|| ISSN(online): 2589-8698 || ISSN(print): 2589-868X ||
International Journal of Medical and Biomedical Studies
Available Online at www.ijmbs.info
NLM (National Library of Medicine ID: 101738825)
Index Copernicus Value 2019: 79.34
Original Research Article
Volume 5, Issue 3; March: 2021; Page No. 78-86

EFFICACY OF COMBINATION OF AMLODIPINE (5MG) AND LOSARTAN (50MG) WITH AMLODIPINE (5MG) MONOTHERAPY IN HYPERTENSIVE PATIENTS.

Sumitra Shrestha[1], Mamita Ghimire[2], Dr. Jeevan Raj Shrestha[3]

[1]*M.Pharm (Clinical Pharmacy) Pokhara University, Senior Quality Assurance Officer Divine Healthcare Pvt. Ltd. Bharatpur-16*
[2]*M.Pharm (Natural product Chemistry) Pokhara University, Quality Control Officer Kasturi Pharmaceuticals*
[3]*BSC (Microbiology), MBBS (Manipal College of Medical Sciences, Pokhara, Medical Officer Barhabise Primary Health Centre Barhabise-9*

Article Info: Received 08 February 2021; Accepted 08 March 2021
DOI: https://doi.org/10.32553/ijmbs.v5i3.1755
Corresponding author: Dr. Jeevan Raj Shrestha
Conflict of interest: No conflict of interest.

Abstract

Objective: Hypertension is the major public health issues, which is the leading causes of mortality and morbidity worldwide. In Nepal the amlodipine and combination of Amlodipine and losartan are the most frequently prescribed antihypertensive drugs. This study was conducted to study antihypertensive effect of Amlodipine (5mg) alone and combination of Amlodipine (5mg) and Losartan (50mg) in hypertensive patients among the community of Bharatpur, chitwan

Method: A prospective study of Hypertensive patient having amlodipine and losartan in Bharatpur, Chitwan, was conducted from 25th July to 10th September 2019. A total of 120 samples were obtained using a random sampling technique.

Result: Of 120 patients 60 patient were administering amlodipine along the maximum number of patient was from the age group 50-60(31.67%). the awareness about medicine and disease were found to be 15 % and 56 % respectively. The average mean of blood pressure reduction found to be 60/28 mmHg by amlodipine + losartan while in monotherapy it was found to be 47/15mmHg.

Conclusion: This study concluded that the mean reduction of blood pressure by the combination therapy was higher than monotherapy hence the combination therapy is found to be more efficious for the reduction of Blood pressure than monotherapy along and the use of PPIs has been extended to other conditions not requiring acid anti secretory therapy.

Keywords: Hypertension, Amlodipine, Losartan

Introduction

Hypertension is the third leading reason for mortality in the whole world and according to WHO, one out of eight deaths occur due to high blood pressure. Hypertension is the prevalent issue with huge cardiovascular risks [1].

The prevalence of Hypertension according to a recent systematic review and meta analysis by 2014 in South Asian countries is Bangladesh-31.5%, India-31.4%, Bhutan-23.9%, Maldives-31.5%, Nepal-33.85, Pakistan-25%, Srilanka-20.9% and moreover, It is higher in woman than man [2]. Hypertension has seen huge uplift from 6% in 1981 to 18% in 2006 in Nepal and It has reached to 33.9% in 2013 [3]. Vast modification in lifestyle including diet and exercise, new pharmacotherapies from different drug classes lower blood pressure risking serious clinical outcomes. One or more than one agent can be used in case of greater risks [4].

The synergistic mechanisms of controlling hypertension and its side effects is a proof that combination therapy is advantageous than mono-therapy [5]. Multiple factors in combination therapy contribute to hypertension and controlling blood pressure. Combination of drugs makes them available accordance to the required dosage format including lowering of individual component dosage, which in turn reduces side effects and improves compliance [6].

Monotherapy with amlodipine is efficacious than losartan monotherapy where it proved to be a milestone in achieving primary end point of reducing mean diastolic and systolic blood pressure. Blood pressure goal of 140/90 Mm of Hg was achieved in 6 weeks with 71.1% of amlodipine and 81.2% of losartan treated patients [7]. The objective of this study was to compare the antihypertensive effect of the combination of amlodipine/losartan with amlodipine monotherapy after 8 weeks of treatment in hypertension patients.

Methods

Study Design

This prospective experimental study was conducted at the Community of Bharatpur, Chitwan, from 25 July 2019 to 10 December 2019. Ethical approval of this study was obtained from the Institutional Review Committee of the College of Medical Sciences Teaching Hospital. Bharatpur, Chitwan.

