IJPSR (2012), Vol. 3, Issue 12 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 24 August, 2012; received in revised form 20 November, 2012; accepted 29 November, 2012

A COMPARATIVE STUDY OF THERAPEUTIC EFFECTS AND TOLERABILITY PROFILE OF CILNIDIPINE VERSUS AMLODIPINE IN MILD TO MODERATE ESSENTIAL HYPERTENSION

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Keywords:
Hypertension, Calcium channel blockers, Cilnidipine, Amlodipine, Tachycardia

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QUICK RESPONSE CODE

IJPSR:
ICV (2011)- 5.07

Website:
www.ijpsr.com

ABSTRACT

High Blood pressure or hypertension is one of the most ubiquitous yet nettle some medical problems that physician and health care provider face in the office. In present study amlodipine and cilnidipine have been selected to evaluate and compare their efficacy and tolerability in mild to moderate essential hypertension. 60 patients of uncomplicated mild to moderate essential hypertension were evaluated for clinical efficacy, effect on biochemical parameters and side effects in 6 weeks of treatment. They were divided into 2 groups of 30 patients each, making a total of 60 patients. First group of 30 patients was given cilnidipine 5-20 mg/day and second group of 30 patients was given amlodipine in dose of 5-10 mg/day and dose was adjusted according to control of blood pressure. In the present study, it was clearly evident that cilnidipine and amlodipine both are effective antihypertensive drugs. Both the drugs were instrumental in decreasing systolic blood pressure significantly ($p<0.05$).. Both the drugs also decreased the diastolic blood pressure significantly ($p<0.05$). There was no significant change in heart rate with cilnidipine therapy ($p<0.05$).. With amlodipine therapy there was significant rise in heart rate ($p<0.05$). The inhibitory effect on the N-type Ca^{2+} channel may bestow an additional clinical advantage for the treatment of hypertension, such as suppression of reflex tachycardia.

INTRODUCTION: Hypertension is one of the leading cardiovascular disorders, which is rising at a rapid pace and becoming a major public health problem in developed as well as developing countries .It is a common, readily detectable, usually easily treatable condition which often leads to life threatening complications, when left untreated [1]. As there is a continuum of risk for cardiovascular ailments with increasing blood pressure, early detection and treatment of hypertension significantly reduces cardiovascular and cerebrovascular disease-related mortality along with an improvement in quality of life [2].

As specified by the JNC 7th report, an individual is classified as hypertensive if blood pressure is more than 140/90 mmHg on mean of two or more properly measured readings on each of two or more office visits.

Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Classification
<120	<80	Normal
120-139	80-89	Pre-hypertension
140-159	90-99	Stage 1hypertension
≥160	≥100	Stage 2 hypertension

Patients with pre-hypertension are at increased risk for progression to hypertension. Systolic blood pressure >140 mmHg is much more important cardiovascular disease risk factor than diastolic blood pressure [3].

Recent Canadian recommendations for management of hypertension have mentioned the important role of calcium channel blockers in hypertension treatment. According to their recommendations, dihydropyridine calcium channel blockers (DHP CCBS) play vital role in the treatment of hypertension with and without other compelling indications, in addition to other antihypertensive agents. The associated compelling indications in which dihydropyridine therapy can be preferred are mention below:

1. ST Segment Elevation-MI or non-ST Segment Elevation MI
2. Left Ventricular Systolic Dysfunction
3. Left Ventricular Hypertrophy
4. Non Diabetic Chronic Kidney Disease
5. Diabetes Mellitus with and without nephropathy
6. Ischaemic Heart Disease

As a part of initial therapy, dihydropyridine calcium channel blockers (DHP CCBS) can be used in treating hypertension without other compelling indications, left ventricular hypertrophy and diabetes mellitus without nephropathy. While in second line therapy, they are preferred in treating diabetes mellitus with nephropathy and angina [4].

Amlodipine besylate is a member of the 1, 4 dihydropyridine group of calcium channel antagonist which is characterized by preferrential activity in vascular smooth muscle compared to myocardium. Amlodipine moves quickly onto the calcium channel to provide quick onset of action and thus vasodilation and unwanted mild tachycardia or increase in a heart rate of about 10 beats per minute. Data from epidemiological studies and clinical trials have demonstrated that elevations in resting heart rate and reduced heart rate variability are associated with higher cardiovascular risk.

In the Framingham heart study, an average resting heart rate of 83 beats per minute was associated with a substantially higher risk of death from a cardiovascular event than the risk associated with lower heart rate levels. Moreover, reduced heart rate variability was associated with an increase in cardiovascular mortality [5].

Cilnidipine is a novel and unique 1, 4 dihydropyridine derivative. It has been developed as a slow onset and long lasting anti-hypertensive drug in Japan [24]. Cilnidipine is a dual calcium channel blocker with action on both L/N type of calcium channels. Cilnidipine lowers blood pressure by inhibiting L-type calcium channels directly associated with vascular tone. Cilnidipine also inhibits N-type calcium channels, thus suppresses sympathetic activity. Cilnidipine has 50 times higher selectivity for N-type of calcium channels than amlodipine. The inhibitory effect on the N-type Ca2+channel may bestow an additional clinical advantage for treatment of hypertension, such as suppression of reflex tachycardia [6].

The present study compared the efficacy and tolerability of Amlodipine and Cilnidipine in mild to moderate essential hypertension.

MATERIAL & METHODS: Present study was carried out in the department of Medicine, Government Medical College/Guru Nanak Dev Hospital, Amritsar. Hypertensive patients were selected at random from the outpatient clinics and indoor wards of Guru Nanak Dev Hospital, Amritsar. Blood pressure was recorded using mercury sphygmomanometer. The diastolic figures were adopted at Kortokoff-V (at disappearance of arterial sounds over the right cubital fossa).It was ensured that none of the patients selected in this study was suffering from the following conditions.

1. Heart failure
2. 2nd and 3rd degree heart blocks.
3. Aortic stenosis

Patients fulfilling the above criteria, before their final inclusion in this study were well acquainted with the type of study to be carried out and their informed consent was obtained.

