ISSN: 2091-2331 (Print) 2091-234X (Online)

Journal of Nobel Medical College

Volume 12, Number 01, Issue 22, January-June 2023, 70-75

Original Article

A Comparative Study of the Safety and Efficacy of Amlodipine and Enalapril when Prescribed as Monotherapy in Patients with Isolated Systolic Hypertension

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Article Received: 6th April, 2023; Accepted: 20th June, 2023; Published: 30th June, 2023

DOI: https://doi.org/10.3126/jonmc.v12i1.56392

Abstract

Background

Most elderly patients with high blood pressure have isolated systolic hypertension. Enalapril and amlodipine are respectively the most commonly prescribed ACE inhibitors and calcium channel blockers in Nepal. The goal of the current study was to compare the adverse drug reaction associated with amlodipine and enalapril in the study population as well as to compare the mean blood pressure and pulse rate reductions caused by amlodipine and enalapril in isolated systolic hypertensive patients.

Materials and Methods

A comparative cross-sectional study was performed on 72 patients of both genders within the age group of 30 to 90 years; with isolated systolic hypertension; attending the out-patients department of Medicine of Nobel Medical College and Teaching Hospital; from December 2022 to February 2023. Mean reductions in systolic and diastolic blood pressure in the two treatment groups over the eight-weeks study period was calculated and then compared. Frequencies of patients developing different side effects was also calculated and compared between the two groups.

Results

Systolic blood pressure was reduced by 16.1% in amlodipine group and by 18.8 % in enalapril group. Enalapril was slightly more efficacious in reducing the systolic blood pressure but such changes were found to be of no significant difference when compared between the two groups. ($p > 0.05$). The incidence of adverse effect was more in the amlodipine group in comparison to the enalapril group. Dry cough, dizziness, headache and fatigue with enalapril; and headache, peripheral edema, shortness of breath, fatigue, and flushing and dizziness with amlodipine were the common adverse effects.

Conclusion

Both amlodipine and enalapril were equally effective in lowering systolic blood pressure without significantly lowering diastolic blood pressure. They were also generally well tolerated, though amlodipine was slightly more likely to cause side effects.

Keywords: *Amlodipine, Comparative study, Efficacy, Enalapril, Safety, Systolic Hypertension*

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Citation
Yadav R, Shah R, A Comparative Study of the Safety and Efficacy of Amlodipine and Enalapril when Prescribed as Monotherapy in Patients with Isolated Systolic Hypertension, JoNMC. 12:1 (2023) 70-75.

