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Physician–Pharmacist Cooperation Program for Blood Pressure Control in Patients With Hypertension: A Randomized-Controlled Trial

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BACKGROUND

The aim of the trial was to evaluate the effectiveness of a program of cooperation between physician and pharmacist to reduce cardiovascular risk factors in patients with mild to moderate hypertension by promoting better blood pressure (BP) control, appropriate changes in antihypertensive medications, and beneficial changes in lifestyle.

METHODS

The 132 subjects in this randomized, controlled trial were in the age range of 40–79 years. The inclusion criteria were: systolic BP (SBP) ranging from 140–179 mm Hg and/or diastolic BP (DBP) ranging from 90-99 mm Hg and treatment-naive (untreated for hypertension); or on a regimen of medication for hypertension. Of these 132 subjects, 124 (94%) were already receiving treatment with antihypertensive medications. Equal numbers of subjects were randomly assigned to one of two groups: a physician–pharmacist intervention group ($n = 66$) and a control group ($n = 66$).

RESULTS

The 6-month follow-up rate was 97% in both groups. At 6 months, the mean decrease in SBP/DBP, as measured at home in the morning, was 2.9/3.3 mm Hg in the intervention group relative to baseline ($P = 0.02$ and $P < 0.0001$ for SBP and DBP, respectively). The mean decrease in home morning SBP in the intervention group was not significantly greater than in the control group. However, the DBP decline was significantly greater in the intervention than control groups, which showed a mean decrease of 2.8 mm Hg (confidence interval: −5.5 to −0.1; $P = 0.04$). The percentage of patients in whom control of home morning BP was achieved was 53% in the intervention group and 47% in the control group ($P = 0.40$). A higher percentage of patients in the intervention group, relative to the control group, were able to reduce the use of antihypertensive medications (31 vs. 8%, $P < 0.0001$), and fewer patients in this group required additional medications or increases in dosage relative to the controls (11 vs. 28%, $P = 0.03$). Patients of the intervention group were more likely to show reduction in body mass index and sodium intake and to stop smoking, as compared with the control group.

CONCLUSIONS

A program of cooperation between physician and pharmacist was successful in reducing cardiovascular risk factors in patients with mild to moderate hypertension by promoting better blood pressure (BP) control, appropriate changes in antihypertensive medications, and beneficial changes in lifestyle.

Keywords: *blood pressure; cardiovascular risk factors; hypertension; lifestyle modification; pharmaceutical services; randomized controlled trial*

American Journal of Hypertension, advance online publication 8 July 2010; doi:10.1038/ajh.2010.127

Despite major advances in pharmacological treatment, hypertension is an increasingly common health problem worldwide.[1] Blood pressure (BP) control in patients on antihypertensive medication has been evaluated as unsatisfactory in the United States, Canada, and other European countries.[2] In Japan, it was estimated that, in the year 2008, 39 million people had hypertension (i.e., nearly 38% of the adult population), almost half of them were untreated,[3] and the control of hypertension in ~50% of those on antihypertensive medication was not satisfactory.[4]

Recent meta-analyses have demonstrated that team-based care involving a pharmacist can improve hypertension control.[5] Most physician–pharmacist comanagement programs are designed to provide a clinically satisfactory control of BP in patients through the addition/substitution of suitable medications, titration of dosages, and/or enhancement of adherence to therapy.[6–8] Although lifestyle modifications are known to enhance the antihypertensive effects of medications and help to reduce the required dosage of drugs,[9] the programs described did not focus on this issue. Pharmacist-based medication counseling, including counseling

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Received 13 December 2009; first decision 10 February 2010; accepted 23 May 2010.

regarding lifestyle modification, could contribute to reductions in both the number and dosage of antihypertensive agents; however, this needs to be confirmed by a thorough analysis. We conducted a randomized-controlled trial to test the *a priori* hypothesis that physician–pharmacist cooperation can reduce antihypertensive medication use and cardiovascular risk factors in patients with mild to moderate hypertension by improving BP control, providing advice on appropriate changes in antihypertensive medication regimens and offering intensive counseling regarding beneficial lifestyle modifications.

METHODS

Setting. This 6-month randomized-controlled trial for hypertension control was conducted at a community-based primary care center, Miho Medical Clinic, located in Ibaraki Prefecture, Japan, which had ~2,000 outpatient visits each month during the fiscal year 2007.

