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Comparative study of effect of amlodipine, atenolol, enalapril and thiazide on arterial blood pressure, heart rate and renal function tests in hypertensive patients

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ABSTRACT

Introduction : Blood pressure can be defined as the force exerted by the blood against any unit area of the vessel wall. The systolic arterial pressure is the maximum pressure in the arteries during systolic phase. Diastolic pressure depends on cardiac output and peripheral vascular resistance. It has long been recognized that mortality and morbidity increase as both systolic and diastolic blood pressure rise. This may lead to changes in heart rate.

Aim&Objectives : To study effect of amlodipine, atenolol, enalapril and chlorothiazide on arterial blood pressure, heart rate and renal function tests.

Materials&Methods : Study type is comparative observational study. Newly diagnosed hypertensive patient will be selected from medicine outpatient department randomly. Their blood pressure and heart rate will be recorded manually while doing selection for study. If blood pressure recorded is ≥ 140/90, then only patient will be included in the study. After that, these 120 patients will be divided in 4 group A, B, C, D. Each cohort contain 30 patients. Patient prescribed with amlodipine will be considered as Group A, likewise prescription of atenolol will be considered as group B, prescription of enalapril will be considered as group C, and prescription of thiazide will be considered as group D. After 15 days all patients will be recalled for follow up. Their blood pressure and heart rate will be recorded. Same procedure will again repeat after 30 days from selection of patients for study. Renal function test will be done before and after the study.Data will be collected for analysis.

Data Analysis: was done by calculating mean & chi square tests.

Results: In terms of effect on systolic blood pressure Enalapril has highest effect. On diastolic blood pressure Atenolol has highest effect. Mean arterial blood pressure was found to be higher decreased by Atenolol. Heart rate was significantly decreased by Atenolol. On blood urea level Atenolol was having maximum effect. Serum creatinine level was higher decreased by Atenolol.

Conclusion: Antihypertensives have effect on blood pressure, heart rate, renal functions. Patients renal function, heart rate should always be considered while prescribing antihypertensive drugs.

Keywords: Hypertension, Heart rate, Renal functions, Cardiovascular complications

INTRODUCTION

Blood pressure is the force exerted by the blood against any unit area of the vessel wall. The systolic arterial pressure is the Maximum pressure in the arteries during systolic phase and diastolic pressure depends upon cardiac output and peripheral vascular resistance. It has long been recognized that mortality and morbidity increase as both systolic and diastolic blood pressure rise. This may lead to changes in heart rate.[1]Hypertensive cardiovascular diseases are a major public health challenge, representing 10% of the global burden of disease. The annual number of deaths caused by cardiovascular disease is expected to rise by more than 33% over the coming two or three decades. Hypertension is among the most important modifiable risk-factors for cardiovascular diseases. Antihypertensive drugs are available which can prevent, or postpone myocardial infarction and stroke. Several clinical trials and systematic reviews have addressed this issue, but have failed to convincingly show that one or more drug-classes are superior to the others.[2]This study effect of amlodipine, atenolol, enalapril and chlorothiazide on arterial blood pressure, heart rate and renal function tests.

Hypertension is very common disease and requires meticulous control to produce the maximum reduction in clinical cardiovascular end points. Approximately 26.4% of the adult population worldwide had hypertension in 2000, and this is expected to increase to 29.2% by 2025.[3] The prevalence of hypertension according to the latest meta-analysis study is 21.9%.[5] Hypertension treatment as a disease is an important public health challenge. Achieving recommended goal appears to be difficult.The variation of Antihypertensive drugs and also extensive clinical studies has led medical practitioners to different ideas for administration of these drugs. The ideal goal is that drug must be efficacious, free from side-effects, enable us to prevent all the complications of hypertension, easy to use and affordable. New onset patients who are diagnosed with uncomplicated hypertension and no compelling indications, choice of first line monotherapy includes angiotensin converting enzyme (ACEI), angiotensin receptor blocker (ARB), calcium channel blocker (CCB) and diuretics. In patients presenting with stage 2 hypertension or beyond, combination therapy is recommended.[4]