Study Population

The Community people aged 20-100 years of age of either gender, with no history of cardiovascular events, Blood

pressure level in the range of 130/90mmHg to 210/110mmHgwho were prescribed monotherapy and combination therapy of amlodipine and losartan. A total of 120 patients were evaluated in the study using a random sampling technique.

Data collection Procedure

Verbal consent was taken from the patients before enrolling them in the study. All information was collected in a well-designed data collection form (Patient profile form), which included age, sex, and diagnosis/chief complaints, past medication history and diagnosis of disease. It also contains the monitoring parameters like Blood pressure, Pulse rate and some common side effects.

Data Analysis

Descriptive statistics were performed using IBM-SPSS 20.0 (IBM Corporation, Armonk, NY, USA). Wilcoxon Signed-rank test was used. The variables were presented as the frequency and their respective percentage, bar diagram and pie chart.

Results

Demographic distribution

Age distribution:

Among 60 patients administering amlodipine alone, maximum number of patients was from age group 50-60(31.67%) followed by age group 60-70years(20%) as shown in table 1. Among 60 patients administering combination of amlodipine and losartan, maximum number of patients was from age group 50-60 (58.33%) followed by 70-80 (38.33%) as shown in table 1.

Table: 1. Age distribution among hypertension patient using amlodipine monotherapy and combination of amlodipine and losartan

Age	Amlodipine (n=60)	Amlodipine+losartan(n=60)	Total (N=120)
20-30	1	0	1
30-40	5	4	9
40-50	7	11	18
50-60	19	16	35
60-70	12	10	22
70-80	8	15	73
80-90	5	3	8
90-100	3	1	4

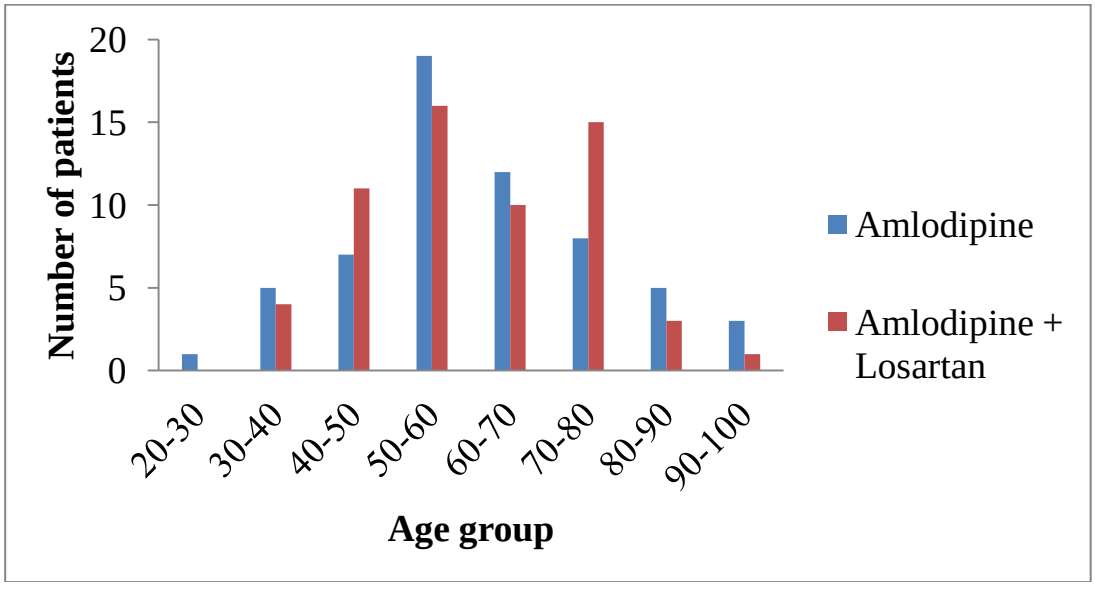

Figure: 1 Age distribution amnong hypertension patient using amlodipine monotherapy and combination of amlodipine and losartan

Gender distribution:

The number of male and female administering amlodipine alone was 32(52%) and 28(47%) respectively as shown in the table 2.The hypertensive cases is more on male than female.

The number of male and female administering combination of amlodipine and losartan was 29(48%) and 31(52%) respectively as shown in the table 2. The hypertensive cases is more on female than male.

