adjusted change	−16.5 (1.0)	−11.3 (0.9)	<0.001
Diastolic			
Randomization	94.1 (10.0)	94.0 (10.2)	0.96
Adjusted change	−11.1 (0.6)	−7.9 (0.6)	<0.001

Blood pressures at randomization are means (SD). Adjusted changes refer to the mean changes (SE) in blood pressure from randomization to the last follow-up visit adjusted for baseline value, sex, age, and body mass index. All within-group changes were significant ($P \leq 0.001$).

At enrolment, all patients were started on monotherapy with 10 mg lisinopril or 50 mg atenolol per day and had a treatment score of 0.5 units. From the second follow-up visit onwards and further throughout the trial, the treatment score was significantly higher in the OBP compared with the HBP group (Fig. 1). At the end of the trial, more HBP than OBP patients could permanently stop antihypertensive drug treatment: 25.6 versus 11.3%; 2.2 versus 1.0 patient per 100 followed-up for 1 month (log rank: $P < 0.001$). The opposite trend was observed for patients proceeding to multiple drug treatment: 38.7 versus 45.1%; 3.3 versus 3.8 patients per 100 followed-up for 1 month (log rank: $P = 0.14$).

In both treatment groups, there was a significant decrease in the electrocardiographic indices of left ventricular mass. These changes were similar in the OBP and HBP group. After adjustment for the baseline values, sex, age and body mass index, the changes in electrocardiographic measurements were −0.03 mV in the OBP group versus −0.03 mV in the HBP group for the *R*-wave in aVl ($P = 0.97$); −0.12 versus −0.09 mV, respectively for

Fig. 1



Treatment scores in patients randomized to treatment based on blood pressure measurement at the office (OBP group) or at home (HBP group). Treatment scores are calculated by assigning a value of 1 to equipotent doses of various study medications. Values are means (SE). *P*-values are for the between-group differences: $*P \leq 0.05$; $\dagger P \leq 0.01$; $\ddagger P \leq 0.001$.

the Sokolow–Lyon index ($P = 0.53$) and -13 versus $-12\,\mu V \times s$, respectively for the Cornell voltage ($P = 0.84$).

The costs of the medications amounted to €2120 and €1688 ($P = 0.002$) per 100 OBP and HBP patients treated for 1 month. The fees of the physicians averaged respectively €1595 and €1411 per 100 patient-months ($P < 0.001$). However, the potential savings in the HBP group associated with less intensive drug treatment and fewer doctor visits, were partially offset by the costs of home monitoring. Overall, expenditure was slightly but significantly higher in OBP compared with HBP patients: €3875 versus €3522 per 100 patient-months ($P = 0.04$).

Discussion

In this randomized clinical trial with a median duration of one year, adjustment of antihypertensive treatment based on home BP instead of office BP led to less intensive drug treatment and marginally lower medical costs, but also to less BP control with no differences in electrocardiographic left ventricular mass. The final differences in SBP and DBP between the randomized groups averaged 6.8 and 3.5 mmHg on conventional measurement at the doctor's office. Blood pressure gradients of this magnitude are clinically relevant for the long-term prognosis. Indeed, a meta-regression analysis of 30 clinical trials in hypertensive or high-risk patients demonstrated that a 5 mmHg difference in SBP over 3–5 years time changed the risk of all cardiovascular complications and stroke by 25–30% [7]. Thus, the present findings do not support the concept that self-measurement at the patient's home might be a better guide to prescribe antihypertensive drugs than conventional BP measurement at the doctor's office.

An important factor limiting the widespread clinical use of self-measurement is the lack of prognostically validated diagnostic thresholds for the initiation or adjustment of antihypertensive treatment. Several experts [8–11] proposed thresholds approximately ranging from 125–140 mmHg for systolic blood pressure (SBP) and from 80–90 mmHg for DBP. Unfortunately, prospective studies on the relation between cardiovascular risk and the self-recorded BP are scarce. Both in a Japanese [12] and in a European [13] study, the self-measured BP was a better predictor of cardiovascular mortality than the conventionally measured BP at screening.

For various reasons, during follow-up, antihypertensive treatment was adjusted only according to DBP. Most outcome trials in hypertension implemented this option [7]. In young and middle-aged subjects of less than 60 years [14] and even in older subjects [15], DBP determines cardiovascular risk. Had both SBP and DBP been used, the treatment strategy should have been more complex. Furthermore, in analogy with the Ambulatory Blood Pressure and Treatment of Hypertension (APTH) Trial [1], treatment was adjusted to achieve the same range of DBP (80–89 mmHg) in the OBP and HBP groups. These design features allowed one physician at the study coordinating office to propose adjustments of treatment in a blinded fashion.

Long-term outcome studies should firmly establish the advantage of further integrating the self-measured and ambulatory BP into the routine care of hypertensive patients. Until such evidence becomes available, conventional sphygmomanometry at the doctor's office in agreement with current guidelines [16] remains the key to the diagnosis and treatment of hypertension. When a raised BP in the doctor's office is the only detectable abnormality or when patients with a normal clinic BP show unexplained target organ damage, self-measurement, ambulatory monitoring, or both techniques, can be used to exclude white-coat hypertension or masked hypertension [17].

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