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Exploring the Efficacy of Telmisartan and Cilnidipine Combination Therapy in Hypertension: A Cross-sectional Analysis

ABSTRACT

Introduction: Hypertension is a common non-communicable disease and is of major public health concern accounting for 19% of all deaths globally. The lack of awareness about hypertension is a major contributory factor for the delayed diagnosis of asymptomatic cases, thus being labeled as a "silent killer disease." Effective control of blood pressure is a must and for achieving it, a long-acting antihypertensive agent is required. Telmisartan is one of the angiotensin II receptor blockers whereas cilnidipine is a novel calcium antagonist. Cilnidipine has shown prolonged and desirable antihypertensive effects. The present questionnaire-based study conducted on various clinicians across different parts of the country analyses the pattern of patients with hypertension and other comorbidities in their clinical practice along with the trend in the prescription of antihypertensives either mono and/or combination therapy. **Materials and Methods:** The present study is a questionnaire-based cross-sectional study consisting of 25 validated structured questions. The study was approved by the Institutional Ethical Committee. All the completed forms were included in the study whereas incomplete form was excluded from the study. **Observation and Results:** The survey reflects that 87% of the patients have diabetes mellitus as one of the most common comorbid conditions associated with hypertension. About 86.5% of the clinicians (86.5%) are of the opinion that more than 30% of the patients required combination therapy of telmisartan and cilnidipine with the addition of diuretics in uncontrolled hypertension. The combination also offers many other benefits such as its anti-atherosclerotic properties and end-organ protection. **Conclusion:** The study highlights that combination therapy is very effective in treating hypertension even if associated with other comorbid conditions such as diabetes and chronic kidney disease.

Key words: Cilnidipine, Combination therapy, Diuretics, Hypertension, Telmisartan

INTRODUCTION

Hypertension is a common non-communicable disease and is of major public health concern accounting for 19% of all deaths globally.[1] Hypertension is defined as blood pressure (BP) of at least 130 mmHg systolic and 80 mmHg diastolic, with the corresponding 24-h ambulatory BP readings being 125 mmHg systolic and 75 mmHg diastolic.[2] An estimated 1.28 billion adults in the age range of 30–79 years worldwide are having high BP and out of them, two-thirds are residing in lower-to-middle-income countries. Nearly 46% of them are unaware of their hypertension condition. Only, around 42% of the cases are diagnosed and treated with only about 21% of the cases having control over their hypertension.[3]

The lack of awareness about hypertension is a major contributory factor for the delayed diagnosis of asymptomatic cases, thus being labeled as a "silent killer disease" as it is an independent risk factor for the initiation and causation of coronary artery disease, cerebrovascular accidents, myocardial infarction, and chronic kidney diseases. If remains undiagnosed or uncontrolled, it is a major cause of mortality or permanent disability. If hypertension is diagnosed on time, then, it can be controlled the mentioned sequelae can be prevented and its incidence can be reduced. Hence, periodic health surveillance including the record of the BP is a must for early diagnosis and treatment and special stress needs to be given to the group of patients with positive family history of hypertension, diabetes mellitus, etc.[4]

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In every patient with hypertension, effective control of BP is a must and for achieving the same, a long-acting antihypertensive agent is essential to be in the prescription. Telmisartan is one of the angiotensin receptor blockers (ARBs) with a terminal elimination half-life of 24 h and has a large volume of distribution due to its high lipophilicity and this property enhances its tissue penetration, intracellular absorption, and bioavailability. Telmisartan acts by blocking the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1 receptor in many tissues, such as vascular smooth muscle and the adrenal gland.[5]

Cilnidipine is a novel calcium antagonist with a dual mode of action on the calcium channels. It blocks both the L-type and N-type calcium channels and this simultaneous blockade of both results in a significant reduction of BP without causing reflex tachycardia. The dual mode of action of cilnidipine permits vasodilation and sympathetic blockade. Due to its lipophilic and avidly binding properties, cilnidipine has shown prolonged and desirable antihypertensive effects.[6,7]

The present questionnaire-based study has been done on various clinicians who are dedicated to the treatment of hypertension and other comorbid conditions associated with it. The study analyses the pattern of patients with hypertension and other comorbidities in their clinical practice along with the trend in the prescription of antihypertensives either mono and/or combination therapy. The study also tried to focus on the patient's response and compliance to the treatment whether the desired outcome of controlling hypertension and prevention of complications has been achieved and also the challenges observed when the same has not been achieved.