Table: 2 Genderwise distribution of amlodipine monotherapy and combination of amlodipine and losartan

Gender	Amlodipine 5mg (n= 60)	Amlodipine 5mg and losartan 50 mg (n=60)
Male	32	29
Female	28	31

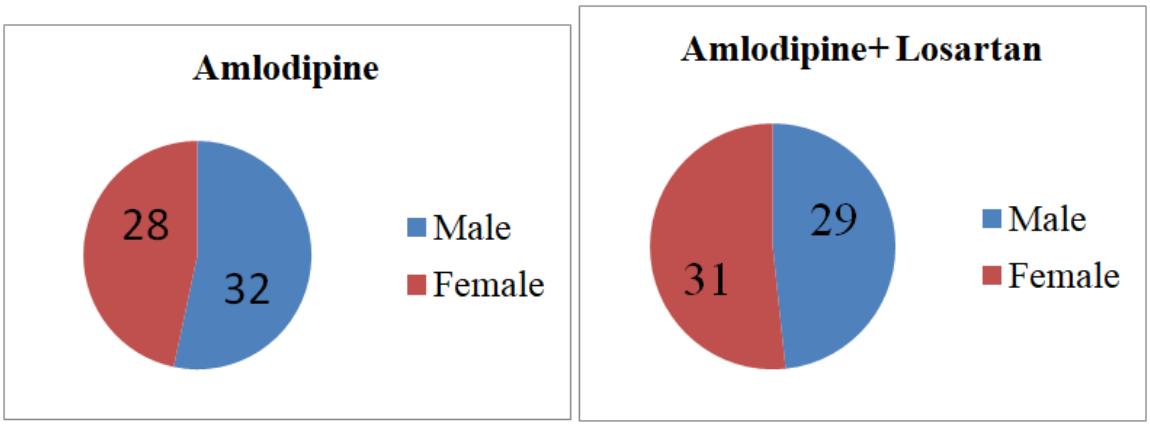

Figure: 2 Gender wise distribution of amlodipine monotherapy and combination of amlodipine and losartan.

Distribution by weight:

In our study we found maximum number of patients administering amlodipine alone are in between the weight range 70-80 kg (22 patients) and the number of patients administering combination of amlodipine and losartan are in between the weight range 60-70 kg (25 patients) as shown in the figure 3.

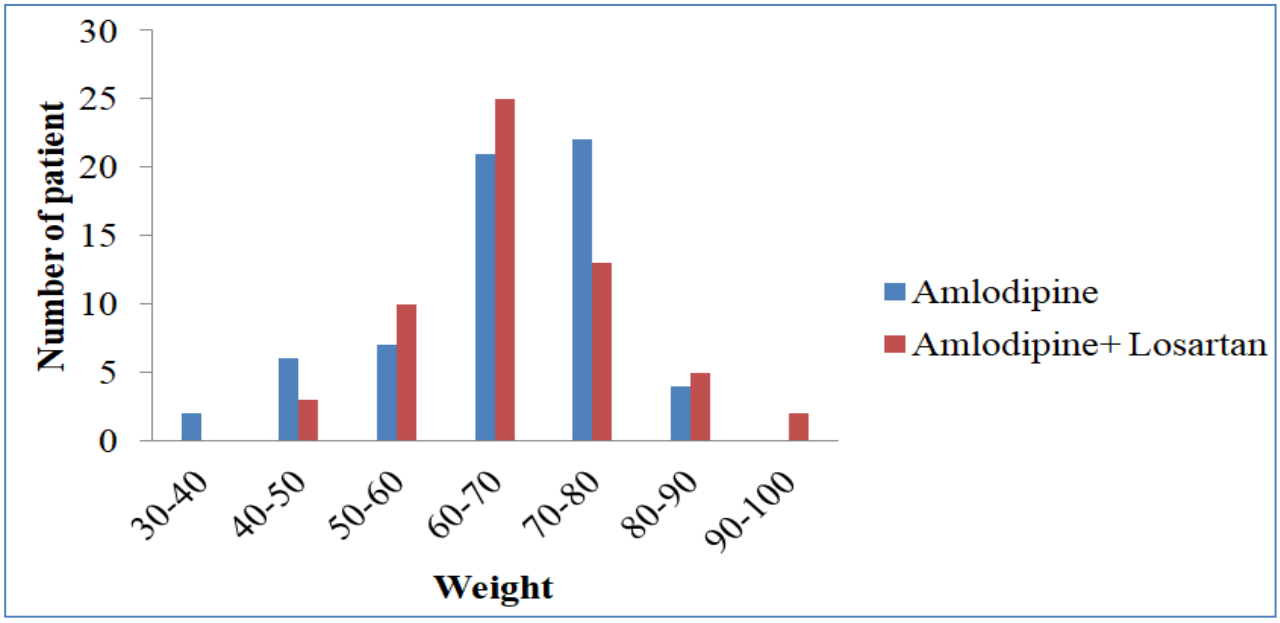

Figure 3: Weight distribution among hypertensive patient using amlodipine monotherapy and combination of amlodipine and losartan.

