Am J Cardiovasc Dis 2021;11(5):601-610
www.AJCD.us /ISSN:2160-200X/AJCD0136932

Original Article

Effectiveness and safety assessment of beta-blockers, calcium channel blockers, and angiotensin receptor blockers in hypertensive patients: a prospective study

Nilay Solanki[1], Dhruvi Pandit[1], Shubha Desai[2]

[1]Department of Pharmacology, Ramanbhai Patel College of Pharmacy, Charotar University of Science and Technology, CHARUSAT Campus, Changa 388421, Gujarat, India; [2]Research Department, Dr. Jivraj Mehta Smarak and Health Foundation, Ahmedabad, Gujarat, India

Received July 2, 2021; Accepted August 23, 2021; Epub October 25, 2021; Published October 30, 2021

Abstract: Background: Hypertension is most common prevailing cardiovascular disease worldwide. In this condition the effectiveness and safety of already available and many time-tested medications should be regularly reviewed. Methodology: Ethical approval of study was obtained from human research ethics committee of the hospital. 180 patients were enrolled with three groups of antihypertensive medication groups as calcium channel blocker (amlodipine), beta blocker (metoprolol) and angiotensin receptor blocker (telmisartan) over a span of eight months. The data was obtained from week zero to twelve (SBP: Systolic Blood Pressure and DBP: Diastolic Blood Pressure). Safety of Beta blocker, calcium channel blocker and angiotensin receptor blocker were investigated. Results: Comparison of efficacy between the beta blocker, calcium channel blocker and angiotensin blocker receptor blocker were shown to be non-significant. It indicated that all drug therapies have the same successful reduction of SBP (P-0.4819). No significant adverse reactions were observed in either class of the medicines. Conclusion: The study showed the efficacy of Calcium Channel Blocker, Beta Blocker and Angiotensin Receptor Blocker in reduction of SBP & DBP was same, while Calcium Channel Blockers were superior to other two medications.

Keywords: Calcium channel blocker, beta blocker, angiotensin receptor blocker, safety, efficacy

Introduction

Hypertension is a common root of disease and mortality worldwide [4]. Systolic blood pressure above 140 mmHg and diastolic blood pressure beyond 90 mmHg is characterized as hypertension [18]. Approximately 50 million population in the USA and 1 billion all over the world are affected by hypertension [17]. Cardiac output and peripheral vascular resistance are circumstances of BP (Blood Pressure) [4]. Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) in its 7th report of 2003 defined pre-hypertension as 120-139 mmHg systolic or 80-89 mmHg diastolic, whereas the European Society of Hypertension Guidelines (2007) [17]. British Hypertension Society (BHS) IV (2004) uses optimum, normal, and high normal categories to subdivide pressures lower than 140 mmHg systolic and 90 mmHg diastolic [8]. A joint guideline that updated the recommendations of the JNC7 report is published by the American Heart Association and the American College of Cardiology [9]. Cardiovascular risks can be decreased by monitoring and regulating BP in its normal range [2]. Hypertension is accompanied by cardiovascular complications, stroke, and renal diseases [1]. Hypertension can be classified as essential and secondary. 90-95% of hypertensive cases belong to the introductory class with no medical history of hypertension [4, 24] and 5-10% cases of secondary hypertension due to endocrine and kidney disease [19, 24]. A correlation was demonstrated through observational, epidemiological, and cohort studies between elevated systolic BP (SBP) and diastolic BP (DBP) with increased cardiovascular risks [6, 16, 25, 25, 31]. Pre-hypertension is an indicator of

CVD. Lifestyle changes and medicaments can reduce CV complications [3]. Cardiovascular disease has been seen mostly in men rather than women for many years. The proportion of all deaths due to cardiovascular disease is lower among men (37%) than women (43%). Furthermore, the prevalence of this disease has seen to be decreased in men and uplifted in women in the last ten years [5]. CV risks can also be extrapolated with higher BMI as per epidemiological studies [22, 23]. As per the WHO report, 62% of cerebrovascular disease and 49% of the ischemic heart disease result from sub-optimal BP (>115 mmHg) with minor deviations by gender [9].

Adults

People aged 18 years or more suffering from hypertension are prone to have more than 129 or 139 mmHg systolic, 89 mmHg diastolic pressure as per the guideline. Other approaches are used if measurements are obtained from home monitoring or 24 hours ambulatory (135 mmHg systolic or 85 mmHg diastolic) [5, 6].

Children

Around 0.2 to 3.0% of newborns come up with hypertension; however, in healthy newborns, the BP is not measured routinely [11]. Hypertension is more common in newborns. Birth weight, Gestational age, postconceptional age are the variety of factors influencing BP [10]. Hypertension and pre-hypertension are identified and classified using similar criteria as in adults is proposed by BP [11].