Participants and recruitment. **Figure 1** provides a flow chart of the recruitment process of patients participating in this study. The study subjects were 412 patients with hypertension who visited the Miho Medical Clinic between April 2007 and June 2007. Enrollment in the study began on 1 July 2007 and was completed on 30 September 2007. The eligible participants were men and women 40–79 years of age, either taking antihypertensive medications under a stable regimen or treatment-naive and with a systolic BP (SBP) of 140–179 mm Hg and/or diastolic BP (DBP) of 90–109 mm Hg, as determined at two or more occasions during the recruitment period. On the basis of medical records, we excluded patients with a history of cardiovascular disease (stroke, transient ischemic attack, coronary heart disease, or heart failure), rheumatoid arthritis, endocrine diseases, and diabetes mellitus requiring medications, all of which usually require aggressive BP control. Patients on exercise restriction (>20-min brisk walking or cycling per day) as identified after a face-to-face interview with a physician, were also excluded. We also excluded patients with secondary hypertension, as diagnosed by a physician on the basis of the clinical history, physical examination, and if appropriate, laboratory tests of the patients. None of the patients had renal dysfunction (defined as serum creatinine ≥2.0 mg/dl) or was on regular treatment with nonsteroidal anti-inflammatory drugs.

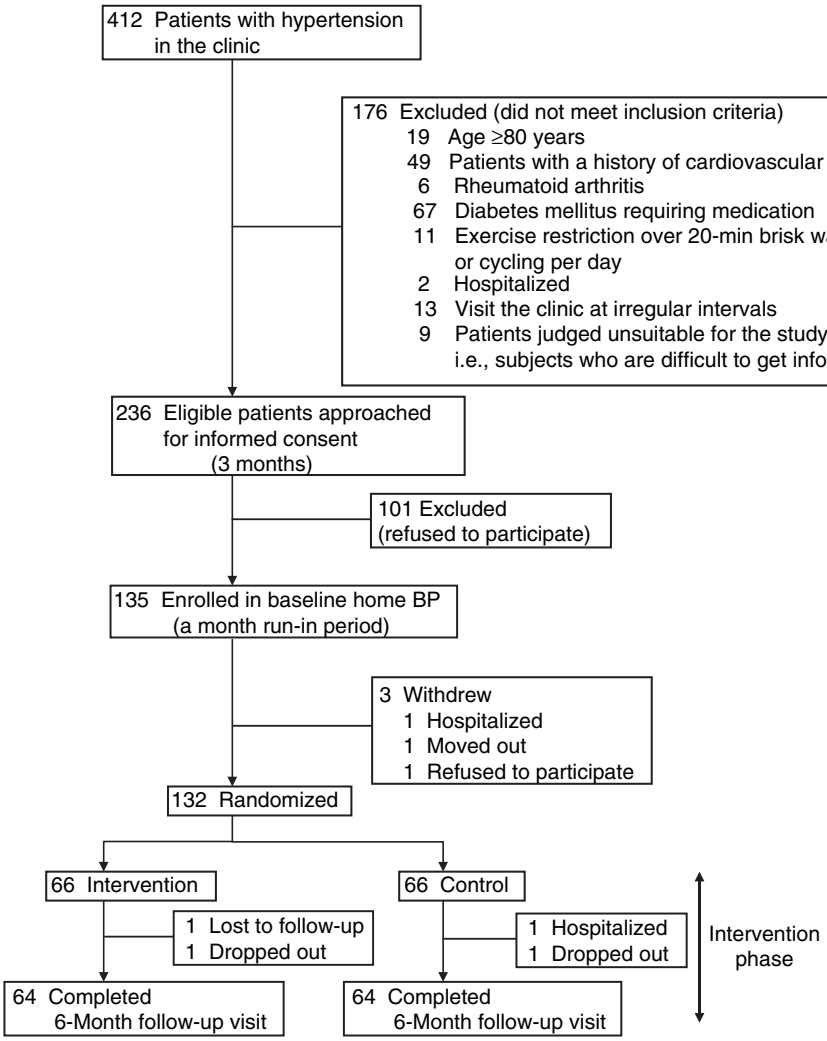

Figure 1 | Flow diagram of the patient selection process. BP, blood pressure.

The study was approved by University of Tsukuba and Osaka University Ethics Committees, and written informed consent was obtained from each patient before enrollment.

Physician–pharmacist program of cooperation. After a 1-month run-in period, the participants were randomized into the intervention or control group in a 1:1 ratio, using a computer-generated random number sequence provided by a statistician who had no contact with the participants. The randomization assignment details were revealed to participants as well as study personnel only after the completion of baseline data collection. The study team comprised five physicians and a pharmacist who had been trained to measure office BP in accordance with the Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2004),[10] and all the personnel adhered to the study protocol. The pharmacist had worked in the clinic for >10 years and had participated in research activities involving provision of health services at Tsukuba University.

