Research Paper

Impact of Concomitant Use of Beta blocker, Statin, Aspirin, and Metformin on Central Hemodynamics and Arterial Stiffness in Hypertension

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Abstract

Objective: To assess the impact of concomitant use of aspirin, BB (metoprolol), statin (atorvastatin), and metformin on central haemodynamics and arterial stiffness parameters in treated hypertensive patients. **Materials and Methods:** We did a cross-sectional study on 476 treated hypertensives. Oscillometric PWA was accomplished by Mobil-o-Graph (IEM, Germany) and groups were stratified using low-dose aspirin, statin, BB, or metformin. Parameters studied were brachial hemodynamics (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). **Results:** All pairs were matched by or comparable for major confounding factors except concomitant use of drugs. The use of BB, aspirin, and statin had favorable effect on brachial and central hemodynamics. Metformin use had effect more on central than brachial hemodynamics. BB and metformin had negative, statin had indifferent, and aspirin had positive effect on arterial stiffness. Only few of these differences had statistical significance. Frequency of central pulse pressure ≥40 was insignificantly affected by drugs studied. **Conclusions:** Concomitant aspirin, BB, and metformin in hypertensives have favorable effects on hemodynamics, brachial more than central. Arterial stiffness has positive impact of metformin and negative impact of BB use. These effects must be considered in studies focusing hypertensive therapies. It remains inconclusive whether these results are due to drugs or their indication.

Keywords: Arterial stiffness, aspirin, beta-blocker, central hemodynamic, metformin, statin

Introduction

Hypertension has enormous prevalence, threatening future prediction, tremendous impact on cardiovascular health, and cost burden of pharmacotherapy.[1] Most studies of hypertension and pharmacotherapy focus on first-line anti-hypertensives and brachial blood pressure (bBP). BP is just one of many determinants of cardiovascular risk.[2] Parameters about functioning of aorta and heart are more discrete and direct in risk stratification. Routinely measured bBP does not tell about the status of aortic compliance and central hemodynamics. Similarly, along with the first-line anti-hypertensives, drugs such as aspirin, statin, beta-blocker (BB), and antidiabetic drugs are also used in hypertensives. BBs are usually used as the second-line agents with some specific indication and metformin as drug for type 2 diabetes in most cases. Statin is used to treat dyslipidemia, and aspirin is given to prevent ischemic heart disease. These preventive pharmacotherapies indicate both risk of underlying indicator for use as well as benefit offered by correction of the same by the drug. Frequency and concomitant use of these are expected more in our hypertensives with association of diabetes and heart disease in majority, as we previously documented.[3] These drugs are known to affect the pathology of essential hypertension individually and may have impact on some discrete aortic and central hemodynamic parameters.

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Similarly, indications which lead to the use of these drugs also affect these parameters. Our previous study showed no impact of statin on peripheral artery disease.[4] Hence, we could ascertain the same for aorta, the most immediate artery to the heart. Introduction of oscillometric cuff-based devices such as Mobil-o-Graph[5] and validated generalized transfer factor has enabled study of aortic and central hemodynamics.[6] Using same technique in treated hypertensives, we studied effect of the use of low-dose aspirin, BB (metoprolol), statin (atorvastatin), and metformin, on pulse wave analysis (PWA)-associated cardiovascular parameters.

Materials and Methods

Study set up 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 physiology and medicine departments from June 18, 2015 to March 2, 2018. The study protocol was approved by institutional review board of our college.

Inclusion and exclusion criteria

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

Study groups

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

We screened and enrolled 700 hypertensives or diabetics from general medicine outdoor patient department by simple random sampling. Out of these, we excluded 140 new hypertensives (duration <1 year), 239 cases with diagnosed or detected diabetes only without hypertension (as per the American Diabetes Association guidelines 2014), 68 due to history of irregular treatment, 10 due to use of lifestyle modification, 3 due to irregular pulse wave recording, 2 due to morbid obesity, 2 owing to arm circumference beyond available cuff size, and 5 due to body mass index (BMI) that cannot be matched with controls.

