

An Observational Study on the Antihypertensive Management of High-Risk Patients in the Philippines

Michelle Marie Q. Pipo, M.D.*; Marievi A. Lelis, B.Sc.**; Jonas Q. Javelona, M.D.***

Abstract

Background: High-risk hypertensive patients often need immediate and more aggressive treatment to achieve adequate blood pressure (BP) control. There is currently no available Philippine data on the level of BP control and management specific to high-risk patients.

Objective: Primary Objective: To determine the prevalence of BP control in high-risk hypertensive patients.

Secondary Objectives:

1. To observe treatment pattern prescribed for high-risk hypertensive patients with uncontrolled BP.
2. To observe the change in BP after eight weeks of planned treatment modification.

Methods: This was a multicenter, observational disease registry of high-risk hypertensive patients based on the 2007 European Society of Hypertension/European Society of Cardiology guidelines. The study had two cross-sectional phases. Patient data, including level of BP control and any prescribed treatment modification, were collected on the first visit (V1). A second evaluation was done after eight weeks for patients with planned treatment modification (V2).

Results: In 804 patients with high-risk hypertension included in V1, only 37 patients (4.6%) had a baseline BP <130/80 mmHg. Treatment modification was planned in most patients by switching (352/804, 44%), adding antihypertensive agents (193/804, 24%) or increasing the treatment dose (33/804, 4.10%). Of the 325 patients with planned treatment modification evaluated at V2, 112 (34%) had no change in baseline treatment. After a mean treatment period of 5.66 weeks, there was a significant decrease from baseline in mean systolic (-23.95 mmHg) and diastolic (-9.26 mmHg) BP (both $p < 0.0001$). Among patients followed-up, 90% (294/325) achieved target systolic or diastolic BP levels, while 70% (228/325) achieved both target systolic and diastolic BP levels at study completion.

Conclusion: BP control in high-risk hypertensive Filipinos is low. Most physicians modified treatment in patients with uncontrolled BP and this was effective in significantly lowering BP. However, larger trials based on current treatment guidelines for hypertension are needed to compare the relative benefits of different types of treatment modification.

Keywords: hypertension; blood pressure; high-risk; treatment modification

Introduction

Markedly elevated blood pressure (BP) and factors such as concomitant diabetes, metabolic syndrome or evidence of target organ damage increase the risk of adverse cardiovascular outcomes in hypertensive patients. Studies have shown that there are significant and immediate benefits to effective BP control in these patients.¹⁻³

While current international guidelines use different criteria and treatment algorithms, combination therapy is often recommended in high-risk patients.¹⁻³ The 2013 European Society of Hypertension (ESH)/European

Society of Cardiology (ESC) guidelines suggest treatment modification by “dosing up”, “switching” or “adding” antihypertensive medications for patients who do not reach the recommended BP goal.¹ The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC7) specifies that combined treatment with a thiazide diuretic and an additional antihypertensive agent should be initiated for systolic BP (SBP) >20 mmHg or diastolic BP (DBP) >10 mmHg of the target BP (<140/90 mmHg or <130/80 mmHg for patients with diabetes or chronic kidney disease). Certain high-risk conditions are also compelling indications for the use of specific antihypertensive drug classes.²

Hypertension remains largely untreated and there is a need to convey current treatment recommendations to physicians.⁴⁻⁷ Physicians are reluctant to treat hypertension aggressively for fear of possible adverse events and hypotension. They may even delay

*Cardiologist, Manila Doctors Hospital, Manila

**Biometrician, Sanofi Aventis Philippines

***Medical Writer, MIMS Philippines

Corresponding Author: Michelle Marie Q. Pipo, MD, Manila Doctors Hospital, U.N. Avenue, Ermita, Manila, Philippines
E-mail: mich.pipomd@gmail.com

modifying treatment because they perceive that it may take months before the maximal effect of treatment is reached.⁸

In the Philippines, the 2007 Philippine Heart Association – Council on Hypertension Report on Survey of Hypertension and Target Organ Damage (PRESYON 2-TOD) noted that only 13% of hypertensive Filipinos had controlled BP, and up to 75% of treated patients were on monotherapy.⁹ There is currently no local data on BP control and the approach of physicians specific to the management of high-risk hypertensive patients. This study aims to assess the level of BP control in high-risk Filipinos with hypertension and evaluate the manner by which physicians in the Philippines modify treatment for this group of patients.

