Research Paper

Effect of Antihypertensive Pharmacotherapy on Oscillometric Pulse Wave Analysis Parameters in Treated Gujarati Hypertensives: A Cross-Sectional Study

Jayesh Dalpatbhai Solanki, Hemant B. Mehta, Sunil J. Panjwani¹, Hirava B. Munshi¹, Chinmay J. Shah Departments of Physiology and ¹Medicine, Government Medical College, Bhavnagar, Gujarat, India

Abstract

Objective: To study the effect of different classes and combinations of antihypertensive agents on arterial stiffness and central hemodynamic parameters. **Materials and Methods:** A cross-sectional study was conducted in 446 treated apparently healthy hypertensives. Oscillometric PWA was performed by Mobil-o-Graph (IEM, Germany) to derive cardiovascular parameters that were further analyzed in groups stratified by antihypertensive used. Study parameters were brachial hemodynamics (blood pressure (BP), heart rate, and rate pressure product); arterial stiffness (augmentation pressure, augmentation index, pulse wave velocity, total arterial stiffness, and pulse pressure amplification); and central hemodynamics (central BP, cardiac output, and stroke work). Statistical significance was kept at P < 0.05. **Results:** All groups were selected by matching of age, gender, and body mass index. They were comparable with major confounding factors. There was no difference between study parameters in hypertensives taking exclusive angiotensin-converting enzyme inhibitor (ACEI), calcium channel blocker (CCB), or angiotensin II receptor blocker. Multitherapy showed better hemodynamics and monotherapy showed better stiffness parameters. Addition of CCB to ACEI did not make a difference except with diastolic BP. For most comparisons, most of the results lacked statistical significance. **Conclusion:** Discrete PWA parameters showed no class difference in hypertensives, treated by conventional monotherapy or combination, ACEI appears to be the best drug. This also indicates that early diagnosis and blood pressure control are more important than antihypertensive used.

Keywords: Antihypertensive, arterial stiffness, blood pressure, hemodynamic, pulse wave analysis

INTRODUCTION

Hypertension is prevalent in 33% of urban Indians and there is enormous cost of pharmacotherapy for the same.^[11] Hypertension is the cause of major cardiovascular morbidity and mortality^[2] and known to inflict at younger age. Measuring brachial blood pressure (bBP) is a routine, but it is not a direct measure. BP is not the only determinant of cardiovascular risk.^[3] Parameters inferring about functioning of aorta and heart are more discrete in this regard. Normal bBP does not ensure about the status aortic compliance and accelerated hemodynamics. Similarly, different antihypertensives are used with varying mechanism, results, and combinations across the globe.^[4] Antihypertensives have different modes of action for this primary essential disease, and normally, it is studied with respect to peripheral BP. These drugs have some difference in effect on central BP (cBP), hemodynamics,

Access this article online Quick Response Code: Website:

www.jpharmacol.com

DOI: 10.4103/jpp.JPP_59_18

and arterial stiffness^[5] that is suggested but not adequately tested, especially in Indians. In this case, there is a need for a bBP independent tool^[6] that infers about central hemodynamics and arterial stiffness. Pulse wave analysis (PWA) gives an opportunity to measure these parameters simultaneously, noninvasively, and objectively.^[7] Introduction of oscillometric cuff-based devices such as Mobil-O-Graph^[8] and invention-generalized transfer factor has enabled the

> Address for correspondence: Dr. Jayesh Dalpatbhai Solanki, F1, Shivganga Appartments, Plot No. 164, Bhayani Ni Waadi, Opposite Bawaliya Hanuman Temple, Gadhechi Wadlaa Road, Bhavnagar - 364 001, Gujarat, India. E-mail: drjaymin 83@yahoo.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Solanki JD, Mehta HB, Panjwani SJ, Munshi HB, Shah CJ. Effect of antihypertensive pharmacotherapy on oscillometric pulse wave analysis parameters in treated Gujarati hypertensives: A cross-sectional study. J Pharmacol Pharmacother 2018;9:153-9. Received: 08-05-2018 Revised: 05-08-2018 Accepted: 17-08-2018

153

measurement of aortic and central hemodynamic parameters validated against intraoperatively invasively measured direct results.^[9] Using same technique in treated hypertensives, we studied the effect of antihypertensive drugs, as monotherapy or combination, on cardiovascular parameters measured by PWA.

Materials and Methods

Study setup and design

We conducted a cross-sectional study on medicine outdoor patients of a tertiary care teaching government hospital attached to a government medical college under the guidance of the departments of physiology and medicine from June 18, 2015 to March 2, 2018. Our study protocol was approved by the Institutional Review Board of our college.

