Effect of Anti-Hypertensive Medication Withdrawal in Well-Controlled Treated Hypertensive Patients: Preliminary Results

Peera Buranakitjaroen MD, DPhil*, Meta Phoojaroenchanachai MD*,
Pavitra Thongma BNS**, Raiwin Wimonsophonkitti MD***

** Division of Hypertension, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
*** Faculty of Nursing, Chulalongkorn University, Bangkok, Thailand*
**** Division of Cardiology, Department of Medicine, Phramongkutklao College of Medicine, Phramongkutklao Hospital, Bangkok, Thailand*

Objective: *To determine prevalence of hypertensive (HT) patients whose BP can be normalized (hospital BP <140/90 mmHg) for at least a year and still remained normotensive (NT) after 12-week anti-HT drug withdrawal. Clinical characteristics of this group of patients were assessed.*
Material and Method: *At least a year of well controlled HT patients by hospital BP without target organ damage and diabetes mellitus who were treated with single low-to-standard dose anti-HT medication in hypertension clinic, Siriraj Hospital were screened. After an informed consent was signed, epidemiologic data, cardiovascular risks and laboratory data done within a year was collected. The anti-HT drug taken would be discontinued and a series of home blood pressure (HBP) was measured twice a day (wake-up time and bed time) for 2 weeks. The anti-HT drug was still discontinued in normal HBP group (average HBP <135/85 mmHg) and reassessed hospital BP 10 weeks later (week 12). Previous anti-HT medications were resumed in high HBP group (average HBP ≥135/85 mmHg), at week 2. At week 12, those who became hypertensive (hospital BP ≥140/90 mmHg) would be advised to continue the drug.*
Results: *Ninety-five patients were recruited. Six patients were excluded since they did not complete HBP measurement data. After 2 weeks of antihypertensive drug discontinuation, 16 out of 89 patients enrolled were found to be HT by HBP. The rest 73 patients (82.0%) were remained NT. At week 12, 7 patients (7.9%) self-administrated drug prior to the visit date. Therefore, 66 patients (74.1%) were left for further analyses. Of them, 55 patients (61.8%) were still NT by hospital BP and 11 patients (12.3%) turned to be HT. There were no significant differences of all risk factors studied between those NT and HT, except male was found in a higher proportion than female (p = 0.021).*
Conclusion: *Fifty five patients (61.8%) out of 89 enrolled patients are still NT and able to stop anti-HT drug after 12 weeks follow-up. Male had a higher rate to remain NT than female.*

Keywords: *Antihypertensive drug withdrawal*

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Antihypertensive (anti-HT) drugs were usually prescribed and maintained lifelong for cardiovascular disease prevention. However, the dosage and number of anti-HT drugs could be reduced after BP could be controlled for at least a year (step-down therapy)[1]. In addition, the prevalence of white-coat hypertension (WCH) was found 12-53.2% in clinical practice. Usually, they do not need pharmacological therapy unless target organ damage was detected. Unnecessary anti-HT drug therapy led to waste of resources and potential occurrence of adverse drug reaction (ADR). Moreover, benefits and harms of treating mild hypertension in primary prevention patients are not known at present[2]. Existing evidence comparing the health outcomes between treated and untreated individuals with mild hypertension (systolic blood pressure of 140-159 mmHg and/or diastolic blood pressure of 90-99 mmHg) showed no differences between treated and untreated

Correspondence to:
Buranakitjaroen P, Division of Hypertension, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkoknoi, Bangkok 10700, Thailand.
Fax: +66-2-4197790
E-mail: peera.bur@mahidol.ac.th

individuals in heart attack, stroke, and death[2]. Therefore, updated ESH/ESC 2013 guidelines emphasized more specific lifestyle recommendations such as limiting salt intake to 5-6 grams/day and lowering body mass index (BMI) to 25 mg/kg^2 among patient with mild hypertension[3].

Recent guidelines have underlined the paucity of data for treating stage 1 hypertension[4]. Treatment was recommended only after confirming high blood pressure (BP) by 24-hour ambulatory blood pressure monitoring (24-hr ABPM) to rule out WCH. Treatment was restricted to stage 1 HT patients with signs of target organ damage or at high total cardiovascular disease risk. Therefore, it is possible to gradually diminish or discontinue anti-hypertensive therapy in patients with mild hypertension whose BP are well controlled and maintain lifestyle modifications thereafter.