MATERIALS AND METHODS

The present study is a questionnaire-based cross-sectional study. The validated questionnaire consisted of 25 structured questions with response printed on it. The study was approved by the Bangalore Ethics Committee (Registration number ECR/355/Indt/KA/2022). After the approval from the Ethics Committee, the questionnaire was distributed among clinicians who are into the practice of hypertension and its associated comorbid conditions, and the survey was conducted over a span of 6 months covering the whole of India. All the completed forms were included in the study whereas incomplete form was excluded from the study. After applying the selection criteria as mentioned above, a total of 635 completed and properly filled questionnaires were received and the data were entered in the Microsoft Excel sheet and the data were statistically analyzed.

OBSERVATION AND RESULTS

The interpretation of the survey is that 87% of the patients have diabetes mellitus as one of the most common comorbid conditions associated with hypertension, it was followed by dyslipidemia as a second most comorbid condition among 16% of patients, chronic kidney disease was seen in 8% of patients, around 2% had associated hypothyroidism, and 24% of patients had various combination of the comorbidities associated with hypertension.

The survey found that 45% of clinicians are having up to 25% of their hypertensive patients also having diabetes mellitus as a comorbid condition, whereas 22.5% of the clinicians have more than 25% of their patients having both hypertension and diabetes mellitus [Figure 1].

Most of the clinicians (86.5%) are of the opinion that more than 30% of the patients required combination therapy of telmisartan and cilnidipine [Figure 2].

When the clinicians were asked about their habit of assessing cardiovascular risk by the SCORE system, 72% of them were of the opinion that they do so in some cases, only whereas 24% of clinicians had the habit of always scoring the cardiovascular risk assessment before initiation the treatment. Very few (3.6%) clinicians did not have the habit of assessing the same.

A total of 258 (42%) clinicians prefer combination therapy of angiotensin receptor blocker and calcium channel blocker (CCB) in 25% of their hypertensive patients, a diuretic was also added in uncontrolled hypertension in addition to the above combination therapy [Figure 3].

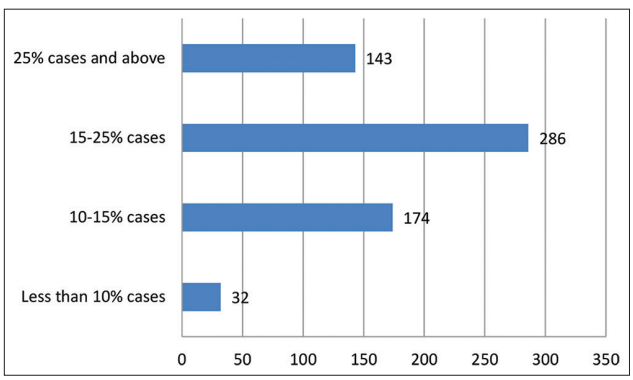

Figure 1: Percentage of hypertension patients having diabetes mellitus as comorbidity

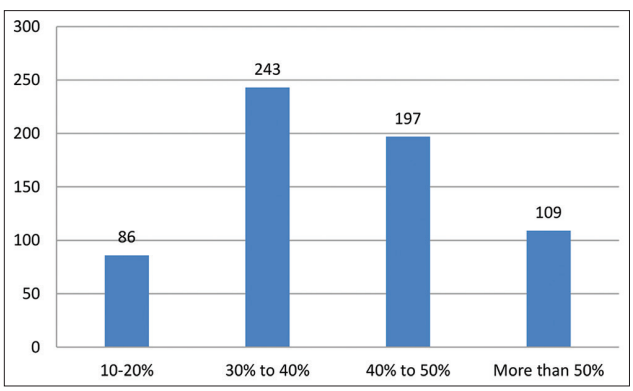

Figure 2: Percentage of patients requiring combination therapy for the initial management of hypertension

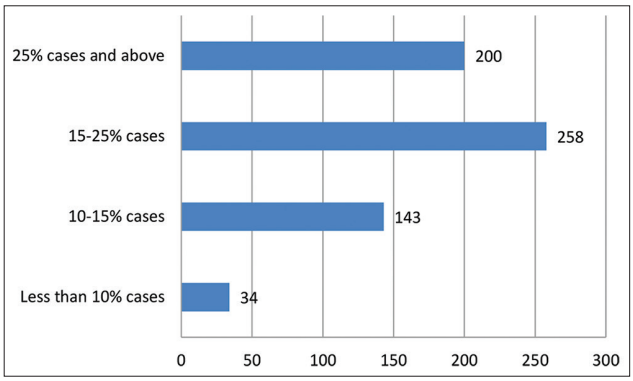

Figure 3: Percentage of patients with hypertension on combination of ARBs and calcium channel blocker