Subject assessment and definitions

All participants were personally interviewed in the form of questionnaires including general features, demographic characteristics, risk factor, and relevant history. Detailed history of pharmacotherapy used was elicited from each hypertensive, and regularity was confirmed by patient's case report chart. Systolic BP (SBP) ≥140 mmHg and diastolic BP (DBP) ≥90 mmHg or use of antihypertensive medication was defined as hypertension. SBP <140 mmHg and DBP <90 mmHg were taken as BP control. Overall, the prevalence of hyperlipidaemia (as defined by use of statins or lipidemic control-low-density lipoprotein ≥100 mg/dL, high-density lipoprotein ≤50 mg/dL, and TGAs ≥150 mg/dL) was 30% (142 out of 474) and associated diabetes was 41% (195 out of 474) in the study group, for which patients were on statin and metformin, respectively. Similarly, BB was used by 27% (129 out of 474) due to resistant hypertension for better BP control, and aspirin was given to 24% (112 out of 474) participants as prophylactic agent. Use of statin, metformin aspirin, and BB were the factors to be studied.

Instrument used

We used portable, personal computer-attached, calibrated[7] and validated[8] 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 the 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 derives central aortic pulse wave by validated generalized transfer factor. It further undergoes point-based and area-based analysis by computer to derive various cardiovascular parameters.

Measurement protocol

A BP cuff of appropriate size (midarm 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 the left arm using 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.[7]

Parameters measured

The following parameters are measured using Mobil-o-Graph[8,9]

1. Heart rate (HR), BMI, and body surface area
2. bBP – systolic (bSBP), diastolic (bDBP), pulse (bPP), and mean (bMBP)
3. Central BP (cBP) – systolic (cSBP), diastolic (cDBP), and pulse (cPP)
4. Central hemodynamic – cardiac output, cardiac index, and systemic vascular resistance
5. Arterial stiffness – augmentation pressure, augmentation index at HR 75/min (AIx@75), reflection magnitude percentage (Ref %), pulse wave velocity.

Parameters derived

A few parameters were derived from parameters measured by Mobil-o-Graph[8,9]

1. Rate pressure product (RPP) = (HR per minute) × (systolic BP) ×10^{-2}

2. Stroke volume (SV) = cardiac output/HR
3. SV index = stroke volume/body surface area
4. Stroke work = (pulse pressure) × (stroke volume) × 0.0144
5. Total arterial stiffness = pulse pressure/stroke volume.

Comparison groups

To compare the effect of preventive pharmacotherapy, we used four subgrouping patterns of pairing.

Each time we selected participants matched by age, gender, and BMI and discarded few who were not matched by age or BMI to counterpart.

We formed four pairs based on use or nonuse of four drugs as follows:

1. Metformin (1500-3000 mg per day)– the most commonly prescribed oral hypoglycemic in our set up
2. Metoprolol (upto 100 mg per day) – only prescribed BB in our set up
3. Aspirin (150 mg per day) – in low dose used for prophylaxis in coronary artery disease
4. Atorvastatin (up to 80 mg per day)- the most commonly used statin in our set up.

Statistical analysis

The data were entered in and sorted by Excel Spreadsheet. All numerical data were expressed as mean ± standard deviation until indicated specifically, and all qualitative data were expressed as number (percentage). Statistic calculations were done on GraphPad InStat 3 software (demo version free software of GraphPad Software, Inc., California, USA) and MedCalc Statistical Software version 16.4.3 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2018). Each set data was checked for parametric or nonparametric distribution by normality test and based on these further tests were selected. Numerical data were compared by the difference in mean/median distributions using unpaired *t*-test or Mann–Whitney test. We compared distribution of qualitative data by normality test or Chi-square test. Statistical significance level was taken as $P < 0.05$.

Results

Table 1 shows comparison of BB users/nonusers and metformin users/nonusers matched by number, age, gender, and BMI. Both pairs had comparable subgroups except higher prevalence of diabetes and BP control in BB users than BB nonusers and higher prevalence of angiotensin-converting enzyme inhibitor (ACEI) and BB use in metformin users than metformin nonusers. BB users had significantly better bBP and cBP, RPP, and BP control but significantly worse profile of arterial stiffness than BB nonusers. Central hemodynamics and cardiac workload were not statistically significantly different. Metformin users and nonusers had comparable brachial hemodynamics, central hemodynamics, and BP control. HR and RPP were significantly lower, while arterial stiffness and workload were higher in metformin users than nonusers [Table 1].