METHODOLOGY

The study was carried out after permission from institutional ethics committee. Total 120 patients with hypertension were included in the study. These patients were assigned to one of the 4 groups randomly. [4] There was 30 patients in each group. Patient prescribed with tablet amlodipine 5mg or 10 mg was be considered as Group A, likewise, prescription of tablet atenolol 25 mg or 50 mg was be considered as group B,prescription of tablet enalapril 2.5 mg or 5 mgwas considered as group Cand prescription of tablet thiazide diuretics 12.5 mg or 25 mg was be considered as group D.

Table 1 : Treatment Groups

Study medication	**Group A**	**Group B**	**Group C**	**Group D**
Medicine	Amlodipine	Atenolol	Enalapril	Thiazide
Dose	5 mg or 10 mg	25 mg or 50 mg	2.5 mg or 5 mg	12.5 mg or 25 mg
Dosage	Once a day	Once a day	Once a day	Once a day

It was a comparative observational study. Newly diagnosed hypertensive patient was selected from medicine outpatient department randomly. Their blood pressure and heart rate will be recorded manually while doing selection for study. If blood pressure recorded is equal to or more than ≥ 140/90, then only patient will be included in the study. After that, these 120 patients was divided in 4 group A, B, C, D. Each cohort contain 30 patients having prescribed data of tab amlodipine, atenolol, enalapril and chlorothiazide respectively.After 1 month all patients was recalled for follow up. Their blood pressure and heart rate was recorded. Same procedure will again repeat after 3 month from selection of patients for study. Data will be collected for analysis. Renal function test was done before and after the study.Analysis of data was done by calculating mean, standard deviation and p value.

Inclusion criteria

1) All newly diagnosed hypertensive patient will be included in study.
2) At the time of screening their blood pressure should be equal to or more than 140/90 mmHg.

Exclusion criteria

1) All patient having emergency condition like myocardial infarction, strokeetc. shall not be included in study.

2) All pregnant patientsshall be excluded from study.
3) Patients with nephropathy were excluded from the study.
3) Patients who will not be ready to give consent shall be excluded from study.

Statistical Analysis

Intension to treat analysis (ITT) for safety data and per protocol analysis for efficacy data was performed. Mean SBP, DBP and mean BP were calculated as mean ± standard deviation (SD) and compared between the groups/baseline values using *t*-test. Fischer's exact test was applied to observe if there was significant difference between responder rates and to observe if there were significant difference between proportions of subjects having peripheral edema not attributable to any concomitant drug.

RESULT

Many factors determine the successful management of hypertension & choice of drug class is one that seems to be of limited importance. Thus, clinicians should probably focus more on issues such as limiting adverse events, improving adherence and better follow up of patients rather than on which drug to select. There is considerable variation in costs across different antihypertensive agents, thus cost-effectiveness assessments may be important for decisions about choice of medications. [11,12.13] This study analysed the effect of various antihypertensives on blood pressure, heart rate and renal function test. This study gives values about changes in heart rate. Heart rate & blood pressure are the main indicator of cardiovascular status.[14,15.16] In terms of effect on systolic blood pressure Enalapril has highest effect. On diastolic blood pressure Atenolol has highest effect. Mean arterial blood pressure was found to be higher decreased by Atenolol. Heart rate was significantly decreased by Atenolol. On blood urea level Atenolol was having maximum effect. Serum creatinine level was higher decreased by Atenolol.

Mean Arterial pressure

Method which was used to calculate mean arterial pressure is as follows:

Mean arterial pressure = Diastolic BP + 1/3 (SP-DP)

Comparison of effects on systolic blood pressure (mmHg)

The effects of drugs on systolic blood pressure (mmHg) before & after was studied. Mean change in systolic blood pressure was analyzed by chi square test. It was statistically significant. Highest decrease in blood pressure was seen by Enalapril followed by thiazides, Atenolol & Amlodipine.