Before the patients were enrolled in the trial, a washout period of at least 2 weeks was observed during which all medications were discontinued. Due care was taken not to withdraw the earlier therapy abruptly. Blood pressure at the end of the washout period was taken as base line. This was an open study where the patient, the observer and the supervisor were having clear knowledge of anti-hypertensive drug used. Established cases of mild to moderate essential hypertension without any cardiac, renal, hepatic or respiratory complications qualified for this study. They were divided into 2 groups of 30 patients each, making a total of 60 patients.

First group of 30 patients will be given cilnidipine 5-20 mg/day, dose was adjusted according to the effective control of blood pressure i.e. either blood pressure was brought to normotensive range or there was a fall of systolic blood pressure by 10-15 mmHg and/or diastolic blood pressure by 5-10 mmHg, whichever was earlier. Second group of 30 patients will be given Amlodipine in dose of 5-10 mg/day was adjusted according to control of blood pressure.

Each patient was made to lie down and take rest for 5 minutes, then systolic and diastolic blood pressure was recorded in supine position. Thereafter, blood pressure was recorded in standing position after standing for 3 minutes. It was made sure that patient had not have smoked or had taken tea/coffee for half an hour before the blood pressure recording.

Periodic Observation: After washout period of 2 weeks, blood pressure recording was done at weekly intervals for 6 weeks after required dose of the drug had been adjusted. Levels of blood urea, serum creatinine, serum cholesterol, fasting blood sugar and urine protein (albumin) was determined in the beginning of the study (ending with the washout period) and again at the end of 6 weeks trial.

Observation and Tabulation: The results of the above parameters of the individual patient were pooled for each group. Their respective mean values were calculated along with standard errors. Their results were finally displayed in the tables and relevant findings were plotted for simplicity and comparison.

Analysis of Data: Data for the above mentioned parameters was compiled, tabulated and statistically analysed for their significance. Utilising the student's 't' test, 'p' value was determined to finally evaluate the levels of significance. 'p' value of <0.05 was considered significant. The relevance of the results in the light of statistical analysis was displayed and discussed.

Observations: Present study was carried out in the department of Medicine, Govt. Medical College/Guru Nanak Dev Hospital, Amritsar, on 60 patients of uncomplicated mild to moderate essential hypertension to compare the clinical efficacy and side effects in six weeks of treatment with cilnidipine and amlodipine given once daily. Patients included in group I were given cilnidipine whereas patients in group II were given amlodipine. Following observations have been made. **Table 1** shows distribution of sex in both groups was nearly equal.

TABLE 1: SHOWING SEX DISTRIBUTION AMONG THE PATIENTS BETWEEN GROUP I AND GROUP II

Sex	Group I (Cilnidipine)		Group II (Amlodipine)	
	No. of cases	Percentage (%)	No. of cases	Percentage (%)
Male	16	53.33	15	50
Female	14	46.67	15	50
Total	30	100	30	100

In the present study, supine systolic blood pressure of group I (cilnidipine) lowered from 160±3.56 mmHg to 133.02±1.63mmHg after 6 weeks of treatment. The fall in supine systolic blood pressure was 26.8 mmHg which was statistically significant. The percentage fall in systolic blood pressure with cilnidipine was 5.00% after 1st week of treatment and in the next five week of treatment it was 16.86% (**Figure 1**) indicating there was effective fall in supine systolic blood pressure with cilnidipine therapy in 1st week and thereafter the blood pressure continued to fall smoothly upto 6 weeks of treatment. In group II (amlodipine) supine systolic blood pressure fell progressively from initial value of 160.86±5.24 mmHg to 135.33±2.98mmHg at the end of 6 weeks which was statistically significant(Figure 1). Mean percentage fall in supine systolic blood pressure was 5.09% at the end of 1stweek and 15.87% at the end of 6th week. But when both groups were compared (**Table 2**) there was no significant difference between percentage fall of supine systolic blood pressure (p<0.05).

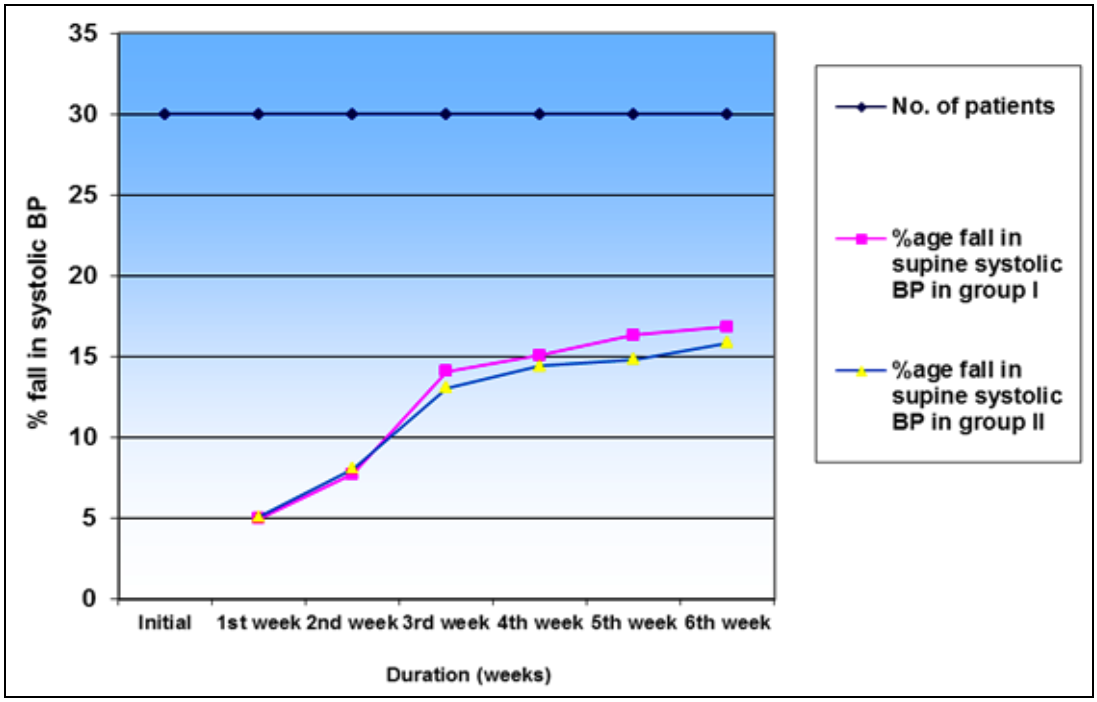

FIGURE 1: COMPARISION OF PERCENTAGE FALL IN SUPINE SYSTOLIC BLOOD PRESSURE AT WEEKLY INTERVAL IN GROUP I AND GROUP II PATIENTS