Dietary habit:
The detail of dietary habits are given in table 3. In our study most of the patients were non vegetarian than vegetarian. Among 120 patients 47 were vegetarian and remaining 83 were non vegetarian.

Table 3: Dietary habit of patients administering amlodipine monotherapy and combination of amlodipine and losartan

Diet	Amlodipine 5mg (n= 60)	Amlodipine 5mg and losartan 50 mg (n=60)
Vegetarian	22	15
Non vegetarian	38	45

In our study, among 60 patients who were administering amlodipine monotherapy most of them were non vegetarian. The number of non-vegetarian patients were 38 and vegetarian patients were 22. Similarly, in our study patients who were administering combination 0f amlodipine and losartan maximum patients were non vegetarian among which 45 were non vegetarian and 15 were vegetarian. The details are given in the figure 4

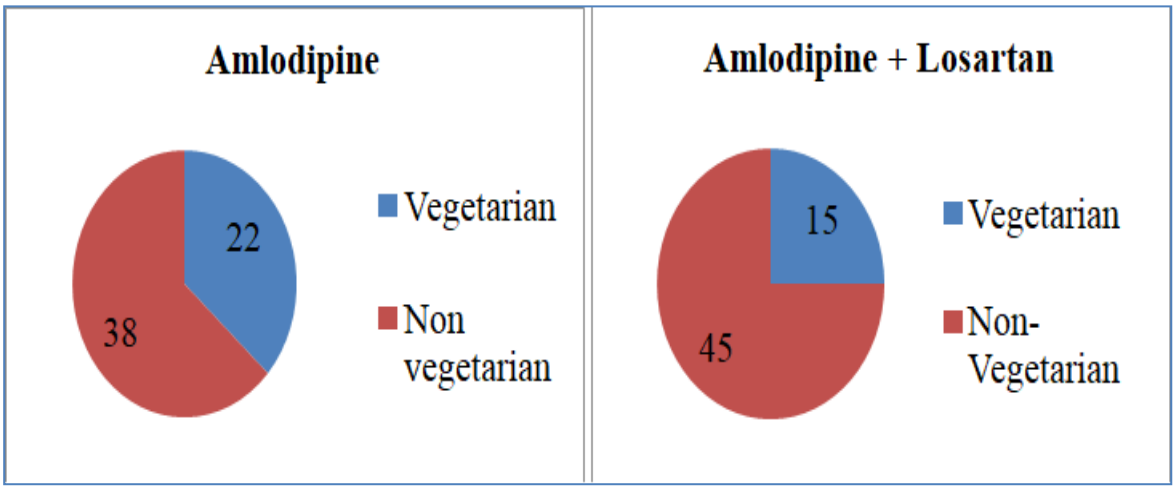

Figure 4: Dietary habit of patients administering amlodipine monotherapy and combination of amlodipine and losartan

Smokers and Alcoholism: In our study among 120 hypertensive patients most of the patients were alcoholics where 15 (12.5%) were smokers and 22(18.3%) were alcoholics as shown in the table 4.

Table 4: Patients who were consuming smoking and alcohol.

Habit	Number of patients (percentage)
Smokers	15(12.5%)
Alcoholism	22(18.3%)

Distribution by disease:
In our study, the maximum number of patients who were administering amlodipine monotherapy and combination of amlodipine and losartan were diabetic which was 5 and 14 patients respectively as shown in the table 5.

Table 5: Different disease of patients who were administering amlodipine monotherapy and combination of amlodipine and losartan

Disease	Amlodipine 5mg (n= 60)	Amlodipine 5mg and losartan 50 mg (n=60)
Diabetes	5	14
Asthma	4	5
Thyroid	1	2
Gout	1	0

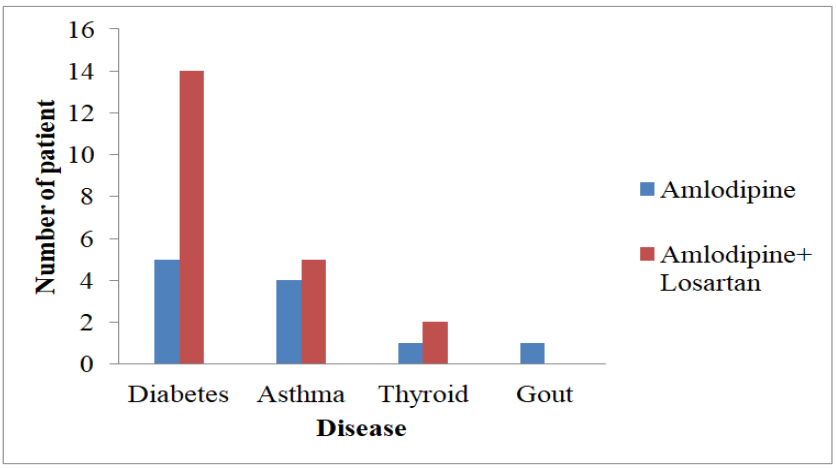

Figure 5: Different disease of patients who were administering amlodipine monotherapy and combination of amlodipine and losartan.