Classification of hypertension

Classification based on etiology [14, 15]

Essential hypertension: The cause for hypertension is an idiosyncrasy in 90% of patients with elevated arterial BP. Genetic make-up, blood relatives, and indicating these are the effective factors for essential hypertension.

Secondary hypertension: Less than 1/10th% of patients suffer from secondary hypertension.

Remediable hypertension: Very negligible patients have a spirit to prevent the hypothesis, which is occurred by renal disease, adrenal disease, and so on. The most curable case of hypertension is renovascular hypertension which comprises 0.5% of cases.

Drug-induced hypertension: Twenty patients consuming oral contraceptives were associated with hypertension. Females were less prone to hypertension due to estrogen, but progestin can elevate the BP.

Classification as per WHO [12]

Staging of normal, high normal, stage-1 mild, stage-2 moderate and stage-3 severe SBP (mmHg) are 130, 130-139, 140-159, 160-179, greater than 180 respectively, while staging of Normal, high normal, stage-1 mild, stage-2 moderate and stage-3 severe DBP (mmHg) are less than 85, 85-89, 90-99, 100-109, greater than 110 respectively.

Classification as per JNC [13]

Staging of normal, pre-hypertension, stage-1 and stage-2 SBP (mmHg) are less than 120, 120-139, 140-159 and greater than 160 respectively; while staging of Normal, pre-hypertension, stage-1 and stage-2 DBP (mmHg) are less than 80, 80-89, 90-99 and greater than 100 respectively.

Diagnosis includes an overview of the medical history of individuals and family, physical examination, laboratory tests, and other co-morbidity associations [7].

Extreme high blood pressure is not curable because the cause is not identified. But if uncontrolled, several body vital organs such as the heart, brain, kidney, and retina can be affected. Blood pressure regulation is therefore important and must be maintained at normal or near-normal levels. Antihypertensive agents help to regulate and monitor BP [27, 44], surpass the CV diseases [30] and reduce the rate of death and morbidity associated with CVD [32, 33]. Since different groups have various pharmacodynamics and kinetics, they can also be combined.

Calcium channel blockers, beta-blockers, and ARBs are the three most used, time-tested types of antihypertensives. B-blockers were found to be partially cardio-selective membrane stabilizers, intrinsic sympathomimetic agents [29]. While there have long been in use

Table 1. Classification of hypertension according to JNC 7

	SBP	No. of Patients	DBP	No. of Patients
Normal	>120	0	>90	13
Pre hypertension	120-139	104	80-89	153
Stage-1 Hypertension	140-159	66	90-99	14
Stage-2 Hypertension	>160	10	>100	0
Total		180		180

for hypertension, in this age of newer and newer molecules that come on the market and are used, it's also important to reassess and repeatedly compare the efficacy and protection of these old medicines. We, therefore, planned to carry out this future analysis.

Methodology

Study site

The study was conducted at the multi-specialty hospital, Ahmedabad. Hospital is fully equipped, excellent staffed, and with fully air-conditioned ICCU with 14 beds and an ICU of 6 beds, to cater to acute cardiac disorders and emergencies.

Study design

The prospective observational research has been performed in hypertensive patients. Adult Patients with outdoor as well as indoor hypertension were included in the study.

Study duration

The study was performed from the period of June 2018 and February 2019.

Number of participants

180 patients.

Selection criteria

Inclusion criteria: 1. Patients were selected randomly having essential hypertension; 2. Age: Above 18-years; 3. Patients of both sexes were included after appropriate consent; 4. Systolic Blood pressure is more than 140 mmHg, and Diastolic Blood Pressure is more than 90 mmHg.

Exclusion criteria: 1. Age <18 years; 2. Patients who were not treated with hypertension medications; 3. Females who are pregnant or breastfeeding or on the oral contraceptive pill; 4. Individuals with Diabetes Mellitus.

Ethical approval

Ethical approval was obtained from the institutional ethics committee from the Research Department at Shree Jivraj Mehta Smarak and Health Foundation (ECR/274/inst/GJ/2013/RR-19).

Data collection

Patients' data were collected in preapproved CRF (case record form), consisting of patient history, prescribed drugs, presenting complaint, co-morbid condition, and adverse events, if any. The informed consent form was acquired from the patients. All patients were recorded with age, gender, body weight, and height. Blood pressure pre-therapy was reported, and patients were graded as per JNC 7 classification (**Table 1**).