Material and Method

Study objectives

To determine the prevalence of mild HT patients who's BP were well controlled with a single low dose antihypertensive drug for at least a year and remain normotensives (NT) after 12-week anti-HT drug withdrawal, and obtained clinical characteristics of this group.

Study design

This is a prospective cohort study approved by the Ethic Review Committee, Siriraj Hospital. It was carried out by reviewing the outpatient files of HT patients who attended the Hypertension Clinic at the Outpatient Department, Siriraj Hospital between October 2012 and June 2013. These patients received usual care provided at the OPD. Only those essential HT patients of both sexes, aged >35 years, treated with single low-to-standard dose of anti-HT medications were reviewed. Major exclusions were those with secondary hypertension, high CVD risk, e.g., type 2 diabetes mellitus (T2DM), metabolic syndrome, and those with target organ damage, e.g., 5left ventricular hypertrophy (LVH), chronic kidney disease (CKD) (CrCl <60 ml/minute) and preexisting cardiovascular disease (CVD), etc. Only those whose BP was well controlled (BP <140/90 mmHg) for at least a year, willing to stop medication and sign informed consent were recruited. Their medical records were then carefully reviewed for family history of hypertension, duration of hypertension and demographic data, e.g., baseline BP before drug treatment if available, recent clinic BP levels, weight and height to calculate body mass index (BMI), etc. Personal histories of smoking or alcohol drinking, high salt intake behavior and exercise status were also collected.

High salt intake was defined as a tendency to add salt or condiments to ready cooked food, a high frequency (≥3 days/week) of taking instant, canned or preserved food, and fast food. Ever alcoholic drinkers included those occasional social drinkers and habitual drinkers. Regular exercise included daily homework, e.g., floor cleaning, washing of clothes by hands, car washing, etc. and walking or running for >20 minutes/day of >3 times a week.

Laboratory findings within a year before recruitment, i.e., fasting plasma glucose (FPG), serum sodium, potassium, blood urea nitrogen (BUN), creatinine (Cr), uric acid, total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), etc., were collected. Estimated creatinine clearance (CrCl) was determined by using the Cockroft-Gault formula[5] adjusted by body surface area[6].

Hyperlipidemia and the adequacy of lipemic control were defined according to the Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP-III)[7]. Obesity and overweight were defined according to the WHO guidelines (BMI cut-off points for Asian population: ≥23.0 for overweight)[8]. Since, this is a "real life study", modification of the dose or adding on the number of the given lipid lowering drugs was allowed.

All data mentioned above will be filled up in a predesigned case record form. Co-administered drugs were also recorded. Patients who personally feel uncomfortable to stop medication after recruitment and took anti-HT drug prior to revisit were not enrolled.

After giving an informed consent, every patient had to stop anti-HT drug used. An automatic BP measurement device (OMRON model IA2) and a HBP record from will be provided for recruited patients to take home. They were instructed how to use the device correctly and to fill the form. Home blood pressure (HBP) was measured twice a day (wake-up time and bed time) for 2 weeks and filled in the form provided. Availability of ≥80% evaluable HBP data was required prior to enrollment. Normal HBP group, high HBP group was defined as patients who had average HBP <135/85, ≥135/85 mmHg, respectively. Anti-HT drug was still discontinued in normal HBP group and

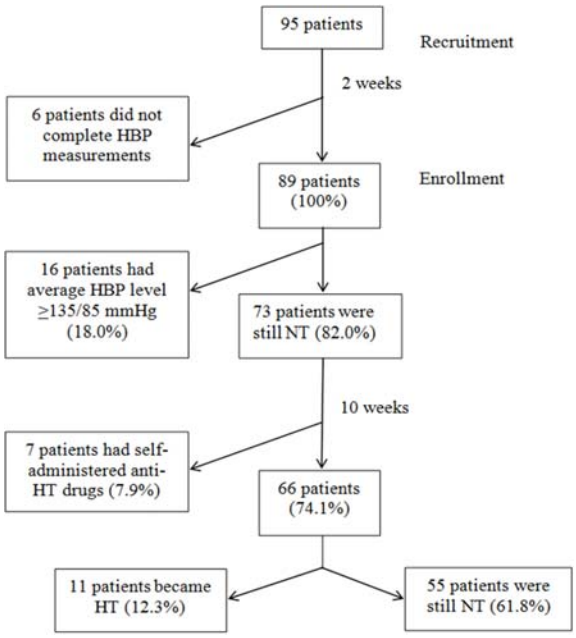
reassessed office BP 10 weeks later (week 12). Previous anti-HT medications were resumed in high HBP group and they were excluded from the study.