Side effect: In our study we found only few patients have side effects. Among 120 patients 3 complaint of headache and 11 complaint of edema as shown in the table 6.

Table 6: Side effect of patients who were administering amlodipine monotherapy and combination of amlodipine and losartan.

Side effect	Amlodipine (5mg)	Amlodipine (5mg) and losartan (50mg)
Edema	9	2
Headache	2	1

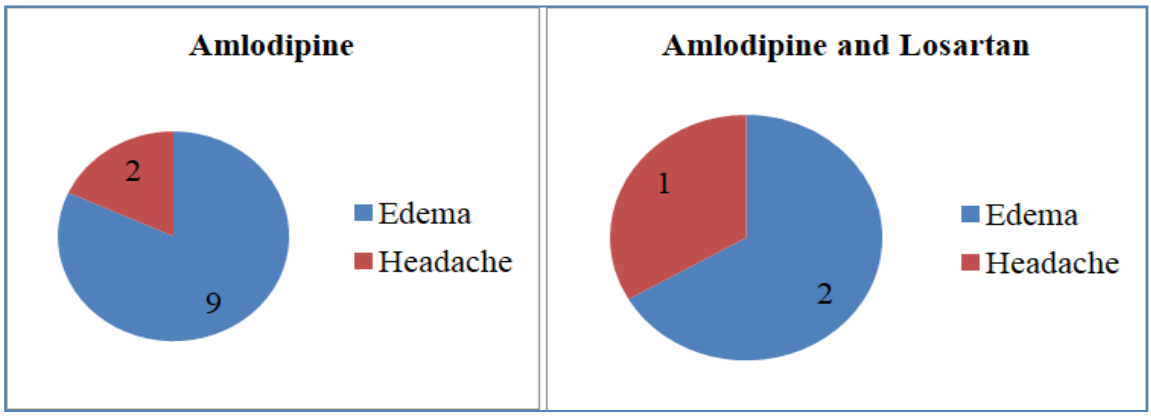

Figure 6: Side effect of patients who were administering amlodipine monotherapy and combination of amlodipine and losartan.

Awareness regarding medicine and disease:

Among 120 patients only 18 patients were aware about medicine and rest of them did not have knowledge about the medicine because maximum number of patients were illiterate as shown in the table 7. Among 120 patients only 18 patients were aware about medicine and rest of them did not have knowledge about the medicine because maximum number of patients were illiterate as shown in the table 7. Among 120 patients only 68 patients were aware about disease and rest of them did not have knowledge about the disease as shown in the table 7.

Table 7: Number of patients regarding awareness about medicine and disease:

Aware about medicine	18 (15%)
Aware about disease	68 (56%)

Statistical Analysis.

Reduction of blood pressure by amlodipine alone and combination of amlodipine and losartan:

During our study period, we found that the average blood pressure was 177.67/103 mmHg at base line and after 8 week by using amlodipine + losartan blood pressure was 117.833/75.13mm Hg, where average blood pressure reduction by using amlodipine + losartan was 60/28mmHg. Similarly the average blood pressure was 160/96mmHg at base line and after 8 week by using amlodipine monotherapy was 113/81 mmHg, where the average mean of blood pressure reduction by using amlodipine monotherapy was 47/15mmHg as shown in the figure 5.7. Hence, our study concluded that the combination therapy was better than amlodipine monotherapy.

Table 8: Mean and Standard deviation of Amlodipine monotherapy and combination of Amlodipine and Losartan.

Duration	N	Mean	Standard Deviation
SBPC0	60	177.67	25.8
DPBC0	60	103.17	11.273
SPBC4	60	138.47	18.824
DPBC4	60	87.98	10.557
SBPC8	60	117.83	7.023
DPBC8	60	75.13	6.601
SBP0	60	162.83	15.414
DPB0	60	97.00	8.887
SBP4	60	141.1	13.894
DPB4	60	87.32	6.342
SBP8	60	128.98	9.700
DPB8	60	81.23	5.334

SBPC0=Systolic blood pressure with combination at baseline.
DBPC0= Diastolic blood pressure with combination at baseline
SBPC4= Systolic blood pressure with combination at 4 week.
DBPC4= Diastolic blood pressure with combination at 4 week.
SBPC8= Systolic blood pressure with combination at 8 week.
DBPC8 = Diastolic blood pressure with combination at 8 week.
SBP0= Systolic blood pressure with monotherapy at baseline.
DBP0= Diastolic blood pressure with monotherapy at baseline.
SBP4=Systolic blood pressure with monotherapy at 4 week.
DBP4= Diastolic blood pressure with monotherapy at 4 week.
SBP8=Systolic blood pressure with monotherapy at 8 week.
DBP8= Diastolic blood pressure with monotherapy at 8 week.

