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RESEARCH ARTICLE

A comparative study of the efficacy of cilnidipine and amlodipine used for the treatment of hypertension at tertiary health-care center

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ABSTRACT

Background: One of the major problems in treatment patients of hypertension (HTN) is controlling their systolic blood pressure (SBP) and diastolic BP (DBP). **Aims and Objectives:** This study aims to study the efficacy of cilnidipine and amlodipine used for the treatment of HTN at tertiary health-care center. **Materials and Methods:** The present study was undertaken by the Department of Pharmacology in collaboration with the Department of Medicine on newly diagnosed patients of HTN attending medicine outpatient department of Bidar Institute of Medical Sciences, Bidar, for a period of 9 months from May 2018 to January 2019. 100 patients aged 18–60 years of either sex were included in the study. Data were analyzed using the SPSS version 22.0. Quantitative data are presented as means and standard deviation (SD) (mean ± SD). **Results:** After 8 weeks of treatment, a gradual decline in SBP from 149.2 ± 12.57 at baseline to 131.04 ± 6.02 and DBP from 94.22 ± 6.76 at baseline to 84.36 ± 1.79 was noted in cilnidipine group. Gradual decline in SBP from 151.56 ± 10.21 at baseline to 132.72 ± 4.91 and DBP from 95.4 ± 5.70 at baseline to 82 ± 2.55 was noted with amlodipine group. Statistical analysis using paired *t*-test was obtained which is statistically significant, $P = 0.00001$. **Conclusion:** It can be concluded that both the drugs significantly reduced BP, but cilnidipine found superior to amlodipine for reducing systolic BP and equally efficacious in reducing DBP.

KEY WORDS: Cilnidipine; Amlodipine; Systolic Blood Pressure; Diastolic Blood Pressure

INTRODUCTION

Hypertension (HTN) is one of the most common diseases afflicting humans throughout the world and due to the associated morbidity and mortality and the cost to society, it is an important public health challenge as well.[1] HTN may be defined as that the level of blood pressure (BP) at which the institution of therapy reduces BP-related morbidity and mortality.[2]

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HTN is graded as mild/Stage/Grade 1 (systolic BP [SBP] between 140 and 159 and diastolic BP [DBP] between 90 and 99), moderate/Stage/Grade 2 (SBP between 160 and 179 and DBP between 100 and 109), and severe/Stage/Grade 3 (SBP ≥180 and DBP ≥110).[3]

HTN doubles the risk of cardiovascular diseases including coronary heart disease, congestive heart failure, ischemic and hemorrhagic stroke, renal failure, and peripheral arterial disease if not effectively treated.[4,5]

Literature quotes numerous studies which show that for the maximum reduction in the clinical cardiovascular end points, a tight check and control of the BP is required.

One of the recent studies indicated that approximately 14% reduction in the risk of stroke and ischemic attacks occurs

by fall in approximately 2-mmHg of average DBP. The same study also showed a simultaneous 6% reduction in risk of the development of coronary artery disease. Data from various other studies also indicate that lowering of BP might also be beneficial.[6-9]

Several classes of antihypertensive agents have been in clinical use, including diuretics, α-blockers, β-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and organic calcium channel blockers (CCBs). All these drugs are being currently used in the treatment of HTN and various disease conditions of the heart either alone or in combination.[10]

One of the CCBs with outstanding pharmacokinetic and pharmacodynamic profile is amlodipine. The only problem encountered with this medication is the presence of peripheral edema. Data from various studies show that approximately up to 30% of the hypertensive cases on amlodipine show the presence of peripheral edema while cilnidipine a newer generation of CCB is known to inhibit sympathomimetic activity.[11]

Hence, in this prospective study, an attempt has been made to compare the efficacy of cilnidipine and amlodipine in hypertensive patients.

MATERIALS AND METHODS

Source of Data

The present study was undertaken by the Department of Pharmacology in collaboration with the Department of Medicine on newly diagnosed patients of HTN attending medicine outpatient department of Bidar Institute of Medical Sciences, Bidar, for a period of 9 months from May 2018 to January 2019.