Calcium blocker (Amlodipine), beta-blocker (Metoprolol), ARB (Telmisartan) was selected for either class. Blood pressure measurement was conducted on a weekly basis (SBP: Systolic Blood Pressure and DBP: Diastolic Blood Pressure), and data were reported in the case record form from week 0 to week 12. Patients were often interviewed during each appointment for any new symptoms or raised severity of symptoms. All complaints have been recorded in the CRF. A master diagram was prepared for patients, and all information was collected using a statistical approach (the t-testing of blood pressure values pre and post-treatment).

Evaluating parameters

1) Effectiveness of antihypertensive drugs was analyzed through Blood pressure measurement (SBP: Systolic Blood pressure and DBP: Diastolic Blood Pressure) was carried out by hospital staff, and data were collected from week 0 to week 12. 2) Safety of Beta-blocker, Calcium channel blocker, and Angiotensin receptors blockers were analysed.

Table 2. Distribution of hypertensive patients

	Gender	No. of patients	Mean ± SEM
Age (years)	Male	104	63.902 ± 7.621
	Female	76	64.671 ± 4.552
	Total	180	64.285 ± 6.086
BMI (kg/m^2)	Male	104	27.815 ± 1.309
	Female	76	28.092 ± 1.343
	Total	180	27.953 ± 1.326
SBP (mm of Hg)	Male	104	154.40 ± 0.811
	Female	76	158.023 ± 0.913
	Total	180	156.2115 ± 0.862
DBP (mm of Hg)	Male	104	83.991 ± 0.708
	Female	76	85.384 ± 0.832
	Total	180	85.687 ± 0.77
Pulse (min)	Male	104	89.68 ± 5.37
	Female	76	90.80 ± 5.57
	Total	180	90.24 ± 5.47

Table 3. Classification of BMI in hypertensive patients

Classification	BMI (kg/m^2)	Male (%)	Female (%)	Total (%)
Underweight	<18.50	0 (00)	2 (2.63)	2 (1.11)
Normal range	18.50-24.99	28 (26.92)	18 (23.68)	46 (25.55)
Overweight	25.00-29.99	41 (39.42)	30 (3.94)	71 (39.44)
Obese	≥30.00	35 (33.65)	27 (35.52)	62 (34.44)
Total		104 (100)	76 (100)	180 (100)

Table 4. Associated co-morbidity with hypertension

Co-morbidity	No. of patients	% Of patients
CAD	40	30.79
CKD	5	3.84
CV stroke	8	6.15
Diabetes	65	50
Heart disease	1	0.76
Hyperlipidaemia	2	1.53
Hyperthyroidism	4	3.07
IHD	5	3.84

Statistical analysis

- Blood Pressure (BP) data were illustrated as the mean ± SEM (Standard error of mean).
- Distribution of condition (Hypertension) was mentioned as mean ± SEM.
- The effectiveness of antihypertensive drugs was assessed by change in BP from the baseline by paired t-test and mentioned as mean ± SEM. *P*-value ≤0.05 was considered significant.

Results

Demographic and clinical parameters of hypertensive patients

Table 2 shows the distribution of hypertensive patients according to Age, Body mass index (BMI), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP).

Classification of hypertension according to JNC 7

Out of 180 patients, no patient was under the normal group (SBP>120). One hundred four patients were pre-hypertensive (120-139). Sixty-six patients were in Stage-1 Hypertension (140-159) and ten patients in Stage-2 hypertension (>160). In Diastolic Blood Pressure, out of 180 patients, 13 patients belonged to the Normal group (>90) and 153 patients in Pre-Hypertension (80-89). Fourteen patients were shown in Stage-1 Hypertension (140-159) and zero patients under Stage-2 Hypertension (>100).

Hypertensive patients with BMI rating

Most patients fall within a spectrum of overweight (39.44%). Many male patients displayed overweight and obesity compared to females (**Table 3**).

Related hypertension co-morbidity

In the current study, the majority of hypertensive patients between 50 and 79 years evidenced co-morbidities. Most common was diabetes Mellitus 65 (50%), followed by coronary artery disease 40 (30.79%), Hypothyroidism 4 (3.07%), and Hyperlipidemia 2 (1.53%), Chronic Kidney Failure & Ischemic Heart Disease 5 (3.84%) (**Table 4**).