Table 2 shows comparison of statin users/nonusers and aspirin users/nonusers matched by number, age, gender, and BMI. Both pairs had comparable subgroups except higher prevalence of ACEI and BB use in statin/aspirin users than nonusers. Statin users had better bBP and cBP, RPP, BP control, and central hemodynamics but insignificantly different arterial stiffness and cardiac workload than statin nonusers. Aspirin users had better bBP and cBP, RPP, arterial stiffness, and central hemodynamics but insignificantly different BP control and cardiac workload than aspirin nonusers [Table 2].

Discussion

This is possibly the first study using Mobil-o-Graph-based PWA in urban Indian hypertensives. Apart from physiological and pathological factors affecting PWA, there are pharmacological factors which can modify the pathophysiology and hence the cardiovascular parameter in hypertension. In another unpublished part of our research work, we demonstrated no significant class difference among the first-line anti-hypertensives on PWA parameters in the same hypertensive participants. Hence, by this paper, we tried to compare effect of other four commonly used pharmacotherapeutic agents, namely, aspirin, BB, statin, and metformin. We selected four pairs of groups by careful matching for confounders[9,10] such as age, height, and BMI. We studied some directly measured and some derived cardiovascular parameters to have complete profile offered by PWA.

BBs are second-line anti-hypertensives that are used along with the first-line agents and more so in cases when BP is not optimally controlled by conventional monotherapy. BB metoprolol users had significantly better bBP and cBP and overall BP control. This is line with the previous studies.[10,11] It highlights importance of sympathetic nervous system as a cause in the development of hypertension[12] and benefit by its correction in our hypertensives. BB significantly reduced HR but was not affecting workload or central hemodynamics and these point to inferiority of same as the first-line antihypertensive drug.[13] Arterial stiffness had negative impact of BB use. This is due to metoprolol which is not offering benefit of vasodilatation like other agents in the group – carvedilol and nebivolol[11] which were used by three participants only in our sample, which we excluded from the calculation. Reduced HR and RPP are advantage. However, late return of reflected pulse wave during diastole increases augmentation index that has adverse effect on coronary circulation with added cardiac afterload.[13]

Metformin is most commonly used drug with or without sulfonylurea in our set up. It is efficacious and cost-effective but does not offer protective advantages of newer drugs such as pioglitazone, empagliflozin, and liraglutide.[14] They are suggested to benefit by combination with metformin, but we could have only 11 participants with use of these so we discard them from the study. Study results of discrete PWA parameters for mertformin use versus nonuse should also be viewed more

Table 1: Comparison of study parameters between hypertensives receiving and not receiving beta-blocker and metformin (each pair matched by age, gender, and body mass index)