Table 2: Comparison of effect of drugs on systolic blood pressure

Groups	Mean systolic blood pressure (mmHg)		Mean change in blood pressure (mmHg)	P-value
	Before (Mean ± SD)	After (Mean ±SD)		
Group 1 Amlodipine	162.45± 4.89	110.67±7.38	51.78	<0.05
Group 2 Atenolol	176.89±23.43	117.27 ±9.54	59.62	<0.05
Group 3 Enalapril	210.56±3.65	129.67 ±08.56	80.89	<0.05
Group 4 Thiazide	188.45±23.28	124.67 ±12.29	63.78	<0.05

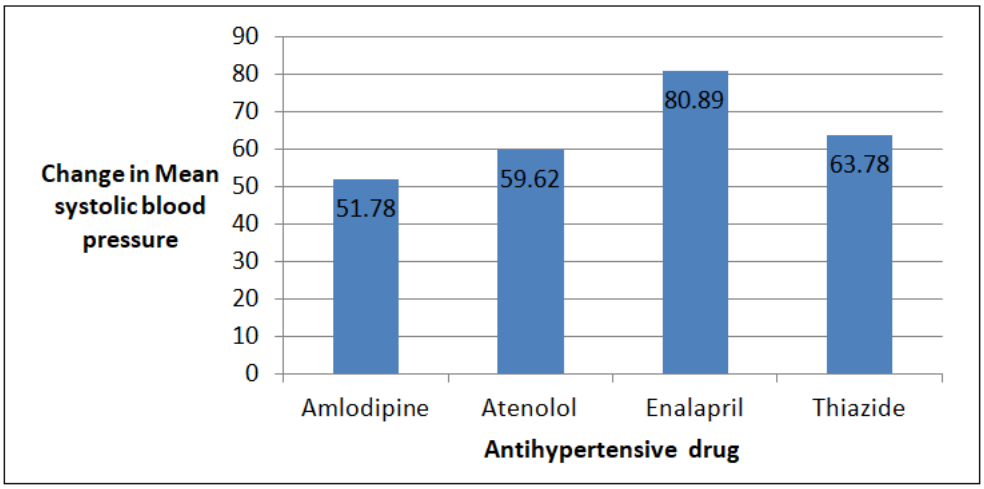


Fig 1:Changein Mean systolic blood Pressure (mmHg)

Comparison of effects on diastolic blood pressure (mmHg)

The effects of drugs on systolic blood pressure (mmHg) before & after was studied. Mean change in diastolic blood pressure was analyzed by chi square test. It was statistically significant. Highest decrease in blood pressure was seen by Atenolol followed by amlodipine, enalapril & thiazide.

Table 3: Mean change in diastolic blood pressure before & after

Groups	Mean diastolic blood pressure (mmHg)		Mean change in blood pressure (mmHg)	P-value
	Before (Mean ±SD)	After (Mean ±SD)		
Group 1 Amlodipine	123.45±14.29	83.67±7.38	39.78	<0.05
Group 2 Atenolol	121.89±23.43	80.27 ±9.54	41.62	<0.05
Group 3 Enalapril	127.56 ±23.65	92.67 ±08.56	34.89	<0.05
Group 4 Thiazide	116.45 ±23.28	86.67 ±12.29	29.78	<0.05