Statistical analyses

Kolmogorov-Smirnov test was used to identify type of distribution. Results were demonstrated as mean ± standard deviation (SD), mean (95% confidence interval) or percent (%) where appropriate. Statistical analyses were carried out using Statistical Packages for Social Sciences (SPSS 11.5). Comparison was made by using Chi-square or Fisher's exact test, paired sample t-test and independent sample t-test where appropriate.

Results

Ninety-five HT patients were recruited. Six of them were excluded since they did not complete HBP measurement data for whatever reasons (Fig. 1). After 2 weeks, 89 HT patients who had completed HBP measurements were enrolled in this study (Table 1). Sixteen of them (18.0%) were found HT (average HBP ≥135/85 mmHg). The rest, 73 participants (82.0%), were remained NT (average HBP <135/85 mmHg). Those patients who turned to be hypertensive had average baseline office SBP and DBP higher than those patients



All percentages given computed from 89 patients enrolled (100%)

Fig. 1 Over all study results of anti-HT drug withdrawal.

who were still normotensive significantly. In addition, they have significant higher average BMI and higher rate of overweight/obese.

During the follow-up period, 7 patients from 73 patients who were still normotensive by HBP had self-administrated anti-HTdrug prior to the appointment date. Among them, 3 receiving ARB, 3 receiving CCB and a patient receiving diuretics were observed. The common reasons were anxiety or feeling not well when not taking anti-HT drug. Therefore, 66 patients (74.1%) were left for analyses at the end of the 12th week (Table 2, 3). Of them, 55 were still NT (61.8%) and 11 turned to be HT (12.3%) (Fig. 1). Average office SBP/DBP levels were significantly increased in 66 patients from 119.8±10.1/68.4±7.7 mmHg at week 0 to 134.5±10.8/77.9± 9.3 mmHg at week 12 (p<0.01 for both SBP and DBP levels). The mean changes of SBP/DBP levels were 14.7/9.5 mmHg (95% CI = 11.3-18.1/7.2-11.7). Similar findings were also found in NT group, i.e. average office SBP/DBP increased from 120.0±9.2 mmHg/ 68.4±7.4 mmHg at week 0 to 131.5±8.3 mmHg/76.4±7.6 mmHg at week 12 (p<0.01 for both SBP and DBP levels). The mean changes of SBP/DBP were 11.5/8.0 (95% CI = 8.4-14.5/5.9-10.1).

As expected, there was significant higher average SBP/DBP levels of the HT group at the end of the 12th week as compared to that of the NT group; SBP of 149.6±9.1 mmHg vs. 131.5±8.3 mmHg, p<0.01, 95% CI = 12.5-23.7 and DBP of 85.6±13.1 mmHg vs. 76.4±7.6 mmHg, p<0.01, 95% CI = 3.5-14.9. However, after 12 weeks of follow-up, there was no significant difference in the amount of losing weight between the NT and the HT groups; 0.1 kg (95% CI = -0.3-0.4) vs. -0.3 kg (95% CI = -1.0-0.4), p = 0.83 (data not shown).

Concerning type of antihypertensive drugs on the effect of 2-week drug withdrawal, there were one case of diuretics (12.5%), 7 cases of calcium channel blocker (CCB, 24.1%), 2 cases of beta-blockers (15.4%), and 6 cases of angiotensin receptor blocker (ARB, 15.8%) who became hypertensive. There were no significant differences between the rates of re-prescribing in each anti-HT drug-class (Table 4). Cumulative drug withdrawal at the end of study was 3 cases (37.5%) of diuretics treated group, 12 cases (41.4%) of CCB treated group, 4 cases (30.8%) of beta-blockers treated group, 14 cases (36.8%) of ARB treated group and a case of ACEI treated group (Table 4).

