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Expert Perspectives on the use of Cilnidipine in Hypertensive Patients with Diabetic Kidney Disease in Indian Settings

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Abstract

Objective: To assess clinicians' preferences and perceptions regarding the use of cilnidipine, both as monotherapy and in combination with telmisartan, for managing hypertension in patients with diabetic kidney disease (DKD) in Indian settings.

Methodology: The cross-sectional study was conducted using a structured 23-item, multiple-response questionnaire designed to capture the perspectives of clinicians involved in the management of hypertension in patients with DKD. The questionnaire focused on current prescribing practices, clinical observations, treatment preferences, and experiences related tocilnidipine both as mono and combination therapy. Data were analyzed using descriptive statistics, and categorical variables were summarized as percentages to highlight prevailing trends and patterns in clinical practice.

Results: The study was conducted among 601 clinicians and revealed that approximately 96% preferred cilnidipine as the calcium channel blocker of choice for patients with hypertension and DKD. Approximately half (50.08%) reported using cilnidipine as a first-line therapy in 21% to 30% of such patients, while 47% used it in 11% to 20% of cases. Most respondents (67.39%) agreed with the RSSDI guideline recommending cilnidipine in combination with angiotensin receptor blockers (ARBs) for enhanced cardiovascular and renal protection. Specifically, 83% favored telmisartan as the ARB of choice in this combination, and 55% reported that 11% to 20% of their patients were on a single-pill cilnidipine-telmisartan regimen. About 66% noted benefits of cilnidipine beyond blood pressure control, including reduced pedal edema, renal protection, and fewer cardiovascular events. Additionally, 47% observed a reduction in microalbuminuria in 26% to 50% of their patients. Around 39% commonly prescribed the cilnidipine-telmisartan single-pill combination for patients with uncontrolled hypertension and diabetes.

Conclusion: Cilnidipine, alone or combined with telmisartan, is widely preferred by Indian clinicians for managing hypertension in patients with DKD, due to its additional benefits beyond BP control, including reno-protection and CV risk reduction.

Introduction

With the increasing worldwide prevalence of type 2 diabetes mellitus (T2DM), diabetic kidney disease (DKD) has emerged as a significant contributor to the global disease burden.[1] DKD ,or diabetic nephropathy, is the most common cause of chronic kidney disease(CKD) in those with diabetes and is the leading attributable cause for incident end-stage renal disease (ESRD).[2] The burden of hypertension is even greater in those with comorbid CKD, with prevalence risingparallel with disease severity. A nationally representative U.S. survey estimated hypertension in 23.3% of individuals without CKD, compared to 35.8% in stage 1, 48.1% in stage 2, 59.9% in stage 3, and 84.1% in stages 4-5.[3] Globally, hypertension affects approximately 70% to 90% of patients with diabetic nephropathy, with prevalence increasing parallelly with CKD severity. [3] The Indian Chronic Kidney Disease (ICKD) study found that 87% of CKD patients in the country are hypertensive, and 37% have diabetes.[4]

Effective blood pressure (BP) management in this subset of patients presents a therapeutic challenge, requiring agents that not only ensure optimal BP control but also provide cardio-renal protection. Among the available antihypertensive therapies, calcium channel blockers(CCBs) have garnered considerable attention due to their efficacy and safety profile. [5] Cilnidipine, a fourth-generation dihydropyridine CCB with dual L/N-type CCB activity, has gained attention for its potential reno-protective and cardio-protective benefits beyond BP reduction.[6] This unique pharmacologic profile is proposed to offer advantages beyond BP control, including a reduction in sympathetic overactivity, a lesser incidence of pedal edema, improved renal outcomes, and favorable metabolic effects such as improved insulin sensitivity.[7,8]

As per the Joint National Committee (JNC) 8 recommendations, CCB is recommended as initial therapy in patients with hypertension, including those with diabetes.[9] Cilnidipine is used in the management of hypertension and comorbid conditions either as a monotherapy or as a combination therapy with angiotensin receptor blockers (ARBs). [10, 11] This is achieved through a reduction in urinary albumin excretion and an increase in the ratio of Ang (1–7) to Ang II in plasma.[12] The Research Society for the Study of Diabetes in India (RSSDI) has recommended the use of cilnidipine in combination with ARBs such as telmisartan for enhanced cardiovascular and renal protection. [13] This study is intended to gather expert opinion on the use of cilnidipine and its combination with telmisartan for managing hypertension with DKD in Indian settings.

Methodology

We carried out a cross-sectional study among experts managing hypertensive patients with DKD in Indian clinical settings from June 2024 to December 2024. Clinicians from diverse specialties, including

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general physicians, diabetologists, and cardiologists, were invited to participate. The study was conducted after receiving approval from Bangalore Ethics, an Independent Ethics Committee, which was recognized by the Indian Regulatory Authority, the Drug Controller General of India (ECR/355/Indt/KA/2022).