In the present study, in group I (cilnidipine) the diastolic blood pressure in supine position lowered from 98.00±2.29mmHg to 82.53±1.48 mmHg respectively after 6 weeks (**Fig. 2**). The fall was statistically significant ($p<0.05$). In group II (amlodipine) supine diastolic blood pressure fell progressively from initial value of 99.53±2.90 mmHg to 83.13±1.71mmHg at the end of 6 weeks which was statistically significant. ($p<0.05$) (Fig. 2). When both groups were compared with each other there is no significant difference (Table 2) between percentage fall in diastolic blood pressure in supine position.

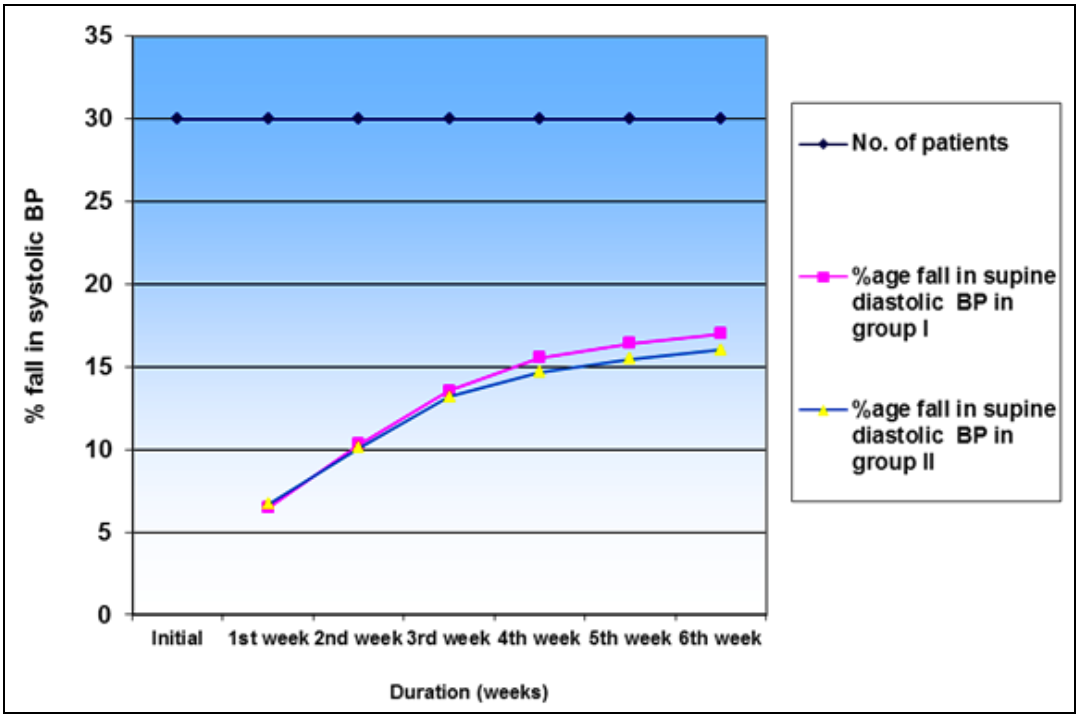

FIGURE 2: COMPARISION OF PERCENTAGE FALL IN SUPINE DIASTOLIC BLOOD PRESSURE AT WEEKLY INTERVAL IN GROUP I AND GROUP II PATIENTS

TABLE 2: SHOWING COMPARISION OF FALL IN SYSTOLIC BLOOD PRESSURE, DIASTOLIC BLOOD PRESSURE IN SUPINE IN GROUP I AND II AT WEEKLY INTERVAL

PERIOD	GROUP	Mean±S.D (sitting SBP) mmHg	Mean fall in SBP (sitting)	%age fall	Difference in fall	p-value	Mean±S.D (sitting DBP) mmHg	Mean fall in DBP (sitting)	%age fall	Difference in fall	p-value
Initial	I	160±3.56	-	-	-	-	98±2.28	-	--	-	-
	II	160.86±5.24	-	-	-	-	99.53±2.95	-	-	-	--
1st week	I	152±5.01	8.00	5.00	0.20	Non significant	91.73±2.55	6.26	6.39	0.30	Non significant
	I I	152.66±4.49	8.20	5.09			92.86±2.90	6.66	6.69		
2nd week	I	147.6±3.03	12.4	7.75	0.60	Non Significant	88.20±2.69	9.80	10.00	0.10	Non significant
	I I	147.86±4.16	13.00	8.08			89.46±2.45	10.06	10.10		
3rd week	I	137.46±3.63	22.53	14.09	1.53	Non Significant	85.40±2.63	12.60	12.86	0.33	Non significant
	I I	139.86±2.40	21.00	13.05			86.40±1.99	13.13	13.19		
4th Week	I	135.86±2.67	24.13	15.08	0.93	Non Significant	83.40±1.49	14.60	14.98	0.31	Non significant
	I I	137.66±2.46	23.20	14.42			85.13±2.20	14.40	14.67		
5th Week	I	133.86±2.09	26.13	16.33	1.86	Non Signifcant	82.93±1.55	15.06	15.40	0.07	Non signifcant
	I I	134.00±3.22	23.86	14.83			84.13±1.81	15.40	15.47		
6th week	I	133.2±1.62	26.80	16.86	0.10	Non significant	82.53±1.48	15.46	15.76	0.24	Non significant
	I I	133.33±2.98	25.53	15.87			83.06±1.61	15.93	16.00		

In group I (cilnidipine) heart rate fell progressively from initial value of 80.13±3.92 bpm to 78.60±4.03 bpm at the end of 6 weeks as shown in **Table 3**. Mean percentage fall of heart rate was 0.38, 0.84, 1.18, 0.67, 1.59 and 1.74 in at the end of 1st, 2nd, 3rd, 4th, 5th and 6th week respectively which is statistically non-significant.

