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Original Research Paper

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COMPARISON OF HEMODYNAMIC AND VASCULAR PARAMETERS BETWEEN PATIENTS WITH CKD AND ASSOCIATED HYPERTENSION TREATED WITH AMLODIPINE AND CILNIDIPINE

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ABSTRACT

Background: Hypertension is more prevalent in patients with chronic kidney disease (CKD) and has a strong risk of cardiovascular disease. This study was aimed to assess and compare amlodipine with cilnidipine on hemodynamic parameters of central blood pressure and arterial stiffness in patients with CKD on dialysis and with associated hypertension.

Methods: This was a prospective study conducted between October 2018 and October 2019. Patients of either sex with CKD on dialysis and with associated hypertension and receiving either amlodipine or cilnidipine were included in the study. Mobil-O-Graph® PWA was used assess peripheral BP, vascular age, augmentation index (AI) and pulse wave velocity (PWV).

Results: A total of 87 patients were included (group 1, amlodipine, n=55; group 2, cilnidipine, n=22). The majority of patients were men (n=55). Proportion of patients with normal, average and abnormal vascular age and arterial stiffness was comparable between the treatment groups. However, in amlodipine group, frequency of patients with normal vascular age (42.2% vs 31.8%) was comparatively higher and frequency of patients with average vascular age (32.8% vs 40.9%) was comparatively lower, compared to cilnidipine group.

Conclusion: Both amlodipine and cilnidipine showed equal efficacy on hemodynamic parameters of central blood pressure and arterial stiffness in studied population.

KEYWORDS : Augmentation index, blood pressure, cardiovascular, pulse wave

INTRODUCTION

Hypertension is more prevalent in patients with chronic kidney disease (CKD) and has a strong risk of cardiovascular disease. Elevated blood pressure leads to decline the kidney function in CKD patients. Therefore, treatment of hypertension plays a central role in the management of CKD.

Hypertension accelerates vascular aging which leads to aortic stiffening. Increased arterial stiffness (pulse wave velocity [PWV]) is associated with increased systolic blood pressure (SBP). However antihypertensive drug has achieved better controlling effect on diastolic blood pressure (DBP) than SBP. PWV may remain same or not after the antihypertensive drug therapy, which directly implies SBP response to the treatment [1].

Antihypertensive regimens commonly include angiotensin-converting enzyme (ACE) inhibitor and angiotensin receptor blocker (ARB), calcium channel blocker (CCB), and beta blockers [2]. The mechanism of action of CCB, including amlodipine which inhibits N-type calcium channel and cilnidipine which inhibits both L and N-type calcium channels, in hypertension is due to its inhibition of calcium influx into vascular smooth muscle cells (VMC) that causes relaxation of VMC, decreased after load and systemic blood pressure. Both amlodipine and cilnidipine have significant impact on blood pressure and arterial stiffness [3-5]. However, amlodipine associated with higher incidence of adverse events like pedal edema leads to discontinuing the treatment. Studies have reported the similar antihypertensive action between amlodipine and cilnidipine [6, 7]. However, cilnidipine is superior in terms of improving artificial stiffness and central aortic pressure [8, 9] with greater antiproteinuric effect [10, 11].

There is still a scarcity of clinical trials comparing effects of amlodipine and cilnidipine on arterial stiffness and vascular aging in patients with CKD associated hypertension. Therefore, the present study aimed to assess and compare amlodipine with cilnidipine on hemodynamic parameters of central blood pressure and arterial stiffness in patients with CKD on dialysis and with associated hypertension.

METHODS AND MATERIALS

Study design:

The present prospective study was conducted in the department of Nephrology of Grant Government Medical College and Sir J. J. Group of Hospitals, Mumbai, Maharashtra, India from October 2018 to October 2019. Patients of either sex with CKD on dialysis and with associated hypertension were included in the study. Patient with any known drug allergy, or with any history of systemic illness and presence of pre-existing edema, nephritic syndrome, anaemia was excluded from this study.

Study procedure:

The complete medical history and demographic details (age, sex, body mass index (BMI), BP) were collected for each patient. Central blood pressure (cBP) and AS were measured using the Mobil-O-Graph® PWA (I.E.M. GmbH, Stolberg, Germany). A common cuff was centered on the left upper arm. Cuff size was chosen according to the circumference of the mid-upper arm. Mobil-O-Graph® PWA provides information about peripheral BP, vascular age, augmentation index (AI) and PWV.

Patients who were taking either amlodipine or cilnidipine were categorised into group 1 and group 2, respectively. BP and pulse rate value were analysed and the average value was recorded.