At the end of study (week 12), the increment of SBP/DBP levels from baseline (week 0) among those 66 patients who completed a 3-month study were 13.5/ 3.0 mmHg (95% CI = -4.9-31.9/-6.1-12.1) for diuretics

Table 1. Baseline clinical characteristics of HT patients who completed HBP measurement compared normotensive group and hypertensive group (identified by HBP ≥135/85 mmHg)

Parameter at baseline	Mean ± SD or n (%)			*p*-value
	All (n = 89)	NT (n = 73)	HT (n = 16)	
Age (years)	57.5±9.3	57.2±9.3	59.0±9.4	0.48
Elderly	37 (41.6)	28 (38.4)	9 (56.3)	0.19
Male	29 (32.6)	22 (30.1)	7 (43.8)	0.29
Office SBP (mmHg)	121.6± 9.9	120.3±9.9	127.7±7.6	<0.01*
Office DBP (mmHg)	69.5±8.1	68.5±7.6	74.0±9.0	0.01*
Ever smoking	8 (9.0)	6 (8.2)	2 (12.5)	0.44
Ever drinking alcohol	18 (20.2)	14 (19.2)	4 (25.0)	0.41
High salt intake	19 (21.3)	17 (23.3)	2 (12.5)	0.28
Ongoing exercise	79 (88.8)	65 (89.0)	14 (87.5)	0.57
Duration of HT (years)	6.7±3.8	6.7±3.9	6.6±3.4	0.92
Family history of HT	69 (77.5)	57 (78.1)	12 (75.0)	0.51
BMI (kg/m^2)	23.9±3.1	23.5±3.0	25.7±2.9	0.01*
Overweight/obese	54 (60.7)	40 (54.8)	14 (87.5)	0.02*
Dyslipidemia	28 (31.5)	21 (28.8)	7 (43.8)	0.24
Average HSBP (mmHg)	126.9±11.1	124.4±10.0	138.1±8.6	<0.01*
Average HDBP (mmHg)	74.9±9.5	73.2±9.1	82.3±8.2	<0.01*

NT = normotension; HT = hypertension; SBP = systolic blood pressure; DBP = diastolic blood pressure; HSBP = home systolic blood pressure; HDBP = home diastolic blood pressure; Elderly = age ≥60 years; n = number; BMI = body mass index; * *p*-value considered significant at <0.05

Table 2. Baseline clinical characteristics of 66 HT patients who finished study at 3 months, compared normotensive group and hypertensive group

Parameter at baseline	Mean ± SD or n (%)			*p*-value
	All (n = 66)	NT(n = 55)	HT (n = 11)	
Age (years)	56.7±9.2	56.7±9.1	56.9±10.6	0.95
Elderly	25 (37.9)	20 (36.4)	5 (45.5)	0.40
Male	18 (27.3)	18 (32.7)	0	0.02*
Office SBP (mmHg) at week 0	119.7±10.1	120.0±9.2	118.6±14.2	0.67
Office DBP (mmHg) at week 0	68.7±7.8	68.6±7.5	68.9±9.5	0.91
Ever smoking	6 (9.1)	6 (10.9)	0	0.32
Ever drinking alcohol	10 (15.2)	10 (18.2)	0	0.14
High salt intake	15 (22.7)	14 (25.5)	1 (9.1)	0.22
Ongoing exercise	58 (87.9)	49 (89.1)	9 (81.8)	0.40
Duration of HT (years)	6.9±3.9	6.7±3.7	7.9±5.0	0.33
Family history of HT	51 (77.3)	44 (80.0)	7 (63.6)	0.21
BMI (kg/m^2)	23.4±2.9	23.4±3.0	23.0±2.2	0.68
Overweight/obese	34 (51.5)	29 (52.7)	5 (45.5)	0.66
Dyslipidemia	20 (30.3)	16 (29.1)	4 (36.4)	0.44
Office SBP (mmHg) at week 12	134.0±10.8	131.2±8.2	149.5±9.1	<0.01*
Office DBP (mmHg) at week 12	77.7±9.4	76.2±7.7	85.6±13.1	<0.01*