Study Population

After approval by the Institutional Ethics Committee (IEC), 100 adult patients aged 18–60 years of either sex of newly diagnosed mild and moderate hypertensive patients were included in the study. The subjects were informed about the study and written informed consent was taken.

Study Design

The present study is a prospective, open-label, parallel group, comparative study.

Inclusion Criteria

1. Newly diagnosed mild and moderate hypertensive patients.
2. Age between 18 and 60 years
3. Patients of either sex are included.

Exclusion Criteria

The following criteria were excluded from the study:
1. Patients aged <18 years and >60 years.
2. History of severe hepatic, renal disease, and severe cardiac disease.
3. Pregnant and lactating mothers.
4. Major depressive disorder with psychotic symptoms.
5. Patients on drugs with known drug interactions with the study of drugs.

Method of Collection

After approval by the IEC, 100 consenting patients were screened in two steps, initial clinical examination by a physician followed by required biochemical investigations. A detailed history which included information regarding comorbidities, allergies, past hospital admissions, reproductive history, and addictions was obtained. Fifty patients each on cilnidipine and amlodipine were randomly chosen and grouped as follows:

a. Group A – 50 patients who were prescribed tablet cilnidipine (5–10 mg/day).
b. Group B – 50 patients who were prescribed tablet amlodipine (2.5–10 mg/day).

General physical examination and systemic examination were performed during this time. The radial pulse was examined for the pulse rate and BP was recorded with a mercury sphygmomanometer in upright position. Complete cardiovascular and respiratory system evaluation was also performed.

Patients were recruited for a period of 8 weeks and were called for follow-up visit at the 2nd, 4th, and 8th weeks. The data collected were entered into a specially designed pro forma (case recording form) for the study.

Routine investigations were performed in hospital laboratory which included complete blood count, random blood glucose levels, liver function test (aspartate aminotransferase and alanine aminotransferase), and renal function test (urea and creatinine), lipid profile, and urine routine also performed before and after institution of therapy according to the scheduled requirements.

Statistical Analysis

All the data collected were entered into a preapproved, case recording form and tabulated using Microsoft Office® Excel software. Quantitative data are presented as means and standard deviation (SD) (mean ± SD). Change of BP readings from baseline to end of the study was compared using ANOVA and paired *t*-test. Intergroup analysis was done using paired Student's *t*-test. Statistical significance was defined as $P < 0.05$.

RESULTS

Figure 1 shows the distribution of patients according to the grade of HTN. Table 1 shows a gradual decline in SBP from 149.2 ± 12.57 at baseline to 131.04 ± 6.02 after 8 weeks of treatment with cilnidipine. Statistical analysis using paired *t*-test was obtained which is statistically significant, $P = 0.00001$. Table 2 shows gradual decline in DBP from 94.22 ± 6.76 at baseline to 84.36 ± 1.79 after 8 weeks of treatment with cilnidipine. Statistical analysis using paired *t*-test was obtained which is statistically significant, $P = 0.00001$. The score showed a gradual decline in SBP from 151.56 ± 10.21 at baseline to 132.72 ± 4.91 after 8 weeks of treatment with amlodipine. Statistical analysis using paired *t*-test was obtained which is statistically significant, $P = 0.0001$ [Table 3]. Table 4 shows a steady decline in DBP from 95.4 ± 5.70 at baseline to 82 ± 2.55 after 8 weeks of treatment with amlodipine. Statistical analysis using paired *t*-test was obtained which is statistically significant, $P = 0.00001$. Application of ANOVA test gives us $P = 0.132$. The difference between the two groups is statistically not significant, but both the drugs are equally efficacious in reducing SBP [Table 5]. On application of ANOVA test gives us $P = 0.0001$ at the end of 8 weeks, the difference between the two groups is statistically significant. Both the drugs are equally efficacious in reducing DBP [Table 6]. On application of ANOVA test gives us $P = 0.46$ at the end of 8 weeks, the difference between the two groups is statistically not significant. Both the drugs are equally efficacious in reducing heart rate [Table 7]. On application of ANOVA test gives us $P = 0.003$ at the end of 8 weeks, the difference between the two groups is statistically significant [Table 8].