With amlodipine heart rate increases progressively from initial value of 78.33±3.40bpm to 85.20±2.26 bpm at the end of 6 weeks as shown in Table 3. Mean percentage increase in heart rate was 3.52, 7.57, 9.70, 10.46, 10.03 and 8.75 in at the end of 1st, 2nd, 3rd, 4th, 5th and 6th week respectively. There was significant increase in heart rate in group II as compared to group I($p<0.05$) as shown in **Fig. 3**.

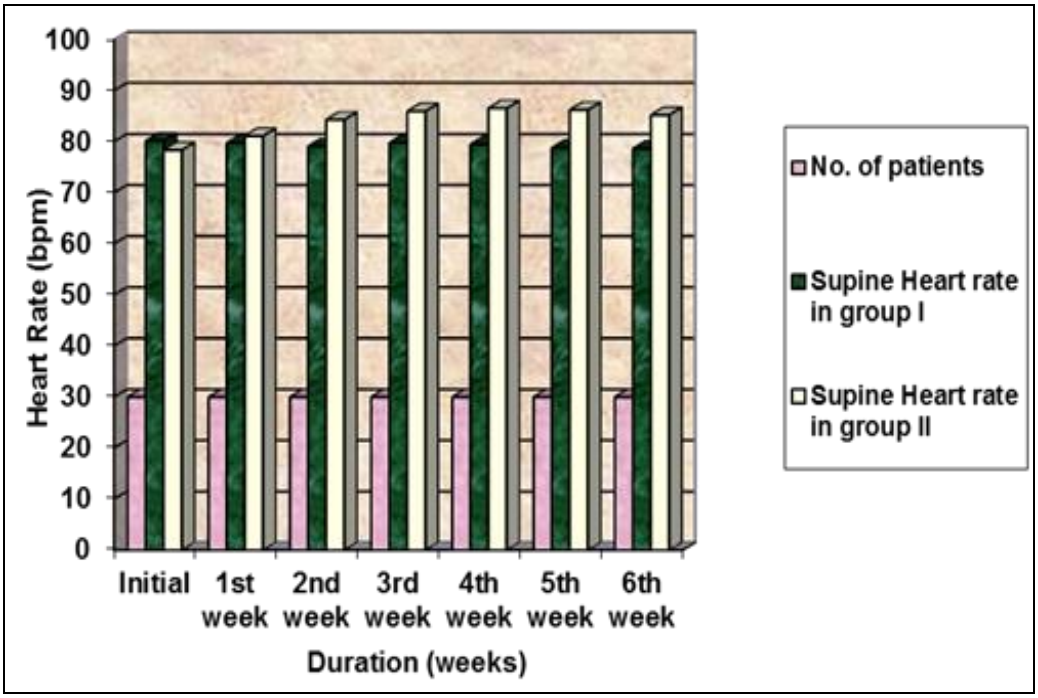

FIGURE 3: COMPARISION OF SUPINE HEART RATE AT WEEKLY INTERVAL IN GROUP I AND GROUP II PATIENTS

TABLE 3: SHOWING COMPARISION HEART RATE IN SUPINE IN GROUP I AND II AT WEEKLY INTERVAL

PERIOD	GROUP	Mean±S.D (standing HR) bpm	Mean fall/increase in HR (standing)	%age fall/ increase	Difference in increase	p-value
Initial	I	80.13±3.92	-	-		
	II	78.33±3.40	-	-		
Ist week	I	80.13±3.92	-0.40	-0.38	3.90	Significant
	II	81.10±3.95	2.76	3.52		
2nd week	I	79.33±3.79	-0.80	-0.84	8.41	Significant
	II	84.26±3.22	5.93	7.57		
3rd week	I	79.06±4.22	-1.06	-1.18	10.88	Significant
	II	85.93±2.43	7.60	9.70		
4th week	I	79.46±4.23	-0.66	-0.67	11.43	Significant
	II	86.53±2.28	8.20	10.46		
5th week	I	78.73±3.87	-1.40	-1.59	11.62	Significant
	II	86.20±2.69	7.86	10.03		
6th week	I	78.6±4.03	-1.53	-1.73	10.48	Significant
	II	85.2±2.26	6.86	8.75		

In standing position, a fall in systolic blood pressure with cilnidipine (Group I) was from initial 158.86±3.22 to 134.60±1.59 mmHg after 6 weeks of treatment (**Fig. 4**). Total mean fall was 24.26 mmHg. Mean percentage fall in standing blood pressure was 4.94 &15.27% at the end of 1st and 6th week respectively as shown in Table no4. With amlodipine standing systolic blood pressure fell progressively from initial value of 158.86±5.29 mmHg to 132.86±2.20mmHg at the end of 6 weeks (Fig. 4).The fall was statistically significant ($p<0.05$) .Total fall in sitting diastolic blood pressure after 6 weeks was 26.00 mmHg. Mean percentage fall in systolic blood pressure in group II was 4.99 and 16.36% at the end of 1st and 6th week respectively (Fig. 4).. As seen in Table no. 4 there is no significant difference in percentage fall in standing blood pressure when compared both groups. ($p<0.05$)