Methods

Study objectives

Primary objective

The primary objective of this study was to assess the current level of BP control in high-risk hypertensive patients.

Secondary objectives

There were two secondary objectives:

1. To assess treatment modification prescribed for high-risk hypertensive patients with uncontrolled BP; and,
2. To evaluate the change in BP after eight weeks of planned treatment modification.

Study design

This was a multicenter, observational, disease registry of adult patients with high-risk essential hypertension in 13 sites across the Philippines collected from January 2, 2010 to September 24, 2010. The study had a preliminary six-month recruitment phase followed by two cross-sectional phases at Day 0 (V1) and eight week (V2). Any follow-ups between V1 and V2 were done according to the physician's usual practice. (Figure 1). Eight hundred four patients were included at V1 and of these, 325 were included for evaluation and analysis of secondary outcomes at V2.

Evaluation criteria

Primary evaluation criteria

The primary evaluation criteria was the proportion of high-risk hypertensive patients who currently had a SBP of <130 mmHg and DBP of <80 mmHg.

Secondary evaluation criteria

The two secondary evaluation criteria were:

- (1) the proportion of patients for whom treatment

modification by dosing up, adding or switching to another agent was prescribed; and, (2) the change in BP in the different groups after planned treatment modification.

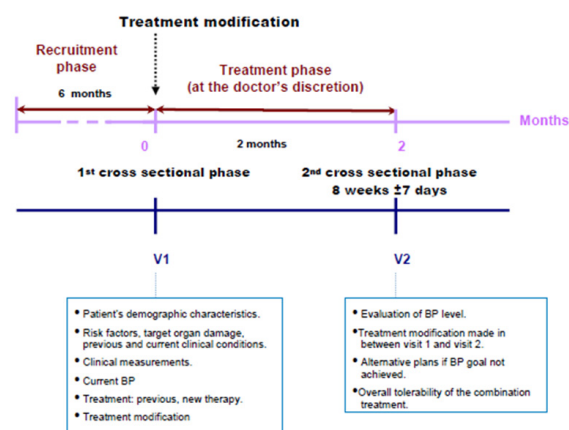


Figure 1: Study design

*V1, Visit 1; V2, Visit 2; BP, blood pressure.

Study population and selection criteria

Investigator and patient recruitment

The study included 804 patients of 72 participating physicians nationwide. Physicians were selected based on their level of expertise and were representative of doctors who manage high-risk patients with essential hypertension. Before beginning the trial, physicians involved in the study had signed the study protocol and had agreed that collected results may be published. Study patients were selected based on predetermined inclusion and exclusion criteria. Data release consent forms were signed by all patients or their legal representative before inclusion in the study.

Patient inclusion criteria

First cross-sectional phase

Patients were males or females ≥ 18 years of age diagnosed with essential hypertension and classified as high or very high risk based on the 2007 ESH/ESC guideline criteria (Table 1).⁵

Second cross-sectional phase

The second cross-sectional phase of the study included patients from the first cross-sectional phase who were previously or currently on antihypertensives and for whom treatment modification was planned.

Patient exclusion criteria

Pregnant and lactating patients, those with mild to moderate hypertension and no additional risk factors, or those with secondary hypertension were excluded from the study.

Table 1: High/Very high risk subjects based on 2007 ESH/ESC guidelines*

- BP ≥ 180 mmHg systolic and/or ≥ 110 mmHg diastolic
- Systolic BP > 160 mmHg with low diastolic BP (< 70 mmHg)
- Diabetes mellitus
- Metabolic syndrome
- ≥ 3 cardiovascular risk factors
- One or more of the following subclinical organ damages:
 - Electrocardiographic (particularly with strain) or echocardiographic (particularly concentric) left ventricular hypertrophy
 - Ultrasound evidence of carotid artery wall thickening or plaque
 - Increased arterial stiffness
 - Moderate increase in serum creatinine
 - Reduced estimated glomerular filtration rate or creatinine clearance
 - Microalbuminuria or proteinuria
- Established cardiovascular or renal disease

ESH, European Society of Hypertension; ESC, European Society of Cardiology; BP, blood pressure.

*Adapted from Mancia G, et al. 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens 2007;25:1105-87.

Study procedures and data collection

Visit schedules

First cross-sectional phase (V1)

The following data were collected by physicians for patients screened and enrolled in the study: patient demographics, existing risk factors, target organ damage, associated clinical conditions, current BP (measured with a standard calibrated sphygmomanometer and taken in the seated position, five to 10 minutes after the cuff was applied), baseline antihypertensive treatment and prescribed antihypertensive treatment.