NT = normotension; HT = hypertension; SBP = systolic blood pressure; DBP = diastolic blood pressure; HSBP = home systolic blood pressure; HDBP = home diastolic blood pressure; Elderly = age ≥60 years; n = number; BMI = body mass index; * *p*-value considered significant at <0.05

Table 3. Baseline laboratory findings of HT patients who finished study at 3 months, compared normotensive group and hypertensive group

Parameter	Mean ± SD or n (%)			*p*-value
	All (n = 66)	NT (n = 55)	HT (n = 11)	
FPG (mg/dL)	96.0±7.7	95.6±7.8	98.3±7.1	0.62
Serum Na (mmol/L)	141.5±2.1	141.5±2.1	141.1±2.1	0.79
Serum K (mmol/L)	4.0±0.3	4.0±0.3	4.0±0.3	0.99
BUN (mg/dL)	12.9±4.0	13.1±4.2	12.0±2.5	0.05
Cr (mg/dL)	0.8±0.2	0.8±0.2	0.8±0.1	0.17
CrCl (ml/min/1.73 m^2)	81.8±17.5	82.4±17.9	78.7±15.7	0.89
Uric acid (mg/dL)	5.12±1.2	5.2±1.2	4.7±1.5	0.26
Total cholesterol (mg/dL)	199.9±28.9	200.3±29.0	198.1±29.7	0.95
Triglyceride (mg/dL)	101.8±51.2	97.3±51.3	123.7±47.2	0.99
HDL-cholesterol (mg/dL)	64.8±17.8	66.0±18.7	58.7±11.3	0.10
LDL-cholesterol (mg/dL)	116.1±24.5	116.4±25.1	114.7±22.5	0.61

NT = normotension; HT = hypertension; n = number; FPG = fasting plasma glucose; Na = sodium; K = potassium; BUN = blood urea nitrogen; Cr = creatinine; CrCl = estimated creatinine clearance; HDL-cholesterol = high density lipoprotein cholesterol; LDL-cholesterol = low density lipoprotein cholesterol; * *p*-value considered significant at <0.05

Table 4. Percentages of patients who became hypertensive at week 12 classified by types of antihypertensive drugs

Type	Baseline (n)	Patients who became hypertensive (n/%)
Diuretics	7	2 (28.6)
CCB	26	9 (34.6)
Beta-blockers	13	4 (30.8)
ARB	35	11 (31.4)
ACEI	1	1 (100.0)
All	82	27 (32.9)

NB: 89 patients enrolled minus 7 patients who were self-prescribed without evidence of BP measurement = 82 patients. No significant difference in the conversion rate between each type of antihypertensive drugs.
CCB = calcium channel blockers; ARB = angiotensin receptor blockers; ACEI = angiotensin converting enzyme inhibitors

treated group, 14.6/10.5 mmHg (95% CI = 8.9-20.3/7.0-14.0) for CCB treated group, 8.4/6.7 mmHg (95% CI = -3.6-20.4/-2.4-15.8) for beta-blockers treated group, and 17.0/11.3 mmHg (95% CI = 11.9-22.0/8.0-14.5) for ARB treated group (Table 5). No adverse event was observed among those who became HT or remained NT. Moreover, no significant differences in re-medication rates between each type of anti-HT drug at the end of study (week 12) (Table 4).

Of the 66 patients, there were no significant differences of cardiovascular risk factors at baseline between the patients who did and did not remain NT after 12 weeks of drug withdrawal. Such risk factors included age, BMI, clinic BP levels, duration of HT, status on smoking, salty food consumption, alcoholic consumption, elderly (≥60 years), overweight (BMI ≥23 kg/m^2), rate of physical inactivity, coexisting dyslipidemia, and positive family history of hypertension. However, a significant higher rate of male sex who remained NT after 12 weeks of drug withdrawal as compared to that of female was noted (p = 0.02) (Table 2). There were also no significant differences in baseline laboratory values between the NT and the HT groups (Table 3).