In the first 20 min of the first session, printed educational leaflets about treatment of hypertension were distributed to the participants. The intervention group received subsequent 15-min sessions of monthly individual counseling for 6 months (**Table 1**). On the basis of each patient's baseline data, including responses to lifestyle questionnaires,[11,12] the pharmacist met with each patient separately in the first session to set up individual goals. At each visit, depending on the predetermined protocol, the pharmacist offered the patient bold messages[11] which translated into individual goals, e.g., restriction of miso soup to one bowl or less per day, and reducing the size of the evening meal. Patients with body mass index (BMI) ≥25 kg/m^2 and those who walked <30 min/day, were advised to record their body weights and total duration of physical activity on a daily basis. On the basis of the patients' BP data, the pharmacist also offered physicians the following recommendations, as appropriate: reduction of drug dose by one-half or discontinuation of drug for patients who achieved the target BP; switching of the timing of medication, most often from wake-up time to bedtime, addition of a different class of drug, or increase in drug dose for patients who did not achieve target BP; and change in drug class for patients who had side effects or did not respond to treatment. The pharmacist offered physicians a choice of drugs that could be prescribed for the patients: α-adrenergic antagonists and/or β-blockers as tapering drugs, and angiotensin-converting enzyme inhibitors, calcium channel blockers, and/or low-dose diuretics as added drugs. The pharmacist attached counseling reports and recommendations about those medication changes and downloaded the home BP data into the patients' medical record as feedback to the physician. The physicians constructed a treatment plan, taking into account the pharmacist's recommendations, based on the JSH 2004.[10] The physicians discussed the treatment plan with the pharmacist over the telephone, or face-to-face if necessary, during the examination of the patient.

The follow-up protocol for patients of the control group was similar to that for the intervention group, but the pharmacist's monthly sessions and reports to the physician were omitted (**Table 1**). Adherence to medication was evaluated by pill counts and the prescription refills at each visit, and expressed as a percentage of the predicted dose. For ethical reasons, patients in the control group were given the same counseling sessions in the 6 months after the end of the intervention period.

Table 1 | Follow-up procedures for the intervention and control groups

Intervention	Control
At enrollment (baseline):	
Pharmacist counseling (20 min)	Same
Orientation about the program	
Education about hypertension	
Practice in use of home BP device	
Questions about salt intake and lifestyle	Same
Explanation of results of medical examination and tests (by mail)	Same
At 1–5 months:	
Pharmacist counseling (15 min/month)	None
Setting individual goals of lifestyle modifications:	
3–5% reduction in body weight (if BMI ≥25 kg/m^2)	
Reduction of daily salt intake	
Increase in vegetable intake to ≥3 portions/day	
Quitting smoking	
Reduction in alcohol intake to <23 g ethanol/day	
Walking at least 30 min/day	
Stressing the importance of individual goals	
Education about antihypertensive drug therapy	
Sending reports of counseling sessions to physicians with recommendations about medication changes	
At 6 months:	
Pharmacist counseling (15 min)	None
Stressing the importance of individual goals	
Sending reports of counseling sessions to physicians	
Questions about salt intake and lifestyle	Same
Explanation of results of medical examination and tests (by mail)	Same
Monthly (1–6 months):	
Physicians' formulated treatment plans	None
Sending home BP records to physicians and patients	Same
Pharmacists' consultation about medication at pharmacy counter	Same

BP, blood pressure; BMI, body mass index.

Outcomes

Distribution of antihypertensive medications. Physicians were instructed by the pharmacist to follow a standardized regimen for all antihypertensive medications in both groups, modified where necessary only in accordance with the JSH 2004 guidelines. This was done in order to eliminate bias from unblinding of the groupwise assignment of patients. The target BP levels were: office BP <130/85 mm Hg (<65 years) and <140/90 mm Hg