An invitation was sent to leading clinicians in managing hypertensive patients with DKD in the month of March 2024 for participation in this Indian survey. About 601 clinicians from major cities of all Indian states, representing the geographical distribution, shared their willingness to participate and provide necessary data. The questionnaire booklet titled NEPCAR (Nephro Cardio protective calcium channel blocker) was sent to clinicians who were interested in participating in this study. The NEPCAR study questionnaire comprised 23 questions focusing on current practices, clinical observations, and specialist experiences in managing hypertension in patients with DKD, with particular emphasis on the routine use of cilnidipine, both as monotherapy and in combination with telmisartan. Clinicians had the option to skip any questions they preferred not to answer. They were instructed to complete the questionnaire independently, without consulting their colleagues. Written informed consent was obtained from all participants before the study commenced.

Statistical analysis

The data collected were analyzed using descriptive statistics. Categorical variables were presented as percentages to provide a clear insight into their distribution. The frequency of occurrence and the corresponding percentage were used to represent the distribution of each variable. To visualize the distribution of the categorical variables, graphs and pie charts were created using Microsoft Excel 2013 (version 16.0.13901.20400).

Results

The study included 601 experts, and approximately 40% of them reported that 21% to 30% of patients with hypertension presenting to the routine settings have both comorbid diabetes and CKD. Around 45% of clinicians stated that 26% to 50% of patients with DKD and hypertension experience BP variability, while 44% reported that 11% to 25% of such patients suffer from BP variability. A significant majority (95.51%) of respondents identified cilnidipine as the most preferred CCB for managing hypertension in patients with DKD (Figure 1).

Half of the experts (50.08%) reported using cilnidipine as a first-line therapy in 21% to 30% of patients with hypertension and DKD, while 47% stated they prescribe it in 11% to 20% of such patients (Table 1). About 31% of clinicians observed that cilnidipine improves renal parameters, including urinary protein-to-creatinine ratio (UPCR), urinary protein excretion (UPE), and estimated glomerular filtration rate (eGFR)in some patients.

About 49% of the clinicians stated that they were unsure whether cilnidipine improves creatinine levels compared to amlodipine in patients. More than half (58.07%) of the participants reported that approximately 11% to 20% of patients with hypertension have elevated creatinine levels. According to 45% of the experts, hypertensive patients aged 46 to 60 years commonly exhibit high creatinine levels.

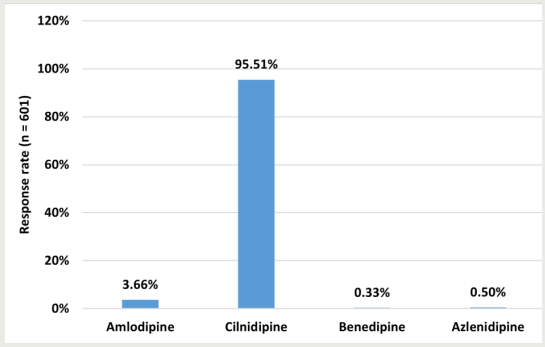

Figure 1: Distribution of responses on the most preferred CCB in patients with hypertension and DKD

Table 1: Distribution of responses on the use of cilnidipine as first-line therapy in patients with hypertension and DKD

Proportions	Response rate (n = 601)
10%	2.83%
11-20%	47.09%
21-30%	50.08%

A majority of clinicians (67.39%) agreed that, according to the RSSDI guidelines for managing hypertension in patients with diabetes mellitus, cilnidipine is recommended in combination with angiotensin receptor blockers (ARBs) to enhance cardiovascular and renal protection in diabetic hypertensive patients (Figure 2). As reported by 43% of the respondents, about 10% to 20% of patients with hypertension achieve control with monotherapy.

The majority of clinicians (82.7%) reported preferring the combination of cilnidipine with telmisartan as the specific ARB for use in diabetic hypertensive patients (Figure 3). More than half (54.91%) of the experts stated that 11% to 20% of their patients are currently on the single-pill combination of cilnidipine and telmisartan (Table 2). Nearly half of the clinicians (47.75%) reported that 21% to 30% of their patients, who are currently receiving a combination of a renin–angiotensin–aldosterone system (RAAS) blocker and a diuretic, could be shifted to a cilnidipine and telmisartan combination.

About 66% of the participants reported a lower incidence of pedal edema, renal protection, and a reduction in cardiovascular (CV) events as clinical outcomes observed in patients receiving cilnidipine, beyond its BP-lowering effects (Figure 4). Approximately 48% of the participants stated that 11% to 30% of hypertensive patients tested positive for proteinuria.