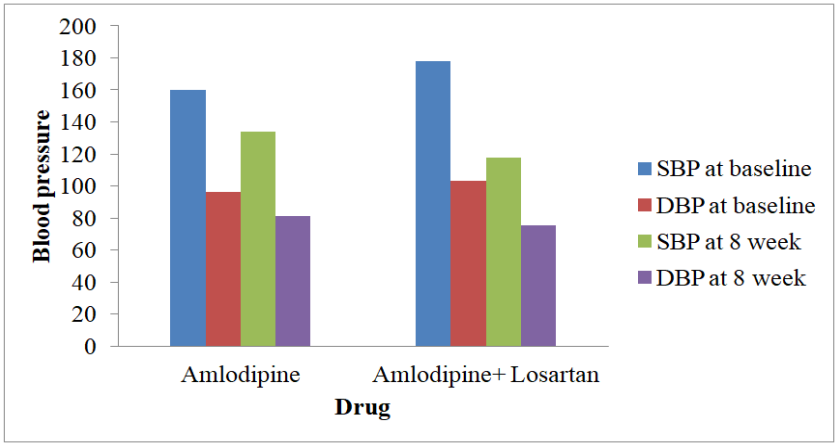

Figure: 7. Reduction of blood pressure by amlodipine monotherapy and combination of amlodipine and losartan.
Median (IQR) of blood pressure after 8 week in patients administering amlodipine alone and combination of amlodipine and losartan.

Table 9: Median (IQR) of blood pressure after 8 week in patients administering amlodipine alone and combination of amlodipine and losartan

Blood pressure (mmHg)	Amlodipine (5mg) Median (IQR)	Amlodipine (5mg) and Losartan (50mg) Median (IQR)	P value
SBP	128(12)	118(9)	<0.001
DBP	100(10)	76(9)	<0.001

Table 10: Median and Interquartile range (IQR) of Amlodipine alone and combination of Amlodipine and Losartan.

Duration	N	Median(IQR)	P value
SBPC0	60	180(40)	<0.001
DBPC0	60	100(20)	<0.001
SBPC8	60	118(14)	<0.001
DBPC8	60	76(9)	<0.001
SBP0	60	160(30)	<0.001
DBP0	60	100(10)	<0.001
SBP8	60	128(12)	<0.001
DBP8	60	81(6)	<0.001

In our study, the median blood pressure of hypertensive patients in combination therapy was reduced by 43% were the patients in amlodipine monotherapy the blood pressure was reduced by 22.5%.

Table 11: Demographic distribution

Variable	**AmlodipineAmlodipine+Losartan**	
Age Group		
20- 30	1(2%)	0
30- 40	5(8%)	4(7%)
40- 50	7(12%)	11(18%)
50- 60	19(32%)	16(27%)
60- 70	12(20%)	10(17%)
70- 80	8(13%)	15(25%)
90- 90	5(8%)	3(5%)
90-100	3(5%)	1(2%)
Gender		
Male	32(53%)	29(48%)
Female	28(47%)	31(52%)
Habit		
Vegetarian	22(37%)	15(25%)
Non-vegetarian	38(63%)	45(75%)
Disease		
Diabetes	5 (8%)	14(23%)
Asthma	4 (7%)	5(8%)
Thyroid	1 (2%)	2(3%)
Gout	1 (2%)	0
Side effect		
Edema	9 (15%)	2(3%)
Headache	2 (3%)	1(2%)

Variable	**Total Number N=120 (%)**
Lifestyle	
Smoking	15(12.5%)
Alcohol	22(18.3%)
Awareness regarding medicine	18(15%)
Awareness regarding disease	68(56%)

Blood pressure	**Mean(Std)**	
	Amlodipine	**Amlodipine+losartan**
SBP	128.98(9.7)	177.67(7.03)
DBP	81.23(5.3)	75.13(6.60)

Discussion

Among 60 patients administering amlodipine alone, maximum number of patients was from age group 50-60 (31.67%) followed by age group 60-70years (20%) as shown in table 1.This is similar to the study done by Sreevalsa Unniachan, et al. where 36% of patients were of age group (55-60) patients [8]. Another research done by Chataut J, et al. where maximum number of patients were from the age group 18-29(27%) [9]. Among 60 patients administering combination of amlodipine and losartan, maximum number of patients was from age group 50-60(58.33%) followed by 70-80 (38.33%) as shown in table 1. This is similar to the study done by Syed Md. Javed et al. where 29% of patients were of age group (56-60) patients [10].