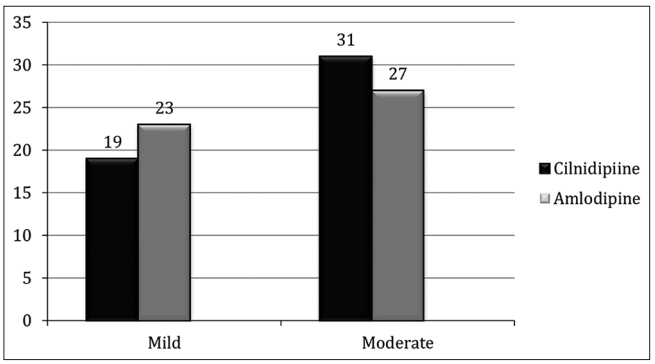

Figure 1: Distribution of patients according to the grade of hypertension

Table 1: Assessment of antihypertensive efficacy of cilnidipine (*n*=50) in the reduction of SBP

Time instance (weeks)	Mean SBP	SD
Baseline	149.2	12.57
2	143.76	10.57
4	137.28	7.76
8	131.04	6.02

SBP: Systolic blood pressure, SD: Standard deviation

Table 2: Assessment of antihypertensive efficacy of cilnidipine (*n*=50) in the reduction of DBP

Time instance (weeks)	Mean DBP	SD
Baseline	94.22	6.76
2	89.56	4.06
4	86.28	2.74
8	84.36	1.79

DBP: Diastolic blood pressure, SD: Standard deviation

Table 3: Assessment of antihypertensive efficacy in amlodipine (*n*=50) group in the reduction of SBP

Time instance (weeks)	Mean SBP	SD
Baseline	151.56	10.21
2	145.44	8.34
4	139.16	6.07
8	132.72	4.91

SBP: Systolic blood pressure, SD: Standard deviation

Table 4: Assessment of antihypertensive efficacy in amlodipine (*n*=50) group in the reduction of DBP

Time instance (weeks)	Mean DBP	SD
Baseline	95.4	5.70
2	89.92	4.09
4	85.84	2.93
8	82	2.55

DBP: Diastolic blood pressure, SD: Standard deviation

Table 5: Comparison of efficacy in SBP reduction by both the groups

Time instance (weeks)	Mean SBP in cilnidipine group	Mean SBP in amlodipine group	*P* value
Baseline	149.2±12.57	151.56±10.21	0.305
At 2	143.76±10.57	145.44±8.34	0.380
At 4	137.28±7.76	139.16±6.07	0.00001
At 8	131.04±6.023	132.72±4.91	0.132

SBP: Systolic blood pressure

Table 6: Comparison of efficacy in DBP reduction by both the groups

Time instance (weeks)	Mean DBP in cilnidipine group	Mean DBP in amlodipine group	*P* value
Baseline	94.22±6.76	95.4±5.70	0.34
At 2	89.56±4.06	89.92±4.09	0.66
At 4	86.28±2.74	85.84±2.93	0.44
At 8	84.36±1.79	82±2.55	0.0001

DBP: Diastolic blood pressure

Table 7: Assessment of heart rate of both the groups

Drugs	At baseline mean	8 weeks mean
Cilnidipine	78.24	75.14
Amlodipine	78.36	75.46

Table 8: Assessment of pulse rate of both the groups

Drugs	At baseline mean	8 weeks mean
Cilnidipine	77.02	75.30
Amlodipine	74.94	74.22

DISCUSSION

Figure 1 depicts that patients were also segregated based on the grade of HTN. It was observed that 31 (62%) and 27 (54%) patients in cilnidipine and amlodipine group, respectively, had maximum patients with moderate HTN.