Inclusion and exclusion criteria

We included apparently healthy nonathletic individuals, taking antihypertensives since at least 1 year, aged 15–65 years, of either sex, nonsmoking, nonalcoholic, not known for any acute or chronic systemic disease, and ready to give written consent. Apart from lack of these criteria, we excluded participants using any alternative system of medicines/lifestyle managements such as yoga and meditation.

Study groups

The sample size was calculated by Raosoft software (Raosoft, Inc., free online software, Seattle, WA, USA). To have 95% confidence level, 5% precision, and considering response distribution 33%, a sample size of 474 was adequate for population of the city (6 lakhs).

We screened and enrolled 700 apparently healthy hypertensives from general medicine outdoor patient department by simple random sampling. Out of these, we excluded 140 new hypertensives (duration <1 year), 68 due to the history of irregular treatment, 10 due to use of lifestyle modification, 3 due to irregular pulse wave recording, 2 due to morbid obesity, and 2 owing to arm circumference beyond available cuff size.

Subject assessment and definitions

All participants were personally interviewed in the form of questionnaires including general features, demographic characteristics, risk factor, and relevant history. A detailed history of pharmacotherapy used was elicited from each hypertensive and regularity was confirmed by patient's case report chart. Systolic BP (SBP) \geq 140 mmHg and diastolic BP (DBP) \geq 90 mmHg or use of antihypertensive medication were defined as hypertension. SBP <140 mmHg and DBP <90 mmHg were taken as BP control.

Instrument used

We used portable, personal computer attached calibrated^[8] and validated^[9] instrument Mobil-O-Graph (IEM Gmbh, Stolberg, Germany) of physiology department to record brachial pulse wave. It undergoes oscillometric PWA as per protocol designed

by European Society of Hypertension and analysis of pressure pulse wave.

Pressure oscillations are generated by brachial arterial pulsation which are transmitted to bBP cuff and measured by transducer to be fed into microprocessor. Computerized software records pulse wave of brachial artery and by validated a generalized transfer factor derives central aortic pulse wave. It further undergoes point-based and area-based analysis by computer to derive various cardiovascular parameters.

Measurement protocol^[6]

A BP cuff of appropriate size (mid-arm circumference: 20-24 cm = small size, 24-32 cm = medium size, and 32-38 cm = large size) was chosen based on measured mid-arm circumference and applied to left arm using a standard protocol. All readings were taken after rest for 10 min, in postabsorptive phase while participants avoiding smoking or alcohol for 12 h before measurement, in a calm room without external influences or avoiding arm movement.^[6]

Parameters measured^[10]

- 1. Heart rate (HR), body mass index (BMI), and body surface area (BSA)
- 2. bBP: Systolic (brachial SBP), diastolic (brachial DBP [bDBP]), pulse (brachial pulse pressure [PP]), and mean (brachial mean BP)
- 3. cBP: Systolic (central SBP), diastolic (central DBP [cDBP]), and pulse (central PP [cPP])
- 4. Central hemodynamic: Cardiac output (CO), cardiac index, and systemic vascular resistance
- Arterial stiffness: Augmentation pressure, augmentation index at HR 75/min (AIx@75), reflection magnitude percentage (Ref %), and pulse wave velocity (PWV).^[10]

Parameters derived^[10]

- 1. Rate pressure product (RPP): (HR per minute) \times (systolic BP) \times 10⁻²
- 2. Stroke volume (SV): CO/HR
- 3. SV index (SVI): SV/BSA
- 4. Stroke work: (PP) \times (stroke volume) \times 0.0144
- 5. Total arterial stiffness (TAS): PP/stroke volume.^[10]

Comparison groups

To compare the effect of antihypertensive pharmacotherapy, we did four subgrouping pattern. Each time we selected participants matched by age, gender, and BMI and discarded a few who were not matched by age or BMI to counterpart.

- 1. We compared exclusively use of calcium channel blockers (CCBs) users and equal numbered patients exclusively taking angiotensin-converting enzyme inhibitors (ACEIs) which were matched to former group by age, gender, and BMI
- 2. Similarly, we compared patients exclusively taking angiotensin II receptor blockers (ARB) with an equal number of patients taking exclusively ACEI. Both groups were matched by age, gender, and BMI

- 3. We compared three groups taking monotherapy, dual combination therapy, and multitherapy
- 4. We compared ACEI users (age, gender, and BMI matched) with or without CCB use.