Introduction

The treatment of hypertension is the most frequent reason patients visit a doctor and use chronic prescription drugs, and hypertension is highly prevalent throughout the world [1, 2]. Among the leading causes of morbidity and mortality worldwide right now is hypertension. It has been estimated that 7.1 million deaths worldwide were attributable to hypertension, and that there may be as many as 1 billion people who have it [3]. Non-optimal blood pressure causes roughly two-thirds of strokes and half of ischemic heart disease worldwide [4]. At the moment, 19.7% of Nepalis have hypertension [5]. Systolic-diastolic hypertension (SDH), isolated systolic hypertension (ISH), and isolated diastolic hypertension (IDH) are just a few of the many variations of hypertension [6, 7]. Systolic blood pressure alone is elevated in ISH. In isolated systolic hypertension, the systolic blood pressures is greater than or equal to 130 mm Hg and diastolic blood pressure is equal to or less than 90 mm Hg. About 50% of individuals over the age of 60 years have ISH, which is the most prevalent type of high blood pressure in elderly patients [8]. This kind of high blood pressure can also occur in younger people. Due to the epidemic of overweight and obesity, the prevalence of ISH has also risen among young adults in recent decades [9, 10]. ISH is due to loss of elasticity of arteries. When arteries become stiff and less elastic; they can't expand and contract in a normal way causing systolic blood pressure to go up. Diastolic blood pressure goes down because of less elasticity and less peripheral resistance. Without treatment, ISH can damage organs just like other types of untreated hypertension. Kidney failure, cardiovascular diseases, and death are all risks associated with isolated systolic hypertension. The treatment to lower systolic blood pressure must prevent the diastolic blood pressure from falling too low, which can lead to other complications, in order to control ISH and prevent health issues. Systolic hypertension can be brought down to safe levels with the help of medication as well as dietary and lifestyle change [11, 12]. Typical treatments for systolic hypertension include thiazide-type diuretics (TTD), calcium channel blockers (CCB), angiotensin converting enzyme inhibitors (ACEI), or a combination of two medications from the aforementioned groups [13]. Enalapril and amlodipine, respectively, are the calcium channel blockers and ACE inhibitors that are most frequently prescribed in Nepal, according to a study [14]. ACE inhibitors include captoril, enalapril, fosinopril, lisinopril, ramipril, moexipril, etc. and most ACE inhibitors are oral medications. These drugs inhibit the vasoconstrictive and aldosterone-secreting effects by stopping the production of a hormone called angiotensin II. The starting dose of enalapril (the most frequently prescribed ACE inhibitor) in adults of 18 years and older is 5 mg taken by mouth once per day. The daily dosage usually ranges between 10 to 40 mg. Dizziness, weakness, skin rash, and cough are some of the more frequent enalapril side effects that can happen. Serious side effects include: trouble breathing or swallowing, hoarseness, tightness in chest, yellowing of skin or the sclera of eyes, fainting, inability to pass urine, change in the amount of urine passed, blood in urine, weight gain, numbness or tingling, shortness of breath, irregular heartbeat, swelling (angioedema) of face, throat, tongue, lips, eyes, hands, feet, ankles, or lower legs and fever, sore throat, chills. The following medications are calcium antagonists: amlodipine, diltiazem, felodipine, isradipine, nicardipine, nifedipine, nisoldipine, and verapamil. Due to its slow but complete absorption and moderately high bioavailability (64–90%), amlodipine is one of the most commonly used 1, 4-dihydropyridine calcium channel antagonists [14]. Amlodipine reduces the contractility and vasodilatation of vascular smooth muscle by blocking the entry of calcium ions through L-type calcium channels, which are primarily found in vascular smooth muscle cells [15]. Amlodipine typically comes in a once-daily dose because of its prolonged half-life, which is good for patient compliance. With a daily dose of 10 mg, a starting dose of 5 mg is typically advised. Constipation, palpitations, fatigue, flushing, headache, nausea, rash, swelling in the feet and lower legs, and dizziness are just a few of the side effects of calcium channel blockers that may occur.

There aren't many studies comparing these drugs' safety and efficacy, and the ones that do exist are all done on western populations. Information about the population of South Asia is lacking.

The present study was conducted to compare the mean reduction in BP and pulse rate by amlodipine and enalapril in isolated systolic hypertensive patients and to compare the adverse drug reaction (ADR) associated with amlodipine and enalapril in the study population.

Materials and Methods

A cross-sectional and comparative study was designed among the patients attending outpatient door (OPD) at Nobel Medical College

Teaching Hospital (NoMCTH) and was diagnosed with isolated systolic hypertension for a period of December 2022 to February 2023. The study was carried after getting the approval from institutional review committee (IRC), NOMCTH. Written informed consent was collected from all eligible patients in their native language. Patients; in the age range of 30-90 yrs and regardless of sex were selected from the medicine opd on the basis of a known systolic blood pressure exceeding 140 mm Hg but not exceeding 200 mm Hg and a diastolic blood pressure less than 90 mm Hg. They were either newly diagnosed cases, previously diagnosed cases who had not yet begun treatment, or previously diagnosed cases who had stopped taking their antihypertensive medication at least one week (two weeks in the case of diuretics) prior to enrolling in the study. Patients were excluded if they had a history of ischemic heart disease, accelerated hypertension, a serious systemic illness, asthma, a known allergy to ACE inhibitors or calcium antagonists, or if they were taking medication that had the potential to raise blood pressure. (e.g. NSAIDs, steroids) Patients suffering from secondary hypertension, patients prescribed with more than one antihypertensive drug, pregnant women and lactating women were also excluded. The study considers 95% confidence interval and 80% power to evaluate the sample size. Since all the population were a diagnosed case of isolated systolic hypertension and considering the prevalence of monotherapy with amlodipine to be 60 % from previous related studies. Now using the formula, $n= z^2 p q/l^2$ where Z= 1.96 at 95% confidence interval, p =60% [14], q=40% and l=20% of p i.e.; 12. Putting in the formula n= 64 i.e. 32 in each group but 36 cases in each group were included to compensate any dropouts. Convenience sampling method was employed in the study.