In Table 1, mean SBP score recorded in cilnidipine group at baseline was 149.2 ± 12.57 and showed a gradual decline over 8 weeks to about 131.04 ± 6.023. This decline was found to be statistically significant on application of paired *t*-test as depicted.

Similarly, in Table 2, there was a reduction of DBP for cilnidipine group from 94.22 ± 6.76 baseline values to 84.36 ± 1.79 at the end of 8 weeks. It was found to be statistically significant with $P = 0.00001$.

As Table 3, the scores of SBP in amlodipine group showed a steady decline in SBP from a baseline value of 151.56 ± 10.21 to 132.72 ± 4.91 at the end of 8 weeks. Likewise, this was statistically significant with $P = 0.0001$.

While in Table 4, there was reduction of DBP in amlodipine group from baseline value of 95.4 ± 5.70 to 82 ± 2.55 at the end of 8 weeks. It was found to be statistically significant with $P = 0.00001$.

Table 5 compared the efficacy of cilnidipine with amlodipine by measuring the mean reduction in SBP after 8 weeks of treatment. On application of unpaired *t*-test, we got $P = 0.132$ which is not statistically significant. Thus concluding that, although both cilnidipine and amlodipine produced statistically significant reduction in SBP, there is no difference between the treatment groups. They are both equally efficacious in the treatment of HTN.

Similarly, in Table 6, DBP values were compared between cilnidipine and amlodipine. Both were equally effective in reducing DBP, but we obtained $P = 0.0001$ which is statistically significant reduction in DBP on comparison of both groups indicating that cilnidipine is better than amlodipine.

Table 7 shows that on application of ANOVA test gives us $P = 0.46$ at the end of 8 weeks, the difference between the two groups is statistically not significant. Both the drugs are equally efficacious in reducing heart rate.

Similarly, Table 8 shows that on application of ANOVA test gives us $P = 0.003$ at the end of 8 weeks, the difference between the two groups is statistically significant. Both the drugs are equally efficacious in reducing pulse rate.

The results of the study conducted previously by Adake *et al*.[12] showed that there was a significant reduction in systolic and DBP ($P < 0.05$) in both groups compared to baseline data. However, there was no significant difference in the antihypertensive efficacy of both drugs ($P > 0.05$).

As per the study by Ando *et al*.,[13] both cilnidipine (systolic and diastolic BP, after treatment: 130.40 ± 13.93/73.37 ± 10.20 mmHg) and amlodipine (129.65 ± 13.33/71.75 ± 9.79 mmHg) equally decreased BP and the changes were not different between the groups (systolic and diastolic BP: $P = 0.88$ and $P = 0.51$, respectively). The PR was unaffected by either drug (after treatment: 74.19 ± 11.96 and 74.19 ± 11.63 bpm), and the change was not significant between the two groups ($P = 0.46$).

A study by Babu[14] showed that the mean SBP in the amlodipine group and the cilnidipine group was 139.1 and 144.2 mmHg, respectively, while the mean DBP in the amlodipine group and cilnidipine group patients was 80.2 and 85.3 mmHg, respectively. Non-significant results were obtained while comparing the mean SBP and DBP among patients of the two study groups ($P < 0.05$).

The study by Shanbhag *et al*.[15] showed that the subjects in cilnidipine group had a significantly higher mean heart rate at baseline compared to the subjects in amlodipine group ($P < 0.049$).

The study by Singh *et al*.[16] showed that in amlodipine, there was no significant reduction in the mean pulse rate at the end of the study in comparison to the baseline values. These results were similar to the results of our study.

The strength of our study is that the study is randomized, there is no bias in allocation of subjects. There is frequent monitoring of BP with good patient's compliance. There are no conflicts of interest in our study.

Limitations of this study are, it is an open-labeled study. Only 8-week follow-up is not sufficient. Adverse drug reaction monitoring had to be done.

CONCLUSION

It can be concluded from our study that both the drugs significantly reduced BP, but cilnidipine found superior to

amlodipine for reducing systolic BP and equally efficacious in reducing DBP.

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