Statistical analysis

The data sorting was done on Excel Spreadsheet and all descriptive results were expressed as mean \pm standard deviation unless indicated specifically and all qualitative data were expressed as number (percentage) All calculations were done on InStat 3 software (GraphPad, Inc., California, USA) and MedCalc Statistical Software version 16.4.3 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2018). Quantitative data were compared by difference in mean or median distributions using unpaired *t*-test, Mann–Whitney test, ANOVA, or Kruskal–Wallis test. We compared the distribution of qualitative data by Normality test. *P* < 0.05 was considered statistically significant.

RESULTS

Patient groups using CCB and ACEI had comparable confounding factors except comparatively higher prevalence of diabetes and concomitant use of beta blockers in the latter group. ACEI users have marginally better brachial hemodynamics, central hemodynamics, and arterial stiffness parameters but all were statistically significant except PP amplification [Table 1].

Patient groups using ARB and ACEI were comparable in confounding factors, but ACEI users had a higher percentage of aspirin, beta blocker, and statin usage. ACEI users had lower brachial hemodynamics, central hemodynamics, and arterial stiffness parameters but all were statistically not significant [Table 1].

We compared mono, dual, and multitherapy users for PWA parameters. Brachial and central hemodynamics were lower and arterial stiffness parameters were higher in multitherapy user than mono or dual therapy users. However, statistical significance was evident only for bDBP and aortic DBP, PP index, HR, and RPP (lower in multitherapy users) and for reflection magnitude (lower in monotherapy users) [Table 2].

ACEI + CCB users were compared to ACEI users, both groups being comparable with reference to major confounding factors. ACEI + CCB group had higher brachial and central hemodynamics and arterial stiffness than ACEI only group. All results were statistically not significant except TAS and prevalence of cPP \geq 40 [Table 3].

DISCUSSION

To the best of our knowledge, by far, this is the first study using Mobil-O-Graph-based PWA in urban Indian hypertensives. Before studying other factors, we studied the effect of various drugs used for BP lowering in treated patient for class difference, if any. To accomplish it further, we selected group by meticulous comparing from the pool of 474 cases and matching was done for confounders^[10,11] such as age, height, and BMI. Most comparisons showed that groups were also comparable with respect to other confounders such as BP control, physical activity percentage, associated diabetes, and use of other therapeutic agents. We used some measured and some derived parameters to encompass complete profile of discrete cardiovascular parameters offered by PWA.

ACEI, CCB, and ARB were commonly used first-line antihypertensive agents in study participants, first two being used in the government setup and the last being used by the patients treated by private practitioners. We compared the use of any of these alone, on PWA parameters in subgroups with matched or comparable confounders. As compared to ARB or CCB, ACEI showed small but statistically insignificant better profile of BP (brachial and aortic), central hemodynamics, and arterial stiffness. These three first-line antihypertensives had no class difference across the spectrum of multiple PWA parameters, in line with others.^[5,12-15] This is explained by BP-lowering effects, common to these vasodilators that improve distensibility,^[14] and vascular remodeling given a duration of minimum 1 year to act adequately. ARB is being used more in the Western world, but we found it to be no superior to ACEI, which is (1) widely used,^[4] (2) cost-effective,^[16] (3) with comparatively lesser side effect, and (4) having convincing baking up data.^[15] Although the same should be viewed in the light of higher percentage of use of beta-blockers (51% vs. 11%), antidiabetics (49% vs. 29%), and statins (42% vs. 18%) in ACEI users than ARB users. Hence, ACEI/ARB/CCB is no different in their effect on central hemodynamics and aortic stiffness in chronic hypertensives. It supports previous literature but with respect to more vivid parameters and in population lacking such evidence. We previously reported no class difference of antihypertensives for QTc interval^[17] and HR variability^[18] in hypertensives. Hence, early detection of pathology has more to do with, than choosing for pharmacotherapy in hypertension.

ACEI, after beta-blocker, was combined with CCB mostly in our study population. However, we did not find any significant effect of CCB combination with ACEI, as compared to the use of ACEI without CCB. This is in contrast to Neutel et al.[19] This can be explained by the fact that in most patients CCB is added to ACEI when the BP is not controlled by the latter. Owing to higher coexistence of type 2 diabetes in hypertensives, as we previously reported,^[20] ACEI is used before CCB in most cases. ACEI + CCB group, rather ACEI + CCB group, had a small, though, better profile of all parameters except cDBP and bDBP which was better in ACEI + CCB group (2 mmHg mean difference). Addition of CCB thus reduces DBP, but the SBP, MBP, and PP are not benefited much. This emphasizes predominant cardioprotective, renoprotective, and cardiovascular risk reducing property of ACEI,^[21] which was common in both groups. We previously reported a significantly better profile of lower limb peripheral arterial disease, measured by ankle brachial index, in hypertensive type 2 diabetics receiving ACEI.^[22] Hence, both peripheral arterial and central arterial parameters are suggested to be benefitted by