In this present study showed that the number of male and female administering amlodipine alone was 32(52%) and 28(47%) respectively as shown in the table 2. The hypertensive cases is more on male than female. The research done by Sreevalsa Unniachan et al. support our research where 72% were male 28% was female. [8] Another research done by Robert A. et al. where male and female were 141(63.5%) and 81(36.5%) [11] Whereas the study done by Chataut J et al. the percentage of male and female was 40.6% and 59.4% respectively [9]. In this study the number of male and female administering combination of amlodipine and losartan was 29(48%) and 31(52%) respectively as shown in the table 2. The hypertensive cases are more on female than male. This is similar to study done by Reza Jafarzadeh Esfehani et al. where 49.9% were male and 50.1% were female [12]. But the study done by Richard N. et al. the percentage of male and female were 65% and 45% respectively [13].

In this present study we found maximum number of patients administering amlodipine alone are in between the weight range 70-80 kg (22patients) and the number of patients administering combination of amlodipine and losartan are in between the weight range 60-70kg (25 patients) as shown in the figure 3.

In our study most of the patients were non-vegetarian than vegetarian. Among 120 patients 47 were vegetarian and remaining 83 were non-vegetarian. Our study support the literature done by Chatuat J.et al. where maximum number of the patients were non vegetarian that is 46 were vegetarian and 486 were non vegetarian [9].

In our study among 120 hypertensive patients most of the patients were alcoholics where 15(12.5%) were smokers and 22(18.3%) were alcoholics as shown in the table 4. The research done by Dr.A.P. Singh et. al support our study where in their study 14.67% were smokers and 4% take alcohol [14]. Another research done by Chataut J et, al. show 41% consumed alcohol and 40% were smokers [9].

In our study, the maximum number of patients who were administering amlodipine monotherapy and combination of amlodipine and losartan were diabetic which was 5 and 14 patients respectively as shown in the table 5. The research conducted by Dr.A.P Singh et. al also showed that maximum hypertensive patients were diabetic [14].

In our study we found only few patients have side effect like headache and edema, whereas others side effects were well tolerated that is no any complaint.

In this present study, among 120 patients only 18 patients were aware about medicine and rest of them did not have knowledge about the medicine because maximum number of patients were illiterate as shown in the table 7. The research done by Iram Shafail et. al showed 48.4% hypertensive patients were aware about medicine [15]. Among 120 patients only 68 patients were aware about disease and rest of them did not have knowledge about the disease as shown in the table 7. The research done by Dr. A.P. Singh et.al show 75% of hypertensive patients were aware of their condition. [14]

During our study period, we found that the average blood pressure was 177.67/103 mmHg at base line and after 8 week by using amlodipine + losartan blood pressure was 117.833/75.13mm Hg, where average blood pressure reduction by using amlodipine + losartan was 60/28mmHg. Similarly the average blood pressure was 160/96mmHg at base line and after 8 week by using amlodipine monotherapy was 113/81 mmHg, where the average mean of blood pressure reduction by using amlodipine monotherapy was 47/15mmHg as shown in the figure 5.7. Hence, our study concluded that the combination therapy was better than amlodipine monotherapy.

In our study, after 8-week combination therapy of amlodipine (5mg) and losartan (50mg) resulted the highest systolic blood pressure reduction (50%) and diastolic blood pressure reduction (35%). Similarly, after 8 week amlodipine mono-therapy resulted systolic blood pressure reduction (39.1%) and diastolic blood pressure reduction (18.75%). In a study by RezaJafarazadesh showed that systolic blood pressure reduction by 38 % after 8 week with amlodipine and losartan combination treatment [16].

During our study, in combination therapy blood pressure was reduced by 44% and in amlodipine mono-therapy 31%. Our result supports the literature done by Sung Hae Kim et. al. where in their research blood pressure reduction was by 52.1% in combination therapy and 33.3% in monotherapy out of 148 patients after 8 week. In our study we found that percentage of reduction of blood pressure in combination therapy is better than amlodipine monotherapy [17].

In our study, the median blood pressure of hypertensive patients in combination therapy was reduced by 43% were the patients in amlodipine monotherapy the blood pressure

was reduced by 22.5%. The research done by Servicio de Nefrologiasupport our research where the median blood pressure reduction in combination therapy was 48.4% and amlodipine monotherapy was 29.5% [18].