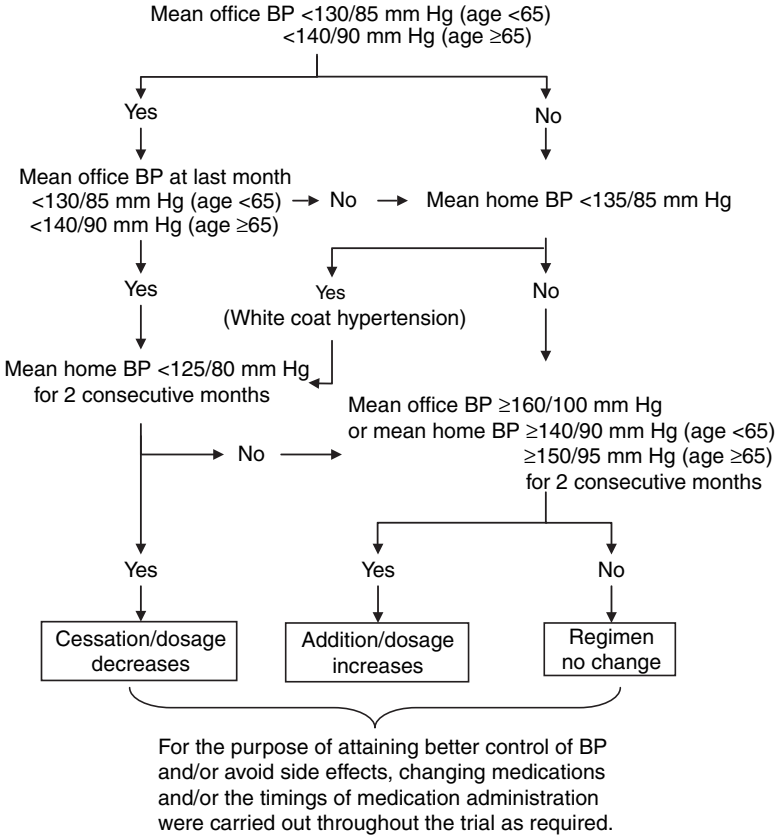

Figure 2 | Flow chart of antihypertensive medication regimens. BP, blood pressure.

(≥65 years) and mean home BP <135/85 mm Hg. At each visit to the clinic during the study, the average value of all available home BP logs was considered as mean home BP. We considered only the morning BP logs in calculating the mean home BP when the mean difference in the SBP readings between morning and evening was >15 mm Hg.[13] In order to attain the target BP levels, physicians prescribed antihypertensive drugs for both the intervention and control groups based on a standardized regimen (**Figure 2**). For the purpose of attaining better control of BP and/or avoid side effects, changing medications and/or the timings of medication administration were carried out throughout the trial as required.

All the recommendations made by the pharmacist regarding the prescription medications were approved by the physicians.

BP measurements. In accordance with the guidelines of JSH 2004, both office and home BPs were measured. Office BP represented the average of two readings taken by a physician using a mercury manometer after the participant had rested for 5 min in a seated posture. When the difference in two consecutive SBP or DBP readings was >5 mm Hg, another measurement was taken, and the office BP represented the average of three readings. Office BP at baseline (August–October, 2007) was calculated as the average of BP measurements on two separate visits taken before the randomization, and the average BP at the end of 6 months (April–May, 2008) was calculated as the average of the measurements taken at two visits before the 6-month follow-up.

The home BP logs and readings were recorded using automatic validated oscillometric manometers UA-767PC (A and D, Tokyo, Japan),[14] certified by the British Hypertension Society. The pharmacist and the physicians were blinded with respect to home BP measurements. The pharmacist trained all the patients at the time of enrollment to use the device appropriately to measure BP, with a special emphasis on keeping the arm-cuff at heart level, and extending and relaxing the arm using a supporting pillow. Measurements were taken twice daily after 2 min of rest in a seated position with feet flat on the floor, once within 1 h after waking up in the morning and the other just before bedtime. If the participants took two or more BP measurements at each of the two indicated time periods, the first reading was used for the analysis. These procedures were followed in every instance, and have been described in detail previously.[15] All the patients were also advised to record in writing the BP readings at the time of measurement of BP using the automated device. Measurements taken outside the predefined morning and evening time frames (2 AM–12 AM or 6 PM–2 AM range) and daytime values were discarded. Home BPs were calculated as the average of 7-day qualified BP measurements in October 2007 (before the randomization) and April 2008 (at 6-month follow-up).

Reduction in cardiovascular risk factors through modification of lifestyles. The secondary endpoint was reduction of cardiovascular risk factors and lifestyle modification, as defined in JSH 2004. BMI was calculated as body weight in kilograms

divided by the square of the height in meters (kg/m^2). The questionnaires included questions on the smoking status (yes/no), alcohol consumption (g ethanol/day), daily exercise, and eating habits.[12] Whether the patient was doing physical exercise equivalent to brisk walking for >30 min/day was estimated from the responses to the following questions: (i) what sort of exercise do you do? (ii) how often do you spend exercising in a week? (iii) how long do you spend exercising at one time? and (iv) how long do you walk per day?