Parameter, unit	CCB + (n = 46)	ACEI + (n = 46)	Р	ARB + (n = 45)	ACEI + (n = 45)	Р
Age, years	48.63±6.42	48.65±6.65	0.98	47.53±7.08	47.40±6.68	0.94
Male, <i>n</i> (%)	20 (43)	20 (43)	1.00	22 (49)	22 (49)	1.000
Height, cm	161.13±6.32	159.74±5.64	0.13	162.44±5.66	159.93±6.27	0.12
Weight, kg	63.87±12.04	63.43±10.73	0.86	65.73±11.45	61.84±8.84	0.07
BMI, kg/m ²	24.47±4.01	24.34±3.86	0.99	24.82±3.51	24.18±2.98	0.36
PA, <i>n</i> (%)	8 (17)	7 (15)	1.000	7 (16)	7 (16)	1.000
Duration	5.26±3.71	4.93±3.86	0.57	4.29±3.29	5.98±6.69	0.56
BPC, <i>n</i> (%)	19 (41)	21 (46)	0.83	19 (42)	22 (49)	0.52
Diabetes (+/-)	13 (28)	26 (57)	0.01*	13 (29)	22 (49)	0.08
Drugs use						
BB, <i>n</i> (%)	22 (48)	24 (52)	0.84	5 (11)	23 (51)	< 0.0001
Diuretics, n (%)	1 (2)	1 (2)	1.00	1 (2)	1 (2)	1.00
Aspirin, n (%)	8 (17)	9 (20)	1.00	7 (16)	14 (31)	0.13
Statin, <i>n</i> (%)	16 (35)	12 (26)	0.50	8 (18)	19 (42)	0.02*
bBP (mmHg)						
SBP	136.46±18.00	135.57±18.71	0.82	139.27±18.28	135.93±19.52	0.41
DBP	88.24±13.99	85.89±10.48	0.36	92.27±14.10	87.29±12.56	0.19
MBP	110.33±14.31	107.52±12.46	0.29	113.89±15.13	108.98±14.62	0.15
PP	48.11±14.20	48.46±14.66	0.89	46.78±11.89	47.53±12.69	0.78
PPI	0.35±0.08	0.35±0.07	0.87	0.33±0.07	0.35±0.07	0.55
HR, bpm	88.33±12.87	89.07±14.61	0.80	90.49±14.86	88.22±12.92	0.57
RPP, mmHg (bpm)	121.12±27.31	120.51±25.05	0.91	126.39±28.38	119.86±24.42	0.24
Art stiffness						
AP, mmHg	10.37±5.68	11.04±6.84	0.95	10.16±6.06	9.93±5.46	0.94
Ref (%)	66.57±6.20	66.22±7.81	0.81	63.87±8.07	65.80±5.75	0.16
AIx@75 (%)	32.59±11.70	34.5±11.71	0.44	34.89±10.82	32.98±9.39	0.64
PWV, m/s	7.49±0.97	7.53±1.15	0.84	7.47±0.98	7.36±1.05	0.62
TAS, ml/mmHg	0.82±0.21	0.84±0.22	0.86	0.79±0.20	0.82±0.19	0.55
PPA	1.37±0.17	1.30±0.15	0.0331*	1.35±0.15	1.33±0.13	0.74
cBP (mm Hg)						
cSBP	126.30±16.37	125.26±16.59	0.76	126.30±16.37	125.26±16.59	0.76
cDBP	90.17±14.24	87.65±10.59	0.34	90.17±14.24	87.65±10.59	0.34
cPP	36.35±10.61	37.61±11.77	0.77	36.35±10.61	37.61±11.77	0.77
cPP ≥40, <i>n</i> (%)	16 (35)	15 (33)	1.000	16 (36)	15 (33)	1.000
Central hemodynamics						
CO, L/min	5.15±0.86	5.07±0.78	0.61	5.32±0.89	5.05±0.67	0.29
PR, mmHg/mL	1.30±0.14	1.29±0.16	0.85	1.30±0.12	1.30±0.13	0.88
CI, L/min/m ²	3.08±0.57	3.04±0.42	0.68	3.13±0.59	3.08±0.52	0.93
SV, ml/beat	58.78±8.82	58.06±11.00	0.73	59.80±10.64	58.30±10.24	0.50
SVI, ml/m ² /beat	35.04±5.99	35.00±6.92	0.98	40.10±11.24	35.48±7.04	0.13
SW, g/beat	116.76±29.77	115.02±33.07	0.79	121.49±34.23	115.87±32.29	0.43