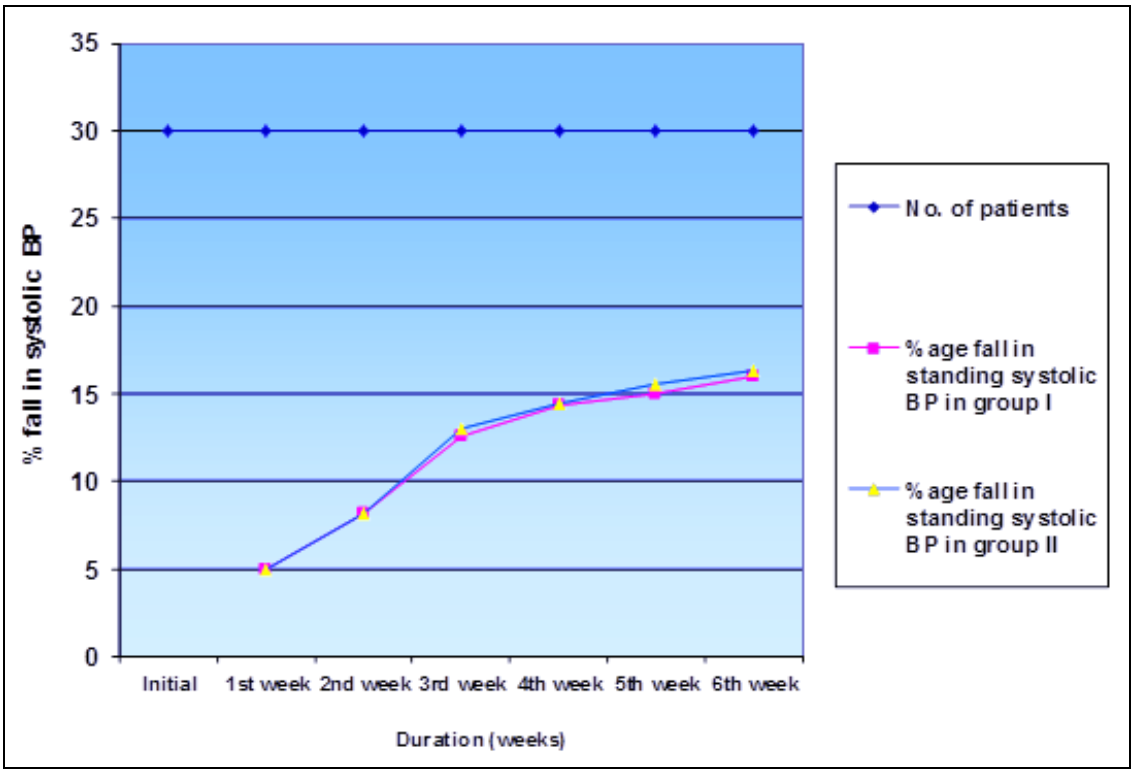

FIGURE 4: COMPARISION OF PERCENTAGE FALL IN STANDING SYSTOLIC BLOOD PRESSURE AT WEEKLY INTERVAL IN GROUP I AND GROUP II PATIENTS

With cilnidipine standing diastolic blood pressure fell progressively from initial value of 98.00±2.29 mmHg to 82.53±1.48mmHg at the end of 6 weeks as seen in **table 4**.

Mean percentage fall in standing diastolic blood pressure was 6.39 and 15.78% at the end of 1st and 6th week respectively (fig no.5). In group II the diastolic blood pressure in standing position reduced from 98.52±2.90mmHg to 83.13±1.71 mmHg respectively after 6 weeks. Mean percentage fall in standing diastolic blood pressure was 6.69 and 16.00% at the end of 1st and 6th week respectively. When both compared with each other there no significant difference in fall of standing diastolic blood pressure. ($p<0.05$) as shown in table 4.

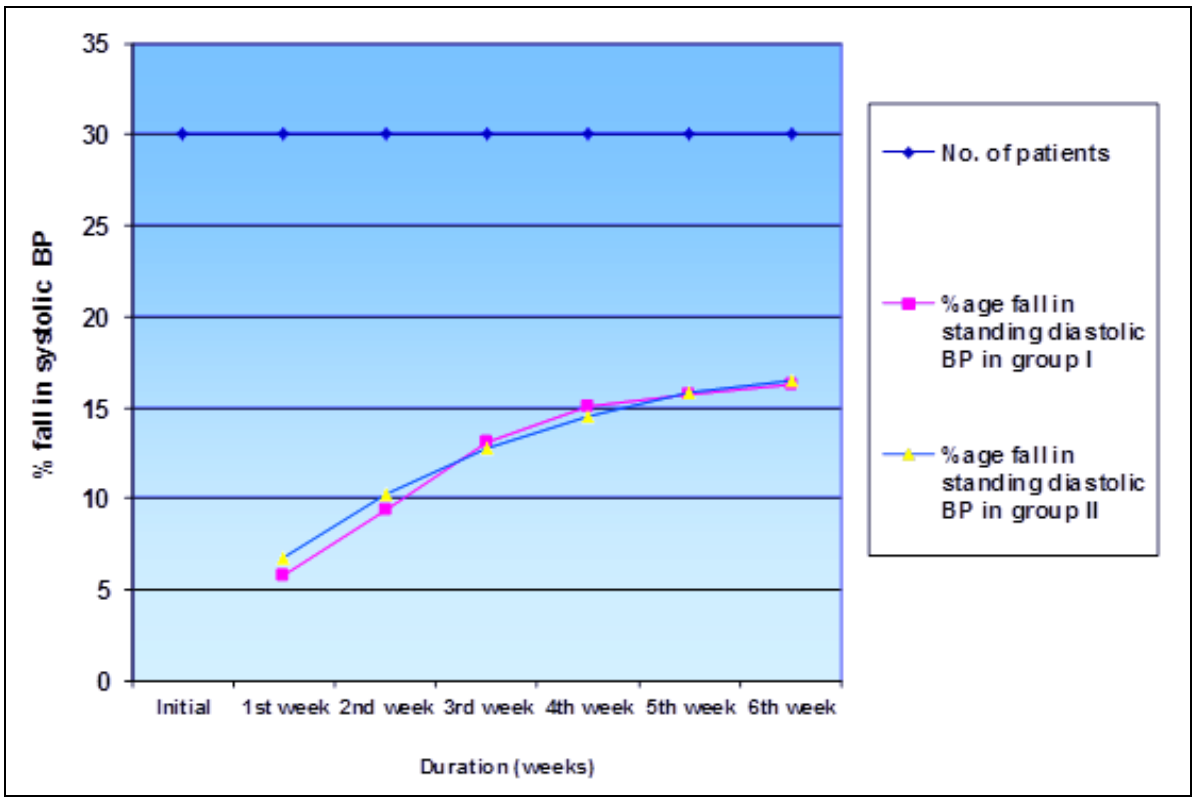

FIGURE 5: COMPARISION OF PERCENTAGE FALL IN STANDING DIASTOLIC BLOOD PRESSURE AT WEEKLY INTERVAL IN GROUP I AND GROUP II PATIENTS