The sodium reduction score was calculated for each individual by adding one point for each of 10 sodium-reducing behaviors. This scoring system has been validated previously.[11,16] The correlation between sodium reduction score and sodium excretion has also been determined previously. Age- and sex-adjusted mean 24-h sodium excretion values across quintiles of the baseline sodium reduction score (n = 1,674) were 203, 195, 183, 180, 168 mmol/day (P for trend <0.0001).[16] Data relating to 24-h sodium excretion values are not reported for this study because of the limited sample size (84/132 patients, 64%). All laboratory assays, blinded as to identification of the patient, were analyzed at Kotobiken Medical Laboratories (Tsukuba, Japan), using standard methods.

Statistical analysis. Our planned sample size of ≥63 patients per group had to be randomized to detect 7 or 5 mm Hg reductions in SBP and DBP, respectively, with significance set at 5% and power at 90%. That expected reduction in BP was similar to or more than the level improved by lifestyle modification, i.e., SBP/DBP reduction of 2.5/2.0 mm Hg by reduction in sodium intake by 77 mmol/day,[17] and SBP/DBP reduction of 4.4/3.6 mm Hg by weight loss of 5.1 kg.[18] Also, we assumed s.d. of 8/6 mm/Hg for SBP/DBP, on the basis of earlier reports of morning BP measurements recorded at home in Japanese individuals with hypertension.[13,19] We estimated a dropout rate of <5% in our study, because the participants had easy access to the primary care center, the largest community clinic in Miho village. Out of the 135 patients enrolled, 128 completed the study and provided the required information in this trial. The involvement of only one pharmacist could provide the higher precision in BP measurements and the more conservative sample size calculations.

Analyses were performed according to the intention-to-treat principle. Differences in baseline characteristics between the intervention and control groups were tested for significance using the independent t, the Wilcoxon rank sum, or χ^2-tests. Fisher's exact test was used to assess differences in adherence to medication. We compared 6-month changes in BP levels, and clinical and lifestyle variables between the two groups using the analysis of covariance for continuous outcomes and multiple logistic regression model for binary outcomes. We controlled for potential baseline confounding by BMI (kg/m^2), which was the only baseline characteristic having a P value <0.10 for between-group comparisons, home morning SBP ≥135 and/or DBP ≥85 mm Hg (yes or no), and antihypertensive medication use (yes or no).

Two-tailed P values of <0.05 were considered statistically significant. In order to minimize the hypotheses tested, we considered home morning BP and reductions in antihypertensive medications as the primary outcomes. All analyses were performed using SAS software version 9.1 (SAS Institute, Cary, NC).

RESULTS

Study flow and baseline characteristics

Of the 236 eligible patients who met the entry criteria, 132 (56%) agreed to be enrolled in the study (**Figure 1**). The proportion of those of age >60 years was somewhat higher among those who consented to enroll than in the general pool of eligible patients, probably more of the younger, working-age patients could not spare the time required for the study. Of the 132 patients enrolled (66 in each group), 64 from each group attended the 6-month follow-up; the follow-up rate in each group was therefore 97%. Four patients did not complete the study: one was lost to follow-up; two dropped-out, and one underwent surgery during the follow-up phase. Throughout the trial none of the patients developed cardiovascular events that required hospitalization. The baseline characteristics and antihypertensive medications were similar in the patients in the two groups (**Tables 2–4**). The total number of visits to the physicians and the pharmacist during the intervention period was not significantly different between the intervention and control groups: median (interquartile range), 4 (4–5) vs. 4 (3–5)

Table 2 | Baseline characteristics of the intervention and control groups

Variables	Intervention (n = 66)	Control (n = 66)	P value for difference
Age, mean (s.d.), years	61.7 (6.9)	61.6 (8.5)	0.95
Male patients	42 (63)	45 (68)	0.59
Family history of cardiovascular diseases	22 (33)	24 (36)	
Antihypertensive medication classes			0.60
None	4 (6)	4 (6)	
1	23 (35)	25 (38)	
2	26 (39)	27 (41)	
≥3	13 (20)	10 (15)	
Categories of antihypertensive medication used			
Calcium channel blockers	53 (80)	54 (82)	0.83
Angiotensin-converting enzyme inhibitors	12 (18)	9 (14)	0.48
Angiotensin receptor blockers	33 (50)	27 (41)	0.30
α-Adrenergic antagonists	7 (11)	6 (9)	0.77
β-Blockers	13 (20)	12 (18)	0.83
Diuretics	1 (2)	2 (3)	0.56
Duration of treatment with antihypertensive agents, Mean (s.d.), years			
	7.7 (8.0)	7.8 (7.4)	0.90
Statin use	15 (23)	12 (18)	0.52

Number (%) of patients unless otherwise indicated.