Second cross-sectional phase (V2)

Data collected at V2 included the current BP, any treatment modifications made between V1 and V2, attainment of target BP, treatment plan if target BP was not achieved and drug tolerability.

Data collection form entry and validation

Physicians or their designated representatives entered all data in data collection forms (DCFs) distributed by the sponsor. All corrections to the DCFs were dated and initialed by the study personnel. Completed original DCFs were collected by the sponsor while the physicians retained a duplicate copy of the DCFs.

Computerized handling of the DCFs was done by the sponsor and the investigator was obligated to respond to any generated additional requests by confirming or modifying the data in question. Requests and responses were appended to the DCFs held by both the investigator and sponsor. Data collection and validation procedures were detailed in appropriate operational documents.

Withdrawal of patients from study

Investigators were tasked to make every effort to contact patients who failed to follow-up at V2, identify the reasons for failure to attend the visit, and determine their health status. Patients who failed to complete the study and for whom no endpoint data were available were considered lost to follow-up.

2.6 Statistical methodology

Determination of sample size

BP control rate was set at 13% based on the result of the PRESYON 2-TOD study.⁹ The sample size was computed for a 3.0% precision rate and a 5% level of significance. The following formula was used: $n = (Z^2 \cdot P(1-P))/d^2$; where, $Z=1.96$; $p=0.13$ (BP control rate); $d=0.03$ (precision rate); and $n=483$. At least 537 patients were targeted to allow for a 10% drop-out rate.

Statistical analysis

Statistical analysis was done on all patients eligible for the registry. Data were summarized using mean, median, standard deviation, range for continuous parameters and counts and percentages for categorical parameters. All statistical tests were performed using two-tailed tests with a 5.0% level of significance. Subgroup analyses based on the manner of treatment modification were performed for secondary outcomes.

Results

Primary Evaluation Criteria

A total of eight hundred four (804) high-risk hypertensive patients were included in the first phase of the study. Among these, only 37 or 4.6% had controlled hypertension (BP $< 130/80$ mmHg). The number of patients with BP $< 140/90$ mmHg was 123 or 15.3%.

Patient baseline characteristics, risk factors and hypertensive medical history

Forty-seven percent of enrolled patients were males. The mean age of the overall population was 56.16 ± 11.93 years and baseline BP was $150.46/89.99$ mmHg. The average duration of hypertension was 7.34 ± 5.91 years and approximately 10% (77/804) of patients were newly diagnosed at the time of inclusion in the study. Eighty-four percent (677/804) had received antihypertensive treatment, with 51.87% (417/804) on monotherapy. Other baseline characteristics are listed in Table II.

Seventy-five percent (602/804) had at least three cardiovascular risk factors. Sedentary lifestyle (560/804, 69.65%), history of smoking (409/804, 50.87%) and old age (262/804, 32.59%) were among the risk factors noted.

Table II: Baseline characteristics and hypertensive medical history of patients with uncontrolled versus controlled blood pressure

Characteristics	Uncontrolled	Controlled	Total	p-value
No. of patients (% of total)	767 (95.40)	37 (4.60)	804 (100)	
Males, n=784 (% of total)	367 (47.85)	13 (35.14)	380 (47.26)	0.2030
Age (years), n=799	55.94±12.03	60.84±8.45	56.16±11.93	0.0051
SBP (mmHg), n=804	152.36±17.56	111.08±8.43	150.46±19.29	<0.0001
DBP (mmHg), n=804	91.13±9.79	66.54±4.89	89.99±10.91	<0.0001
Height (cm), n=784	162.07±7.04	163.72±6.59	162.14±7.02	0.2555
Weight (kg), n=786	65.69±9.99	65.94±9.17	65.7±9.95	0.4125
BMI (kg/m ²), n=783	25.05±3.75	24.57±2.81	25.02±3.71	0.3604
BMI≥23 kg/m ² (%)	527 (68.71)	24 (64.86)	551 (68.53)	0.6228
BMI≥25 kg/m ² (%)	330 (43.02)	15 (40.54)	345 (42.91)	0.7656
Previously diagnosed (%)	690 (89.96)	37 (100)	727 (90.42)	0.0173
Duration of hypertension (years)*, n=504	7.3±5.97	8.26±4.67	7.34±5.91	0.0467
Previous anti-hypertensive treatment† (%)	641 (83.57)	36 (97.30)	677 (84.21)	0.0169
Monotherapy (%)	396 (51.63)	21 (56.76)	417 (51.87)	0.1272
Combination therapy (%)	239 (31.16)	15 (40.54)	254 (31.59)	

SBP, systolic blood pressure; DBP, diastolic blood pressure;

BMI, body mass index.