Parameter, unit	BB+ (*n*=127)	BB− (*n*=127)	*P*	Metformin+ (*n*=178)	Metformin− (*n*=178)	*P*
Age, years	50.32±6.14	50.15±6.09	0.88	49.70±6.48	49.72±6.46	0.96
Male, *n* (%)	66 (52)	66 (52)	1.000	88 (49)	88 (49)	1.000
Height, cm	160.76±5.55	161.12±5.96	0.55	161.55±5.57	161.10±5.38	0.40
Weight, kg	63.90±9.66	63.75±9.48	0.82	65.62±8.84	64.96±9.28	0.63
BMI, kg/m^2	24.72±3.08	25.06±5.54	0.98	25.16±3.23	24.97±3.12	0.64
PA, *n* (%)	26 (20)	38 (30)	0.12	36 (20)	36 (20)	1.000
Duration	4.98±3.43	5.50±4.47	0.97	5.56±4.04	5.19±3.97	0.30
BPC, *n* (%)	52 (41)	28 (22)	0.0018*	67 (38)	66 (37)	1.000
Diabetes, *n* (%)	46 (36)	66 (52)	0.0162*	178 (100)	0	-
Hyperlipidemia, *n* (%)	49 (36)	42 (33)	0.43	55 (31)	51 (29)	0.73
Drugs use, *n* (%)						
ACEI	106 (83)	106 (83)	1.00	145 (81)	124 (70)	0.0134*
BB	127 (100)	0	-	67 (38)	92 (52)	0.0104*
CCB	48 (38)	48 (38)	1.00	51 (29)	69 (39)	0.06
Diuretics	7 (6)	10 (8)	0.62	20 (11)	25 (14)	0.53
ARB	18 (14)	21 (17)	0.73	24 (13)	29 (16)	0.55
Aspirin	42 (33)	46 (36)	0.69	42 (24)	46 (26)	0.71
Statin	46 (36)	41 (32)	0.59	55 (31)	50 (28)	0.64
bBP (mmHg)						
SBP	137.05±20.05	139.79±17.72	0.25	138.87±19.83	138.56±19.34	0.86
DBP	87.06±12.98	90.84±11.25	0.0042*	88.92±11.80	89.27±13.07	0.79
MBP	109.69±14.85	111.23±12.65	0.0417*	111.69±13.99	111.71±14.82	0.77
PP	49.98±14.52	49.05±14.69	0.43	49.94±15.63	49.01±13.53	0.89
PPI	0.36±0.07	0.35±0.07	0.13	0.35±0.07	0.35±0.07	0.65
HR, bpm	86.45±14.57	92.12±12.88	0.0011*	93.89±14.42	86.69±15.58	<0.0001*
RPP, mmHg bpm	119.01±28.72	129.28±27.09	0.0033	130.57±28.45	120.68±29.29	0.0017*
Art stiffness						
AP, mmHg	11.18±5.68	10.43±5.41	0.92	10.74±6.42	10.84±6.72	0.97
Ref (%)	67.02±7.00	65.07±6.45	0.0298*	65.75±6.52	66.13±7.21	0.42
AIx@75 (%)	32.45±12.04	35.28±9.50	0.0446*	35.62±11.15	32.97±11.22	0.0366*
PWV, m/s	7.66±1.03	7.70±0.94	0.78	7.67±1.00	7.64±0.98	0.79
TAS, ml/mmHg	0.84±0.25	0.83±0.21	0.63	0.85±0.25	0.80±0.23	0.0197
PPA	1.32±0.14	1.36±0.14	0.0308*	1.34±0.15	1.33±0.14	0.74
cBP (mmHg)						
cSBP	127.19±18.50	129.65±15.84	0.38	128.71±18.05	128.38±17.35	0.94
cDBP	88.86±13.31	91.94±13.46	0.0081*	90.38±13.33	91.04±18.56	0.99
cPP	38.37±12.50	36.91±11.66	0.33	37.72±12.73	37.33±11.28	0.84
cPP ≥40, *n* (%)	46 (36)	46 (36)	1.000	67 (38)	66 (37)	1.000
Central hemodynamics						
CO, L/min	5.17±0.90	5.34±0.81	0.13	5.34±0.88	5.26±0.87	0.31
PR, mmHg/mL	1.28±0.16	1.29±0.14	0.78	1.27±0.15	1.28±0.16	0.67
CI, L/min/m^2	3.1±0.57	3.2±0.57	0.23	3.13±0.54	3.12±0.56	0.81
SV, ml/beat	60.79±11.00	58.51±8.40	0.06	57.80±10.49	62.07±13.33	0.0014*
SVI, ml/m^2/beat	36.37±7.19	34.87±6.16	0.08	33.91±6.56	36.75±9.06	0.0006*
SW, g/beat	121.54±34.42	119.21±29.12	0.56	118.40±34.89	125.03±36.28	0.08

*Statistical significance. BP=Blood pressure, CCB=Calcium channel blocker, ACEI=Angiotensin-converting enzyme inhibitor, ARB=Angiotensin II receptor blocker, BMI=Body mass index, PA=Physical activity, BPC=BP control, BB=Beta-blocker, bBP=Brachial BP, SBP=Systolic BP, DBP=Diastolic BP, MBP=Mean BP, PP=Pulse pressure, PPI=Pulse pressure 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=Pulse pressure amplification, cSBP=Central SBP, cDBP=Central DBP, 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

as presence versus absence of diabetes as a risk factor in hypertensives. bBP and cBP had small and insignificant effect of associated metformin use. Lack of significant impact is in contrast to others[15] and may be explained by poor glycemic control which was in just 23% of metformin users, being the hallmark of our diabetics.[4] Metformin had negative impact

Table 2: Comparison of study parameters between hypertensives receiving or not receiving statin and aspirin (each pair matched by age, gender, and body mass index)