Table 3 | Blood pressure values and medication changes in the intervention and control groups

Variables	*n*	Intervention	*n*	Control	Estimated difference between groups or odds ratio at 6 months (95% CI)	*P value for difference
At office						
SBP (95% CI)						
Baseline, unadjusted mean	66	138 (135 to 141)	66	139 (136 to 142)		
Change at 6 months	64	−2.4 (−5.7 to +0.8)	64	−0.9 (−4.2 to +2.3)	−1.9 (−6.1 to +2.3)	0.36
DBP (95% CI)						
Baseline, unadjusted mean	66	81 (80 to 83)	66	83 (81 to 85)		
Change at 6 months	64	−2.3 (−4.2 to −0.3)	64	−3.1 (−5.1 to −1.2)	−0.7 (−3.4 to +1.9)	0.59
At home, morning						
SBP (95% CI)						
Baseline, unadjusted mean	66	135 (132 to 138)	66	135 (132 to 138)		
Change at 6 months	64	−2.9 (−5.5 to −0.4)	64	−1.2 (−3.8 to +1.3)	−0.6 (−4.1 to +2.9)	0.73
DBP (95% CI)						
Baseline, unadjusted mean	66	83 (81 to 85)	66	84 (82 to 86)		
Change at 6 months	64	−3.3 (−4.8 to −1.8)	64	−1.4 (−2.9 to +0.1)	−2.8 (−5.5 to −0.1)	0.04
Pulse (95% CI)						
Baseline, unadjusted mean	66	68 (66 to 70)	66	66 (64 to 68)		
Change at 6 months	64	−0.7 (−2.0 to +0.7)	64	+1.5 (+0.1 to +2.8)	−0.6 (−3.8 to +2.6)	0.72
BP control, *n* (%)[a]						
Baseline	66	26 (40)	66	25 (38)		
6 months	64	34 (53)	64	30 (47)	1.4 (0.6 to 3.1)	0.40
At home, evening						
SBP (95% CI)						
Baseline, unadjusted mean	61	125 (122 to 128)	60	126 (123 to 129)		
Change at 6 months	63	−0.1 (−2.8 to +2.6)	60	+3.4 (+0.6 to +6.2)	−1.9 (−6.3 to +2.5)	0.39
DBP (95% CI)						
Baseline, unadjusted mean	61	75 (73 to 77)	60	77 (75 to 79)		
Change at 6 months	63	−0.9 (−2.5 to +0.8)	60	+0.9 (−0.8 to +2.6)	−2.0 (−5.3 to +1.3)	0.22
Pulse (95% CI)						
Baseline, unadjusted mean	61	73 (71 to 76)	60	71 (69 to 74)		
Change at 6 months	63	−2.4 (−4.0 to −0.8)	60	−0.9 (−2.6 to +0.7)	−1.2 (−4.4 to +2.1)	0.48
Any changes in antihypertensive medication, n (%)	64	47 (73)	64	31 (48)	3.2 (1.5 to 6.9)	0.003
Cessation/dosage decreased, *n* (%)	64	20 (31)	64	5 (8)	9.8 (2.8 to 41.1)	<0.0001
Calcium channel blockers		10		0		
ACE		3		1		
ARB		6		1		
α-Adrenergic antagonists		1		2		
β-Blockers		4		1		
Diuretics		1		0		
Addition/dosage increases, *n* (%)	64	7 (11)	64	18 (28)	0.3 (0.1 to 0.8)	0.03
Calcium channel blockers		5		5		
ACE		1		0		
ARB		2		6		
α-Adrenergic antagonists		1		2		

Table 3 | Continued on next page

Table 3 | Continued

Variables	*n*	Intervention	*n*	Control	Estimated difference between groups or odds ratio at 6 months (95% CI)	*P value for difference
β-Blockers		3		0		
Diuretics		0		7		
Switching drug, *n* (%)	64	10 (16)	64	9 (14)	1.2 (0.4 to 3.2)	0.73
Within the same class		4		3		
To the other class		6		6		
Changing the timing of medication, n (%)	64	24 (38)	64	9 (14)	3.9 (1.6 to 10.1)	0.003

ACE, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure.
[a]Home morning BP <135/85 mm Hg.
**P* values are based on between-group differences adjusted for the following baseline variables: body mass index (kg/m^2), home morning, SBP ≥135 and/or DBP ≥85 mm Hg (yes or no), and antihypertensive medication use (yes or no).