*n=223, unknown duration of hypertension; †n=6, unknown treatment.

Table III: Existing risk factors for uncontrolled versus controlled hypertensive patients

Existing risk factors	Uncontrolled	Controlled	Total	p-value
No. of patients	767	37	804	
≥ 3 CV risk factors	571 (74.45)	31 (83.78)	602 (74.88)	0.2009
Age (Male >55 years; Females >65 years)	248 (32.33)	14 (37.84)	262 (32.59)	0.4854
Smoker	393 (51.24)	16 (43.24)	409 (50.87)	0.3420
Sedentary lifestyle	533 (69.49)	27 (72.97)	560 (69.65)	0.6528
Diabetes	337 (43.94)	18 (48.65)	355 (44.15)	0.5730
Dyslipidemia	464 (60.50)	32 (86.49)	496 (61.69)	0.0015

Family history of premature CV disease	392 (51.11)	12 (32.43)	404 (50.25)	0.0265
--	-------------	------------	-------------	--------

Other risk factors	21 (2.74)	2 (5.41)	23 (2.86)	0.2862
--------------------	-----------	----------	-----------	--------

CV, cardiovascular.

Dyslipidemia and diabetes were observed in 61.69% (496/804) and 44.15% (355/804), respectively (Table III). Fifty-two percent (418/804) had evidence of target organ damage such as left ventricular hypertrophy (318/804, 39.55%), microalbuminuria (231/804, 28.73%) and increased plasma creatinine (156/804, 19.40%) (Table IV).

Table IV: Target organ damage in patients with uncontrolled versus controlled hypertension

Target organ damage	Uncontrolled	Controlled	Total	p-value
No. of patients	767	37	804	
At least one target organ damage	385 (50.20)	33 (89.19)	418 (51.99)	<0.0001
Microalbuminuria	208 (27.12)	23 (62.16)	231 (28.73)	<0.0001
Increased plasma creatinine	136 (17.73)	20 (54.05)	156 (19.40)	<0.0001
Left ventricular hypertrophy	288 (37.55)	30 (81.08)	318 (39.55)	<0.0001

The study population included patients with a history of cerebrovascular accidents (transient ischemic attack (TIA) or stroke, (133/804) 16.54%), coronary heart disease (199/804, 24.75%), atrial fibrillation (43/804, 5.35%), congestive heart failure (134/804, 16.67%), peripheral arterial disease (59/804, 7.34%) and retinopathy (47/804, 5.85%) (Table V).

Prescribed antihypertensive treatment

Majority of patients (493/804, 61.32%) at the end of V1 were prescribed angiotensin II receptor blockers (ARBs), followed by a fixed-dose combination of ARB plus hydrochlorothiazide (181/804, 22.51%), calcium channel blockers (162/804, 20.15%) and beta blockers (94/804, 11.69%). Most were maintained on monotherapy (429/767, 55.93%). The number of patients prescribed combination therapy increased from 31.59% (254/804) at baseline to 43.28% (348/804) at the end of V1. Most patients on combination therapy were given two different classes of antihypertensives (298/804, 37.06%) (Table VI).

Table V: Associated clinical conditions in uncontrolled versus controlled hypertensive patients

Associated clinical conditions	Uncontrolled	Controlled	Total	p-value
No. of patients	767	37	804	
≥ 1 associated or previous clinical condition (%)	327 (42.63)	30 (81.08)	357 (44.50)	<0.0001
Cerebrovascular [stroke, TIA] (%)	130 (16.95)	3 (8.11)	133 (16.54)	0.1575
Coronary heart disease (%)	174 (22.69)	25 (67.57)	199 (24.75)	<0.0001
Atrial fibrillation (%)	35 (4.56)	8 (21.62)	43 (5.35)	0.0004
Congestive heart failure (%)	116 (15.12)	18 (48.65)	134 (16.67)	<0.0001
Peripheral arterial disease (%)	52 (6.78)	7 (18.92)	59 (7.34)	0.0143
Retinopathy (hemorrhages, papillary edema) (%)	46 (6.00)	1 (2.70)	47 (5.85)	0.7176

TIA, transient ischemic attack.

