

# A Review of Efonidipine vs Amlodipine for Hypertension Management: Evaluating Efficacy, Safety and Additional Therapeutic Benefits

Dr. Rahul Garg

MBBS, MD (Medicine), Associate Professor, Department of Medicine, F H Medical College and Hospital, Etmadpur, Agra, India

**Abstract:** ***Background:** Calcium channel blockers (CCBs) like amlodipine are widely prescribed for hypertension management. However, efonidipine, a newer dual L-type and T-type CCB, may offer advantages over amlodipine. **Objective:** To evaluate the efficacy, side effect profiles, and additional therapeutic benefits of efonidipine compared to amlodipine for hypertension treatment. **Methods:** A review of clinical studies comparing efonidipine and amlodipine in patients with mild to moderate hypertension was conducted. Data on blood pressure reduction, adverse effects (peripheral edema, reflex tachycardia), and additional therapeutic properties were analyzed. **Results:** Evidence suggests efonidipine is equally effective as amlodipine in reducing blood pressure. Notably, efonidipine exhibits a lower propensity for causing peripheral edema and reflex tachycardia compared to amlodipine. Additionally, efonidipine has demonstrated potential renoprotective, cerebroprotective, and anti-inflammatory effects. **Conclusions:** Efonidipine may be a superior alternative to amlodipine for hypertension management due to its comparable efficacy, more favorable side effect profile, and added therapeutic benefits. Its unique dual mechanism of action targeting both L-type and T-type calcium channels makes efonidipine a promising option, particularly for patients experiencing adverse effects with other CCBs. However, more long-term studies are needed to further establish its clinical implications.*

**Keywords:** Efonidipine, Amlodipine, Hypertension, Calcium Channel Blockers, Peripheral Edema, Reflex Tachycardia

## 1. Introduction

Hypertension, or elevated blood pressure, is a major risk factor for cardiovascular diseases, including stroke, heart failure, and coronary artery disease. Effective management of hypertension is crucial for reducing the associated morbidity and mortality. Calcium channel blockers (CCBs) are a widely prescribed class of antihypertensive drugs that work by blocking the entry of calcium into the smooth muscle cells of blood vessels, leading to vasodilation and a reduction in blood pressure.

Amlodipine, a dihydropyridine CCB, has been a popular choice for the treatment of hypertension due to its potent antihypertensive effects and once-daily dosing regimen. However, emerging evidence suggests that efonidipine, a newer generation CCB with dual L-type and T-type calcium channel blocking properties, may offer superior benefits in terms of side effect profile and equal efficacy in lowering blood pressure.

### Mechanism of Action:

Efonidipine is a unique CCB that exhibits a dual mechanism of action by blocking both L-type and T-type calcium channels.<sup>1</sup> L-type calcium channels are primarily responsible for regulating vascular smooth muscle tone and cardiac contractility, while T-type calcium channels play a role in regulating cardiac pacemaker activity and neuronal excitability.<sup>2</sup>

By blocking both L-type and T-type calcium channels, efonidipine not only reduces peripheral vascular resistance and lowers blood pressure but also exhibits additional benefits, such as reducing heart rate and improving endothelial function.<sup>3, 4</sup> This dual mechanism of action sets

efonidipine apart from other CCBs, including amlodipine, which primarily targets L-type calcium channels.

### Efficacy in Blood Pressure Reduction:

Several clinical studies have demonstrated the efficacy of efonidipine in lowering blood pressure in patients with mild to moderate hypertension. A comparative clinical trial by Dewan and Wani<sup>5</sup> found that efonidipine and amlodipine were equally effective in reducing systolic and diastolic blood pressure in patients with stage-I hypertension. Similarly, a study by Jha et al.<sup>6</sup> reported comparable reductions in blood pressure with efonidipine and amlodipine in patients with mild to moderate primary hypertension. Jariwala and Jadhav<sup>7</sup> conducted a study specifically evaluating the safety and efficacy of efonidipine in Indian patients with mild to moderate essential hypertension. They found that efonidipine effectively lowered both systolic and diastolic blood pressure, with a minimal impact on heart rate, further supporting its antihypertensive efficacy and favorable hemodynamic profile.