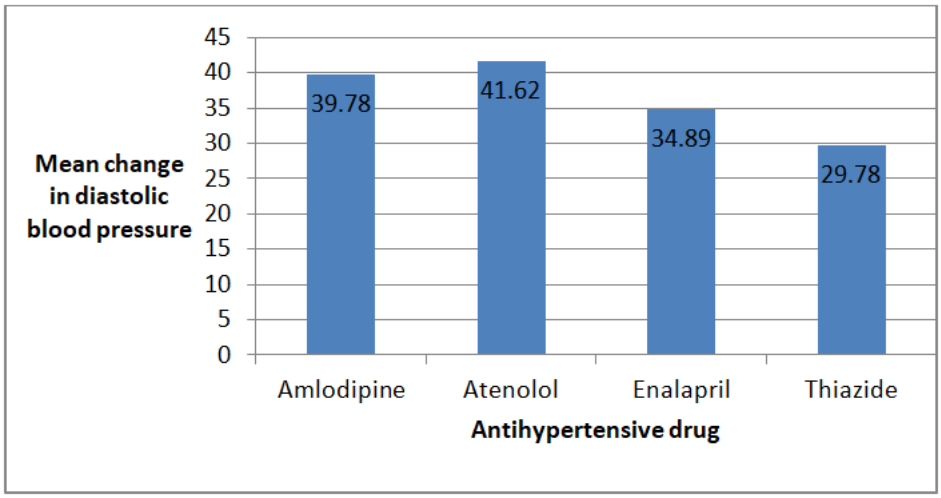


Fig 2: Mean change in diastyolic blood pressure before & after (mmHg)

Comparison of effects on mean arterial pressure (MAP) (mmHg)

The effects of drugs on systolic blood pressure (mmHg) before & after was studied. Mean change in mean arterial blood pressure was analyzed by chi square test. It was statistically significant. Highest decrease in mean arterial pressure was seen by Atenolol followed by amlodipine, enalapril & thiazides.

Table 4: Change in mean arterial pressure(MAP) before & after

Groups	Mean mean arterial pressure (mmHg)		Mean change in blood pressure (mmHg)	P-value
	Before (Mean ± SD)	After (Mean ±SD)		
Group 1 Amlodipine	110.45 ±14.29	74.67±7.38	39.78	<0.05
Group 2 Atenolol	103.56±23.43	69.94 ±9.54	41.62	<0.05
Group 3 Enalapril	99.90±23.65	80.34 ±08.56	34.89	<0.05
Group 4 Thiazide	92.45±23.28	74.01 ±12.29	29.78	<0.05

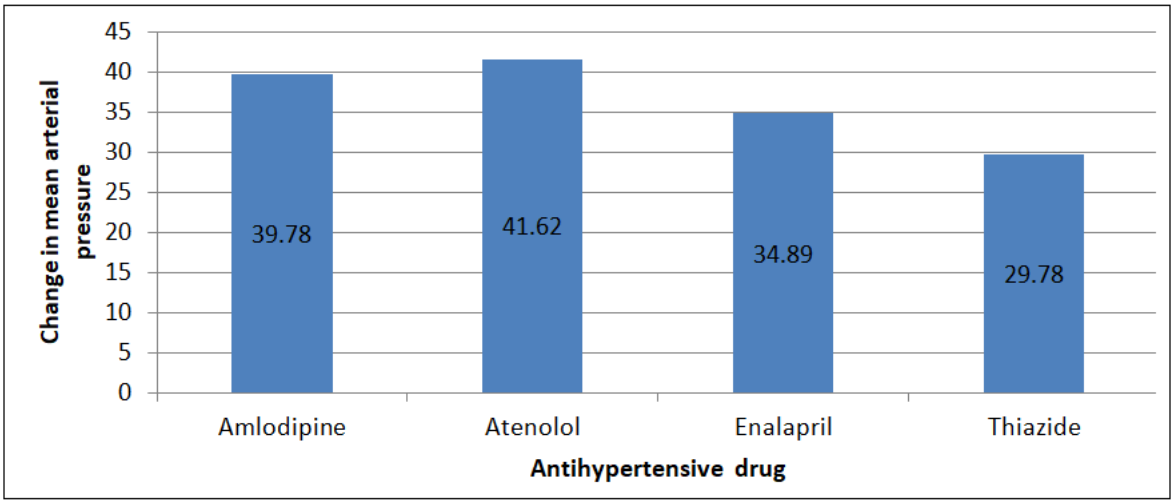


Fig 3: Change in mean arterial pressure (MAP) before & after

Comparison of effects on heart rate

The effects of drugs on systolic blood pressure (mmHg) before & after was studied. Mean change in systolic blood pressure was analyzed by chi square test. It was statistically significant. Highest decrease in blood pressure was seen by Atenolol followed by amlodipine, enalapril & thiazides.