Table VI: Prescribed antihypertensive treatment in uncontrolled versus controlled hypertensive patients

Antihypertensive treatment	Uncontrolled	Controlled	Total	p-value
No. of patients	767	37	804	
Treatment regimen*				
Monotherapy (%)	429 (55.93)	22 (59.46)	451 (56.09)	0.0408
Combination therapy (%)	334 (43.55)	14 (37.84)	348 (43.28)	
2 (%)	286 (37.29)	12 (32.43)	298 (37.06)	
3 (%)	43 (5.61)	2 (5.41)	45 (5.60)	
4 (%)	5 (0.65)	0 (0.0)	5 (0.62)	
Beta blockers (%)	82 (10.69)	12 (32.43)	94 (11.69)	<0.0001
Diuretics (%)	39 (5.08)	1 (2.70)	40 (4.98)	0.5151
ACE inhibitors (%)	40 (5.22)	5 (13.51)	45 (5.60)	0.0320
Angiotensin II receptor blockers (%)	468 (61.02)	25 (67.57)	493 (61.32)	0.4242
Calcium channel blockers (%)	155 (20.21)	7 (18.92)	162 (20.15)	0.8485
ARB+HCTZ (Fixed-dose) (%)	180 (23.47)	1 (2.70)	181 (22.51)	0.0031
Others/Fixed-dose combinations (%)	5 (0.65)	0 (0.0)	5 (0.62)	0.06597

ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker; HCTZ, hydrochlorothiazide.

*n=5, antihypertensive medications were not specified.

Secondary evaluation criteria**Treatment modification**

The proportion of patients for whom physicians decided to modify antihypertensive treatment was 71.89% (578/804). Forty-four percent (352/804) were switched to a new class of antihypertensive, 24% (193/804) were given additional antihypertensive agents and 4.10% (33/804) were maintained on the same drug/s at a higher dose (Table VII). Thirty-four percent of those for whom treatment modification was planned (112/325) and were included for a second visit (V2) had not changed their baseline hypertensive treatment at follow-up.

Table VII: Treatment approach of physicians for patients with uncontrolled and controlled hypertension at baseline

Treatment approach	Uncontrolled	Controlled	Total
No. of patients in the cross-sectional phase	767	37	804
With treatment modification (%)	577 (75.23)	1 (2.70)	578 (71.89)
Increased dose (%)	33 (4.30)	0 (0.0)	33 (4.10)
Added new treatment (%)	193 (25.16)	0 (0.0)	193 (24.0)
Switched to a new treatment (%)	351 (45.76)	1 (2.70)	352 (43.78)
No change (%)	190 (24.77)	36 (97.30)	226 (28.11)

Change in blood pressure

Table VIII shows the change in BP of patients with or without treatment modification at follow-up. There was a significant overall decrease in BP in patients with or without treatment modification who were seen at V2 after an average of 5.66 ± 3.55 weeks ($p < 0.0001$). Mean SBP decreased to 124.35 ± 11.68 mmHg from a baseline of 150.46 ± 19.29 mmHg. Mean DBP also decreased to 78.11 ± 7.94 mmHg at follow-up from 89.99 ± 10.91 mmHg at baseline.

SBP decreased by 29.41 ± 16.49 mmHg in patients whose treatment was modified. This reduction was significantly greater than the decrease in SBP noted in patients whose treatment had not changed (-13.57 ± 16.81 mmHg). Likewise, the mean decrease in DBP was significantly greater in patients with treatment modification than in those maintained on the same treatment (-10.55 ± 9.03 versus -6.8 ± 11.22 mmHg, respectively). However, after adjusting for differences in BP levels at baseline, mean changes in SBP and DBP were significantly in favor of patients whose treatment was not modified.

BP reduction from baseline was significant in patients switched to a new antihypertensive agent or given additional antihypertensive medications (both $p < 0.0001$). Although there was no significant BP improvement in six patients whose treatment doses were increased, the study was not powered enough to detect the true effect of increasing the antihypertensive dose in this small group (Table IX).