Parameter, unit	Statin+ (*n*=137)	Statin− (*n*=137)	*P*	Aspirin+ (*n*=111)	Aspirin+ (*n*=111)	*P*
Age, years	49.77±6.45	49.54±6.27	0.77	50.14±6.40	49.86±6.40	0.80
Male, *n* (%)	70 (51)	70 (51)	1.000	62 (56)	62 (56)	1.000
Height, cm	161.05±5.56	161.47±5.67	0.71	161.29±5.31	161.99±5.19	0.25
Weight, kg	65.39±8.34	65.95±8.70	0.59	65.45±8.17	66.40±8.09	0.26
BMI, kg/m^2	25.19±2.66	25.25±2.83	0.87	25.17±2.64	25.29±2.77	0.74
PA, *n* (%)	30 (22)	26 (19)	0.65	52 (16)	39 (16)	0.10
Duration	5.34±4.27	6.17±4.80	0.26	5.39±4.42	5.55±4.14	0.85
BPC, *n* (%)	63 (46)	45 (33)	0.0354*	52 (47)	39 (45)	0.52
Diabetes, *n* (%)	62 (45)	67 (49)	0.63	51 (46)	53 (48)	0.89
Hyperlipidemia, *n* (%)	137 (100)	0	-	93 (84)	19 (17)	<0.0001*
Drugs use, *n* (%)						
ACEI	101 (74)	103 (75)	0.89	90 (81)	78 (51)	0.08
BB	71 (52)	51 (37)	0.0207*	72 (65)	42 (2)	<0.0001*
CCB	50 (36)	49 (36)	1.00	34 (31)	40 (31)	0.48
Diuretics	24 (18)	14 (10)	0.11	20 (18)	11 (42)	0.0039*
ARB	23 (17)	19 (14)	0.62	16 (14)	17 (2)	1.000
Aspirin	91 (66)	9 (7)	<0.0001*	111 (100)	0 (31)	-
Statin	137 (1000)	0	-	92 (83)	19 (17)	<0.0001*
bBP (mmHg)						
SBP	134.58±21.82	139.29±19.20	0.0117*	135.14±22.60	139.67±16.98	0.0228*
DBP	87.00±13.71	90.48±12.33	0.0123*	87.45±13.73	88.60±12.39	0.51
MBP	108.77±16.09	112.64±14.24	0.0066*	109.41±16.76	111.74±12.93	0.06
PP	47.59±15.81	48.40±14.07	0.38	97.96±15.10	50.71±14.38	0.11
PPI	0.35±0.08	0.34±0.07	0.57	0.35±0.07	0.36±0.08	0.29
HR, bpm	88.33±13.90	88.82±14.80	0.78	86.86±14.90	91.61±14.13	0.0156*
RPP, mmHg bpm	118.86±26.77	124.05±28.08	0.07	117.76±28.69	128.50±27.76	0.005*
Art stiffness						
AP, mmHg	10.18±6.79	10.71±6.84	0.48	10.14±6.85	11.17±6.54	0.18
Ref (%)	66.27±6.68	65.09±7.66	0.23	66.28±6.63	66.50±7.59	0.48
AIx@75 (%)	32.88±11.72	33.68±10.65	0.55	31.87±11.89	35.10±11.34	0.0399*
PWV, m/s	7.52±1.02	7.64±1.01	0.35	7.57±1.01	7.67±0.98	0.45
TAS, ml/mmHg	0.80±0.26	0.80±0.23	0.70	0.79±0.22	0.86±0.22	0.0290*
PPA	1.32±0.13	1.33±0.14	0.68	1.33±0.16	1.33±0.15	0.55
cBP (mmHg)						
cSBP	125.03±19.38	129.26±17.94	0.015*	125.41±19.80	129.10±15.73	0.0474*
cDBP	88.71±13.94	91.51±14.31	0.0181*	89.07±14.13	88.70±16.39	0.42
cPP	36.24±12.27	37.07±12.24	0.54	36.23±11.32	38.59±12.21	0.18
cPP ≥40, *n* (%)	45 (33)	49 (36)	0.70	35 (32)	44 (40)	0.26
Central hemodynamics						
CO, L/min	5.11±0.90	5.30±0.80	0.0065*	5.18±0.95	5.38±0.38	0.0064*
PR, mmHg/mL	1.29±0.17	1.29±0.15	0.96	1.28±0.17	1.26±0.14	0.34
CI, L/min/m^2	3.02±0.58	3.1±0.50	0.0458*	3.04±0.58	3.13±0.47	0.0326*
SV, ml/beat	59.34±11.89	61.09±13.57	0.32	60.77±11.99	59.52±9.27	0.39
SVI, ml/m^2/beat	34.92±7.18	35.98±9.33	0.51	35.78±7.40	34.70±6.09	0.24
SW, g/beat	117.35±39.70	123.75±35.60	0.06	120.72±40.27	120.73±28.02	0.99