Table 5: Comparison of effect of drugs on heart rate

Groups	Mean heart rate		Mean change in heart rate	P-value
	Before (Mean ±SD)	After (Mean ±SD)		
Group 1 Amlodipine	110.45 ±14.29	74.67±7.38	9.78	<0.05
Group 2 Atenolol	103.56±23.43	69.94±09.54	4.62	<0.05
Group 3 Enalapril	99.90 ±23.65	80.34 ±08.56	4.89	<0.05
Group 4 Thiazide	92.45 ± 23.28	74.01 ±12.29	9.78	<0.05

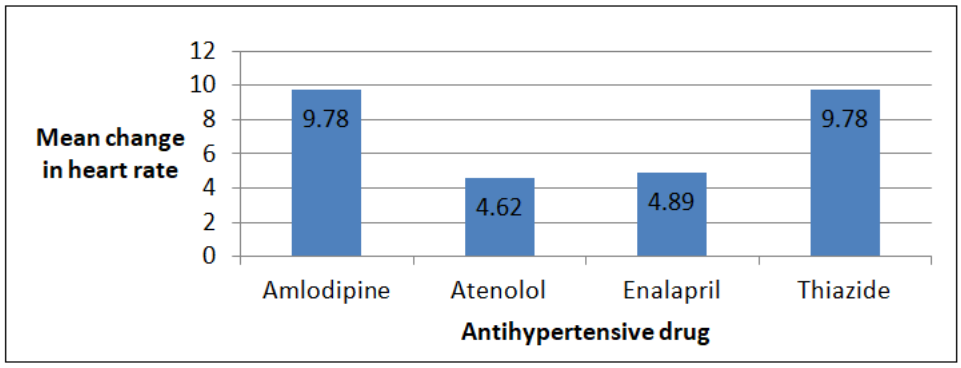


Fig 4: Mean change in heart rate before & after

Comparison of effects on blood urea level (mg/dl)

The effects of drugs on systolic blood pressure (mmHg) before & after was studied. Mean change in blood urea was analyzed by chi square test. It was statistically significant. Highest decrease in blood urea level was seen by Thiazides followed by enalapril, amlodipine & atenolol.

Table 6: Mean change in blood urea level before & after

Groups	Mean blood urea level (mg/dl)		Mean change in blood urea level (mg/dl)	P-value
	Before (Mean ± SD)	After (Mean ± SD)		
Group 1 Amlodipine	20.89 ± 4.29	12.72 ± 5.45	8.17	<0.05
Group 2 Atenolol	21.03 ± 3.43	13.23 ± 3.61	7.80	<0.05
Group 3 Enalapril	19.81 ± 3.65	09.28 ± 6.68	10.53	<0.05
Group 4 Thiazide	21.36 ± 3.28	10.06 ± 2.41	11.30	<0.05