The OPD ticket was duly filled by interns or attending doctors. It included information about the patient, their history with medications and medical conditions, their complaints, and their diagnosis. Additionally, it included the patient's medication that had been prescribed by the attending physician as well as monitoring data like blood pressure and pulse rate. Measurement of blood pressure in the study population was done using a mercury sphygmomanometer. Properly maintained device with appropriate size cuff was used. Patient was allowed to sit in a quiet room for at least 5 minutes in chair with feet on the floor and arm supported at heart level before beginning BP measurement. Tight clothing's were removed and patients were instructed to avoid talking before and during blood pressure measurement. In a seated position, an average of two blood pressure readings was taken in both hands. We considered the arm with the higher average BP. Pulse rate measurement: The researcher felt the radial artery over a radial bone to manually record the pulse rate.

The 72 patients in this prospective, parallel group study; which lasted for 8 weeks; were of both genders; and they ranged in age from 30 to 90 years old; an was diagnosed with isolated systolic hypertension; attending the out- patients department of Medicine of Nobel Medical College and Teaching Hospital. Patients were randomized by the technique of minimization in an observer-blind study. Nurse performing the blood pressure measurements was not aware of the patient's treatment though the patient and the treating doctor and the researcher were aware of the type of medication the particular patient was receiving. Eligible patients were randomly divided into groups A and B. In Group A patients; treated with daily dose of amlodipine (5-10 mg) of a particular brand were included and in group B; patients treated with daily dose of enalapril (5-20 mg) of a particular brand were included. Patients were advised to take it regularly after lunch. Patients were instructed to take their medication at home. They were then checked in at the out-patient department (OPD) after four weeks, and their blood pressure and pulse rate were once more recorded on the patient profile form. Patients were advised to keep taking their medication regularly. After eight weeks patients we rechecked in at OPD again. At eight weeks, patients' blood pressure and pulse rate were once more noted on the patient profile form. Based on patient complaints and patient interviews, the ADR experienced by the study population were documented in the patient profile form.

The data analysis tool of choice was SPSS. The mean and standard deviation of every quantitative variable were used to describe them. Utilizing an independent samples t-test, the mean decrease in blood pressure and pulse rate in the two treatment groups over the course of the eight-week study were calculated and compared. p value of ≤ 0.05 was considered significant.

Results

A total of 72 patients participated in the study and consisted of 41 males (56.95%) and 31females

(43.05%) (Table 1). Distribution of patients in the age group of 31-40 years was 23.6%; 41-50 years were 19.4%; 51-60 years were 19.4%; 61-70 years were 29.2% and above 70 years were 8.3%. (Table 2)There was no significant difference in baseline blood pressure (Both systolic and diastolic) and pulse rate between the two groups ($p > 0.05$) (Table 1). The results of the study demonstrated that the systolic and diastolic blood pressure varied from zero to 8th week in each test group significantly. (Table 3) Despite the fact that both groups' blood pressure reductions were significant ($p < 0.05$) between the two treatments it was statistically insignificant. ($p > 0.05$) (Table 4).

Mean systolic blood pressure was reduced from 161 to 135 mm Hg (amlodipine) and 165 to 134 mm Hg (enalapril) after 8 weeks treatment. Mean diastolic blood pressure was reduced from 82 to 74 mm Hg (amlodipine) and 85 to 75 mm Hg (enalapril) after 8 weeks treatment. The pulse rate was reduced from 77 to 74 beats per minute (amlodipine) and from 75 to 70 beats per minute. (enalapril) At the end of 8 weeks treatment, the systolic blood pressure had fallen by 26 mm Hg and diastolic blood pressure had fallen by 8mm Hg in the subjects treated with amlodipine whereas we found that systolic blood pressure had fallen by31 mm Hg, and diastolic blood pressure had fallen by 10 mm Hg in the subjects treated with enalapril. The pulse rate had fallen by 3 and 5 beats per min in amlodipine an enalapril group respectively.