Hypertensive patients' age distribution

Table 5 represent age-wise patient distribution. In our sample, hypertension prevalence in the

Table 5. Age distribution of hypertensive patients

Age	Male (%)	Female (%)	Total (%)
20-29	0 (00)	4 (5.26)	4 (2.22)
30-39	4 (3.84)	3 (3.94)	7 (3.88)
40-49	11 (10.57)	2 (2.63)	13 (7.22)
50-59	24 (23.07)	13 (17.10)	37 (20.55)
60-69	30 (28.84)	21 (27.63)	51(28.33)
79-79	19 (18.26)	24 (31.57)	43 (23.88)
80-89	14 (13.46)	7 (9.21)	21 (11.66)
90-99	2 (1.92)	2 (2.63)	4 (2.22)
Total	104 (100)	76 (100)	180 (100)

Table 6. Side effects in gender group

Class of drug	Gender wise patients	
	Male	Female
Beta blocker	14	10
Ca channel blocker	5	8
ARB	6	9

20-29 year age group was 2.22%, rising from 50-79 years to 28.33%. In the elderly, 51.8% prevalence was found in 60-69 years.

Side-effect profile based on gender

In beta-blocker, the male had more side effects than female whereas calcium channel blocker and ARB more side effects were observed in female than male (**Table 6**).

Efficacy of hypertensive patients treatment

Blood Pressure was successfully lowered by all three classes of medications. It was evidenced that one factor of effectiveness in systolic blood pressure was removed between the group analyzes of Beta Blocker, Calcium Channel Blocker, and Angiotensin Receptor Blockers by ANOVA (*P*-value-0.481856, F-value-0.73313). This research showed that the effectiveness of all three classes of antihypertensive drugs substantially decreased diastolic blood pressure. Beta-blocker, calcium canal blocker, and angiotensin receptor blocker by ANOVA were found to be a factor in the effectiveness of the diastolic blood pressure (*P*-value <0.00001, F-value-16.20) (**Tables 7**, **8**).

Safety assessment of antihypertensives

Mild to moderate degrees of side effects for all three medications were observed. Patients administering β-blockers had Cough (3.70%), dry mouth (33.33%), fatigue (7.40%), nausea (3.70%), stomach discomfort (7.40%), skin rashes (44.44%). Complaints about calcium channel blockers include Sedation (66.66%), vomiting (13.33%), stomach pain (6.66%), and swelling (13.33%). However, ARB induced cough (15.78%), headache (21.05%), nausea (31.57%), skin rashes (31.57%). All these side effects were mild and did not require drug dose monitoring because they confined themselves and needed no further care (**Table 9**).

Discussion

The current study contains 180 patient's enrollment, and data collection was done in Case record form consisting of 104 males and 76 females.

Age ranging from 20-99years was included. The majorly affected age group was 61-69 years, with a total of 51 (28.33) subjects having 30 (28.84) males and 21 (27.63) females. One drug utilization study showed that out of two hundred patients, 115 (57%) patients were females and 85 (43%) were males, which is slightly different from current study results [48]. The average age was found to be 53.36 years in an open-labeled study [20]. In one study, cardiovascular disease patients were observed of the age group 51-60 years (37.5%) followed by 61-70 years (20%), where Male patients (63%) had a higher prevalence of Cardiovascular disease than females (37%) [46].

As per JNC 7 classification, in the case of systolic BP 104 (120-139) patients were pre-hypertensive, followed by 66 patients under Stage-1 Hypertension (140-159). While for diastolic BP, 153 patients were observed in the Pre-Hypertension group (80-89), followed by 14 patients were shown in Stage-1 Hypertension (140-159).

BMI-based classification showed that prominent patients were included in the over-weight range (39.44%). The obese and overweight males showed higher BMI compared to females. In our study, most of the hypertensive patients fall under the age range of 50-79 years, along with other co-morbidities. A study observed that overweight criteria were linked with 2 to 6 fold increased risk of developing hypertension. The study suggested that 10% increases in the weight give increase of 6.5

Table 7. Effectiveness of hypertensive patients (systolic BP)

Class of Drugs	Before ± SEM	After ± SEM	Difference	*P* value
Beta Blocker	157.43 ± 8.76	138.93 ± 2.66	18.5	0.0000069
Ca channel Blocker	160.77 ± 9.45	138.88 ± 3.58	21.89	0.0000014
ARB	153.78 ± 9.93	137.1 ± 2.33	16.68	0.0001670

Table 8. Effectiveness of hypertensive patients (diastolic BP)

Class of Drugs	Before ± SEM	After ± SEM	Difference	*P* value
Beta blocker	89.91 ± 4.56	84.08 ± 1.43	5.83	0.00308069
Ca channel blocker	89.09 ± 4.61	82.03 ± 0.84	7.06	0.000403974
ARB	83.0 ± 3.87	80.58 ± 0.52	2.42	0.027018544

mmHg in systolic pressure [29]. It was also noted that 78% of cases of hypertension in males and 65% in females are linked with obesity [21, 29]. A recent study showed a causal relationship between BMI with hypertension [9, 22]. However, these studies were done in the western population. The WHO showed that the occurrence of overweight (BMI≥30 kg/m^2) was higher in the Americans 27% obese and 61% overweight or obese in both sexes. In contrast, the Korean community has a lower obese population (4.6% obese and 31% overweight or obese in both sexes). However, The United States and Korea have the same prevalence of hypertension (9.4% vs. 8.4% respectively) [23, 33].

