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TO STUDY CLINICAL AND BIOCHEMICAL EFFECTS OF AMLODIPINE AND CILNIDIPINE IN NEWLY DIAGNOSED CASES OF HYPERTENSION

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ABSTRACT: Introduction: Hypertension is a major global health challenge and a significant contributor to cardiovascular diseases and death. Calcium channel blockers (CCBs) are effective in managing various stages of hypertension. The aim of study was to compare the safety and effectiveness of amlodipine and cilnidipine in newly diagnosed patients of hypertension. **Material and Methods:** This prospective, randomized, open-label, parallel-group study was conducted at Guru Nanak Dev Hospital, Amritsar. Sixty newly diagnosed mild to moderate hypertensive patients were randomly assigned to two groups. Group A received amlodipine 5 mg, and Group B received cilnidipine 10 mg once daily for 12 weeks. Blood pressure, heart rate and biochemical parameters were recorded at baseline, 4, 8, and 12 weeks. Adverse events were monitored, and data was analysed. **Observations:** Baseline characteristics were largely similar in two groups, except total cholesterol, which differed significantly ($p = 0.043$). Both groups showed significant reduction in SBP and DBP over the 12-week period ($p < 0.001$), with no notable difference between two groups ($p > 0.05$). Heart rate was slightly increased in Group A ($p = 0.782$) but a significant decrease in Group B ($p < 0.001$), with evident intergroup difference at weeks 8 and 12 ($p < 0.05$). Significant decrease in triglycerides ($p = 0.012$) in Group B was seen. Group A suffered more adverse effects of pedal oedema, headache and fatigue. **Conclusion:** Both amlodipine and cilnidipine effectively reduced blood pressure over 12 weeks. However, cilnidipine had fewer side effects and added benefits on heart rate and triglycerides.

INTRODUCTION: Hypertension, often called "the silent killer," is a major global health issue contributing to about 13% of all deaths worldwide. It significantly increases the risk of cardiovascular diseases, including heart attacks and strokes [1]. In India, especially in rural and younger populations, hypertension is on the rise.

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Globally, over 1.28 billion adults aged 30–79 are affected, with two-thirds living in low- and middle-income countries [2]. Yet, about 46% are unaware of their condition, and only 21% manage to control it effectively [3].

Most cases are due to essential (idiopathic) hypertension, where factors like genetics, high salt intake, and sympathetic over activity play key role. Salt sensitivity, seen in 50–60% of hypertensive individuals, contributes significantly to the disease. Key mechanisms include increased salt and water retention, overactive sympathetic nervous system, and dysregulated renin-angiotensin-aldosterone system (RAAS).

These lead to high peripheral resistance and organ damage like heart failure and kidney disease. RAAS and sympathetic over activity promote vasoconstriction and fluid retention, raising blood pressure. Elevated sympathetic nerve activity, especially in muscles, increases vascular tone and contributes to complications. Arterial stiffness, functional or structural, is also linked to hypertension with genetic and metabolic factors playing a role. Over 1,000 gene regions have been associated with blood pressure regulation [4].

Diagnosis includes confirming hypertension, ruling out secondary causes, and assessing cardiovascular risk [5]. Treatment includes several drug classes: ACE inhibitors, ARBs, calcium channel blockers (CCBs) diuretics, and beta-blockers. CCBs are widely used, especially the dihydropyridine (DHP) type, which cause blood vessel relaxation by blocking calcium channels in smooth muscle. Older DHPs like nifedipine act quickly but can cause side effects due to short half-lives. Newer DHPs such as amlodipine and cilnidipine are longer-acting and better tolerated [6].

Cilnidipine is a newer-generation DHP that blocks both L- and N-type calcium channels. It offers smoother blood pressure control, fewer side effects, and is particularly beneficial for heart and kidney protection. Unlike amlodipine, cilnidipine causes less ankle swelling due to its dual action on blood vessels [7]. This study aimed to compare the safety and effectiveness of amlodipine and cilnidipine in newly diagnosed hypertensive patients.