Around 47% of clinicians reported that cilnidipine reduced microalbuminuria in 26% to 50% of their patients (Table 3). Approximately 66% of participants identified reduced pedal edema as a key advantage of cilnidipine. As reported by 64% of experts, the combination of telmisartan with cilnidipine is preferred for BP control and cardiorenal protection in middle-aged patients.

Around 39% of participants reported that they commonly prescribe a single-pill combination of telmisartan with cilnidipine for patients with uncontrolled hypertension and diabetes (Table 4). Almost half of the clinicians (49.75%) were unsure about considering cilnidipine as their preferred antihypertensive agent in the

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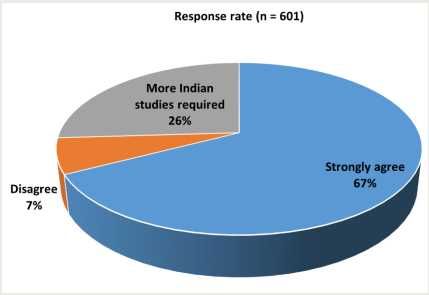

Figure 2: Distribution of responses on the clinicians' opinions on the RSSDI guideline recommendation of cilnidipine with ARBs for managing hypertension in diabetic patients

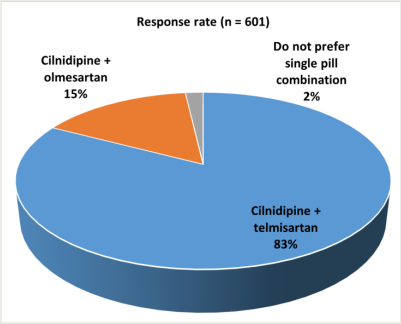

Figure 3: Distribution of responses on the preferred ARB combined with cilnidipine in diabetic hypertensive patients

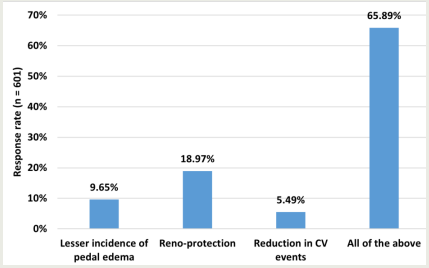

Figure 4: Distribution of responses on the clinical outcomes observed with cilnidipine beyond BP control

Table 2: Distribution of responses on the proportion of patients on the single-pill combination of cilnidipine and telmisartan

Proportions	Response rate (n = 601)
10%	7.15%
11-20%	54.91%
21-30%	37.94%

Table 3: Distribution of responses on the clinicians' experience with cilnidipine in reducing microalbuminuria among patients with DKD

Proportions	Response rate (n = 601)
10%	6.99%
11-25%	33.94%
26-50%	46.59%
51-75%	10.98%
>75%	1.5%

Table 4: Distribution of responses on the subset of patients who most commonly use telmisartan with cilnidipine single pill combination

Subset of patients	Response rate (n = 601)
Uncontrolled hypertension with CV risk factors	22.8%
Uncontrolled hypertension with diabetes	38.94%
Uncontrolled hypertension with CKD	16.97%
All the above	21.3%

management of hypertension. According to approximately 45% of clinicians, low awareness about hypertension may be a contributing factor to CV disease-related deaths in patients aged 40 to 59 years.

Approximately 44% of clinicians opined that cilnidipine also improves insulin resistance in obese hypertensive patients, while 42% indicated that improvement in insulin resistance is observed only in a few cases. Around 47% of clinicians reported conducting monthly follow-ups for patients with uncontrolled hypertension and DKD.

Discussion

In the present study, the majority (95.51%) of the clinicians preferred cilnidipine as the CCB of choice for managing hypertension in patients with DKD, reflecting growing clinical confidence in its reno-protective properties. In line with this, Mehta et al. stated that cilnidipine is the most common CCB used antihypertensive agent due to its effectiveness in reducing BP, along with its good tolerability and evidence of reducing hypertension, related cardiovascular and renal diseases.[12] Srivathsan et al. concluded that cilnidipine is more effective in reducing proteinuria or preventing its progression, while demonstrating comparable effects on serum creatinine and estimated glomerular filtration rate (eGFR) in hypertensivepatients.[14] Similarly, Chakraborty et al. recommended cilnidipine as a novel first-line CCB for managing hypertension, either as monotherapy or in combination.[10]

The present study also revealed that clinicians frequently prescribed cilnidipine as a first-line treatment in patients with hypertension and DKD, indicating its growing acceptance in routine clinical practice. Supporting this, the J-CIRCLE study evaluated 70 hypertensive patients with chronic kidney disease who continued to have albuminuria despite amlodipine therapy. After switching to cilnidipine for three months, patients showed a significant reduction in the urinary albumin-to-creatinine ratio, despite no significant change in blood pressure. Notably, cilnidipine also reduced uric acid levels in patients with elevated baseline values, highlighting additional metabolic benefits beyond its antihypertensive effects.[15]