Discussion

After HBP monitoring was performed for 2 weeks before enrollment, those patients who cannot stop the medication since their BP's rose shortly after discontinuation of anti-HT drugs and those who had anxiety or drug withdrawal effects were excluded. There were73 patients (82%) out of 89 patients enrolled who could stop anti-HT drugs at the end of the 2nd week. Sixteen patients (18.0%) who became HT had a higher BMI and a higher rate of overweight/obese compared to those who were still NT. BP may rise from anxiety about drug withdrawal. After 2 weeks of HBP measurement, 16 patients were excluded because some of them informed to have high BP by using their

Table 5. Changes of SBP/DBP levels among 66 patients who were able to complete the 3-month study classified by types of antihypertensive drugs

Type	Average BP (mean ± SD) (n = 66)		ΔBP from baseline (mean & 95%CI) (week 12-week 0)	
	SBP/DBP week 0 (mmHg)	SBP/DBP week 12 (mmHg)	ΔSBP (mmHg)	ΔDBP (mmHg)
Diuretics	121.0±10.2/68.2±8.1	134.5±14.5/71.2±5.5	13.5 (-4.9-31.9)	3.0 (-6.1-12.1)
CCB	121.2±7.2/68.8±6.0	135.8±8.6/79.3± 9.3	14.6 (8.9-20.3)	10.5 (7.0-14.0)
Beta-blockers	120.6±13.2/70.3±7.2	129.6±14.5/77.6±10.5	8.4 (-3.6-20.4)	6.7 (-2.4-15.8)
ARB	118.1±10.8/67.0±8.6	135.1±9.8/78.3±9.4	17.0 (11.9-22.0)	11.3 (8.0-14.5)
ACEI	123/81	144/85	21	4
All	119.8±10.1/68.4±7.7	134.5±10.8/77.9±9.3	14.7 (11.3-18.1)	9.5 (7.2-11.7)

NB: Change of SBP/DBP represent in mean (95% CI).
SBP = systolic blood pressure; DBP = diastolic blood pressure; CCB = calcium channel blockers; ARB = angiotensin receptor blockers; ACEI = angiotensin converting enzyme inhibitors

own home BP measurement devices while others had anxietyor withdrawal symptoms even though their BP's were still NT. In addition, seven patients (7.9%) self-administered antihypertensive drug under phone permission before the appointment. Therefore, BP control rate after antihypertensive drug withdrawal could be higher if they could comply to the protocol and remained in the study.

After excluded those who became HT, 55 patients (61.8%) out of 66 patients were still NT in this 3-month study. It was comparable to 62% reported from DeFelice et al ($p = 0.94$) in a 28-day-study[9]. Similarly, the study by Jenning et al[10] on the effect of anti-HT drug withdrawal showed that 28% out of 83 patients required re-institution of drug within 10 weeks[10]. It was comparable to the present study which found that 30.3% (18.0% at 2 weeks plus 12.3% at 3 months) of the studied population resumed anti-HT drugs.

It was possible that those patients who remained NT after discontinuing anti-HT drugs still ad hered to lifestyle modification, since significantly lower BMI & lower rate of overweight/obese were noted in the NT group compared to the HT group at week 2. However, these findings disappeared at week 12. The BP control rate at the end of this study (61.8%) was not significantly different from those remaining NT (78%) reported among the stage 1 HT patients who were assigned to the Established Recommendation which focused on total energy intake, the amount of sodium and alcohol intake plus DASH (Diet Approaches to Stop Hypertension) diet intervention group after 6 month follow-up[11]. There was no adverse event among those who became HT or those who remained NT observed at the end this short-term study. This finding was similar to the study by Hajjar and co-workers who reported on the effect of short-term (<3-4 weeks) withdrawal of anti-HT therapy in older HT patients which appeared to be safe in spite of mild elevation of BP levels[12]. The United States Food and Drug Administration (FDA) had confirmed that there were no differences in the risks associated with short-term placebo-controlled anti-HT clinical trials. Every placebo-controlled clinical trials submitted to the FDA on new antihypertensive drugs from 1973 through 2001 was analyzed. Clinical events were collected across 12,658 patient-years of observation; no differences in irreversible harmful outcomes between placebo and active drug treated patients were found[9]. The findings on the feasibility and safety of anti-HT drug withdrawal confirmed by this meta-analysis of the short-term placebo-controlled trials were beneficial. Therefore, the majority of stage 1 hypertension patients who performed lifestyle modifications had a good chance toremain NT after drug withdrawal without significant adverse events.

A high successful rate of anti-HT drug withdrawal was unlikely to be explained by BP measurement error since nearly all of them were instructed to do lifestyle modification before anti-HT drug administration. However, it is possible that those mild HT patients had WCH and they were treated due to ignorance of physicians.