No patients were withdrawn from the study; neither from the amlodipine group nor from the enalapril group because the adverse effects encountered were mild to moderate. In the amlodipine group, 24 patients (66.7%) were kept on a dose of 5 mg per day throughout the study, while 12 patients (33.3%) needed to be titrated to 10 mg per day. In the enalapril group, seven additional patients (19.4%) were titrated to 20 mg daily, while sixteen patients (44.4%) received 10 mg and thirteen patients (36.1%) were maintained on 5 mg daily. The average dose of enalapril was 10.1mg, and the average dose of amlodipine was 6.7mg. The side effects that the patients in the enalapril and amlodipine groups experienced are displayed in Table 5.

Table 1: Baseline characteristics of patients of isolated systolic hypertension receiving Amlodipine and Enalapril as monotherapy ($n_1 = 36$) and ($n_2 = 36$) (Total N= 72)

Baseline characteristics		Amlodipine group	Enalapril group	*P* value
Number of patients		36	36	
Age range (in years)		30-90	30-90	
Sex (male/female)		21/15	20/16	
Dietary habits	Vegetarian	4	4	
	Non-vegetarian	32	32	
Education	Literate	16	13	
	Illiterate	20	23	
Occupation	Service	7	6	
	Business	8	5	
	Teacher	2	3	
	Farmer	5	6	
	Housewife	13	13	
	Others	1	3	
Systolic BP (mm of Hg)		161.22(±16.22)	165.11(±22.02)	*P* >0.05
Diastolic BP (mm of Hg)		82.11 (±7.49)	85 (±5)	*P* >0.05
Pulse (beats per minute)		77.61 (±14.19)	75.39 (±13.18)	*P* >0.05
Habitat	Rural	16	14	
	Urban	20	22	

Table 2: Age group distribution of the study population

Description	Category	Amlodipine (n_1=36)	Enalapril (n_2=36)	Total N=72
Age (in years)	31-40	10	7	17
	41-50	7	7	14
	51-60	7	7	14
	61-70	10	11	21
	> 70	2	4	6

Table 3: Changes in the BP and Pulse Rate in Amlodipine (Group – A) and Enalapril (Group - B) expressed as (Mean ±SD) and student paired t test

Parameter	Groups	Mean ± SD At 0 weeks	At 4 weeks	At 8 weeks	*P* value 0 weeks versus 8 wks
Systolic BP (mm Hg)	Amlodipine Group	161.22 (±16.22)	141.31 (± 12.74)	135.64 (± 11.65)	P < 0.0001
	Enalapril Group	165.11(±2 2.02)	137.06 (±14.66)	134.28 (±11.40)	
Diastolic BP (mm Hg)	Amlodipine Group	82.11 (±7.49)	76.86 (±8.99)	74.85 (±8.44)	P < 0.0001
	Enalapril Group	85 (±5)	79.33 (±7.2)	75.17 (±8.12)	
Pulse (Beats per min)	Amlodipine Group	77.61 (±14.19)	75.31 (±11.05)	74.83 (±8.52)	P < 0.0001
	Enalapril Group	75.39 (±13.18)	70.53 (±8.16)	70.78 (±6.35)	

Table 4: Inter group comparison of Blood pressure and Pulse Rate at Baseline and at 8 weeks

Parameter	Mean ± SD Baseline Amlodipine Group	Enalapril Group	*P*	Mean ± SD At 8 Weeks Amlodipine Group	Enalapril Group	*P*
Systolic BP (mm Hg)	161.22 (±16.22)	165.11(±2 2.02)	*p*>0.05	135.64 (± 11.65)	134.28 (±11.40)	*p*>0.05
Diastolic BP (mm Hg)	82.11 (±7.49)	85 (±5)	*p*>0.05	74.85 (±8.44)	75.17 (±8.12)	*p*>0.05
Pulse (Beats per min)	77.61 (±14.19)	75.39 (±13.18)	*p*>0.05	74.83 (±8.52)	70.78 (±6.35)	*p*>0.05