Table 1: Study parameters between hypertensives receiving angiotensin-converting enzyme inhibitor and calcium channel blocker (n=46 each; matched by age, gender and body mass index)

+ Means present, - Means absent. *Statistical significance. CCB=Calcium channel blocker, ACEI=Angiotensin converting enzyme inhibitor, ARB=Angiotensin II receptor blocker, BMI=Body mass index, PA=Physical activity, BP=Blood pressure, BPC=BP control, BB=Beta blocker, bBP=Brachial BP, SBP=Systolic BP, DBP=Diastolic BP, MBP=Mean BP, PP=Pulse pressure, PPI=PP index, HR=Heart rate, RPP=Rate pressure product, AP=Augmentation pressure, Ref=Reflection percentage, AIx@75=Augmentation index at heart rate 75 bpm, PWV=Pulse wave velocity, TAS=Total arterial stiffness, PPA=PP amplification, cBP=Central BP, cSBP=Central systolic BP, cDBP=Central diastolic BP, cPP=Central PP, CO=Cardiac output, PR=Peripheral resistance, CI=Cardiac index, SV=Stroke volume, SVI=Stroke volume index, SW=Stroke work, bpm=Beats per minute

ACEI. Blockade of rennin–angiotensin aldosterone system by ACEI has held its place as a gold standard despite the invention of many newer antihypertensive agents.^[4] Our finding reaffirms the same. It also emphasizes the importance of early diagnosis and initiation of treatment since with aging the reversibility decreases and add-on therapy becomes imperative. Other antihypertensives such as diuretics were used in small number of cases, so, were not studied.

We tested parameters with respect to varying combination of drugs in three groups – mono, dual, or multitherapy users. Multitherapy adds an advantage of use of multiple mechanism of modifying pathology of the diseases hypertension, which

Parameter, unit	ACEI + CCB ($n=54$)	ACE $-$ ICCB ($n=54$)	Р
Age, years	48.98±5.99	48.93±5.67	0.96
Males, <i>n</i> (%)	27 (50)	27 (50)	1.00
Height, cm	162.20±5.29	160.67±6.23	0.17
Weight, kg	65.85±9.55	64.00±9.33	0.31
BMI, kg/m ²	24.97±3.42	24.75±3.00	0.73
PA, n (%)	13 (24)	13 (24)	1.000
Duration	5.56±3.22	5.20±4.30	0.20
BPC, <i>n</i> (%)	18 (33)	18 (33)	1.00
Diabetes, n (%)	28 (52)	34 (63)	0.33
Pharmacotherapy, n (%)			
ACEI	54 (100)	54 (100)	-
BB	0	0	-
CCB	54 (100)	0	-
Diuretics	0	0	-
ARB	0	0	-
Aspirin	5 (9)	8 (15)	0.56
Statin	16 (30)	14 (26)	0.83
bBP (mm Hg)			
SBP	140.54±17.80	138.44±17.96	0.24
DBP	88.11±8.12	90.80±11.08	0.15
MBP	112.20±10.86	111.61±13.07	0.80
PP	52.43±16.13	44.87±13.67	0.026*
PPI	0.37±0.07	0.33±0.07	0.012*
HR, bpm	93.91±13.77	94.46±12.96	0.58
RPP, mmHg (bpm)	131.96±26.28	126.08±23.92	0.23
Vascular stiffness			
AP, mmHg	11.65±7.89	9.24±5.70	0.11
Ref (%)	65.89±7.41	63.91±6.48	0.09
AIx@75 (%)	36.67±9.77	33.70±9.83	0.12
PWV, m/s	7.69±0.94	7.45±1.00	0.21
TAS, ml/mmHg	0.90±0.21	0.80±0.19	0.0109*
PPA	1.34±0.14	1.35±0.13	0.85
cBP (mmHg)			
cSBP	129.81±16.74	126.76±16.35	0.34
cDBP	90.09±8.30	92.17±11.15	0.28
cPP	39.72±14.22	34.41±11.16	0.06
cpp ≥40, <i>n</i> (%)	24 (44)	12 (22)	0.0241*
Central hemodynamics			
CO, L/min	5.39±0.75	5.25±0.84	0.38
PR, mmHg/mL	1.26±0.14	1.28±0.13	0.07
CI, L/min/m ²	3.16±0.51	3.13±0.54	0.77
SV, ml/beat	58.24±9.64	57.61±10.25	0.74
SVI, ml/m ² /beat	34.08±6.61	34.42±7.16	0.80
SW, g/beat	119.39±31.66	115.09±33.66	0.50