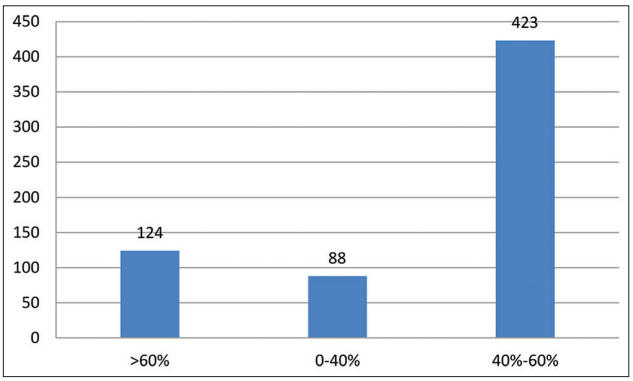

Figure 5: Percentage of patients achieving target blood pressure at 3 months of therapy

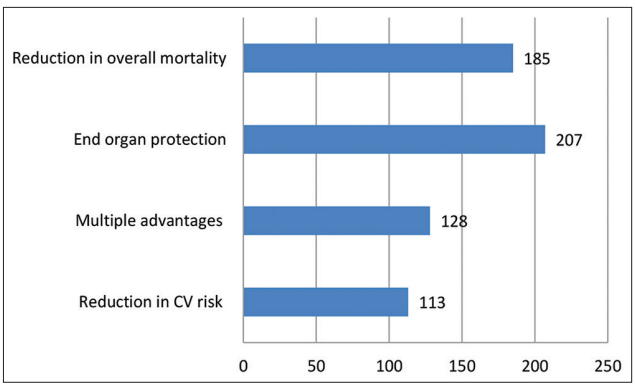

Figure 4: Clinical outcomes observed with cilnidipine and telmisartan combination

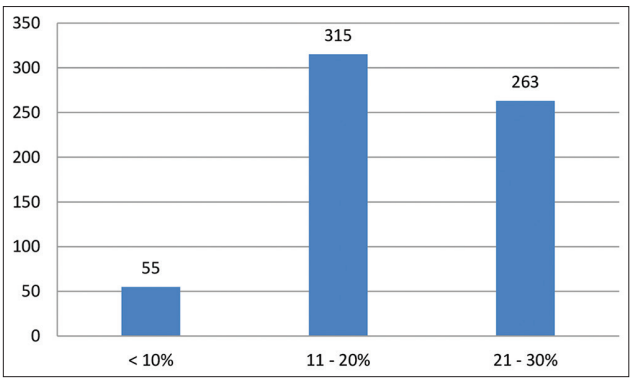

Figure 6: Percentage of patients above 45 years with uncontrolled hypertension

Most of the clinicians (75%) prescribe a combination of angiotensin receptor blockers and diuretics in 10–25% of their hypertensive cases.

Telmisartan 40 mg with cilnidipine 10 mg combination was most commonly used by clinicians in around 95% of their hypertensive patients in comparison to telmisartan 80 mg with cilnidipine 10 mg combination [Figure 4].

Fifty percent of the clinicians are of the opinion that they require combination therapy of telmisartan and cilnidipine in more than 40% of their patients to control the BP, whereas 40% of the clinicians are required the same combination in around 30% of their patients.

The clinicians are very optimistic about the multiple benefits of cilnidipine and telmisartan. The end-organ protection was the most beneficial aspect and is believed by more than 32% of the clinicians in the present survey. Reduction in cardiovascular accidents was another benefit seen by more than 15% of the clinicians and many also believed multiple combinations of the above benefits, thus resulting in a reduction in the overall mortality as a consequence of hypertension.

There was remarkable control of BP at 3 months of 140/90 mm of mercury with the combination therapy and 66.6% of the clinicians achieved the same in 40–60% of their patients, 19.5% of the clinicians have achieved the target BP control in over 60% of their patients [Figure 5].

As per the survey, 49.6% of clinicians are of the opinion that 11–20% of the hypertensive population are above 45 years old and are having uncontrolled BP, whereas 41% experienced the same to be between 21% and 30% [Figure 6]. The preferred drug of choice for managing such cases of uncontrolled hypertension was angiotensin receptor blockers and in cases where target BP was still not achieved then a diuretic is also added to it. Apart from that, regular exercise, a healthy diet plan along with the incorporation of a Yoga routine schedule were also told and counseled as a part of the lifestyle modification plan. This was also suggested by a study done by Ahmadi *et al.*,[8] the study has also suggested that educational programs should be developed to increase the patient's acceptance of lifestyle modification and physical activity.