MATERIAL AND METHODS: This prospective, randomized, open-label, parallel-group comparative study was conducted at Guru Nanak Dev Hospital, Government Medical College, Amritsar, over a period of 9 months from April to December 2024. After obtaining approval from the Institutional Ethics and Thesis Committees, 60 patients (aged 18–60 years, either sex) meeting inclusion criteria were recruited from the Medicine OPD. Written informed consent was obtained from all participants in their local language. Sample size was calculated with 95% confidence level, 80% power, and 5% margin of error, resulting in 30 patients per group (n=60). Patients were randomly assigned to two groups using computer-generated randomization:

- **Group A:** Amlodipine 5 mg once daily
- **Group B:** Cilnidipine 10 mg once daily

Patients were followed monthly for 3 months. Exclusion criteria included patients over 60 years, pregnant or lactating women, and those with severe hepatic, renal, or cardiac disease, psychiatric illness, or known drug interactions. Patients were assessed for heart rate and blood pressure on day 0, 4^{th}, 8^{th}, 12^{th} week. Baseline and post-treatment investigations included CBC, LFT, RFT, and lipid profile.

RESULTS: A total of sixty patients completed the study, with thirty patients in each treatment group. The mean age for Group A (Amlodipine) was 48.70±5.99 years, and for Group B (Cilnidipine) was 49.53±7.93 years. The age distribution was similar between the groups, with the majority of patients in both groups falling within the 41−50 years and 51−60 years age groups. Group A comprised 12 females (40%) and 18 males (60%), while Group B had 15 females (50%) and 15 males (50%).

TABLE 1: COMPARISON OF STUDY PARAMETERS AT BASELINE AND WEEK 12IN GROUP A AND B (MEAN ± SD)

Parameters		Group A (Baseline)	Group A (week 12)	Group B (Baseline)	Group B (week 12)	P value (week 12)
	HB	12.41±1.46	12.23±1.75	11.68±1.37	11.53±1.67	0.237
CBC	TLC	7570.10±1625.60	7655.33±1966.71	7149.20±1441.53	7203.67±1802.63	0.688
	Platelet	3.74±5.36	2.66±0.65	3.83±4.58	2.86±0.55	0.241
	Bilirubin	0.79±0.21	0.81±0.30	0.80±0.16	0.85±0.22	0.117
LFT	SGOT	43.33±19.67	43.40±21.10	45.47±15.64	45.60±15.28	0.864
	SGPT	49.97±22.19	50.17±24.04	55.30±17.76	55.43±19.56	0.861
	ALP	86.87±21.41	91.27±24.73	85.80±18.67	88.10±23.73	0.229
	TC	192.70±21.10	193.53±22.18	203.57±18.33	204.53±18.81	0.072
Lipid	HDL	58.40±7.55	58.47±8.19	56.73±11.06	56.70±11.61	0.937
Profile	LDL	107.90±22.10	107.97±23.40	118.70±24.54	119.03±25.58	0.515
	TG	132.77±20.46	133.53±21.57	138.57±17	139.70±18.35	0.012*

	Urea	30.57±6.72	31.47±8.02	34.17±6.94	34.23±7.89	0.898
RFT	Creatinine	1.11±0.23	1.09±0.27	1.11±0.22	1.13±0.25	0.275
	Uric Acid	5.46±0.81	5.41±0.99	5.67±0.63	5.66±0.75	0.820
	SBP	137.2±4.69	154.90±7.71	138.6±3.94	155.43±6.17	<0.001*
BP	DBP	73.13±5.93	92.23±8.28	74.27±5.91	94.63±7.77	<0.001*
Heart rate	HR	86.20±7.15	85.93±9.48	83.67±8.26	88.77±10.14	<0.001*