Diabetes 65 (50%) was the most common precipitating condition associated with hypertension in this study, followed by coronary artery disease 40 (30.79%), Cardiovascular Stroke 8 (6.15), Chronic Kidney Failure & Ischemic Heart Disease 5 (3.84%), Hyperthyroidism 4 (3.07), and Hyperlipidemia 2 (1.53%), heart disease 1 (0.76%). A clinical study observed that diabetes (13%) was the highest co-morbid condition along with hypertension, followed by hyperlipidemia (7.5%), Renal disorder, obesity (6.5%), peptic ulcer disease, and stroke (4% each), and congestive cardiac failure (3.5%) [24].

In beta-blockers, males were more prone to side effects than females, whereas, in calcium channel blockers and ARB, females had major side-effect profiles. A study consisting of 14644 patients treated with beta-blockers (65% female, 66.1 years) were like those of the 40676 patients who received other antihypertensive drugs (57% female, 65.9 years). It showed that beta-blocker might be associated with a higher cause of mortality and morbidity and other side effects in female as compared to the male [42]. Another study expressed higher incidences of stroke with β-blockers [34].

As a matter of efficacy, all three classes of antihypertensives showed an efficient reduction in BP. In a study consisting of 1797 patients, 760 (42.3%) were newly, and 1037 (57.7%) were previously diagnosed. Of these, 29.9% were classified as high-risk and 43.2% under very high-risk group. Amlodipine was administered for six months follow-up with the conclusion of high potency and safety [37, 24]. A significant decrease in Blood pressure was noted in 87 patients at a daily dose of 5-10 mg Amlodipine were enrolled in the study [41]. It was found that calcium channel blockers have better efficacy compared to other classes of drugs for long-term treatment and even in combination [39, 40, 28]. 61-91% of patients achieved desired BP with the help of amlodipine [26]. In a previous study, it was shown that 696 patients were assigned, of which 85 patients met all inclusion criteria. Systolic Blood Pressure was calculated, which included that systolic Blood Pressure decreased by a mean of 17.5 mm Hg from baseline [38].

Cough (3.70%, n=1), Dry mouth (33.33%, n=9), Fatigue (7.40%, n=2), Nausea (3.70, n=1), Gastrointestinal pain (7.40, n=2), Rashes on the skin (44.44%, n=12) were the common side-effects observed for β-blockers. A study indicated that side-effects of β-blockers could be due to pharmacological or non-pharmacological consequences. Other Side effects like bronchospasm, heart failure, depression, Bradycardia, nightmares, heart block are associated [43]. They are inferior in terms of side effects compared to calcium channel blockers [35]. They elevated the risk of CV disease, stroke, and mortality than calcium channel blockers [36]. In one study, antiplatelet, Dyslipidemia agents, and Beta-blockers were prescribed as 34%, 19%, and 14%, respective-

Table 9. Side effects reported in angiotensin receptor blocker, beta blocker and Calcium channel blocker

Reported Side Effects	Reported in Angiotensin Receptor Blocker	Reported in Beta Blocker	Reported in Calcium channel Blocker
	No. of Patients (%) (N=19)	No. of Patients (%) (N=27)	No. of Patients (%) (N=15)
Cough	3 (15.78)	1 (3.70)	-
Headache	4 (21.05)	-	2 (13.33)
Nausea	6 (31.57)	1 (3.70)	-
Skin rashes	6 (31.57)	-	-
Dry mouth	-	9 (33.33)	-
Gastrointestinal Pain	-	2 (7.4)	1 (6.66)
Rashes on skin	-	12 (44.44)	-
Fatigue	-	2 (7.4)	-
Sedation	-	-	10 (66.6)
Swelling on legs	-	-	2 (13.33)

ly, while antianginals, ACE inhibitors, and diuretics were prescribed in 11%, 8%, 5%, respectively [46]. Another study showed out of 187 patients received monotherapy, which revealed that calcium channel blockers were the drugs of choice for hypertensive patients because it is prescribed to 54 (28.87%) patient of hypertension as single-drug therapy, followed by the fixed-dose combination (FDC) of β-blockers with amlodipine 42 (22.45%), β-blockers 37 (19.78), angiotensin two receptor blocker 23 (12.29%), diuretics 9 (4.81%), angiotensin-converting enzyme inhibitors 9 (4.81%) [47].