Table VIII: Mean change in baseline blood pressure and level of blood pressure control after eight weeks in patients with or without treatment modification

	No change in treatment	Treatment modified	Total	p-value
No. of patients at baseline	226	578	804	
No. of patients followed-up	112	213	325	
SBP at baseline	135.97±20.81	156.13±15.33	150.46±19.29	<0.0001
SBP at Visit 2	117.95±10.67	127.72±10.75	124.35±11.68	<0.0001
Change in SBP	-13.57±16.81	-29.41±16.49	-23.95±18.21	<0.0001
Adjusted* change in SBP	-26.29	-22.73		0.0113
p-value	<0.0001	<0.0001	<0.0001	
DBP at baseline	83.37±11.89	92.58±9.31	89.99±10.91	<0.0001
DBP at Visit 2	74.11±8.55	80.21±6.72	78.11±7.94	<0.0001
Change in DBP	-6.8±11.22	-10.55±9.03	-9.26±9.98	<0.0001
Adjusted* change in DBP	-11.62	-8.02		0.0001
p-value	<0.0001	<0.0001	<0.0001	
SBP and DBP ≤ Target BP (%)	90 (80.36)	138 (64.79)	228 (70.15)	0.0036
SBP or DBP ≤ Target BP (%)	107 (95.54)	187 (87.79)	294 (90.46)	0.0239
SBP <140 mmHg/DBP <90 mmHg (%)	101 (90.18)	163 (76.53)	264 (81.23)	0.0027
SBP <130 mmHg/DBP <80 mmHg (%)	57 (50.89)	25 (11.74)	82 (25.23)	<0.0001

SBP, systolic blood pressure; DBP, diastolic blood pressure.

*Adjusted for the differences in blood pressure levels at baseline.

Table IX: Mean change in baseline blood pressure and level of blood pressure control after 8 weeks by type of treatment modification

	Change in antihypertensive treatment		
	Add	Increased dose	Switched
No. of patients at baseline	193	33	352
No. of patients followed-up	83	6	124
SBP at baseline	156.78±13.86	156.06±22.63	155.78±15.29
SBP at Visit 2	126.27±9.72	126.67±17.51	128.75±11.02

Change in SBP	-31.45±16.16	-15.00±15.17	-28.75±16.49
p-value	<0.0001	0.0599	<0.0001
DBP at baseline	92.32±8.51	93.03±8.83	92.68±9.78
DBP at Visit 2	79.58±5.64	81.67±9.83	80.56±7.22
Change in DBP	-11.41±8.13	-8.33±11.69	-10.08±9.48
p-value	<0.0001	0.1412	<0.0001
SBP and DBP ≤ Target BP	64 (77.11)	5 (83.33)	69 (55.65)
SBP or DBP ≤ Target BP	77 (92.77)	5 (83.33)	105 (84.68)
SBP <140 mmHg/DBP <90 mmHg (%)	68 (81.93)	5 (83.33)	90 (72.58)
SBP <130 mmHg/DBP <80 mmHg (%)	10 (12.05)	1 (16.67)	14 (11.29)

SBP, systolic blood pressure, DBP, diastolic blood pressure, BP, blood pressure.

Management approach for patients who did not achieve target BP

Of the 325 patients followed up, 294 or 90.46% of patients at follow-up had achieved either their SBP or DBP target, while 70.15% (228/325) achieved both SBP and DBP targets. There were 97 patients who had not reached either their SBP or DBP goal at the end of the study. Management for these patients is described in Table X.

Table X: Percentage of patients who achieved target BP and management approach for patients who did not achieve target blood pressure after 8 weeks

Achievement of Target BP	Frequency	Percentage
No. of followed-up patients	325	100
SBP or DBP ≤ target BP	294	90.46
SBP and DBP ≤ target BP	228	70.15
Management approach for patients who did not achieve target BP	97	29.85
Increase dosage of medication	16	16.49
Use another fixed combination	2	2.06
Use another free combination	1	1.03
Add a drug from another class	2	2.06
Educate the patient about his hypertension	46	47.42
Provide compliance tools	37	38.14
Reinforce lifestyle advice	48	49.48
Other	3	3.09

BP, blood pressure, SBP, systolic blood pressure, DBP, diastolic blood pressure.

Discussion

High-risk hypertensive patients represent a special group that requires different treatment goals and strategies compared with other patients.⁵ Despite the availability of different antihypertensive medications, hypertension remains poorly controlled.^{6,7,9} The approach of physicians to treatment and patient compliance are key factors that directly influence

Physicians modified treatment in patients with uncontrolled BP primarily by switching to a different antihypertensive class or adding additional antihypertensive agents. This approach is consistent with current ESH/ESC and JNC7 guidelines.^{1,2} However, 34% of patients for whom treatment modification was planned at V1 and had been monitored for follow-up (V2) had not changed their baseline treatment regimen. It was not evident if this was due to poor compliance, drug intolerance, or an observed improvement in BP control with baseline treatment.

