International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

To Study Effect of Cilnidipine Inhypertensive Patients with Comorbid Diabetes Mellitus in Tertiary Care Hospital in Uttar Pradesh

Dr. Jugal Kishor, Dr. Umesh Verma, Dr. Anil K. Kem

Abstract: ***Background: Hypertension is a widespread public health problem and a major risk factor. Angiotensin - converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) are first line of treatment in case of albuminuria. When the patients do not respond to ARB monotherapy, diuretics or non - dihydropyridine calcium channel blockers (CCBs) are the second line of drugs. The dihydropyridie CCB, amlodipine is a widely used drug but has no renoprotective property. Cilnidipine, a new Type of CCB which can inhibit L - Type calcium channels but also N - Type calcium channels having anti proteinuric effect. Objective: The objective of the study was to evaluate the effect of cilnidipine by estimating urinary albumin and creatinine levels in hypertension (HTN) with Type 2 diabetes mellitus (DM). Methods: This was a single - center, prospective, open - labeled, randomized study. A total of 80 patients of either gender aged between 30 and 60 with mild - to - moderate HTN with comorbid Type 2 DM visiting OPD at SIMS, Hapur, were included in the study. Urine albumin and serum creatinine were measured at day 1 and end of 6 months. Blood pressure (BP) was measured in all visits. The drug cilnidipine at a dose of 10–20 mg oral was given and the corresponding improvement in the levels of urine albumin and other parameters was identified. Results: There was a significant reduction in the mean SBP and also in DBP in the first, second and third visit. The mean heart rate at visit zero was 77.11 ± 5.04. At the end of 6 months of treatment, there was significant reduction to 71.02 ± 3.04. There was a significant reduction in microalbuminuria from 67.24 ± 8.64 to 37.14 ± 8.24. There was no change in creatinine levels. Conclusion: The study reveals that the drug cilnidipine is safe and effective in reducing the microalbuminuria and also effectively reduces BP in hypertensive patients. Hence, the drug cilnidipine can be safely administered to the patient with diabetes and HTN.***

Keywords: Cilnidipine, Renoprotective, Microalbuminuria, Hypertension, Diabetes mellitus

1. Introduction

Hypertension is a widespread public health problem and a major risk factor. (1) Patients with hypertension are often asymptomatic and disease progress so much that complications slowly and silently develop like stroke, heart failure, CAD, and sudden death. (2)

Diabetic kidney disease produces clinical proteinuria i. e. excretion of protein in urine which is a well - established marker and reliably predicts renal dysfunction even before the reduction of glomerular filtration rate (GFR). Therefore, an early diagnosis, can predict the impending renal dysfunction at initial stages of organ damage (5)

Angiotensin - converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) are first line of treatment in case of albuminuria. When the patients do not respond to ARB monotherapy, diuretics or non - dihydropyridine calcium channel blockers (CCBs) are the second line of drugs. The Dihydropyridine CCB, Amlodipine is a widely used drug but has no renoprotective property (6)

Novel CCBs act on N - and T - Type calcium channels also. N - Type calcium channels are found at nerve endings so they regulate the release of neurotransmitters norepinephrine. Cilnidipine is a novel and unique 1, 4 - dihydropyridine derivatives calcium antagonist with potent inhibitory action against not only L - Type but also N - Type voltage - dependent calcium channels. Hypertension is closely related to increase sympathetic nerve activity so decrease in norepinephrine release helps in decreasing blood pressure and their other effect's. (3)

Diabetic patients have increased sympathetic activity, cilnidipine inhibits this activity by blocking N - Type calcium channels located in the glomerulus of kidneys bringing about dilation of afferent arterioles and efferent arterioles equally, causing no increase in intraglomerular pressure and showing antiproteinuric effects. (4) Cilnidipine improves LV diastolic function in hypertensive heart disease by suppressing cardiac sympathetic over - activity. It exerts vasodilatory action without stimulating sympathetic nervous activity, thus improving insulin sensitivity. (3)

The present study was, therefore, designed and conducted to evaluate the renoprotective effect of cilnidipine by estimating urinary albumin and the serum creatinine levels in hypertensive patients with concomitant Type 2 DM and albuminuria.

