Introduction

Hypertension remains a major cause of premature death worldwide though blood pressure (BP) lowering has proven benefits on the reduction of cardiovascular (CV) events.[1,2] Global hypertension control rates continue to stand at a dismal 20%. This scenario is grimmer in India where nearly 1/3rd of the adult population suffers from hypertension with BP control rates of ~8%.[3,4]

Thus an effective BP-lowering agent which enhances compliance and minimises side effects is the need of the hour. Though the latest guidelines recommend initiating therapy with any of the main five classes of antihypertensive agents i.e. angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), beta-blockers, calcium channel blockers (CCBs) and diuretics, some cause-specific differences do exist between the therapeutic agents.[5]

Amlodipine controls BP and enhances patient outcomes

CCBs were introduced more than 3 decades ago and were primarily used for the treatment of coronary heart disease (CHD). Over time, their efficacy as antihypertensive agents took precedence along with their effectiveness in other correlated conditions such as peripheral vascular disease, angina and certain arrhythmias.[6]

Amongst the antihypertensive agents, clinicians consider the dihydropyridine CCB, Amlodipine, as the gold standard in BP reduction.[7] This belief has been reaffirmed by a plethora of landmark trials that have shown that Amlodipine-based therapy decreases CV morbidity and mortality. The Antihypertensive Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT; n=33,000) showed that Amlodipine was as effective as a diuretic in decreasing CV outcomes. In the Valsartan Antihypertensive Long-term Use Evaluation (VALUE; n=15,245) trial, greater BP reduction was observed with the Amlodipine-based regimen, especially in the initial period of the trial which resulted in a better impact on myocardial infarction (MI).[8,9]

Similarly, both Anglo-Scandinavian Cardiac Outcomes Trial - Blood Pressure Lowering Arm (ASCOT-BPLA; n=19257) and Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension (ACCOMPLISH; n=11,506) trials reinforced the efficacy of the Amlodipine-based regimen on reducing CV events and mortality along with enhancing renoprotection in high-risk hypertensive patients.[6,8]

A meta-analysis of 7 large-scale, actively-controlled, long-term outcome trials (n=87,257) showed that compared to non-CCB antihypertensive therapy, Amlodipine-based regimens significantly reduced the risk of MI, stroke, total CV events and total mortality by 9%, 16%, 10% and 7%, respectively.[9]

Amlodipine - Part of guideline-directed therapy

The BP-lowering of Amlodipine is accompanied by high tolerability and minimal side effects.[10] Its long half-life ensures 24hr BP control and its once-daily administration enhances patient compliance.[10,11] Moreover, data from real-world evidence involving 4.9 million patients showed that Amlodipine (administered in 85% of patients initiated with CCB therapy) was as effective as the agents from other antihypertensive classes in reducing CV outcomes.[12] These unique properties also make it an effective agent when used in combination with other antihypertensive drugs.[10]

The European Society of Cardiology/European Society of Hypertension (ESC/ESH) 2018 hypertension guidelines reiterate that the outcome trials on CCBs are mainly based on Amlodipine.[5] On the other hand, the Hypertension, brain, cardiovascular and renal Outcome Prevention and Evidence in Asia (HOPE Asia) guidelines recommend the use of long-acting CCBs such as Amlodipine for the prevention of subsequent CV events.[13] Thus real-world evidence, trial evidence and guideline recommendations endorse the efficacy of Amlodipine as a part of monotherapy and combination therapy regimens for the management of hypertension (Table).[5,10,12,13]

Table: Evidence supporting Amlodipine's efficacy

Study	Remarks
HOPE Asia Network guidelines 2020[13]	The need for strict 24 hr BP control is essential and hence long-acting antihypertensive agent such as CCBs are recommended
ESC/ESH 2018 guidelines[5]	RCT-based evidence on the beneficial impact of CCBs on outcomes have utilized dihydropyridines, specifically Amlodipine
Lancet 2019 real word evidence[12]	Data from 4.9 million patients showed that Amlodipine therapy (used by 85% of the patients on CCB therapy) was as effective as agents from other classes for CV outcomes
Review of trial evidence by *Fares H et al.* 2016[6]	Amlodipine is effective and safe. Its efficacy is additionally supported by robust evidence from large RCTs for CV event reduction and should be considered as a first-line antihypertensive agent.

HOPE - Hypertension, brain, cardiovascular and renal Outcome Prevention and Evidence, **BP -** Blood Pressure, **CCB** – Calcium Channel Blockers, **ESC/ESH -** European Society of Cardiology/European Society of Hypertension, **RCT -** Randomised Clinical Trials, **CV -** Cardiovascular

Conclusion

Amlodipine has been used effectively for the last 2 decades for the treatment of hypertension. Its efficacy, excellent tolerability and once-daily administration have made it an attractive therapeutic choice across patient subgroups. Moreover, its long duration of action ensures 24hr BP control which in turn mitigates the incidence of future CV events. Robust data from landmark trials have helped cement its place in hypertension guidelines, making it one of the preferred choices as a first-line antihypertensive agent.

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