Side-effect profile of calcium channel blockers include Sedation (66.66%, n=10), Headache (13.33%, n=2), Gastrointestinal pain (6.66%, n=1), Swelling in the leg (13.33%, n=2). The study stated major side effects associated with calcium channel blockers such as headache, flushing, palpitations, peripheral Edema, and hypotension [44].

ARBs resulted in cough (15.78%, n=3), headache (21.05%, n=4), nausea (31.57%, n=6), skin rashes (31.57%, n=6). Headache, respiratory infection, dizziness and fatigue were reported with 2.1% on Telmisartan 40 mg, 4.5% on Telmisartan 80 mg [45].

Conclusion

In this study, we observed that diabetes is the most common co-morbid condition associated with hypertension in the effectiveness and protection of the anti-hypertension drug. The most prescribed antihypertensive was amlodipine (calcium channel blocker) followed by Metoprolol (β-blocker) and telmisartan (angiotensin receptor blocker). Three types of antihypertensive drugs were found to reduce systolic and diastolic blood pressure substantially in all patients. Mild to moderate side effects were observed with all three classes of drugs.

Acknowledgements

All the authors are thankful to Ramanbhai Patel College of Pharmacy, Charotar University of Science and technology, CHARUSAT Campus, changa and Dr. Jivraj Mehta Smarak and Health foundation, Ahmedabad for necessary help during the study.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Nilay Solanki, Department of Pharmacology, Ramanbhai Patel College of Pharmacy, Charotar University of Science and Technology, CHARUSAT Campus, Changa 388421, Gujarat, India. E-mail: nivyrx@gmail.com

References

[1] Lackland DT and Weber MA. Global burden of cardiovascular disease and stroke: hypertension at the core. Can J Cardiol 2015; 315: 569-71.

[2] Daniels SR, Kimball TR, Khoury P, Witt S and Morrison JA. Correlates of the hemodynamic determinants of blood pressure. Hypertension 1996; 28: 37-41.

[3] Nakkeeran M, Periasamy S, Inmozhi SR and Ramya P. Oxidative stress, antioxidant status

and Hs-CRP levels in essential hypertension. IOSR J of Den and Med Sci 2017; 16: 100-103.
[4] Poulter NR, Prabhakaran D and Caulfield M. Hypertension. Lancet 2015; 386: 801-12.
[5] Kasper D, Fauci A and Hauser S. Harrison's principle of internal medicine 19th edition. 2012. pp. 15-25.
[6] Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbiagele B, Smith SC Jr, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA Sr, Williamson JD and Wright JT Jr. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Hypertens 2017; 71: 1269-1324.
[7] 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 and Zanchetti A; ESH-ESC Task Force on the Management of Arterial Hypertension. 2017 ESH-ESC practice guidelines for the management of arterial hypertension. J Hypertens 2007; 25: 1751-1762.
[8] Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JF, Sever PS and McG Thom S; British Hypertension Society. Guidelines for management of hypertension: report of the fourth working party of the british hypertension society, 2004-BHS IV. J Hum Hypertens 2004; 18: 139-85.
[9] Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr and 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. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. hypertension. Joint national committee on prevention. JAMA 2003; 289: 2560-72.
[10] Dionne JM, Abitbol CL and Flynn JT. Hypertension in infancy: diagnosis, management and outcome. Pediatr Nephrol 2011; 27: 17-32.
[11] National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 2004; 114: 555-76.
[12] Thomas G. A clinical classification of hypertension. Chin Med 2006; 119: 80-83.
[13] Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr and Roccella EJ; Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. Hypertension 2003; 42: 1206-52.
[14] Herfindal ET and Helms RA. Textbook of therapeutics drug and disease management, 8th Edtion. Philadelphia: Lippincott Williams & Wilkins; 2006. pp. 451-481.
[15] Dipiro JT, Talbert RL, Yee GC, et al. Pharmacotherapy: a pathophysiologic approach, 6th Edtion. MC Graw-Hill; 2005. pp. 186-205.
[16] Gupta R. Trends in hypertension epidemiology in India. J Hum Hypertens 2004; 18: 73-78.
[17] National High Blood Pressure Education Program, 2003.
[18] Henshaw CM. Alteration in blood pressure. In: Copstead Banasik JL, editor. Pathophysiology: Biological and behavioural perspective 2nd edition. Philadelphia: WB Saunders Co.; 2004. pp. 374-92.
[19] Barbara G, Schwinghamme TL, Cecily VD, et al. Pharmacotherapy Handbook, 9th edition. MC Graw-Hill; 2005. pp. 87-101.
[20] Rao NS, Oomman A, Bindumathi PL, Sharma V, Rao S, Moodahadu LS, Patnaik A and Kumar BR. Efficacy and tolerability of fixed dose combination of Metoprolol and amlodipine in Indian patients with essential hypertension. J Midlife Health 2005; 4: 1-8.
[21] Gupta R, Guptha S, Gupta VP and Prakash H. Prevalence and determinants of hypertension in the urban population of Jaipur in Western India. J Hypertens 1995; 13: 1193-200.
[22] Fall T, Hägg S, Mägi R, Ploner A, Fischer K, Horikoshi M, Sarin AP, Thorleifsson G, Ladenvall C, Kals M, Kuningas M, Draisma HH, Ried JS, van Zuydam NR, Huikari V, Mangino M, Sonestedt E, Benyamin B, Nelson CP, Rivera NV, Kristiansson K, Shen HY, Havulinna AS, Dehghan A, Donnelly LA, Kaakinen M, Nuotio ML, Robertson N, de Bruijn RF, Ikram MA, Amin N, Balmforth AJ, Braund PS, Doney AS, Döring A, Elliott P, Esko T, Franco OH, Gretarsdottir S, Hartikainen AL, Heikkilä K, Herzig KH, Holm H, Hottenga JJ, Hyppönen E, Illig T, Isaacs A, Isomaa B, Karssen LC, Kettunen J, Koenig W, Kuulasmaa K, Laatikainen T, Laitinen J, Lindgren C, Lyssenko V, Läärä E, Rayner NW, Männistö S, Pouta A, Rathmann W, Rivadeneira F,