TABLE 4: SHOWING COMPARISION OF FALL IN SYSTOLIC BLOOD PRESSURE, DIASTOLIC BLOOD PRESSURE IN STANDING IN GROUP I AND II AT WEEKLY INTERVAL

PERIOD	GROUP	Mean±S.D (supine SBP) mmHg	Mean fall in SBP (spine)	%age fall	Difference in fall	p-value	Mean±S.D (supine DBP) mmHg	Mean fall in DBP (supine)	%age fall	Difference in fall	p-value
Initial	I	158.86±3.22	-	-	-	-	100.00±2.62	-	--	-	-
	II	158.86±5.29	-	-	-	-	99.53±2.90	-	-	-	--
1st week	I	151.00±2.76	7.86	4.93	0.07	Non significant	93.53±3.70	6.46	6.43	0.32	Non significant
	II	150.93±4.68	7.93	4.99			92.80±3.08	6.66	6.75		
2nd week	I	145.93±3.25	12.93	8.11	0.13	Non Significant	89.66±3.52	10.33	10.31	0.10	Non significant
	II	145.80±4.61	13.06	8.05			89.33±2.45	10.06	10.21		
3rd week	I	138.86±3.18	20.00	12.57	0.60	Non Significant	86.46±2.38	13.53	13.50	0.26	Non significant
	II	138.26±3.05	20.60	12.97			86.80±2.65	13.13	12.76		
4th Week	I	136.00±1.74	22.86	14.36	0.07	Non Significant	84.46±1.79	15.53	15.48	0.90	Non significant
	II	135.93±3.08	22.93	14.43			85.06±2.27	14.40	14.50		
5th Week	I	135.20±1.44	23.66	14.86	1.06	Non Significant	83.60±1.69	16.40	16.35	0.59	Non significant
	II	133.80±2.69	25.06	15.77			83.80±1.91	15.40	15.76		
6th week	I	134.60±1.62	24.26	15.24	1.84	Non significant	83.60±1.69	17.00	16.95	0.53	Non significant
	II	132.86±2.20	26.00	16.36			83.13±1.71	15.93	16.42		

With cilnidipine heart rate fell non-significantly from initial value of 78.86±3.65 bpm to 77.53±4.15 bpm at the end of 6 weeks (**Fig. 6**). With amlodipine heart rate increases progressively from initial value of 78.33±3.40 bpm to 85.20±2.26 bpm at the end of 6 weeks (Fig no.6). When both groups were compared there was significant ($p<0.05$) increase in heart rate in group II as compared to group I as shown in Table no.5.

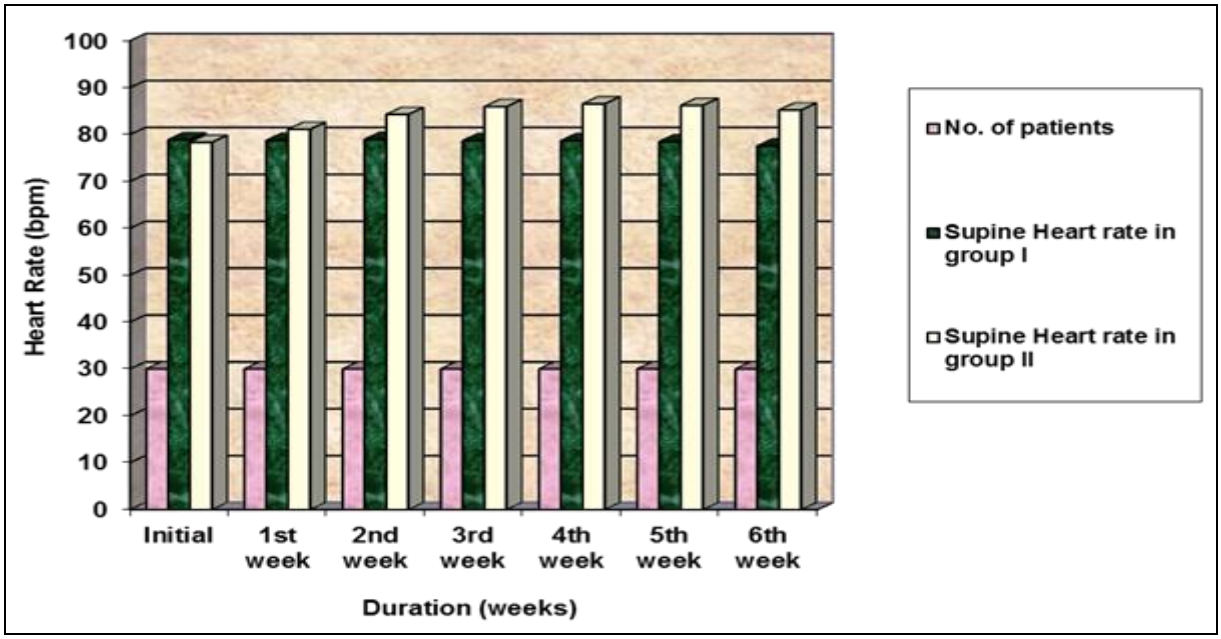

FIGURE 6: COMPARISION OF STANDING HEART RATE AT WEEKLY INTERVAL IN GROUP I AND GROUP II PATIENTS

TABLE 5 : SHOWING COMPARISION OF HEART RATE IN STANDING IN GROUP I AND II AT WEEKLY INTERVAL

PERIOD	GROUP	Mean±S.D (supine HR) bpm	Mean fall/increase in HR (supine)	%age fall/ increase	Difference in increase	p-value
Initial	I	78.66±3.65	-	-		
	II	78.33±3.40	-	-		
Ist week	I	78.73±3.65	0.07	0.16	3.36	Significant
	II	81.10±3.95	2.76	3.52		
2nd week	I	78.93±3.70	0.27	0.39	7.18	Significant
	II	84.26±3.22	5.93	7.57		
3rd week	I	78.66±3.65	0.00	0.00	9.70	Significant
	II	85.93±2.43	7.60	9.70		
4th week	I	78.66±3.65	0.00	0.00	10.46	Significant
	II	86.53±2.28	8.20	10.46		
5th week	I	78.66±3.76	0.11	-0.17	10.20	Significant
	II	86.20±2.69	7.86	10.03		
6th week	I	77.53±4.15	-1.73	-1.38	10.13	Significant
	II	85.2±2.26	6.86	8.75		

DISCUSSION: In the present study, effective fall in both systolic and diastolic blood pressure was noted with cilnidipine and amlodipine. Both cilnidipine and amlodipine showed almost equal efficacy as antihypertensive agents. There was no significant difference in fall in systolic and diastolic blood pressure in both groups. Hoshide [7] and Park both demonstrated that cilnidipine and amlodipine has similar efficacy in lowering both systolic and diastolic blood pressure.