Table 4 | Cardiovascular risk factors and lifestyles in the intervention and control groups

Variables	*n*	Intervention	*n*	Control	Estimated difference between groups or odds ratio at 6 months (95% CI)	*P value for difference
Body mass index (BMI), kg/m^2						
Baseline, unadjusted mean	66	25.0 (24.1 to 25.9)	66	26.1 (25.2 to 27.1)		
Change at 6 months	64	−0.4 (−0.7 to −0.2)	64	0.0 (−0.2 to +0.2)	−0.4 (−0.7 to −0.1)	0.008
Sodium reduction score, points						
Baseline, unadjusted mean	66	4.4 (3.9 to 4.9)	66	4.4 (3.9 to 4.9)		
Change at 6 months	64	+1.3 (+0.9 to +1.7)	64	+0.0 (−0.4 to +0.4)	+1.2 (+0.5 to +2.0)	0.002
Smokers, n (%)						
Baseline	66	17 (26)	66	21 (32)		
6 months	64	9 (14)	64	19 (30)	0.4 (0.2 to 0.9)	0.04
Alcohol consumption >23 g/day, n (%)						
Baseline	66	30 (45)	66	25 (38)		
6 months	64	19 (30)	64	25 (39)	0.6 (0.3 to 1.3)	0.23
Brisk walking >30 min/day, n (%)						
Baseline	66	40 (61)	66	37 (56)		
6 months	64	44 (69)	64	34 (53)	1.9 (0.9 to 4.0)	0.09

**P* values are based on between-group differences adjusted for the following baseline variables: body mass index (kg/m^2), home morning BP level SBP ≥135 and/or DBP ≥85 mm Hg (yes or no), and antihypertensive medication use (yes or no).
BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.

for visits to physicians, $P = 0.42$; and 5 (5–6) vs. 4 (3–5) for visits to the pharmacist, $P = 0.89$. Adherence to medication regimens at the baseline and 6-month follow-up time points were not significantly different between the intervention and control groups: median (interquartile range), 100 (93–100) % vs. 100 (94–100) % at baseline, $P = 0.90$; and 100 (97–100) % vs. 100 (93–100) % at 6-month follow-up, $P = 0.17$. The total time spent per patient on physician consultation, including the physician–pharmacist interaction time, was also not significantly different between the intervention and control groups: median (interquartile range), 17 (13–23) vs. 17 (13–23) min, $P = 0.55$.

Changes in antihypertensive medication regimens

During the intervention period, 20 of 64 patients (31%) in the intervention group discontinued antihypertensive medications or decreased the dosage of these medications as compared to only 5 of 64 patients (8%) in the control group ($P < 0.0001$). There was no significant correlation between reduction in antihypertensive medication and the age of the patient ($P = 0.29$) or the number of antihypertensive drugs taken ($P = 0.25$) (data not shown). On the other hand, 18 patients (28%) in the control group required additional medications or increases in dosage as compared to only 7 patients (11%) in the intervention group ($P = 0.03$).With regard to changes in antihypertensive medication regimens, drug changes were made to ensure equivalent efficacy and not based on the classification of the drug; for example, 5 mg amlodipine was changed to 40 mg telmisartan. The frequency of change in medications was not significantly different between the two groups (10 in the intervention group vs. 9 in the control group, $P = 0.73$); the frequency of

change in the timing of medication administration was higher in the intervention group than in the control group (24 vs. 9, respectively, $P = 0.003$).

BP control

At 6 months, the mean office DBP diminished relative to the baseline in the intervention group (SBP by 2.4 mm Hg, $P = 0.14$, and DBP by 2.3 mm Hg, $P = 0.02$) as well as in the control group (SBP by 0.9 mm Hg, $P = 0.45$, and DBP by 3.1 mm Hg, $P = 0.002$, respectively), but the differences between the two groups in this regard were not significant (Table 3). The mean home morning values of SBP and DBP in the intervention group also decreased relative to the baseline by 2.9 ($P = 0.02$) and 3.3 mm Hg ($P < 0.0001$), respectively. The mean decrease in home morning SBP in the intervention group was not significantly greater than in the control group. However, the DBP decline was significantly greater in the intervention than control groups, which showed a mean decrease of 2.8 mm Hg (confidence interval: −5.5 to −0.1; $P = 0.04$ for between-group comparison). The proportion of patients in whom the control of home morning BP was achieved was 53% in the intervention group and 47% in the control group, and no significant difference was noted in this regard between the groups ($P = 0.40$). At the 6-month follow-up, home evening BP levels were similar to the baseline in the intervention group whereas they had increased in the control group. Similar results were noted after excluding from the analysis data relating to patients who did not receive antihypertensive medications.