Ruokonen A, Savolainen MJ, Sijbrands EJ, Small KS, Smit JH, Steinthorsdottir V, Syvänen AC, Taanila A, Tobin MD, Uitterlinden AG, Willems SM, Willemsen G, Witteman J, Perola M, Evans A, Ferrières J, Virtamo J, Kee F, Tregouet DA, Arveiler D, Amouyel P, Ferrario MM, Brambilla P, Hall AS, Heath AC, Madden PA, Martin NG, Montgomery GW, Whitfield JB, Jula A, Knekt P, Oostra B, van Duijn CM, Penninx BW, Smith GD, Kaprio J, Samani NJ, Gieger C, Peters A, Wichmann HE, Boomsma DI, de Geus EJ, Tuomi T, Power C, Hammond CJ, Spector TD, Lind L, Orho-Melander M, Palmer CN, Morris AD, Groop L, Järvelin MR, Salomaa V, Vartiainen E, Hofman A, Ripatti S, Metspalu A, Thorsteinsdottir U, Stefansson K, Pedersen NL, McCarthy MI, Ingelsson E and Prokopenko I; European Network for Genetic and Genomic Epidemiology (ENGAGE) consortium. The role of adiposity in cardiometabolic traits: a Mendelian randomization analysis. PLoS Med 2013; 10: e1001474.

[23] Holmes MV, Lange LA, Palmer T, Lanktree MB, North KE, Almoguera B, Buxbaum S, Chandrupatla HR, Elbers CC, Guo Y, Hoogeveen RC, Li J, Li YR, Swerdlow DI, Cushman M, Price TS, Curtis SP, Fornage M, Hakonarson H, Patel SR, Redline S, Siscovick DS, Tsai MY, Wilson JG, van der Schouw YT, FitzGerald GA, Hingorani AD, Casas JP, de Bakker PI, Rich SS, Schadt EE, Asselbergs FW, Reiner AP and Keating BJ. Causal effects of body mass index on cardio metabolic traits and events: a mendelian randomization analysis. Am J Hum Genet 2014; 94: 198-208.

[24] Beevers G, Lip GY and O'Brien E. The pathophysiology of hypertension. Br Med J 2001; 322: 912-6.

[25] Malacco E, Leonetti G and Santini F. Comparison of calcium agonist and an ACE inhibitor in the treatment of elderly hypertensive patients. Curr Ther Res 1993; 54: 695-702.

[26] Haria M and Wagstaff AJ. Amlodipine. A reappraisal of its pharmacological properties and therapeutic use in cardiovascular disease. Drugs PMC 1995; 50: 560-86.

[27] ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). JAMA 2002; 288: 2981-97.

[28] Gottwald-Hostalek U, Sun N, Barho C and Hildemann S. Antihypertensive effectiveness of amlodipine in combination with hyperchlorothiazide. Am J Hypertens 1989; 2: 537-41.