Conclusion

Altogether we observe 120 hypertensive patients. Among them 60 patients were using amlodipine monotherapy and remaining were administering combination therapy. The number of male and female administering amlodipine monotherapy was 32 and 28 respectively where as in combination therapy male and female were 29 and 31 respectively. Our study showed that, mostly seen side effect during the period of treatment were edema of leg and headache. Patients who were using antihypertensive drugs have other diseases also like diabetes, asthma, thyroid and gout. Among this diabetes and asthma were commonly observed. Our study revealed that only 15% of the patients were aware about medicine and 56% were aware about disease. Out of 120 patients most of them were non vegetarian (83 patients).

Hypertension is the common public cardiovascular disorder and now regarded as major health problem. In our research among 120 patients, majority of hypertensive patients were male. The mean reduction of the blood pressure by amlodipine monotherapy was 47/15 mmHg and mean reduction of the blood pressure by amlodipine and losartan combination was 60/28 mmHg. Our study found that combination therapy was effective than monotherapy as greater blood pressure was reduced and higher response rates than with monotherapy. In our study fewer side effects were seen in patients who were administering the combination therapy and lastly we concluded that combination therapy of amlodipine and losartan is more efficacious than amlodipine monotherapy in hypertensive patients.

References

1. WHO, Clinical guidelines for the management of hypertension. 2005, p. 1-96.
2. Neupane. D, McLachlan CS, Mishra SR. et al. 2014. *Prevalence of hypertension.* Systematic review and meta analysis.Medicine. 93 (13), pp. 74.
3. WHO 2013. *A Global brief on hypertension*
4. Britsov SA et al. 2013.*Effectiveness and safty of losartan and its combination with amlodipine in therapy of hypertension*.Klin Med (mosk).91(12), pp.7-51
5. Adrogue HJ, and Madias NE.2007.*Sodium and Potassium in the Pathogenesis of Hypertension.*The New England Journal of Medicine. 356(01), pp. 1966-78.
6. Kalra S., Kalra B., Agrawal N. 2010. *Combination therapy in hypertension*.Diabetology and Metabolic Syndrome. 2 (02), pp. 44.
7. Robert A et al., 2003.*The effect of amlodipine compared to losartan in patients mild to moderately severe hypertension*.J Clin.5(1),pp.17-23.
8. SreevalsaUnniachan, et al., 2014.*Evaluation of blood pressure reduction response and responder characteristics to fixed-dose combination treatment of amlodipine and losartan:A post hoc analysis of pooled clinical trials*.Clinical J.16,pp.9
9. Chataut J., Adhikari K., Sinha NP., 2011. *The Prevalence of and Risk factors for Hypertension in Adults Living in Central Development Region of Nepal*.Kathmandu University Medical.J. 33 (1), pp. 13-8.
10. Sayed Md., Mishra J. et al. 2013.*Comparative study of amlodipine with losartan and amlodipine with lisinopril in control of blood pressure.* International. J.Pharma. 18 (2), pp. 42-46.
11. Merck Sharp,Dohme Corp 2014.*Efficacy of losartan +amlodipine alone in the treatment of uncontrolled high blood pressure*.Lancet. 360 (01), pp. 1347-1360.
12. Reza JafarzadehEsfehani 2012.*A comparative study of the management of stage 2 hypertension by combined therapy with Losartan,Amlodipine and HTCZ*. Cardiovasc Res J.6(3),pp.79-83.
13. Richard N et al.,2006.*A randomized trial comparing losartan with amlodipine as initial therapy for hypertension in the early post- transplant period*. Depart of medicine21(1),pp. 1389-1394
14. Dr.A.P.Singh 2013.*The prevalence of hypertension and its modifiable risk factors among medical students of a medical college in Uttar Pradesh,India*. LMcoll J.1(2), pp.53-55.
15. IramShaifali et al.,2014.*A comparative evaluation of losartan/Hydrochlorothiazide(fixed combination)versus amlodipine monotherpy in patients with hypertension.*Int.J.9(2),pp.9-16.
16. Reza JafarzadehEsfehani 2012.*A comparative study of the management of stage 2 hypertension by combined therapy with Losartan,Amlodipine and HTCZ*. Cardiovasc Res J.6(3),pp.79-83.
17. Sung Hae Kim et al.,2011.*Efficacy of fixed dose amlodipine and losartan combination compared with amlodipine monotherapy in stage 2 hypertension*. BioMed central.4(3),pp.461.
18. Servicio de Nefrologia et al,.2010.*Comparision of losartan and amlodipine in renally impaired hypertensive patients.* Kidney international.54 (02).pp., 124-128.