Statistical analysis:

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 23.0. Analysis of categorical variables using Chi-square test and continuous variables using independent sample t-test was done for the assessment of the level of significance. A P value <0.05 was considered statistically significant.

RESULTS

A total of 87 patients were included and majority of patients were men (n=55). The demographics of enrolled patients are summarized in Table 1.

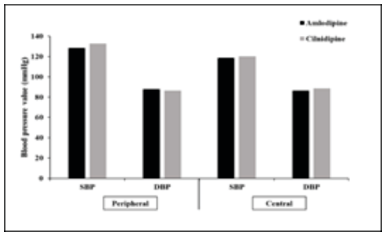
The patients were divided into group 1, patients treated with amlodipine (n=65) and group 2, patients treated with cilnidipine (n=22).

Table 1: Demographic and clinical characteristics of participants

Characteristics	Total (N= 87)
Age (years)	52.83 (12.64)
Sex	
Male, n (%)	55 (63.20)
Female, n (%)	32 (36.80)
BMI (kg/m2)	22.72 (3.33)
Peripheral BP (mmHg)	
Systole	128 (86-201)
Diastole	86 (58-130)
Pulse pressure (mmHg)	40 (19-79)
Heart rate (bpm)	85.49 (17.30)
Arterial BP (mmHg)	105 (76-159)
Augmentation Index (%)	25.83 (11.25)
Pulse wave velocity (m/s)	7.84 (1.65)
Vascular age	
Normal	34 (39.5)
Average	30 (34.9)
Abnormal	22 (25.6)
Central BP (mmHg)	
Systole	119.08 (16.89)
Diastole	88 (59-132)
Arterial stiffness	
Small arteries	26.19 (10.36)
Large arteries	7.84 (1.65)

Data shown as media (SD), unless otherwise specified.
BMI, body mass index; BP, blood pressure

The mean age of patients from group 1 was 53.66 years while the mean age of patients from group 2 was 50.36 years with male predominance in both the groups (60% vs 72.7%). Antihypertensive efficacy of amlodipine and cilnidipine drug therapy was found to be comparable (Figure 1).



SBP, systolic blood pressure; DBP, diastolic blood pressure.
Figure 1. Antihypertensive efficacy of amlodipine and cilnidipine treatment

Proportion of patients with normal, average and abnormal vascular age was comparable between the treatment groups (P=0.675). However, in amlodipine group, frequency of patients with normal vascular age (42.2% vs 31.8%) was comparatively higher and frequency of patients with average vascular age (32.8% vs 40.9%) was comparatively lower, compared to cilnidipine group. Frequency of patients from both the treatment groups was similar when categorized according to small and large arterial stiffness (P = 0.945 and 0.850, respectively). Majority of patients had normal small arterial stiffness in both the groups while average and abnormal levels of large arterial stiffness were commonly observed in both the groups. Mean peripheral BP was comparable between both the groups. The average pulse pressure was slightly higher in patients from cilnidipine group than those from amlodipine group without any significant difference (P=0.093). Augmentation index was comparatively higher in patients taking cilnidipine (P=0.411) compared to those taking amlodipine (P=0.411). Pulse wave velocity was similar between both the group (P=0.565) (Table 2).

DISCUSSION

This study assessed and compared vital hemodynamic parameters of central blood pressure and arterial stiffness measured by oscillometric methods in patients with CKD on dialysis and with associated hypertension treated with two types of calcium channel blockers; amlodipine, a L-type Ca channel blocker and cilnidipine, N/L-type Ca channel blocker. Overall observations demonstrated no significant difference in any of the pulse wave analysis parameters between the two treatment groups indicating similar effect of L-type and N/L-type calcium channel blockers on these patients.

To our knowledge, there is no similar study conducted to compare these observations with amlodipine and cilnidipine. However, several past studies have compared amlodipine with cilnidipine on antihypertensive efficacy and incidence of pedal edema in hypertensive individuals.

Two studies from Southern part of India demonstrated equal efficacy of cilnidipine and amlodipine in reducing blood pressure in hypertensive individuals [6, 7]. However, cilnidipine being N-type and L-type calcium channel blocker, associated with lower incidence of pedal edema compared to only L-type channel blocked by amlodipine.