[29] Wilcox RG. Randomized study of six-beta-blockers and a thiazide diuretic in essential hypertension. Br Med J 1978; 2: 383-85.

[30] Turnbull F; Blood Pressure Lowering Treatment Trialists Collaboration. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively designed overviews of randomized trials. Lancet 2003; 362: 1527-1535.

[31] Dahlöf B, Devereux RB, Kjeldsen SE, Julius S, Beevers G, de Faire U, Fyhrquist F, Ibsen H, Kristiansson K, Lederballe-Pedersen O, Lindholm LH, Nieminen MS, Omvik P, Oparil S and Wedel H; LIFE Study Group. Cardiovascular morbidity and mortality in the Losartan Intervention for Endpoint reduction in hypertension study (LIFE): a randomized trial against atenolol. Lancet 2002: 359: 995-1003.

[32] Dahlöf B, Sever PS, Poulter NR, Wedel H, Beevers DG, Caulfield M, Collins R, Kjeldsen SE, Kristinsson A, McInnes GT, Mehlsen J, Nieminen M, O'Brien E and Ostergren J; ASCOT Investigators. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required. In the anglo-scandinavian cardiac outcomes trial-blood pressure lowering arm (ASCOT-BPLA): a multicentre randomized controlled trial. Lancet 2005; 366: 895-906.

[33] Messeril FH, Grossman E and Goldbourt U. Are β-blockers efficacious as first-line therapy for hypertension in the elderly? A systemic review. JAMA 1998; 279: 1903-1907.

[34] Lindholm LH, Carlberg B and Samuelsson O. Should beta blockers remain first choice in the treatment of primary hypertension? A meta-analysis. Lancet 2005; 366: 1545-1553.

[35] Wiysonge CS, Bradley H, Mayosi BM, Maroney R, Mbewu A, Opie LH and Volmink J. Beta blockers for hypertension. Cochrane Database Syst Rev 2007; 20: 917-922.

[36] Massie BM. Review: available evidence does not support the use of beta-blockers as first-line treatment for hypertension. Evid Based Med 2007; 12: 112.

[37] Valcárcel Y, Jiménez R, Arístegui R and Gil A; Nota Study Group. Effectiveness and safety of amlodipine in newly diagnosed hypertensive patients and in previously diagnosed hypertensive patients not controlled with their usual treatment. Clin drug Investig 2003; 23: 761-770.

[38] Levine CB, Fahrbach KR, Frame D, Connelly JE, Estok RP, Stone LR and Ludensky V. Effect of amlodipine on systolic blood pressure. Clin Ther 2003; 25: 35-57.

[39] Cross BW, Kirby MG, Miller S, Shah S, Sheldon DM and Sweeney MT. A multicentre study of the safety and efficacy of amlodipine in mild to moderate hypertension. Br J Clin Pract 1993; 47: 237-240.
[40] Takagi H and Umemoto T. Revisiting evidence of blood pressure-dependent and independent effects of amlodipine on the risk of stroke. J Clin Hypertens 2011; 13: 781-782.
[41] Habeler G, Lenzhofer R, Pall H, Tomaschek A, Ziebart-Schroth A, Zirm B and Ganzinger U. Effectiveness and tolerance of amlodipine in the treatment of patients with mild to moderate hypertension. Wien Klin Wochenschr 1992; 104: 16-20.
[42] Jørgensen ME, Hlatky MA, Køber L, Sanders RD, Torp-Pedersen C, Gislason GH, Jensen PF and Andersson C. β-blocker-associated risks in patients with uncomplicated hypertension undergoing noncardiac surgery. JAMA 2015; 175: 1923-1931.
[43] Frishman WH. Beta-adrenergic receptor blockers. Adverse effects and drug interactions. Hypertens 1988; 11: II21-9.
[44] Russell RP. Side effects of calcium channel blockers. Hypertens 1988; 11: 42-44.
[45] Abraham HM, White CM and White WB. The comparative efficacy and safety of the angiotensin receptor blockers in the management of hypertension and other cardiovascular diseases. Drug Saf 2015; 38: 33-54.
[46] Solanki N, Patel V and Patel R. Prescribing trends in cardiovascular conditions: a prospective cross-sectional study. J Basic Clin Pharma 2019; 10: 23-26.
[47] Solanki ND and Patel P. Drug utilization pattern and pharmacoeconomic analysis of antihypertensive drugs prescribed in secondary care hospital in Gujarat, India. Asian J Pharm Clin Res 2017; 10: 120-4.
[48] Solanki N and Patel Y. Drug utilization pattern and drug interaction study of antibiotics prescribed to orthopedic patients in private hospital. Arch Pharm Pract 2019; 1: 114-117.