As compared to amlodipine, cilnidipine showed no significant increase in heart rate during treatment. But patients on amlodipine treatment showed increase in heart rate from baseline which was statistically significant. These findings are comparable to the studies done by Hoshide[7] and Park. The inhibitory effect on the N-type Ca^{2+} channel may bestow an additional clinical advantage for the treatment of hypertension, such as suppression of reflex tachycardia.

Both the drugs caused no significant effect on biochemical parameters and ECG in the patients under treatment in the present study. Mild side effects were noticed in patients on cilnidipine as well as in patients on amlodipine therapy. The incidence of side effects was slightly lesser in cilnidipine group. No severe side effect requiring stoppage of treatment was recorded in any of group.

Cilnidipine is observed to be an effective antihypertensive drug in the both the sexes and in all age groups included in this study. This antihypertensive effect is also reported by other workers in their studies like Hoshide [7], Yamagishi [8] and Nagahma [9].

It was found that cilnidipine when given to patients of mild to moderate essential hypertension reduced blood pressure significantly. In the present study supine systolic blood pressure lowered from 160±3.56 mmHg to 133.02±1.63mmHg after 6 weeks of treatment. The fall in supine systolic blood pressure was 26.8 mmHg which was statistically significant.

The percentage fall in systolic blood pressure with cilnidipine was 5.00% after 1st week of treatment and in the next five week of treatment it was 11.86% indicating there was effective fall in supine systolic blood pressure with cilnidipine therapy in 1st week and thereafter the blood pressure continued to fall smoothly upto 6 weeks of treatment

The effect of cilnidipine to lower blood pressure in standing position was also observed and recorded. In standing position, adequate fall in systolic blood pressure with cilnidipine was recorded as compared to that in supine position. Standing systolic blood pressure was reduced from initial 158.86±3.22 to 134.60±1.59 mmHg after 6 weeks of treatment. Total mean fall was 24.26 mmHg. Similarly, significant fall in standing systolic blood pressure has been reported in various studies carried out previously .

Our findings agree with those of Nagahma [9] who demonstrated fall in systolic blood pressure by 24.9 mmHg after 8 weeks of treatment with cilnidipine. Yamagishi [8] reported fall in systolic blood pressure by 29 mmHg with cilnidipine after 8 weeks of treatment. Hoshide [7] reported fall in systolic blood pressure by 28 mmHg with treatment cilnidipine after 12 weeks of treatment.

It is obvious that percentage fall in standing systolic blood pressure was 4.94% after 1st week and 11.33% in the next 5 weeks of treatment, indicating that there was an effective fall in standing systolic blood pressure with cilnidipine in 1st week and thereafter.

Further fall in systolic blood pressure was statistically significant up to 6th week, indicating that cilnidipine therapy starts its action immediately and sustained antihypertensive effect of the drug continued upto 6 weeks. The fall in supine and standing systolic blood pressure was also compared in present study. But the difference in fall in both postures was insignificant and there was no incidence of postural hypotension.

The effect of cilnidipine on diastolic blood pressure in supine and standing position was also observed. In the present study, the diastolic blood pressure in supine and standing position reduced from 100.00±2.67 mmHg and 98.00±2.29mmHg to 83.00±1.55 and 82.53±1.48 mmHg respectively after 6 weeks. The fall was statistically significant.

Net fall in diastolic blood pressure was 17.00 mmHg and 15.78 mmHg in supine and standing position respectively. The studies carried out by other workers also showed significant reduction in diastolic blood pressure with cilnidipine therapy. Yamagishi[8] reported fall in diastolic blood pressure by 19 mmHg with treatment cilnidipine after 8 weeks of treatment. Nagahma[9] demonstrated net fall in diastolic blood pressure after cilnidipine therapy was 12.4 mmHg in 8 weeks of treatment.

The percentage fall in diastolic blood pressure in supine and standing position is 6.46% and 5.76% respectively after 1st week in the present study. Thereafter, the percentage reduction in supine and standing diastolic blood pressure in next 5 weeks is 10.54% and 10.45% respectively. So there is effective fall in diastolic blood pressure in 1st week and it continued to fall smoothly upto 6 weeks.

The effect of cilnidipine on heart rate in supine and standing position was also observed. In the present study, there was no significant change in heart rate of

patients treated with cilnidipine therapy. The heart rate in supine and standing position at the end of 1st week is 79.3±3.77 bpm and 78.86±3.50 bpm. There was no significant change in the heart rate during 1st week. Thereafter, there was no significant change in heart rate in next 5 weeks with cilnidipine therapy. Minami [10]and Kithara [11] both showed that there was slight decrease in heart rate which was not statistically significant

No significant effect was observed on renal function, fasting blood sugar, serum cholesterol, serum sodium and potassium in the patients treated with cilnidipine therapy.

The changes in ECG, which was present at the beginning of the study, persisted at the end of 6 weeks of treatment in cilnidipine therapy group.

The present study has been carried out for 6 weeks and this period is quite short to cause any significant changes in ECG, unless an acute complication of hypertension is observed.

Out of the thirty patients treated with cilnidipine in the present study, one patient complained of edema feet, one patient complained of headache and one patient complained of malaise and fatigue.

It has been observed that unwanted events in patients receiving cilnidipine therapy were mild and therefore, the findings of the present study are comparable to the findings of previous studies [7, 8, 9].

Effect of amlodipine on systolic and diastolic blood pressure was also observed in patients suffering from mild to moderate essential hypertension in the present study. Amlodipine was found to be an effective antihypertensive agent in the present study as is also demonstrated by various studies which have also reported antihypertensive effect of amlodipine. There is rise in heart rate with treatment with amlodipine.