*Statistical significance. BP=Blood pressure, CCB=Calcium channel blocker, ACEI=Angiotensin-converting enzyme inhibitor, ARB=Angiotensin II receptor blocker, BMI=Body mass index, PA=Physical activity, BPC=BP control, BB=Beta-blocker, bBP=Brachial BP, SBP=Systolic BP, DBP=Diastolic BP, MBP=Mean BP, PP=Pulse pressure, PPI=Pulse pressure 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=Pulse pressure amplification, cSBP=Central SBP, cDBP=Central DBP, 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

on HR and RPP, but this is more due to cardiac dysautonomia in diabetic patients that is known to exist with loss of vagal tone as we confirmed previously by our study based on 5 min HR variability.[16] Similarly, arterial stiffness was adverse in metformin users which hint to vascular progeria of diabetes that is evident even before disease itself as we published

before.[8] Hence, it remains a matter to explore whether these are effects of drug or disease (may be before clinical diagnosis) itself.

Atorvastatin was shown to be beneficial with respect to BP, BP control, and central hemodynamics. This is supported by other studies as well.[17,18] It can be explained by its immune-modulatory and anti-inflammatory effect that is causative for oxidative stress and vascular injury otherwise.[19] Atorvastatin was having neutral effect on arterial stiffness parameters in contrast to available literature[17,18] and needs further study for explanation. This can be due to fact that other studies used regional stiffness difference rather than aortic stiffness like us. We found same insignificant effect of statin on the prevalence of peripheral arterial disease in low-risk diabetics.[4] Hence, these vascular changes are suggested to be benefitted insignificantly by statins.

Low-dose prophylactic aspirin was the only tested agent in our study that benefited arterial stiffness beyond brachial and central blood hemodynamics with indifferent effect on cardiac workload. This is more than needed benefit in our population and this in line with a study showing reduced cardiovascular risk in diabetics with poorly controlled BP, by use of concomitant aspirin.[20] Aspirin has antiplatelet effect that prevents vascular inflammation[19] and associated injury. This is, however, offered only after risk of coronary artery symptom or after myocardial infarction. However, once started, the cardiovascular protection is evident.

Hypertension is ever increasing disease with no permanent cure and with cardiovascular risk that has to be tackled by pharmacological interventions. Cardiac health is determinant of overall health, more so in hypertensives; and for betterment of that, preventive pharmacotherapies such as ACEI, aspirin, and BB are needed. Even cost-effective, conventional drugs in these regards are found to be effective in our patients treated in government set up by essential listed drugs. With coexistence of diabetes and hyperlipidemia in majority, hypertensives are further given advantage of metformin and statin, respectively. In our study, beneficial effect of four studied agents must be viewed in light of co-use of most out of these four, in majority of the participants. There was no baseline data and follow-up, so results have to be studied further to confirm whether they are due to use of drug *per se* or due to condition indicating their use, more so with metformin and diabetes. With this baseline study, further studies with vertical follow-up and inclusion of newer class drugs are needed that we intend as future prospect.

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 conventional drugs to compare, absence of use of vasodilating BBs, and lack of follow-up were limitations of our study.

Conclusions

Oscillometric PWA on treated hypertensives shows favorable effect associated with the use of aspirin, BB, and metformin on hemodynamics-brachial more than central. Arterial stiffness has positive impact of metformin use, indifferent impact of statin and aspirin use, and negative impact of BB use. These effects must be considered in studies on hypertensives. It is further to be studied whether these differences are due to drugs or conditions indicating them.

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Conflicts of interest

There are no conflicts of interest.

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