There was a significant decline in mean BP from 150/90 mmHg to 124/78 mmHg after an average treatment period of 5.66 weeks. BP target was achieved in 70% of patients at the end of the study, while 90% had reached either their SBP or DBP goal. Switching or adding antihypertensive treatment resulted in significant BP reductions. Significant reductions in BP were also noted in patients with no treatment modification. Patients in whom treatment had not been changed had significantly lower mean baseline BP than those with treatment modification (135.97/83.37 versus 156.13/92.58, respectively; $p < 0.0001$). SBP and DBP reductions adjusted for differences in baseline BP were also more favorable in these patients.

Limitations of the Study

This study evaluated the treatment prescribed by physicians for high-risk patients with hypertension. However, treatment bias in favor of the study sponsor cannot be discounted. Inclusion in the study may also have led to better patient compliance and closer physician monitoring and may explain the BP improvements observed in patients with no treatment modification at follow-up. Additionally, because of the small follow-up sample size and few patients whose treatment doses were increased, head-to-head comparisons between different types of treatment modification were not possible.

Conclusion

BP control in high-risk Filipinos is poor and more aggressive BP control is warranted. This study supports treatment modification as an effective means of improving BP status and should be considered for the initial management of high-risk individuals. While switching or prescribing additional antihypertensives can significantly lower BP, a more comprehensive multicenter trial involving a larger sample size is needed to compare the relative benefits of switching, adding or increasing treatment dose in high-risk hypertensive patients. It is also recommended that future trials be based on the updated 2013 ESH/ESC guideline criteria.

Disclosure

Dr. Michelle Pipo was an investigator but received no funding as corresponding author for this paper. She develops modules and is invited to do presentations by Sanofi and receives fees for providing these services. Ms. Marievi A. Lelis was an employee of Sanofi and was the Biometrician at the time the study was conducted. Dr. Jonas Q. Javelona did not receive any funding for the services he provided the company.

Acknowledgement

Sanofi-aventis Philippines, Inc. wishes to acknowledge and express gratitude to the following investigators for their invaluable contributions to the study: Dr. Mark Resty Rivera, Dr. Valerie Valdez, Dr. Sharon R. Pascua, Dr. Nicole Reyes, Dr. Odeson Estabello, Dr. Maria Jasmin D. Ortiz, Dr. Kristian Patrick Chan, Dr. Allan Lim, Dr. Maria Cristina M. Jauculan, Dr. Jerelyn Adviento, Dr. Jean D. Alcover, Dr. Camilo G. Te Jr., Dr. Claudine Ong, Dr. Maidenlove Raguero, Dr. Angelo Javier, Dr. Jose Donato Magno, Dr. Michelle Marie Q. Pipo, Dr. Peter Carlo Nierras, Dr. Khristine Tumambiene, Dr. Jill Irene Capistrano, Dr. Michael T. Reyes, Dr. Gino Rel Quizon, Dr. Vin I. Samonte, Dr. Joyce Dico-Go, Dr. Leovino Acharon, Dr. Felimon Flavier, Dr. Joel Paolo Nocom, Dr. Ritchie Go, Dr. Michelleen D. Corrales, Dr. Regina Yao, Dr. Jansen Mancera, Dr. Chris Asido-Regina Yao, Dr. Ma. Cecilia Bondoc, Dr. Gilbert Villela, Dr. Joseph Cal, Dr. Paolo Buenaventura, Dr. Kriska Duff, Dr. Nicolo Salallima, Dr. Irene Celedonio, Dr. Sharon Diego, Dr. Claro Antonio, Dr. Rodney Jimenez, Dr. Alma Carandang, Dr. Joengelee Montalbo, Dr. Gail Culla, Dr. Glenn Gayos, Dr. Francis Fernandez, Dr. Estrelita Bitong, Dr. Michael Rosario, Dr. Danivic Ramirez, Dr. Cristina Chua, Dr. Nerissa Ang, Dr. Jowett Golangco, Dr. Rojohn Maliwat, Dr. Brenda Espinosa, Dr. Daniel Ynzon Jr., Dr. Dick L. Ong, Dr. Chainelyn B. Dacasin, Dr. Gretchen Parayno, Dr. Teoceles D. Olivar, Dr. Melanie Gail Hamoy, Dr. Rosario Franco-Aceron, Dr. Rene Juaneza, Dr. Raymund Darius C. Liberato, Dr. Karen Ann Querequincia, Dr. Hiede Quino, Dr. Suzette H. Solis, Dr. Annalyn Vistudazo, Dr. Noreen April C. Pascual, Dr. Candice Faye Chua-Sanchez, Dr. Aurora Nirisma and Dr. Dharyl Guillermo.