2. Methodology

Study was approved from the Institutional Ethics Committee ofSARASWATHI INSTITUTE OF MEDICAL SCIENCES, HAPUR. Informed consent was obtained from the patient before conducting the study by explaining the study procedures to the patient.

After a detailed history, physical examination, clinical examination (SBP, DBP, and heart rate), and laboratory investigation (CBC, LFT, KFT, RBS, FBS, HBA1C, Serum Creatinine, Urine routine and microscopy, Urine for Albumin, ECG), the recruited patients were given cilnidipine 10–20 mg once daily ½ h after breakfast for 6 months. Patients enrolled in the study were not permitted to use any other medications apart from the antihypertensive drugs given to them. All the recruited patients completed the study. BP, heart rate, proteinuria, and serum creatine were

measured in all patients.

There were four visits (Visit 0 at the start of the study, Visit 1 at 1 month, visit 2 at 3 months and Visit 3 at 6 months). During each visit, the SBP, DBP, and heart rate were measured. Urine albumin and serum creatinine were measured at day 1 and 6 months.

This was a prospective, open - labeled, randomized study conducted for 6 months. A total of 80 patients of either gender aged between 30 and 60 with HTN and Type 2 DM

Inclusion criteria

HTN patients (<160/110mmhg) with Type 2 DM (HBA1C >6.5 %)
Both males and females aged between 30 and 60 years
Urine for albumin in the range of 30– 300 mg/L
Serum creatinine <3 mg/dl

Exclusion criteria

Hypertensive patients with SBP>_ 180mmhg and /or DBP >_ 110mmhg
Patients on two or more antihypertensives
H/o stroke within 3 months of study
Pregnant and lactating women,
Patients with severe heart failure/severe liver dysfunction/ end - stage renal disease
H/o severe side effects of CCBs or ACE inhibitors.

Statistical Analysis

The statistical analysis was based on standard descriptive statistical tests using the IBM SPSS version 25.0 software.

All parameters such as age, body mass index (BMI), BP, heart rate, were expressed as mean±standard deviation (SD).

The Intragroup comparison of systolic, diastolic blood pressure, serum creatinine, and HBA1c was done using the paired students T - test the p value of <0.05 was considered significant.

3. Results

A total of 80 hypertensive patients with concomitant Type 2 diabetes were included in the study. Their characteristics are summarised in Table 1.

Table 2 shows that there was a significant reduction in the mean SBP (from151.04 ± 5.68 to 124.02 ± 5.86) and also in DBP (from 96.52 ± 7.86 to 81.02 ± 2.84) in the first, second and third visit. The mean heart rate at visit zero was 77.11 ± 5.04. At the end of 6 months of treatment, there was significant reduction to 71.02 ± 3.04. There was a significant reduction in microalbuminuria from 67.24 ± 8.64 to 37.14 ± 8.24. There was no change in creatinine levels.

Table 1: Baseline Characteristics of the Hypertensive Patients with Concomitant Type 2 Diabetes

BASELINE CHARACTERISTICS	
AGE (YEARS)	46 ± 9.34
SEX	47 males ; 33 females
WEIGHT (KG)	62.93 ± 12.08
HEIGHT (CM)	152.87 ± 12.17
BMI (KG/M2)	24.23 ± 2.05
FASTING BLOOD SUGAR (MG/DL)	154.162 ± 9.83
POSTPRANDIAL BLOOD SUGAR (MG/DL)	218.52 ± 19.44
SBP (MMHG)	151.04 ± 5.68
DBP (MMHG)	96.52 ± 7.86
HEART RATE (BEATS/MIN)	77.11 ± 5.04
ALBUMINURIA (MG/L)	67.24 ± 8.64
CREATININE (MG/DL)	0.89 ± 0.12
HBA1C (%)	7.716 ± 1.42