In the elderly hypertensive population, clinidipine with telmisartan combination therapy was the most preferred combination of the drug for BP control among 263(41.4%) clinicians, it was followed by the addition of diuretics and other CCBs based on the individual preference of clinicians in accordance with the clinical presentation and comorbidity of the patient [Figure 7]. The clinicians are also of the opinion that

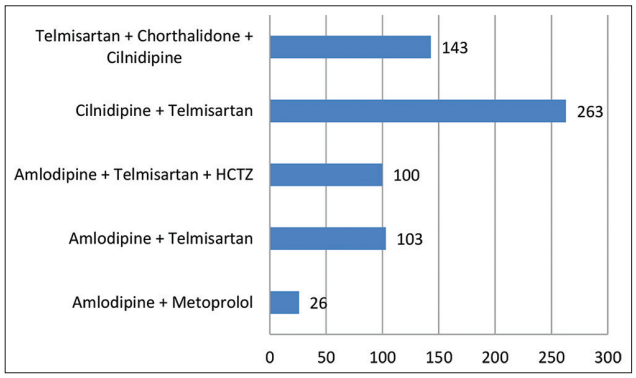

Figure 7: Choice of combination of anti-hypertensives in the elderly population

amlodipine with telmisartan is also a very effective treatment combination for the treatment of uncontrolled hypertension, the combination also provides an added advantage of improved insulin sensitivity and improved quality of life. It was and still is the drug of choice for the treatment of uncontrolled hypertension.

DISCUSSION

The treatment of hypertension though seems to be simple but in the present era where patients present with multiple comorbid conditions, the choice of anti-hypertensive is a very challenging task and also requires a regular follow-up which may range from weekly assessment initially to monthly follow-up. However, physicians are of the opinion that an ideal antihypertensive drug should be efficacious with less of side effects, also the drug should be able to prevent long-term complications of hypertension and be beneficial in view of associated comorbid conditions.

The main point highlighted here is that diabetes mellitus is one of the most common comorbid diseases associated with hypertension and together it is causing a serious health issue and increased health burden on the family and country. Kapil *et al*.[9] have also found a higher association of comorbidity with hypertension in the elderly population of Uttarakhand.

Sawant *et al*.[10] found in their study that telmisartan and cilnidipine once daily were effective and well tolerated in the treatment of newly diagnosed Stage-I hypertension.

Sofogianni *et al*.[11] in their review found that country-specific risk scores, wherever available, should be preferred for cardiovascular risk stratification, they also concluded that these risk scores should be regularly updated with the contemporary epidemiological data.

Kato *et al*.[12] found in their study that switching to combination antihypertensive drugs resulted in an improvement in adherence and a reduction in medication-related expenses, and revealed that patient satisfaction was high.

Most of the clinicians (75%) prescribe a combination of angiotensin receptor blockers and diuretics in 10–25% of their hypertensive cases and the reason could be these patients present with moderate-to-severe hypertension.

Telmisartan 40 mg in combination with cilnidipine 10 mg gives better BP control in moderate hypertension as compared to 80 mg of telmisartan in combination with cilnidipine 10 mg as few patients present with moderate severe cases of high BP and severe cases usually require admission.

The possible reason could be attributed to different severity of the hypertension and also associated comorbidities with hypertension.

A study done by Mori *et al*.[13] has found a reduction in the progression of cardiorenal disease in type 2 diabetes patients who are on the combination therapy of ARB and CCBs. Kaneshiro *et al*.[14] in their study found that telmisartan and cilnidipine have unique properties for inhibiting vascular complications by different mechanisms.

Essential hypertension is the more common cause of hypertension in clinical practice as per 433 (68%) clinicians in the survey, other causes leading to persistent hypertension could be attributed to renal cause, endocrine abnormalities are under the secondary cause and pregnancy-induced hypertension forms an independent entity and are generally for a transient period which usually resolves after the delivery. The most common cause for achieving control of BP was found to be inadequate treatment by the physician as the treatment needs to be individualized after the workup of the patient and also associated comorbid conditions need to be addressed promptly in getting the desired results. Non-compliance to the medications by the patient is a major cause in achieving the desired control of the BP. Obesity, sedentary lifestyle, and unhealthy food habits are the major cause contributing to the causation of hypertension. Inefficient lifestyle modification by the patient has a major role to play in the failure to achieve the target BP.

Poor control of BP above 45 years of age is attributed to the poor compliance of the patient and an unhealthy lifestyle. Lifestyle modification is the most challenging part in the control of hypertension particularly uncontrolled one, the probable reason being the resistance to change their already learned habits. Bekki *et al*.[15] found in their study the beneficial effect of the combination therapy of telmisartan and amlodipine in the treatment of poorly controlled hypertension.

CONCLUSION

The present survey on hypertension clearly highlights combination therapy of telmisartan with clinidipine is very effective in treating hypertension even if associated with other comorbid conditions such as diabetes and chronic kidney disease. The beneficial effect of this combination is attributed to the anti-atherosclerotic property of the CCB and angiotensin receptor blockers, thereby also preventing the incidence of myocardial infarction. Diuretics are also added in some cases as per the level of BP control.

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