Sanofi-aventis Philippines, Inc. also wishes to acknowledge the participation and involvement of the following institutions in this study: Manila Doctors Hospital, Philippine General Hospital, Chinese General Hospital, Jose Reyes Memorial Medical Center, Santo Tomas University Hospital (Cardiology Fellows), Philippine Heart Center, UERM Medical Center, St.

Luke's Medical Center, Makati Medical Center, Baguio General Medical Center, Cebu Doctors Hospital, Iloilo Doctors Hospital and Davao Med Center (Family Medicine Department).

References

1. Mancia G, Fagard R, Narkiewicz K, Redón J, Zanchetti A, Böhm M, Christiaens T, Cifkova R, De Backer G, Dominiczak A, Galderisi M, Grobbee DE, Jaarsma T, Kirchhof P, Kjeldsen SE, Laurent S, Manolis AJ, Nilsson PM, Ruilope LM, Schmieder RE, Sirnes PA, Sleight P, Viigimaa M, Waeber B, Zannad F. 2013 ESH/ESC guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens*. 2013;31:1281-57.
2. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The 7th Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The JNC 7 Report. *JAMA*. 2003;289:2560-72.
3. Whitworth JA; World Health Organization, International Society of Hypertension Writing Group. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. *J Hypertens*. 2003;21:1983-92.
4. Pechère-Bertschi A, Greminger P, Hess L, Philippe J, Ferrari P. Swiss Hypertension and Risk Factor Program (SHARP): Cardiovascular risk factors management in patients with type 2 diabetes in Switzerland. *Blood Pressure*. 2005;14:377-44.
5. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, Grassi G, Heagerty AM, Kjeldsen SE, Laurent S, Narkiewicz K, Ruilope L, Rynkiewicz A, Schmieder RE, Boudier HA, Zanchetti A, Vahanian A, Camm J, De Caterina R, Dean V, Dickstein K, Filippatos G, Funck-Brentano C, Hellemans I, Kristensen SD, McGregor K, Sechtem U, Silber S, Tendera M, Widimsky P, Zamorano JL, Erdine S, Kiowski W, Agabiti-Rosei E, Ambrosioni E, Lindholm LH, Viigimaa M, Adamopoulos S, Agabiti-Rosei E, Ambrosioni E, Bertomeu V, Clement D, Erdine S, Farsang C, Gaita D, Lip G, Mallion JM, Manolis AJ, Nilsson PM, O'Brien E, Ponikowski P, Redon J, Ruschitzka F, Tamargo J, van Zwieten P, Waeber B, Williams B; Management of Arterial Hypertension of the European Society of Hypertension; European Society of Cardiology. 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens*. 2007;25:1105-87.
6. Singh RB, Suh IL, Sing VP, Chaithiraphan S, Laothavorn P, Sy RG, Babilonia NA, Rahman AR, Sheikh S, Tomlinson B, Sarraf-Zadigan N. Hypertension and stroke in Asia: prevalence, control and strategies in developing countries for prevention. *J Hum Hypertens*. 2000;14:749-63.
7. Gu D, Reynolds K, Wu X, Chen J, Duan X, Muntner P, Huang G, Reynolds RF, Su S, Whelton PK, He J; InterASIA Collaborative Group. The International Collaborative Study of Cardiovascular Disease in ASIA. Prevalence, awareness, treatment, and control on hypertension in China. *Hypertension*. 2002;40:920-7.
8. Ferrari P, Hess L, Pechère-Bertschi A, Muggli F, Burnier M. Reasons for not intensifying antihypertensive treatment (RIAT): A primary care antihypertensive intervention study. *J Hypertens*. 2004;22:1221-9.
9. Sison J, Arceo LP, Trinidad E, Bautista AJ, Buan E, Chua P, Lapitan R, Neri R, Punzalan A, Tan M, Torres DJ, Yape IM. Philippine Heart Association – Council on Hypertension Report on Survey of Hypertension and Target Organ Damage (PRESYON 2-TOD*) A report on prevalence of hypertension, awareness, treatment profile and control rate. *Philipp J Cardiol*. 2007;35:1-9.