There were no statistically significant differences (p>0.05) between Group A and Group B at baseline for most parameters, including: Complete Blood Count (CBC), Liver Function Tests (LFT), Renal Function Tests (RFT), Blood Pressure & Heart Rate. No statistically significant changes (p>0.05) were observed in mean levels of CBC, LFT, RFT from baseline to week 12 in either Group A or Group B. Intergroup comparisons at week 12 was not statistically significant (p-values >0.05). Intragroup analysis of lipid profile showed no statistically significant changes in mean levels of total cholesterol (TC), high-density lipoprotein (HDL), or low-density lipoprotein (LDL) in either group over 12 weeks (All p-values > 0.05). However, a statistically significant reduction in mean triglyceride (TG) levels was observed in cilnidipine group (mean change: 1.13 ± 2.33 mg/dL, p=0.012) Intergroup comparison of percentage changes in lipid parameters showed no statistically significant difference (p-values > 0.05).

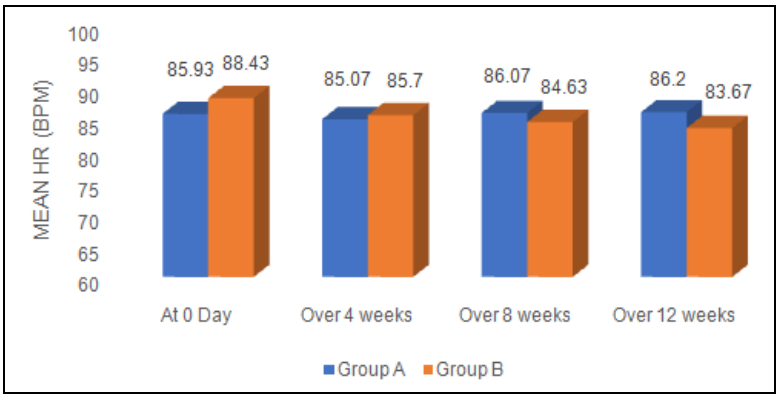

FIG. 1: INTRAGROUP COMPARISON OF MEAN HEART RATE (BPM) OF PATIENTS IN GROUP 'A' & 'B' OVER '12' WEEKS OF TREATMENT

Intragroup comparison of heart rate in Group A showed no statistically significant reduction whereas Group B expressed a statistically significant reduction in heart rate at 4, 8, and 12 weeks (p<0.05 at 4 weeks, p<0.001 at 8 and 12 weeks), with mean changes of 2.73±5.63, 3.80±4.51, and 4.77±6.17 beats per minute. Intergroup comparison revealed statistically significant difference in mean percentage change in HR between the groups at 8 weeks (p=0.002) and 12 weeks (p=0.002).

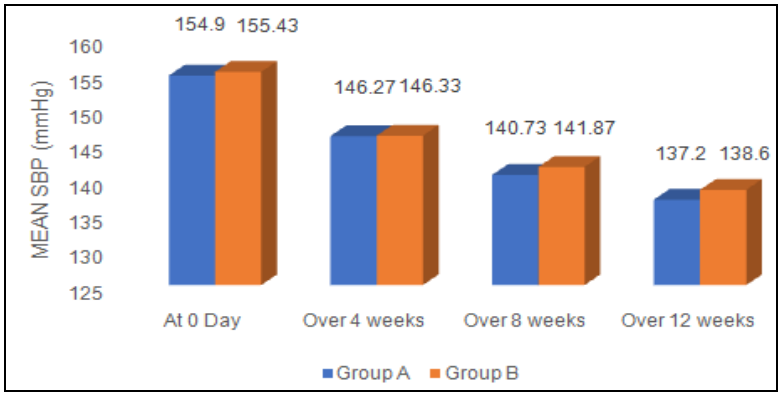

FIG. 2: INTRAGROUP COMPARISON OF MEAN SYSTOLIC BP (MM HG) OF PATIENTS IN GROUP 'A' & 'B' OVER '12' WEEKS OF TREATMENT

Intragroup comparison of systolic blood pressure (SBP) in both Group A and Group B showed highly significant reductions in SBP from baseline to 12 weeks ($p<0.001$). By week 12, the mean SBP reduction was 17.7±6.64 mmHg in Group A and 16.83±5.06 mmHg in Group B. No statistically significant difference ($p>0.05$) was observed on intergroup comparison