Table 2: Study parameters between hypertensive angiotensin-converting enzyme inhibitor users with and without calcium channel blocker use (matched by age, gender, and body mass index)

*Statistical significance. CCB=Calcium channel blocker, ACEI=Angiotensin converting enzyme inhibitor, ARB=Angiotensin II receptor blocker, BMI=Body mass index, PA=Physical activity, BP=Blood pressure, BPC=BP control, BB=Beta blocker, bBP=Brachial BP, SBP=Systolic BP, DBP=Diastolic BP, MBP=Mean BP, PP=Pulse pressure, PPI=PP index, HR=Heart rate, RPP=Rate pressure product, AP=Augmentation pressure, Ref=Reflection percentage, AIx@75=Augmentation index at heart rate 75 bpm, PWV=Pulse wave velocity, TAS=Total arterial stiffness, PPA=PP amplification, cBP=Central BP, cSBP=Central systolic BP, cDBP=Central diastolic BP, cPP=Central PP, CO=Cardiac output, PR=Peripheral resistance, CI=Cardiac index, SV=Stroke volume, SVI=Stroke volume index, SW=Stroke work, bpm=Beats per minute

is essential and primary in majority. However, it is always for the cause of failure of monotherapy and advancement of disease. Our previous studies have shown that young, sedentary first-degree relatives of diabetic,^[10] or hypertensive^[11] parents had accelerated cardiovascular aging. Multitherapy receivers had a small but insignificant advantage over mono or dual therapy users with respect to brachial and central hemodynamic parameters. In contrast, monotherapy users had

Parameter, unit	Mono (<i>n</i> =179)	Dual (<i>n</i> =224)	Multi (<i>n</i> =71)	Р
Age, years	49.17±7.05	49.05±7.37	51.11±6.42	0.06
Males, n (%)	84 (47)	106 (47)	38 (54)	0.61
Height, cm	161.08±5.99	160.91±5.91	161.56±4.34	0.94
Weight, kg	64.45±10.56	64.39±10.13	66.79±8.77	0.20
$BMI, kg/m^2$	24.79±3.35	24.82±3.62	25.54±2.94	0.23
PA, n (%)	39 (22)	41 (18)	16 (23)	0.60
Duration	5.30±4.72	5.30±3.81	5.15±3.50	0.53
BPC, <i>n</i> (%)	59 (33)	90 (40)	28 (39)	0.31
Diabetes, n (%)	96 (54)	94 (42)	26(37%)	0.0169*
Pharmacotherapy, <i>n</i> (%)			~ /	
Aspirin	21 (12)	60 (27)	30 (42)	< 0.0001*
Statin	40 (22)	64 (29)	34 (48)	0.0003*
bBP (mmHg)				
SBP	139.37±17.51	138.44±20.50	137.07±20.69	0.61
DBP	91.72±12.81	87.65±12.65	87.17±11.99	0.0004*
MBP	113.55±13.14	110.67±14.84	110.03±14.96	0.06
РР	47.61±13.81	50.61±15.25	50.04±14.23	0.10
PPI	0.34±0.07	0.36±0.07	0.36±0.07	0.0027*
HR, bpm	91.47±14.12	90.26±15.04	84.70±14.69	0.001*
RPP, mmHg (bpm)	127.74±26.75	125.04±28.37	116.39±29.61	0.0081*
Vascular stiffness				
AP, mmHg	10.15±5.94	11.09±7.55	11.43±6.22	0.26
Ref (%)	65.08±6.40	66.40±7.29	67.11±6.22	0.0251*
AIx@75 (%)	34.72±10.50	34.17±11.48	32.86±11.24	0.43
PWV, m/s	7.59±1.01	7.61±1.10	7.74±1.01	0.58
TAS, ml/mmHg	0.81±0.21	0.85±0.26	0.79±0.23	0.09
PPA	1.34±0.14	1.33±0.15	1.30±0.13	0.20
cBP (mmHg)				
cSBP	129.61±15.86	127.97±18.91	127.44±18.31	0.44
cDBP	93.08±13.55	89.46±12.90	88.87±12.43	0.0011*
cPP	35.97±11.40	38.27±13.11	38.56±11.19	0.09
cPP ≥40, <i>n</i> (%)	56 (31)	87 (39)	27 (38)	0.27
Central hemodynamics				
CO, L/min	5.32±0.83	5.26±0.84	5.25±0.97	0.60
PR, mm Hg/mL	1.29±0.14	1.28±0.17	1.28±0.16	0.88
CI, L/min/m ²	3.13±0.59	3.08±0.52	3.13±0.59	0.09
SV, ml/beat	59.28±12.53	59.68±10.98	62.86±11.75	0.06
SVI, ml/m ² /beat	34.89±6.86	35.33±7.03	36.55±7.52	0.30
SW, g/beat	120.50±33.95	120.32±34.24	122.24±29.75	0.68