Table 5: Adverse effects encountered by the study population in Amlodipine group and enalapril group

Parameter	Amlodipine Group (no. of patients)	Enalapril Group (no. of patients)
Peripheral edema	4	0
Shortness of breath	4	0
Headache	8	2
Palpitation	2	0
Fatigue	3	2
Dizziness	2	3
Flushing	2	0
Tingling sensation	0	1
Dry cough	0	7
Sinusitis	0	0
Rhinitis	0	0
Sore throat	0	0
Taste alteration	0	0
Vomiting	0	0
Chest pain	0	2
Decreased sleep	0	0
Constipation	0	1
Anorexia	0	0

Discussion

Both patient groups shared the same demographic information. After four weeks, amlodipine decreased systolic and diastolic blood pressure from 161.22 (±16.22)/82.11 (±7.49) mm Hg to 141.31 (±12.74)/76.86 (±8.99), and after eight weeks, to 135.64 (±11.65)/74.85 (±8.44) mm Hg. Systolic and diastolic blood pressure dropped with enalapril, going from a mean of 165.11(±22.02)/85(±5) mm Hg at the beginning to 137.06(±14.66)/79.33(±7.2) after four weeks and 134.28(±11.40)/75.17(±8.12) mm Hg after eight weeks. Amlodipine reduced pulse rate from 77.61 (±14.19) to 75.31 (±11.05) after four weeks and to 74.83 (±8.52) bpm after eight weeks. After 4 weeks, enalapril reduced the pulse rate from 75.39 (±13.18) to 70.53 (±8.16), and after 8 weeks, it dropped to 70.78 (±6.35) bpm. Dry cough, lightheadedness, fatigue, peripheral edema, shortness of breath, and headache were the side effects of enalapril. The most typical ADRs were flushing and vertigo when taking amlodipine. Despite being greater in the enalapril group than the amlodipine group, the decrease in systolic and diastolic blood pressure was not statistically significant ($p > 0.05$) when compared between the groups. In this study, individual medications decreased blood pressure on average more than they did in Gryglas P.'s research [16] in Poland and Fowler et al. [17] in Denmark. This may be due to the study population's varied ethnicity and culture. Moreover, it was discovered that enalapril slightly lowers blood pressure more compared to amlodipine, but this difference was not statistically significant. This demonstrates that lowering blood pressure with amlodipine and enalapril is equally effective. The research done by Gryglas P [16] and Fowler et al. [17] and this study are comparable. The exact opposite, however, is true in that amlodipine slightly lowers blood pressure more than enalapril [17]. Once more, this might be a result of the study population's diverse ethnicity and culture.

This study has important limitations. The associated risk factors were not taken into account. Similarly, the impact from the non-pharmacological treatment such as diet and life style changes was not considered.

Conclusion

Over the course of 8 weeks, patients with ISH experienced satisfactory blood pressure reductions with both amlodipine and enalapril. Both medications were reasonably well tolerated and equally effective at lowering systolic blood pressure without significantly lowering diastolic blood pressure with slightly more incidence of side effects with amlodipine.

Acknowledgement: None

Conflict of interest: None

References

[1] Munter P, Carey RM, Gidding S, et al., Potential US Population Impact of the 2017 ACC/AHA High Blood Pressure Guideline. 137:2 (2018) 109-118. DOI: 10.1161/CIRCULATIONAHA.117.032582

[2] Yoon SS, Gu Q, Nwankwo T, et al., Trends in blood pressure among adults with hypertension: United States, 2003 to 2012, Hypertension 65:1 (2015) 54-61. DOI: 10.1161/HYPERTENSIONAHA.114.04012.