The current study findings align with the recommendations of the RSSDI, which suggests that cilnidipine, as a novel CCB, should be used in combination with ARBs for enhanced cardiovascular and renal protection in diabetic hypertensive patients.[13] Supporting this, a randomized controlled trial by Katayama et al. (2006) involving 87 patients with type 2 diabetes and albuminuria found that the combination of cilnidipine and valsartan led to a significantly greater reduction in the urinary albumin-to-creatinine ratio compared to valsartan alone (−44% vs. −9%, P = 0.014).[16] The HOPE-Combi survey carried out by Kario et al. (2020) demonstrated that a single-pill combination of cilnidipine and valsartan effectively reduced morning home systolic BP and pulse pressure in patients with uncontrolled hypertension and sympathetic hyperactivity.[17]

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The majority of the current study clinicians indicated a preference for combining cilnidipine with telmisartan as the ARB of choice in managing diabetic hypertensive patients. Additionally, more than half of the experts reported that 11% to 20% of their patients were receiving the single-pill combination of cilnidipine and telmisartan. Similarly, in a knowledge, attitude, and practice survey conducted by Shete et al., the cilnidipine and telmisartan combination was reported to benefit patients with uncontrolled hypertension (46%), diabetes (43%), and chronic kidney disease (41%), making it a preferred therapeutic option.[18] Jo et al. also suggested that the combination of cilnidipine and telmisartan serves as an effective therapeutic strategy for managing hypertension and its associated complications.[19] Furthermore, a prospective randomized study conducted at three tertiary hospitals in India concluded that this combination significantly reduced blood pressure and improved central hemodynamic parameters, such as the aortic augmentation index, in patients with untreated or uncontrolled hypertension [20].

Majority of the survey respondents cited reduced incidence of pedal edema, reno-protection and reduction in CV events askey clinical outcomes observed in patients receiving cilnidipine, beyond its BP lowering effects. The study also indicated that cilnidipine is effective in reducing microalbuminuria. Kumari et al. similarly reported that cilnidipine demonstrates superior renoprotective effects, as evidenced by a significant reduction in proteinuria among hypertensive patients.[21] Ramya et al. noted satisfactory BP control with negligible side effects and a lower incidence of pedal edema in patients treated with cilnidipine.[22] Chandra and Ramesh found that cilnidipine exhibits renoprotective, cardioprotective, and neuroprotective effects.[6] Pavan Malleshappa also reported that cilnidipine is safe and effective in reducing low-grade albuminuria in hypertensive CKD patients.[23] Additionally, Singh et al. concluded that cilnidipine has an additive effect in reducing microalbuminuria. [24]

The current study reported that clinicians commonly prescribe the single-pill combination of telmisartan and cilnidipine for patients with uncontrolled hypertension and diabetes. Sawant et al. concluded that once daily cilnidipine and telmisartan is effective and well tolerated in the treatment of newly diagnosed stage I hypertension [25]. A cross-sectional survey involving 533 clinicians in India revealed that 76% recommended the cilnidipine and telmisartan combination for diabetic hypertensive patients, citing its efficacy in blood pressure reduction, cardioprotective effects, and the added benefit of attenuating high blood glucose levels.[8]

The study provides valuable insights into clinicians' preferences regarding the use of cilnidipine for managing hypertension in patients with DKD in the Indian context. Despite its strengths, such as a large and diverse sample of clinicians and the use of a structured questionnaire, several limitations should be acknowledged. The study captures expert opinion rather than objective clinical outcomes, which introduces potential bias due to individual differences in clinical judgment, experience, and prescribing patterns. In addition, the cross-sectional design limits the ability to assess trends over time, treatment effectiveness, or patient outcomes. Since the findings are based on clinicians' perceptions, they do not reflect actual patient data, such as changes in kidney function or cardiovascular events, which may reduce the broader applicability of the results. Furthermore, the study may not fully capture evolving treatment practices or the influence of the latest clinical evidence. Future studies should include prospective or observational research involving direct patient data to validate these observations and support more informed treatment strategies for this population.

Conclusion

The study highlights that cilnidipine is widely preferred by Indian clinicians for the management of hypertension in patients with DKD, both as monotherapy and in combination with telmisartan. The preference is supported by its perceived benefits beyond BP control, including reduced incidence of pedal edema, reno-protective effects, and CV risk reduction. The strong alignment with RSSDI guideline recommendations and the frequent use of single-pill combinations underscore the growing clinical confidence in cilnidipine, particularly when paired with telmisartan, as a practical and effective therapeutic option in this high-risk population.

Acknowledgement

We would like to thank all the clinicians who were actively participating in this study.

Disclosure of compliance with ethical principles

The study was conducted after receiving approval from Bangalore Ethics, an Independent Ethics Committee, which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

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