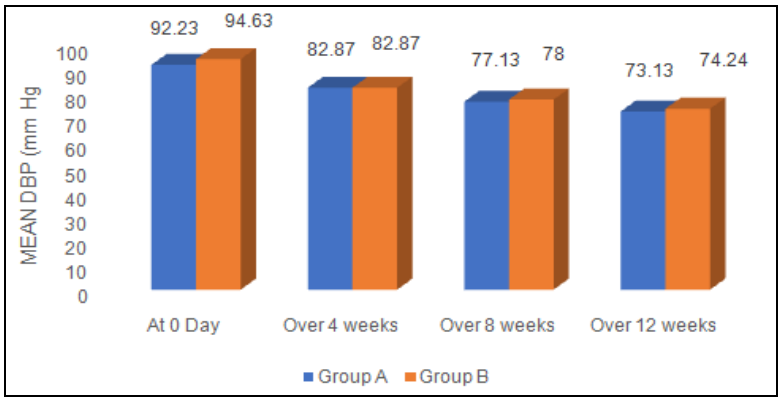

FIG. 3: INTRAGROUP COMPARISON OF MEAN DIASTOLIC BP (MM HG) OF PATIENTS IN GROUP 'A' & 'B' OVER '12' WEEKS OF TREATMENT

Intragroup comparison of diastolic blood pressure (DBP) demonstrated highly significant reductions in DBP from baseline to 12 weeks ($p<0.001$). By week 12, the mean DBP reduction was 19.1±9.56 mmHg in Group A and 20.37±7.47 mmHg in Group B. Similar to SBP, no statistically significant difference ($p>0.05$) was found between the groups indicating comparable efficacy. Adverse effects were less frequent in the cilnidipine group compared to the amlodipine group. Notably, pedal oedema was the most frequently reported side effect in the amlodipine group, affecting 23.33% of patients, compared to only 6.67% in the cilnidipine group. Headache (16.67% vs 6.67%), fatigue (10% vs 6.67%), muscle pain (10% vs 6.67%), abdominal pain (6.67% vs 3.33%), and nausea (6.67% vs 0%) were also more prevalent in the amlodipine group.

DISCUSSION: The escalating prevalence of hypertension remains a significant global health concern, contributing substantially to cardiovascular morbidity and mortality. Calcium channel blockers (CCBs) are a cornerstone in its management, with newer generations offering enhanced efficacy and safety profiles. This prospective, randomized study, conducted at Government Medical College, Amritsar, investigated the clinical and biochemical effects of two CCBs: amlodipine and cilnidipine. Sixty newly diagnosed patients with mild to moderate hypertension were equally randomized into two groups, with 30 receiving amlodipine (Group A) and 30 receiving cilnidipine (Group B). The baseline characteristics of the study participants demonstrated excellent comparability between the two treatment arms. The mean age in the amlodipine group was 48.70±5.99 years, and in the cilnidipine group, it was 49.53±7.93 years, with no statistically significant difference ($p=0.648$). This age homogeneity is crucial, as age can influence blood pressure regulation and drug metabolism. Gender distribution was also well-balanced, with 40% females in the amlodipine group and 50% in the cilnidipine group. At baseline, a comprehensive comparison of haematological, hepatic, renal, and hemodynamic parameters revealed no statistically significant differences ($p>0.05$) between Group A and Group B.

The only minor difference was observed in total cholesterol levels, with Group B showing a slightly higher average (204.53±18.81 mg/dL) compared to Group A (193.53±22.18 mg/dL), reaching statistical significance ($p=0.043$). However, this 11 mg/dL difference is unlikely to be clinically significant, especially given the similar baseline levels of LDL and triglycerides, which are more directly linked to cardiovascular risk. Regarding efficacy, both amlodipine and cilnidipine effectively reduced blood pressure. The intragroup analysis of mean systolic blood pressure (SBP) demonstrated a highly significant reduction ($p<0.001$) in both groups over 12 weeks. Group A experienced a mean SBP reduction of 17.7 mmHg (from 154.9±7.71 to 137.2±4.69 mmHg), while