[3] World Health Report 2002: Reducing risks, Promoting healthy life. Geneva, Switzerland: World Health Organization. 2002. http://www.who.int/hr/2002/. (accessed 15.03.23)

[4] Lawes CMM, Hoorn SV, Law MR, et al., Blood pressure and the global burden of disease 2000. Part II: Estimates of attributable burden, J Hypertens. 24:3 (2006) 423-30. DOI: 10.1097/01.hjh.0000209973.67746.f0.

[5] Sharma D, Manbahadur KC, RajbhandariS et al., Study of prevalence, awareness and control of hypertension in a suburban area of Kathmandu, Nepal. Indian Heart J 58:1 (2006) 34-7. PMID: 18984928.

[6] Mc Eniery CM, Franklin SS, Cockcroft JR, Wilkinson IB. Isolated systolic hypertension in young people is not spurious and should be treated: pro side of the argument. Hypertension 68:2 (2016) 269-75. DOI: 10.1161/HYPERTENSIONAHA.116.06547.

[7] Midha T, Lalchandani A, Nath B, Kumari R, Pandey U, prevalence of isolated diastolic hypertension an associated risk factors among adults in Kanpur, India, Indian Heart J.64:4 (2012) 374-9. DOI: 10.1016/j.ihj.

2012.06.007
[8] Kim NR, Kim HC, Prevalence and trends of isolated systolic hypertension among Korean adults: the Korea National Health and nutrition examination survey, 1998-2012. Korean Circ J. 45:6 (2015) 492-9. DOI: 10.4070/kcj.2015.45.6.492
[9] Grebla RC, Rodriguez CJ, Borrell LN, Pickering TG, Prevalence and determinants of isolated systolic hypertension among young adults: the 1999–2004 US National Health and Nutrition Examination survey, J hypertens. 28:1 (2010) 15-23. DOI: 10.1097/HJH.0b013e328331b7ff.
[10] Liu X, Rodriguez CJ, Wang K. Prevalence and trends of isolated systolic hypertension among untreated adults in the United States. J Am Soc, Hypertens.9:3 (2015) 197-205. DOI: 10.1016/j.jash.2015.01.002.
[11] Musini VM, Tejani AM, Bassett K, Puil L, Wright JM. 'Pharmacotherapy for hypertension in adults 60 years or older', The Cochrane Database of Systematic Reviews. 6:6 (2019) CD000028. DOI: 10.1002/14651858. PMC 6550717. PMID 31167038.
[12] Musini VM, Gueyffier F, Puil L, Salzwedel DM, Wright JM, 'Pharmacotherapy for hypertension in adults age 18 to 59 years', The Cochrane Database of Systematic Reviews. 8 (2017) CD008276. DOI: 10.1002/14651858.CD008276.pub2. PMC6483466. PMID28813123.
[13] Egan BM, Yang J, Rakotz MK, Sutherland SE, Jamerson KA, Wright JT, et al.“Self-Reported Antihypertensive Medication Class and Temporal Relationship to Treatment Guidelines', Hypertension. 79:2 (2022) 338–48. DOI: 10.1161/HYPERTENSIONAHA.121.17102.
[14] Karki N, Kandel K, Prasad P, Khanal J, Antihypertensive Drug Use Pattern in a Tertiary Care Hospital of Western Region of Nepal: A Cross-Sectional Study. J. Lumbini Med. Coll.10:2 (2022) 1-9. DOI: 10.22502/jlmc.v10i2.469.
[15] Law V, Knox C, Djoumbou Y, et al. Drug Bank 4.0: shedding new light on drug metabolism, Nucleic Acids Res. 42 (2014) DI 091-7. DOI: 10.1093/nar/gkt1068.
[16] Gryglas P, The comparison of hypotensive efficiency and tolerability of amlodipine and enalapril in patients with essential hypertension, Pol Arch Med Wewn. 105:2 (2001) 109-15. PMID: 11505744
[17] Fowler G, Webster J, Lyons D et al., A comparison of amlodipine with enalapril in treatment of moderate/severe hypertension, Br J Clin Pharmacol.35:5 (1993) 491-8. DOI: 10.1111/j.1365-2125.1993.tb04175.x.