*Statistical significance. BMI=Body mass index, PA=Physical activity, BP=Blood pressure, BPC=BP control, bBP=Brachial BP, SBP=Systolic BP, DBP=Diastolic BP, MBP=Mean BP, PP=Pulse pressure, PPI=PP index, HR=Heart rate, RPP=Rate pressure product, AP=Augmentation pressure, Ref=Reflection percentage, AIx@75=Augmentation index at heart rate 75 bpm, PWV=Pulse wave velocity, TAS=Total arterial stiffness, PPA=PP amplification, cBP=Central BP, cSBP=Central systolic BP, cDBP=Central diastolic BP, cPP=Central PP, CO=Cardiac output, PR=Peripheral resistance, CI=Cardiac index, SV=Stroke volume, SVI=Stroke volume index, SW=Stroke work, bpm=Beats per minute

a better profile of vascular stiffness – central (aortic PWV), peripheral (augmentation index and PP amplification) and total, as compared to combination users. This suggests that cBP and bBPs are late changes as compared to stiffness parameters, later being not totally dependent on former parameters. Furthermore, it hints vascular changes of aorta preceding incident hypertension and/or diabetes. We do not find disparity between cBP and bBP values in most comparison; though, former was lesser than later, as in accordance with other studies.^[5,14] cPP >40 is a risk factor for end-organ damage to heart, kidney, and brain.^[23] However, we could not attribute its prevalence to overuse of various antihypertensive drugs. Hence, screening and early diagnosis and prompt treatment are of importance to offer reversibility, if any. The same is suggested for Asian and African hypertensives in a recent article with no ethnic difference from non-Asian non-Africans.^[24] Adding to it, with no significant class difference of antihypertensive agents on discrete aortic parameters, we are left with primary prevention by screening to render secondary prevention by antihypertensive drugs.

With increased life expectancy and ever-increasing magnitude and treatment cost of hypertension, more studies are needed to find the missing links. Early diagnosis with the use of ACEI/ ARB/CCB – alone or in combination and strict control and PWA monitoring are suggested. With this early evidence, further study with vertical follow-up and baseline data is needed.

Use of novel oscillometric method and Mobil-O-Graph, meticulous matching for comparison, moderately large size of sampling, inclusion of multiple parameters, and simultaneous measurement of all parameters were the strengths of our study. Lack of baseline data, unavailability of biochemical investigations, availability of limited antihypertensive drugs to compare, the absence of use of vasodilating beta blockers, and absence of follow-up were limitations of our study.

CONCLUSION

Oscillometric PWA parameters showed no significant class difference of conventional antihypertensive drugs, used alone or in combination, in treated Gujarati hypertensives. ACEI was comparable to other drugs alone or in combination, monotherapy being not much differently affecting than multitherapy. It suggests the importance of early diagnosis of hypertension and control of BP more than the antihypertensive class difference and further studies to confirm our results.

Acknowledgments

We are thankful to Physiology and Medicine Departments of our medical college and Sir T Hospital Bhavnagar for giving us the facilities available in the department and to volunteers for participation in this study.

Financial support and sponsorship Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Anchala R, Kannuri NK, Pant H, Khan H, Franco OH, Di Angelantonio E, et al. Hypertension in India: A systematic review and meta-analysis of prevalence, awareness, and control of hypertension. J Hypertens 2014;32:1170-7.
- World Health Organization. Media Centre Fact Sheet. Geneva: World Health Organization; 2015.
- Ulusoy S. Assessment of cardiovascular risk in hypertensive patients: A comparison of commonly used risk scoring programs. Kidney Int Suppl (2011) 2013;3:340-2.
- Gude D. How full is our antihypertensives pipeline? J Pharmacol Pharmacother 2012;3:7-11.
- McGaughey TJ, Fletcher EA, Shah SA. Impact of antihypertensive agents on central systolic blood pressure and augmentation index: A Meta-analysis. Am J Hypertens 2016;29:448-57.
- 6. Steppan J, Sikka G, Hori D, Nyhan D, Berkowitz DE, Gottschalk A, et al. Seeking a blood pressure-independent measure of vascular

properties. Hypertens Res 2016;39:27-38.