Table 2: Comparison of parameters between the treatment groups

Parameters	Group 1 (n=65)	Group 2 (n=22)	P value
Age	53.66 (12.24)	50.36 (13.77)	0.293
Sex, n (%)			
Male	39 (60)	16 (72.7)	0.319
Female	26 (40)	6 (27.3)	
BMI	22.44 (3.33)	23.55 (3.28)	0.177
Vascular age, n (%)			
Normal	27 (42.2)	7 (31.8)	0.675
Average	21 (32.8)	9 (40.9)	
Abnormal	16 (25)	6 (27.3)	
Small arterial stiffness, n (%)			
Normal	37 (56.9)	13 (59.1)	0.945
Average	23 (35.4)	7 (31.8)	
Abnormal	5 (7.7)	2 (9.1)	
Large arterial stiffness, n (%)			
Normal	18 (27.7)	7 (31.8)	
Average	25 (38.5)	7 (31.8)	0.850
Abnormal	22 (33.8)	8 (36.4)	
Peripheral BP			
Systole	128.35 (20.81)	132.77 (15.50)	0.364
Diastole	87.92 (14.15)	86.31 (10.20)	0.626
Pulse pressure	41.41 (12.49)	46.45 (10.39)	0.093
Heart rate	89.94 (17.11)	90.09 (17.42)	0.150
Arterial BP	106.32 (15.70)	107.63 (11.95)	0.721
Augmentation Index	25.24 (11.63)	27.54 (10.12)	0.411
Pulse wave velocity	7.88 (1.64)	7.70 (1.69)	0.656
Central BP			
Systole	118.68 (18.29)	120.27 (12.15)	0.704
Diastole	86.48 (25.50)	88.54 (10.52)	0.713

Data shown as mean (SD), unless otherwise specified.
BMI, body mass index; BP, blood pressure

There are few studies which reported cilnidipine is more effective than amlodipine at improving renal function and arterial stiffness [8] and albuminuria and uric acid metabolism [12] in patients with essential hypertension and in hypertensive patients with CKD, respectively.

Malleshappa P. revealed that urinary albumin excretion was significantly reduced by administration of the cilnidipine in hypertensive CKD patients [13]. He also suggested that early treatment of cilnidipine in hypertensive CKD patients with low-grade albuminuria may prevent cardiovascular disease.

A prospective randomized trial demonstrated by Zaman et al. compared the effects of amlodipine and cilnidipine on blood pressure, heart rate, proteinuria, and lipid profile in hypertensive patients [10]. Both the drugs showed significantly reduced SBP and DBP. Unlike amlodipine, pulse rate and urinary protein excretion were decreased in cilnidipine group. Also, in cilnidipine group patients with diabetes showed reduce serum triglyceride.

A multi-centre study at Japan demonstrated that cilnidipine had greater antiproteinuric effects than amlodipine when used in combination with a renin-angiotensin system (RAS) inhibitor to treat hypertensive patients [14]. Therefore, cilnidipine showed higher antioxidant activity than amlodipine when used in combination therapy. Similar study done by Fujita et al. showed superior effect of cilnidipine in preventing progression of proteinuria more potently than that with amlodipine in hypertensive CKD patients concomitantly with RAS therapy [11]. A randomized trial conducted in hypertensive patients with CKD reported reduction of ambulatory blood pressure and heart rate in the cilnidipine group compared with the control CCBs group. Furthermore, the results showed that cilnidipine is superior to the control CCBs in improving left ventricular hypertrophy [15].

One open labeled study evaluated the effects of amlodipine and cilnidipine on PWV and augmentation pressures in hypertensive patients [9]. Cilnidipine showed significantly higher improvement in aortic blood pressure and aortic augmentation pressure as well as markers of arterial stiffness including PWV and augmentation index compared with amlodipine. However, this study showed that the cilnidipine has a similar antihypertensive action to the amlodipine, but is superior in terms of improving arterial stiffness and central aortic pressures. The present study assessed hemodynamic parameters of central blood pressure and arterial stiffness in CKD patients associated with hypertension using cilnidipine and amlodipine. However, there was no significant difference in the markers of arterial stiffness and central blood pressure between both the groups. Both cilnidipine and amlodipine have shown similar effect in reducing blood pressure in patients with CKD and associated with hypertension.

The present study has several limitations. Firstly, small sample size which may limit the determination of significant effectiveness of drugs. Secondly, this study could not evaluate the levels of hemodynamic and vascular parameters before and after the antihypertensive drug treatment in the patients with CKD and associated with hypertension which could have added a value to the study. Studies with large sample size are required to confirm above results.

CONCLUSION

Both amlodipine and cilnidipine have shown equal efficacy in terms of hemodynamic parameters of central blood pressure and arterial stiffness in patients with CKD on dialysis and with associated hypertension.

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