Amlodipine when administrated to the patients of uncomplicated mild to moderate hypertension reduced supine and standing systolic blood pressure from the mean of 160.86±5.24 mmHg and 158.86±5.29 mmHg to 135.33±2.98 and 132.86±2.20 mmHg respectively after 6 weeks of treatment. Total fall in supine and sitting diastolic blood pressure after 6 weeks was 25.33 and 26.00 mmHg respectively. Our findings agree with Johansen who demonstrated fall in systolic blood pressure by 27mmHg after 8 weeks of treatment with amlodipine therapy. Eguchi also reported fall in systolic blood pressure by 26 mmHg with amlodipine therapy.

The fall in supine and standing blood pressure in the present study is 5.09% and 4.99% respectively after 1st week of therapy and after 5 weeks was 10.78% and 11.37% respectively. Thus there was effective fall in systolic blood pressure after 1st week of treatment, after which the systolic blood pressure fell progressively and smoothly upto 6 weeks of treatment. The fall in supine and standing systolic blood pressure was also compared in present study. But the difference in fall in both postures was insignificant and there was no incidence of postural hypotension.

The effect of amlodipine on diastolic blood pressure in supine and standing position was also observed. In the present study, the diastolic blood pressure in supine and standing position reduced from 99.53±2.95 mmHg and 98.52±2.90mmHg to 83.60±1.61and 83.13±1.71 mmHg respectively after 6 weeks. The fall was statistically significant. There is no significant fall of blood pressure in the supine and standing position after treatment with amlodipine indicating there was no postural hypotension.

The fall in supine and standing diastolic blood pressure was 6.69% and 6.76% respectively after 1st week of treatment and subsequent 5 weeks. The reduction in diastolic blood pressure was 10.71% and 9.31% in supine and standing position respectively. Thus there was effective fall in diastolic blood pressure after 1st week of treatment and diastolic blood pressure continued to fall smoothly till 6 weeks of treatment.

Johansen [12] reported fall in diastolic blood pressure by 16 mmHg with amlodipine therapy after 8 weeks of treatment. Eguchi [13] demonstrated net fall in diastolic blood pressure by 13mmHg after 8 weeks of amlodipine treatment. The fall in diastolic blood pressure in the present study is slightly less than observed by other workers in their respective studies.

This difference may be due to differences in the life style, diet, socio-cultural environment, and weight and body mass index of the different populations.

The effect of amlodipine on heart rate in supine and standing position was also observed. In the present study, there was significant change in heart rate of patients treated with amlodipine therapy. The heart rate in supine and standing position at the end of 1st week is 81.10±3.95 bpm and 81.10±3.95 bpm. There was significant change in the heart rate in 1st week. In the present study, the heart rate in supine and standing position increased from 78.33±3.40 bpm and 78.33±3.40 bpm to 85.20±2.26 bpm and 85.20±2.26 bpm respectively after 6 weeks. The increase was statistically significant. No difference in heart rate was observed in supine and standing postures.

The increase in heart rate in the present study is 3.52% after 1st week of therapy and increase in subsequent 5 weeks was 5.23%. Thus there was effective increase in heart rate after 1st week of treatment, after which the heart rate increased progressively and smoothly upto 3rd week of treatment. After that heart rate continued to increase but this increase was statistically insignificant. Similar effects had been noticed by various workers in their studies. Hoshide [8] and Kojima [14] demonstrated that amlodipine caused statistically significant increase in heart rate.

In the present study, no significant effect was observed on laboratory parameters like fasting blood sugar, blood urea, serum creatinine, serum cholesterol and serum sodium after 6 weeks of treatment with amlodipine.

Changes in ECG, which were present at the beginning of the study, persisted till the end of 6 weeks in amlodipine group. On the scrutiny of the record, it is also observed that there were no significant new changes in patients on amlodipine therapy. This period is quite short to draw any firm conclusions about changes unless it is affected by any acute episode.

The side effects encountered in the present study with amlodipine were mild and did not warrant stoppage of treatment. Out of the 30 patients treated with amlodipine in the present study, 4 complained of palpitation, 2 of edema feet, 1 of headache, 1 of hot flushes and 2 of malaise and fatigue.

In the rapidly changing world of medicine, where a wide variety of drugs is introduced for the treatment of hypertension, it is important to know effectiveness and side effects of different drugs. In the present study, a sincere effort has been made to compare two drugs in terms of efficacy and safety.

SUMMARY AND CONCLUSIONS:

1. The present study was carried out in the department of Medicine, Guru Nanak Dev Hospital / Medical College, Amritsar on 60 patients of uncomplicated mild to moderate essential hypertension to evaluate the clinical efficacy, effect on biochemical parameters and side effects of cilnidipine and amlodipine in 6 weeks of treatment.

2. In the present study, it was clearly evident that cilnidipine and amlodipine both are effective antihypertensive drugs. Both the drugs were instrumental in decreasing systolic blood pressure significantly.

3. Both the drugs also decreased the diastolic blood pressure significantly.

4. There was no significant change in heart rate with cilnidipine therapy. With amlodipine therapy there was significant rise in heart rate. The inhibitory effect on the N-type Ca^{2+} channel may bestow an additional clinical advantage for the treatment of hypertension, such as suppression of reflex tachycardia.

5. The common side effects in both groups were pedal edema, palpitation, headache, flushing, headache and fatigue. The side effects were mild and did not warrant stoppage of treatment.

6. The changes in the ECG pattern before trial persisted in both the groups and no new change was noticed.

7. There was no significant change in biochemical parameters in either group before and after 6 weeks of treatment.

8. Cilnidipine showed better safety and efficacy compared to amlodipine. Cilnidipine is not found to be associated with producing reflex tachycardia. It can be beneficial in peripheral edema. Overall, cilnidipine can be a better therapeutic option than amlodipine.

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How to cite this article:
Kaur M, Sharma AK, Mahajan DS, Takia T and Goel D: A Comparative StudyO Therapeutic Effects And Tolerability Profile Of Cilnidipine Versus Amlodipine in Mild to Moderate Essential Hypertension. *Int J Pharm Sci Res*. 3(12); 5044-5055.