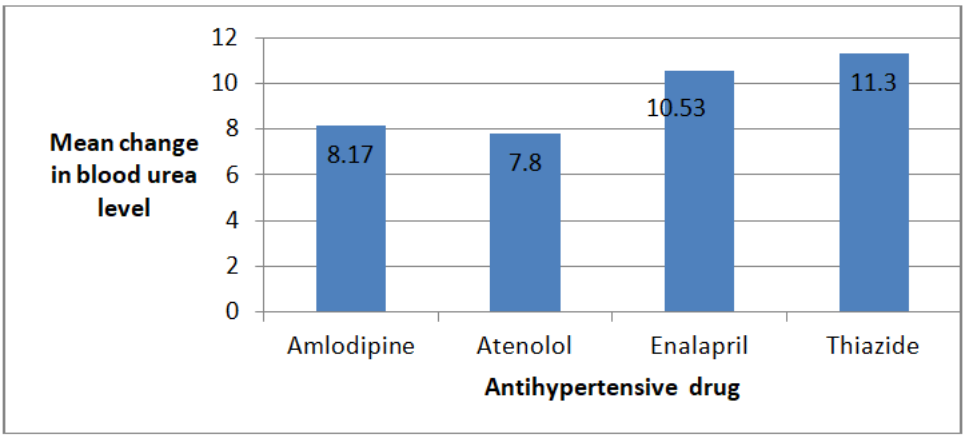


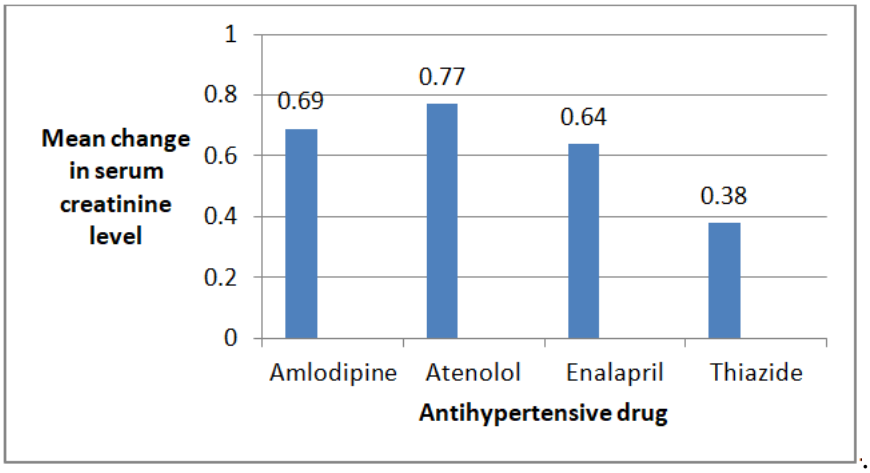
Fig 5: Mean change in blood urea level (mg/dl) before & after

Comparison of effects on serum creatinine level (mg/dl)

The effects of drugs on systolic blood pressure (mmHg) before & after was studied. Mean change in blood urea was analyzed by chi square test. It was statistically significant. Highest decrease in blood urea level was seen by Atenolol followed by amlodipine, enalapril & thiazides.

Table 7: Comparison of effect of drugs on serum creatinine level

Groups	Mean serum creatinine level (mg/dl)		Mean change in serum creatinine level (mg/dl)	P-value
	Before (Mean ± SD)	After (Mean ± SD)		
Group 1 Amlodipine	1.38 ± 4.29	0.69 ± 7.38	0.69	<0.05
Group 2 Atenolol	1.23 ± 3.43	0.46 ± 9.54	0.77	<0.05
Group 3 Enalapril	1.29 ± 3.65	0.65 ± 8.56	0.64	<0.05
Group 4 Thiazide	1.04 ± 3.28	0.66 ± 1.29	0.38	<0.05



Change in serum creatinine level (mg/dl) before & after

Fig 6: Mean change in serum creatinine level (mg/dl) before & after

DISCUSSION

This analysis very comprehensive analysis of the existing data on the comparative effectiveness of different antihypertensive drug-classes. As for most other systematic reviews in this field we find limited evidence of important differences between the various drug-classes.[3] The differences we do find are not easy to put into practice as the ranking of a drug-class depends on which outcome one chooses to emphasize, and no drugs are consistently among the best across all important outcomes. Our ranking of drug-classes may be useful to decision makers, or it may add to the confusion. A study by Brookhart et al. reported that beta blockers like propranolol has prominent effect on heart rate. Our study corresponds with the study. In another study by Majumdar et al., focusing on patients admitted to hospital with community acquired pneumonia, statin users were more likely to be former smokers and have up-to-date immunizations for pneumococcus and influenza. Furthermore, Dormuth et al. reported that for action on mean arterial pressureatenolol had significant effect. Our study correspond to the study. Although the studies differ in terms of design, outcome measure and definition of adherence, they all suggest a healthy adherer or healthy user effect. [4]