Group B had a comparable mean reduction of 16.83 mmHg (from 155.43±6.17 to 138.6±3.94 mmHg). Similarly, mean diastolic blood pressure (DBP) reductions were highly significant ($p<0.001$) in both groups, with Group A showing a 19.1 mmHg decrease and Group B a 20.37 mmHg decrease by week 12. Importantly, no statistically significant intergroup differences ($p>0.05$) were observed for either SBP or DBP, suggesting comparable antihypertensive efficacy. These findings align with previous research by H. Hasan, which also reported similar blood pressure lowering effects for both drugs [8].

However, a key distinction emerged in their effects on heart rate (HR). While amlodipine (Group A) showed no statistically significant change in HR over 12 weeks, cilnidipine (Group B) demonstrated a pronounced and statistically significant reduction in HR, from 88.43±9.56 bpm at baseline to 83.67±8.26 bpm at 12 weeks ($p<0.001$). This sustained HR reduction by cilnidipine contrasts with some studies, like Hasan MH, which observed minimal HR impact from both drugs [8].

In terms of safety, neither drug significantly impacted renal function tests (RFTs), complete blood count (CBC) parameters, or liver function tests (LFTs) over the 12-week period. Intragroup comparisons showed no statistically significant changes in blood urea, serum creatinine, uric acid, haemoglobin, TLC, platelet count, bilirubin, SGOT, SGPT, or ALP for either group. Intergroup comparisons also revealed no significant differences for these parameters. This neutrality regarding renal and hepatic function is largely consistent with existing literature, though a retrospective analysis by Jadhav *et al.* suggested cilnidipine might offer better renal outcomes [9]. A rare case report of amlodipine-induced liver injury highlights the importance of continued monitoring, even though our study found no significant LFT changes.

Regarding lipid profiles, neither drug significantly impacted total cholesterol, HDL, or LDL levels. However, cilnidipine uniquely demonstrated a statistically significant reduction in triglyceride (TG) levels ($p=0.012$), a benefit not observed with amlodipine. Lowering of TG with cilnidipine has also been reported by Kumari K *et al* [10].

A notable difference in tolerability was observed in the adverse effect profiles. The amlodipine group (Group A) experienced a higher overall incidence of adverse effects (22 total) compared to the cilnidipine group (9 total). Specifically, pedal oedema was significantly more prevalent in Group A (23.33%) versus Group B (6.67%). Other adverse effects such as headache (16.67%), fatigue (10%), muscle pain (10%), abdominal pain (6.67%), and nausea (6.67%) were also more common in the amlodipine group. These findings align with Di X *et al.* and Chakraborty RN *et al.*, who similarly reported more adverse events with amlodipine than cilnidipine [11, 12]. This suggests that while both drugs are effective, cilnidipine may be a more preferable option for patients prone to peripheral oedema or those who have shown intolerance to other CCBs.

CONCLUSION: This prospective randomized study concluded that both amlodipine and cilnidipine are effective in significantly reducing systolic and diastolic blood pressure in newly diagnosed mild to moderate hypertension over a 12-week period, with comparable antihypertensive efficacy between the two drugs. However, cilnidipine demonstrated a superior safety profile, with a significantly lower incidence of adverse effects, particularly pedal oedema. Additionally, cilnidipine favourably reduced heart rate and triglyceride levels, which was not observed with amlodipine.

Therefore, cilnidipine may be considered a preferable first-line option for newly diagnosed hypertensive patients, especially those where heart rate control, metabolic profile considerations, or tolerance to peripheral oedema are relevant clinical factors. The drug offers comparable antihypertensive efficacy with improved tolerability, making it an attractive therapeutic option in the management of mild to moderate hypertension.

Limitations: The study was conducted at a single health centre, which may limit the generalizability of findings to diverse populations and healthcare settings. Study duration was restricted to only 12 weeks, as it was an academic project with time-limit.

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CONFLICTS OF INTEREST: Nil

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