Changes in cardiovascular risk factors and lifestyle modification

At 6 months, the decrease in BMI was significantly greater in the intervention group than in the control group (Table 4). Larger proportions of patients in the intervention group improved their sodium reduction scores and achieved smoking cessation as compared to the control group ($P = 0.002$ and $P = 0.04$, respectively, for the two lifestyle changes). As regards reduction in alcohol intake and walking >30 min/day, the percentages of such patients were not significantly different in the two groups ($P = 0.23$, $P = 0.09$, respectively).

DISCUSSION

The physician–pharmacist cooperation in this study, aimed at promoting appropriate changes in antihypertensive medications and dosing regimens and also in the lifestyles of patients with mild to moderate hypertension, was shown to improve the control of home morning DBP and reduce the use of antihypertensive medication. It also resulted in a decrease in BMI, sodium intake, and the use of tobacco. Previous studies have targeted patients with hypertension to improve adherence to medication regimens and to increase the use/dosage of antihypertensive drugs as needed. The novelty of the present study is that it was designed to bring about reductions in BP levels through lifestyle modification and medication changes. Specifically, the approach we adopted was able to achieve BP control in patients even while reducing or discontinuing the use of antihypertensive agents.

Since morning BP readings have been regarded as a good predictor of future cardiovascular disease,[19–21] the control of morning BP used in this program is of value for clinical practice of hypertension control. Although home BP monitoring is described as effective in improving adherence to medications and decreasing home BP in hypertensives,[22] the present physician–pharmacist cooperative approach also improved home morning BP in hypertensives.

In this study, although the magnitude of reduction in home morning BP was relatively small, same as the expected reduction level improved by lifestyle modification,[17,18] it may be of value, given that 3–5 mm Hg of reduction in BP is reported to reduce potential adverse cardiac events and stroke.[23] Moreover, a recent study showed that lifestyle modification improved the outcome of medical treatment; it was shown in patients with hypertension that, over a 10-year period, a reduction in intake of salt by 1 g/day achieved BP control that was equivalent to and far more cost-effective than the use of antihypertensive medications.[24] Consequently, it has been recommended that more emphasis be placed on lifestyle modification to control BP in patients undergoing treatment for hypertension. Physician–pharmacist collaboration is a practical approach to controlling high BP, because the pharmacist could build bridges between patients and physicians through counseling patients about lifestyle improvement and physicians about administration of medications.

The physician–pharmacist interaction was conducted mostly over the telephone at the time of a visit by the patient to the physician's office. Because the total physician consultation time was not different between the intervention and control groups, it was concluded that the cost of the physician–pharmacist interaction was minimal.

Our results suggest that lifestyle modification, especially weight control and reduction in sodium intake, could be effective in hypertension control and allow for reduction in antihypertensive medications. The results also showed that the proportion of patients who quit smoking was significantly larger in the intervention group than in the control group. Nicotine replacement treatment may enhance smoking cessation while minimizing dropouts on account of withdrawal symptoms.

This study has several limitations. First, counseling was conducted by one pharmacist at a single community clinic, and blinding was not feasible. However, to minimize the potential biases, we took the following steps: (i) ensured that the randomization to the two groups was carried out by an independent person; (ii) selected home BP as the primary outcome, using BP auto-measuring devices for uniformity and comparability, (iii) ensured that BMI of patients was measured by nurses who were blinded to the patient group allocation, and (iv) employed standardized counseling scenarios and medication regimens. Second, the study findings may be limited by potential contamination, i.e., physicians examined patients of both the intervention and control groups. BP control may have been better in the intervention if such contamination of data could have been avoided. Third, 43% of eligible patients refused to participate

in the study. The proportion of individuals aged <60 years was slightly higher among the nonparticipants than participants, probably because younger persons were full-time workers and felt uncomfortable in devoting their time to participate in this study. Fourth, this study took place at one outpatient clinic in Japan. Further studies are needed to confirm our findings in various clinical settings.

In conclusion, our physician–pharmacist cooperation intervention, including intensive counseling regarding lifestyle modifications and antihypertensive medication changes, improved the control of home morning BP and reduced the use of antihypertensive medications as well as BMI, sodium intake, and the use of tobacco in patients with mild to moderate hypertension.

Acknowledgments: We thank Dr Terukazu Enami, Sumie Kobayashi, Yumiko Itoga, Chisato Kawarabayashi, Noriko Hosoya, Tomomi Morita, Hiromi Hanari, Hitomi Nakazawa, Maki Yamanaka, and all other staff at Miho Medical Clinic.

Disclosure: The authors declared no conflicts of interest.

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