Furthermore, the 2012 Cochrane reviewed on the treatment for mild hypertension had concluded that

anti-HT drugs used in healthy adults with stage 1 hypertension had not been shown to reduce mortality or morbidity in randomized clinical trials[2]. Therefore, the concept of with holding of an anti-HT drug for a short period with close blood pressure monitoring by using HBP device is feasible and useful. However, significant increase of office SBP/DBP levels to hypertensive range after 12 weeks of anti-HT drug withdrawal should alert physicians on the possibility that their patients did not ad here to lifestyle modification.

There were no significant differences in the withdrawal effects at the end of the 2nd week between each type of anti-HT drugs in terms of the rate and extent of BP elevation (data not shown). These findings were previously confirmed by Hajjar et al[12]. However, types of anti-HT drugs may influence upon the rate of elevation in BP levels if with holding the treatment is carried out for a longer period. The extent of SBP elevation after discontinuing the anti-HT drugs for 3 months was found to be significantly higher among those who previously received ARB as compared to those who previously received beta-blockers, 17.0 vs. 8.4 mmHg. This finding could be explained by the lower blood pressure baseline in the ARB treated group and the different potency of each anti-HT drugs[13]. However, the differences in baseline SBP/DBP levels between the 2 groups was not found. At 3 months of drug withdrawal, the differences in the rate of hypertensive reversal among anti-HT drug classes could not be found in this study, so did the study reported by Mitchell et al[14] and the study conducted by the medical research council working party[15].

Other factor that might influence on those patients who remained NT after discontinuing anti-HT drug was pursued. Withdrawal of beta-blockers that might be a negative predictor, once proposed by some investigators, for success in drug withdrawal was examined[13]. This can be explained by up-regulation of beta receptor secondary to beta blockade. Those patients who received high dose of beta-blockers cannot discontinue the drug abruptly. Otherwise, they will have palpitation and have to resume beta-blockers. However, the association between the discontinuation of beta-blockers and the rate of drug re-institution could not be found in the study, since nearly all of them had a low dose beta-blocker, i.e., atenolol 25 mg/day (data not shown). Smoking, alcohol drinking, high salt intake, exercise, duration of hypertension, family history of hypertension, overweight/obese, and dyslipidemia were not found to be predictors of the success of antihypertensive drug discontinuation, except for male sex which corresponded to that reported by Aylett et al[16]. One plausible explanation is that female patients tend to have more anxiety developed after discontinuation of their medication than male patients.

Conclusion

Fifty five patients out of 89 enrolled patients (61.8%) are still NT and able to stop anti-HT drug after 12 weeks follow-up. No adverse event was found. Male had a significant higher rate to remain NT than female. In addition, with holding of a low to medium dose of an anti-HT drug with close BP monitoring initially for a short period is applicable and quite safe in the patients whom BP's were well controlled for at least a year. On the contrary, anti-HT drug withdrawal should not be considered on HT patients who could not comply with lifestyle modification and those who have high cardiovascular risk or subclinical organ damage.

What is already known on this topic?

Withdrawal of some antihypertensive drug(s) or drug discontinuation could be performed if normalization of blood pressure was achieved for at least a year with the continuation of lifestyle modification.

What this study adds?

This study showed that more than half of those treated mild hypertensive patients could discontinue antihypertensive drugs and remained normotensive after short-term follow-up. However, long-term BP monitoring is needed.

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Potential conflicts of interest

None.

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การศึกษาถึงผลการหยุดยาลดความดันโลหิตในผู้ป่วยความดันโลหิตสูงที่ได้รับการควบคุมความดันโลหิตเป็นปกติ: ผลการศึกษาเบื้องต้น

พีระ บูรณะกิจเจริญ, เมธา ผู้เจริญชนะชัย, ปวิตรา ทองมา, ไรวินทร์ วิมลโสภณกิตติ

วัตถุประสงค์: เพื่อศึกษาหาความชุกของผู้ป่วยความดันโลหิตสูงที่ควบคุมความดันโลหิตที่โรงพยาบาลได้ (<140/90 มม.ปรอท) เป็นเวลาอย่างน้อย 1 ปี ซึ่งสามารถคงความดันโลหิตเป็นปกติหลังหยุดยาเป็นเวลา 12 สัปดาห์ร่วมกับประเมินลักษณะทางคลินิกของผู้ป่วยดังกล่าว