This study a comprehensive one including the most recent studies and clinical outcomes of among patients taking major classes of antihypertensive drugs. However, our study has some limitations, majority of which are implicit to the studies included.[5] The limitation is that our interpretation of sub-meta-analysis findings were based on our clinical judgement that assumed prescription of BBs could occur in patients with worse cardiovascular comorbidity. For instance, patients taking certain antihypertensives like BBs may not necessarily have a worse cardiovascular condition. Similarly, even though ACEIs are good choice of antihypertensives in patients without any comorbidity, they are also preferred drugs in those who had myocardial infarction or systolic dysfunction.[6] On the other hand, the strength of this meta-analysis is that we excluded studies that compared hypertensive patients who were taking RAAS inhibitors to those that were not taking any form of antihypertensive (e.g., on dietary management). This helped us to have comparable groups. [7] We should also point out that the quality of the underlying evidence is not taken into consideration in the ranking, thus the results should be interpreted cautiously, and in conjunction with the drug-comparison findings.[8] Beta-blockers (atenolol) were superior to all drug-classes for all primary outcomes, and although the difference in many cases was non-significant and the quality of the evidence was mixed, this may be seen as evidence against opting for these drugs as the first choice. Beta-blockers and alpha-blockers were the only drug-classes that were not

significantly superior to any drug, for any outcome, which could suggest not recommending these as first line medication. [9,10]

FUTURE RESEARCH AGENDA

Despite the fact that many methodologically sound large-scale trials of anti-hypertensive drugs have been conducted, our confidence in the overall findings ranged from very low to high after assessing the quality of the evidence. Future research to improve the quality of hypertension management should also focus on other issues, such as interventions to improve treatment adherence and on how to organise follow-up of patients more effectively.

CONCLUSION

Antihypertensives have effect on blood pressure, heart rate, renal functions. Patients renal function, heart rate should always be considered while prescribing antihypertensive drugs. By presenting the chance that a drug is among the top three for an outcome, we had hoped that one or two drugs would emerge as first choice candidates by being among the three best drugs across several important outcomes.