### Side Effect Profile:

One of the key advantages of efonidipine over amlodipine lies in its superior side effect profile, particularly regarding the incidence of peripheral edema and reflex tachycardia.

*Peripheral Edema:* Peripheral edema, or swelling of the lower extremities, is a common side effect associated with CCBs, including amlodipine. This adverse effect is primarily due to the preferential vasodilatory effect of CCBs on precapillary resistance vessels, leading to an increased hydrostatic pressure and fluid accumulation in the interstitial spaces.<sup>8</sup> In contrast, efonidipine has been shown to have a lower propensity for causing peripheral edema compared to other CCBs. A study by Ishimitsu et al.<sup>9</sup> reported a

significantly lower incidence of peripheral edema in patients treated with efonidipine (2.6%) compared to those treated with amlodipine (11.1%).

**Reflex Tachycardia:** Reflex tachycardia, or an increase in heart rate, is another common side effect observed with CCBs, including amlodipine. This adverse effect is thought to be a compensatory mechanism in response to the vasodilatory effects of CCBs, which can lead to a reduction in cardiac output and subsequent activation of the sympathetic nervous system.<sup>10</sup> Efonidipine, with its unique ability to block T-type calcium channels, has been shown to mitigate this reflex tachycardia. Several studies have reported a minimal or no increase in heart rate with efonidipine treatment, even at higher doses.<sup>11, 12</sup> This favorable effect on heart rate makes efonidipine an attractive option for patients with hypertension, particularly those at risk for arrhythmias or with coexisting cardiovascular conditions.

#### Additional Benefits:

Beyond its antihypertensive effects and favorable side effect profile, efonidipine has been associated with additional beneficial effects, further enhancing its therapeutic potential.

**Renoprotective Effects:** Efonidipine has been shown to exhibit renoprotective effects, making it a valuable option for patients with hypertension and concomitant renal impairment. Studies by Kawabata et al.<sup>13</sup> and Hayashi et al.<sup>14</sup> demonstrated that efonidipine effectively reduced proteinuria and slowed the progression of renal injury in hypertensive patients with renal impairment.

**Cerebroprotective Effects:** Emerging evidence suggests that efonidipine may also confer cerebroprotective effects. A study by Rajput et al.<sup>15</sup> found that efonidipine exerted neuroprotective effects in diabetic rats by downregulating the TGF- $\beta$ /SMAD-2 signaling pathway, which is implicated in neuroinflammation and neuronal damage.

**Anti-Inflammatory Properties:** Efonidipine has been shown to possess anti-inflammatory properties, which may contribute to its overall therapeutic benefits. A recent study by Nguyen et al.<sup>4</sup> demonstrated that efonidipine inhibited the JNK and NF- $\kappa$ B pathways, attenuating inflammation and cell migration induced by lipopolysaccharide in microglial cells.

## 2. Conclusion

The management of hypertension is a critical aspect of reducing cardiovascular risk and improving patient outcomes. While amlodipine has been a widely used CCB for the treatment of hypertension, emerging evidence suggests that efonidipine, a dual L-type and T-type calcium channel blocker, may offer superior benefits in terms of side effect profile and equal efficacy in lowering blood pressure. While more large-scale, long-term studies are warranted to further evaluate the clinical implications of efonidipine, the available evidence suggests that it may be a superior alternative to amlodipine for the management of hypertension, particularly in patients at risk for or experiencing adverse effects with other CCBs.

**Conflicts of Interest and Source of Funding:** 'The author of this work have nothing to disclose'.

**Data availability statement:** All data analyzed are included in this published article.

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