- Wassertheurer S, Kropf J, Weber T, van der Giet M, Baulmann J, Ammer M, *et al.* A new oscillometric method for pulse wave analysis: Comparison with a common tonometric method. J Hum Hypertens 2010;24:498-504.
- Weiss W, Gohlisch C, Harsch-Gladisch C, Tölle M, Zidek W, van der Giet M, *et al.* Oscillometric estimation of central blood pressure: Validation of the mobil-O-graph in comparison with the sphygmoCor device. Blood Press Monit 2012;17:128-31.
- Weber T, Wassertheurer S, Rammer M, Maurer E, Hametner B, Mayer CC, *et al.* Validation of a brachial cuff-based method for estimating central systolic blood pressure. Hypertension 2011;58:825-32.
- Solanki JD, Mehta HB, Shah CJ. Pulse wave analysed cardiovascular parameters in young first degree relatives of type 2 diabetics- A crosssectional study. Indian Heart J 2018;70:341-5.
- Solanki JD, Mehta HB, Shah CJ. Pulse wave analyzed cardiovascular parameters in young first degree relatives of hypertensives. J Res Med Sci 2018;23:72.
- Manisty CH, Hughes AD. Meta-analysis of the comparative effects of different classes of antihypertensive agents on brachial and central systolic blood pressure, and augmentation index. Br J Clin Pharmacol 2013;75:79-92.
- Janić M, Lunder M, Sabovič M. Arterial stiffness and cardiovascular therapy. Biomed Res Int 2014;2014:621437.
- Miyashita H, Aizawa A, Hashimoto J, Hirooka Y, Imai Y, Kawano Y, et al. Cross-sectional characterization of all classes of antihypertensives in terms of central blood pressure in Japanese hypertensive patients. Am J Hypertens 2010;23:260-8.
- Koumaras C, Tzimou M, Stavrinou E, Griva T, Gossios TD, Katsiki N, et al. Role of antihypertensive drugs in arterial 'de-stiffening' and central pulsatile hemodynamics. Am J Cardiovasc Drugs 2012;12:143-56.
- Wu HY, Huang JW, Lin HJ, Liao WC, Peng YS, Hung KY, et al. Comparative effectiveness of renin-angiotensin system blockers and other antihypertensive drugs in patients with diabetes: Systematic review and Bayesian network meta-analysis. BMJ 2013;347:f6008.
- Solanki JD, Gadhavi BP, Makwana AH, Mehta HB, Shah CJ, Gokhale PA, *et al.* QTc interval in young Gujarati hypertensives: Effect of disease, antihypertensive monotherapy, and coexisting risk factors. J Pharmacol Pharmacother 2016;7:165-70.
- Solanki JD, Basida SD, Mehta HB, Panjwani SJ, Gadhavi BP. Comparative study of cardiac autonomic status by heart rate variability between under-treatment normotensive and hypertensive known type 2 diabetics. Indian Heart J 2017;69:52-6.
- Neutel JM, Smith DH, Weber MA. Effect of antihypertensive monotherapy and combination therapy on arterial distensibility and left ventricular mass. Am J Hypertens 2004;17:37-42.
- Solanki JD, Makwana AH, Mehta HB, Gokhale PA, Shah CJ. A study of prevalence and association of risk factors for diabetic vasculopathy in an urban area of Gujarat. J Family Med Prim Care 2013;2:360-4.
- Ong HT, Ong LM, Ho JJ. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin-receptor blockers (ARBs) in patients at high risk of cardiovascular events: A Meta-analysis of 10 randomised placebo-controlled trials. ISRN Cardiol 2013;2013:478597.
- 22. Solanki JD, Makwana AH, Mehta HB, Gokhale PA, Shah CJ. Hypertension in type 2 diabetes mellitus: Effect of the disease and treatment on development of peripheral artery disease. Int J Diabetes Dev Ctries 2015;35:380-4.
- Kollias A, Lagou S, Zeniodi ME, Boubouchairopoulou N, Stergiou GS. Association of central versus brachial blood pressure with target-organ damage: Systematic review and meta-analysis. Hypertension 2016;67:183-90.
- 24. Brewster LM, van Montfrans GA, Oehlers GP, Seedat YK. Systematic review: Antihypertensive drug therapy in patients of African and South Asian ethnicity. Intern Emerg Med 2016;11:355-74.