REFERENCES

1. 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 randomised trials. Lancet. 2003;362(9395):1527-35. doi: 10.1016/s0140-6736(03)14739-3, PMID 14615107.
2. Law MR, Morris JK, Wald NJ.Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ. 2009;338: b1665-10.1136:b1665. doi: 10.1136/bmj.b1665, PMID 19454737.
3. Wright JM, Lee CH, Chambers GK.Systematic review of antihypertensive therapies: does the evidence assist in choosing a first-line drug?CMAJ. 1999;161(1):25-32. PMID 10420860.
4. Psaty BM, Lumley T, Furberg CD, Schellenbaum G, Pahor M, Alderman MH, Weiss NS.Health outcomes associated with various antihypertensive therapies used as first-line agents: a network meta-analysis. JAMA. 2003;289(19):2534-44. doi: 10.1001/jama.289.19.2534. PMID 12759325.
5. Chrysant SG, Lee J, Melino M, Karki S, Heyrman R. Efficacy and tolerability of amlodipine plus olmesartanmedoxomil in patients with difficult-to-treat hypertension. J Hum Hypertens.2010;24(11):730-8. doi: 10.1038/jhh.2010.5, PMID 20164847.
6. Hong BK, Park CG, Kim KS, Yoon MH, Yoon HJ, Yoon JH, Yang JY, Choi YJ, Cho SY. fficacy and Safety of Fixed-Doseamlodipine/losartan and losartan in Hypertensive Patients Inadequately Controlled with losartan. Am J Cardiovasc Drugs. 2012;12(3):189-95. doi: 10.2165/11597410, PMID 22462558.
7. Economic evaluation of ASCOT-BPLA: antihypertensive treatment with an amlodipine-based regimen is cost effective compared with an atenolol-based regimen. Lindgren P, Buxton M, Kahan T, Poulter NR, Dahlöf B, Sever PS, Wedel H, Jönsson B; ASCOT trial investigators.Heart. 2008 Feb;94(2):e4. doi: 10.1136/hrt.2007.127217. Epub 2007 Oct 4.PMID: 17916665.
8. Sica DA. Calcium channel blocker-related periperal edema: can it be resolved?J Clin Hypertens (Greenwich). 2003;5(4):291-4, 297. doi: 10.1111/j.1524-6175.2003.02402.x, PMID 12939574.
9. J-ELAN study (effect of losartan and amlodipine on left ventricular diastolic function in patients with mild-to-moderate hypertension).Yamamoto K, Hori M. Nihon Rinsho. 2007 Apr 28;65 Suppl 4:513-5.PMID: 17511101.
10. MesserliFH. Vasodilatory edema: a common side effect of antihypertensive therapy. Am J Hypertens.2001;14(9):978-9. doi: 10.1016/s0895-7061(01)02178-1, PMID 11587169.
11. Makani H, Bangalore S, Romero J, Wever-Pinzon O, Messerli FH. Effect of renin-angiotensin system blockade on calcium channel blocker-associated peripheral edema. Am J Med.2011;124(2):128-35. doi: 10.1016/j.amjmed.2010.08.007, PMID 21295192.
12. Makani H, Bangalore S, Romero J, Htyte N, Berrios RS, Makwana H, Messerli FH. Peripheral edema associated with calcium channel blockers: incidence and withdrawal rate-a meta-analysis of randomized trials. J Hypertens.2011;29(7):1270-80. doi: 10.1097/HJH.0b013e3283472643, PMID 21558959.
13. Pedrinelli R, Dell'Omo G, Nuti M, Menegato A, Balbarini A, Mariani M. Heterogeneous effect of calcium antagonists on leg oedema: a comparison of amlodipine versus lercanidipine in hypertensive patients. J Hypertens.2003;21(10):1969-73. doi: 10.1097/00004872-200310000-00026, PMID 14508205.
14. ALLHAT Collaborative Research Group.Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). JAMA. 2000;283(15):1967-75. doi: 10.1001/jama.283.15.1967.
15. Wiysonge CS, Bradley H, Mayosi BM, Maroney R, Mbewu A, Opie LH, Volmink J.Beta-blockers for hypertension. Cochrane Database Syst Rev.2007;(1):CD002003. doi: 10.1002/14651858.CD002003.pub2, PMID 17253471

16. Kodama S, Tanaka S, Saito K, Shu M, Sone Y, Onitake F, Suzuki E, Shimano H, Yamamoto S, Kondo K, Ohashi Y, Yamada N, Sone H.Effect of aerobic exercise training on serum levels of high-density lipoprotein cholesterol: a meta-analysis. Arch Intern Med.2007;167(10):999-1008. doi: 10.1001/archinte.167.10.999. PMID 17533202.
17. Kreger BE, Cupples LA, Kannel WB The electrocardiogram in prediction of sudden death: Framingham Study experience *Am Heart J* 1987 113 377–382.
18. Comparison of actions of irbesartan versus atenolol on cardiac repolarization in hypertensive left ventricular hypertrophy: results from the Swedish Irbesartan Left Ventricular Hypertrophy Investigation Versus Atenolol (SILVHIA). Malmqvist K, Kahan T, Edner M, Bergfeldt L.Am J Cardiol. 2002 Nov 15;90(10):1107-12. doi: 10.1016/s0002-9149(02)02777-7.