Table 2: Effect of Cilnidipine on BP, Heart Rate, Albuminuria, and Serum Creatinine

PARAMETERS	VISIT 0	VISIT1	VISIT2	VISIT3
SBP(MMHG)	151.04 ± 5.68	139.56 ± 7. 06	129.72 ± 6.24	124.02 ± 5.86
DBP(MMHG)	96.52 ± 7.86	88.24 ± 4.52	84.12 ± 3.44	81.02 ± 2.84
HEART RATE (BPM)	77.11 ± 5.04	76.02 ± 4.05	73.7 ±3.45	71.02 ± 3.04
ALBUMINURIA (MG/DL)	67.24 ± 8.64			37.14 ± 8.24
CREATININE (MG/DL)	0.89 ± 0.12			0.9 ± 0.12

4. Discussion

Cilnidipine was extensively studied by researchers in its preclinical and clinical developmental stages and is still being studied. It was proved to have a reno (reducing microalbuminuria), cardio (decrease reflex tachycardia) and neuroprotective effect apart from its BP lowering effect. Hence, this study was conducted which revealed that microalbuminuria was significantly reduced with cilnidipine in patients with HTN and comorbid Type 2 DM. The study also confirmed that the cilnidipine is safe and no serious adverse effect was reported

There was a significant negative correlation between the degree of SBP change and that of PR change after Cilnidipine treatment. Cilnidipine suppressed sympathetic nervous activity, especially under a stress - induced hyperactive condition.

Blood pressure control is important in suppressing the onset of renal dysfunction. It was reported that antihypertensive therapy suppressed the progression of renal dysfunction. Regarding glomerular kinetics, it has been shown that inhibition of angiotensin II suppresses the elevation of glomerular pressure. Among CCBs, Cilnidipine has been reported to reduce glomerular pressure.

5. Conclusion

From this study, we can conclude that cilnidipine can significantly reduce BP, microalbuminuria, and less reflex tachycardia in hypertensive patients with comorbid Type2DM. Hence, it can be used in renal compromised patient.

References

[1] The National High Blood Pressure Education Program Working Group. National high blood pressure education program working group report on hypertension in diabetes. Hypertension 1994; 23: 145 - 58
[2] Giles TD. Hypertension is taking on Business briefing. US Cardiology 2006: 1 - 4.
[3] Takahara A. Cilnidipine: a new generation Ca2+ channel blocker with inhibitory action on sympathetic neurotransmitter release. Cardiovasc Ther 2009; 27: 124 - 39.
[4] Vupputurti S, Batuman V, Bazzano LA. Effect of blood pressure on early decline in kidney function among hypertensive men. Hypertension 2003; 42: 144 - 9.
[5] Singh VK, Mishra A, Gupta KK, Misra R, Patel ML. Reduction of microalbuminuria in Type - 2 diabetes mellitus with angiotensin - converting enzyme inhibitor alone and with cilnidipine. Indian J Nephrol.2015; 25 (6): 334 - 8
[6] Ando K, Ueshima K, Tanaka S, Kosugi S, Sato T, Matsuoka H, et al. Comparison of the antialbuminuric effects of L - /N - Type and L - Type calcium channel blockers in hypertensive patients with diabetes and microalbuminuria: the study of assessment for kidney function by urinary microalbumin in randomized (SAKURA) trial. Int J Med Sci.2013; 10 (9): 1209 - 16.
[7] Shajahan OM, Rajaram S, Ramya R, Ranga Bhashyam SR. A comparative study on efficacy and safety of amlodipine and cilnidipine in the treatment of mild to moderate essential hypertension. Natl J Basic Med Sci 2020; 10: 112 - 23.
[8] Dietz JD, Du S, Bolten CW, Payne MA, Xia C, Blinn JR, et al. A number of marketed dihydropyridine calcium channel blockers have mineralocorticoid receptor antagonist activity. Hypertension 2008; 51: 742 - 8.