วัสดุและวิธีการ: คัดเลือกผู้ป่วยความดันโลหิตสูงที่ได้รับการควบคุมความดันโลหิตที่โรงพยาบาลได้เป็นเวลาอย่างน้อย 1 ปี โดยยังไม่มีการทำลายอวัยวะ ไม่เป็นเบาหวานและได้รับการรักษาด้วยยาลดความดันโลหิตชนิดเดียวในขนาดต่ำถึงปกติที่คลินิกความดันโลหิตสูง โรงพยาบาลศิริราช หลังเซ็นยินยอมเข้าโครงการวิจัย ได้ทำการเก็บข้อมูลทางระบาดวิทยา, ปัจจัยเสี่ยงต่อโรคหัวใจและหลอดเลือดและผลทางห้องปฏิบัติการที่ทำภายใน 1 ปี ผู้ป่วยจะได้รับการแนะนำให้หยุดยาลดความดันโลหิตที่รับประทานอยู่ และวัดความดันโลหิตที่บ้านวันละ 2 ครั้ง (เช้าและก่อนนอน) เป็นเวลา 2 สัปดาห์ ผู้ป่วยที่มีความดันโลหิตเฉลี่ยที่บ้านปกติ (<135/85 มม.ปรอท) จะได้รับการหยุดยาลดความดันโลหิตต่อและประเมินด้วยความดันโลหิตที่โรงพยาบาลอีก 10 สัปดาห์ต่อมา (สัปดาห์ที่ 12) ในกลุ่มที่มีความดันโลหิตเฉลี่ยที่บ้านสูง (ความดันโลหิตเฉลี่ยที่บ้าน ≥135/85 มม.ปรอท) จะให้ผู้ป่วยรับประทานยาเดิม ผู้ที่กลับเป็นความดันโลหิตสูงจากการวัดที่โรงพยาบาลในสัปดาห์ที่ 12 จะได้รับการแนะนำให้รับประทานยาต่อ

ผลการศึกษา: ผู้ป่วย 95 ราย ได้รับการคัดเลือกผู้ป่วย 6 ราย ถูกตัดออกเพราะไม่ได้กรอกข้อมูลความดันโลหิตที่บ้านครบตามกำหนด หลังหยุดยาลดความดันโลหิต 2 สัปดาห์ ผู้ป่วย 16 ราย จาก 89 ราย ที่เข้าโครงการมีความดันโลหิตเฉลี่ยที่บ้านสูง ผู้ป่วย 73 ราย (ร้อยละ 82) ยังมีความดันโลหิตเฉลี่ยที่บ้านปกติ สัปดาห์ที่ 12 ผู้ป่วย 7 ราย กลับไปรับประทานยาเองก่อนวันนัดตรวจ เหลือผู้ป่วย 66 ราย (ร้อยละ 74.1) สำหรับวิเคราะห์ พบผู้ป่วย 55 ราย (ร้อยละ 61.8) ยังคงมีความดันโลหิตวัดที่โรงพยาบาลปกติ และ 11 ราย (ร้อยละ 12.3) มีความดันโลหิตสูง ไม่พบว่ามีความแตกต่างอย่างมีนัยสำคัญในปัจจัยเสี่ยงต่าง ๆ ที่ทำการศึกษาระหว่างผู้ที่มีความดันโลหิตปกติและผู้เป็นความดันโลหิตสูงหลังสัปดาห์ที่ 12 ยกเว้นผู้ป่วยชายจะพบเป็นอัตราส่วนสูงกว่าที่พบในผู้หญิง ($p = 0.021$)

สรุป: ผู้ป่วย 55 ราย (ร้อยละ 61.8) จาก 89 ราย ที่เข้าโครงการวิจัยยังคงมีความดันโลหิตปกติหลังหยุดยาลดความดันโลหิตเป็นเวลา 12 สัปดาห์ พบอัตราผู้ป่วยชายที่ยังคงมีความดันโลหิตปกติสูงกว่าที่พบในผู้ป่วยหญิง