

ROLE OF CILNIDIPINE A NOVEL DIHYDROPYRIDINE DERIVATIVE IN HYPERTENSIVE PATIENTS WITH AMLODIPINE INDUCED EDEMAN. C. Sarkar¹, S. Jain², M. Tilkar³, N. Modi⁴**HOW TO CITE THIS ARTICLE:**

N. C. Sarkar, S. Jain, M. Tilkar, N. Modi. "Role of Cilnidipine a Novel Dihydropyridine Derivative in Hypertensive Patients with Amlodipine Induced Edema". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 36, August 18; Page: 9385-9388, DOI: 10.14260/jemds/2014/3210

ABSTRACT: AIM AND OBJECTIVE: Commonly used L-type calcium channel blocker (CCB) Amlodipine which is used for treatment of essential hypertension. It controls hypertension adequately, but very often produces ankle edema. Our object of study was to see whether Cilnidipine, a novel newer L/N-type CCB can adequately control hypertension without the adverse effect of ankle edema. **MATERIAL AND METHODS:** This was a prospective OPD based study performed on 62 patients with essential hypertension with amlodipine induced edema. Congestive cardiac failure, cirrhosis of the liver, concomitant Nephropathy and secondary hypertension were excluded by clinical examination and appropriate laboratory tests. Amlodipine was substituted in the enrolled cases with cilnidipine as on efficacy equivalent dose. Clinical assessment of blood pressure, pulse rate, body weight, ankle edema and measurement of bilateral ankle circumference were recorded at the beginning of the study and after 6 weeks of Cilnidipine therapy. **RESULT:** Six weeks follow up of patients revealed adequate blood pressure control without any ankle edema. Ankle edema resolved along with a decrease in the bilateral ankle circumference and body weight. **CONCLUSION:** There is complete resolution of amlodipine induced ankle edema with the substitution of cilnidipine. Blood Pressure is also adequately controlled without any other side effect. So cilnidipine a L/N-type CCB, a novel and unique dihydropyridine derivative which adequately control blood pressure without ankle edema.

KEYWORDS: Hypertension, Calcium channel blocker (CCB), Amlodipine (L-type CCB) Ankle edema, Cilnidipine (L/N type CCB).

INTRODUCTION: Commonly used L-type calcium channel blocker (CCB) amlodipine, which is used for treatment of essential hypertension often produces ankle edema. It is self-limited minor effect in most of the cases. In 15% of cases it may be severe.¹ It may lead to reduced drug compliance and even discontinuation of medication.²

The physician usually adds thiazide diuretic and/or change amlodipine with ACE inhibitors or ARBs. The blood pressure control response is not adequate as amlodipine but resolved ankle edema satisfactorily.³ Ankle edema resolved at the cost of poor control of blood pressure, which is not ideally desirable. Substitution of amlodipine with another CCB may be a better option if blood pressure is adequately controlled without any ankle edema.

The 4th generation L/N-type CCB, cilnidipine, a novel and unique dihydropyridine derivative is approved for therapy of essential hypertension. It demonstrated good tolerability, safety and antihypertensive efficacy equivalent to amlodipine as shown by recent Meta-analysis.⁴

But we do not have our own data on the efficacy and tolerability of cilnidipine in patients with amlodipine induced ankle edema. Our objective of the study was to see whether cilnidipine can adequately control hypertension without the adverse effect of ankle edema.

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MATERIALS AND METHODS: This study was done at Sri Aurobindo Medical College and PG Institute, Indore, MP. Informal consent was taken from all the patients who were included in this study.

This was a prospective longitudinal OPD based study to see the effect of substitution of amlodipine with cilnidipine, in hypertensive patients with the amlodipine- induced ankle edema. Exclusion criteria were: I) Congestive Cardiac failure, II) Nephropathy III. Cirrhosis of liver. IV. Hypothyroidism V. Varicose vein.

We studied 62 patients. Their blood pressure was well controlled with antihypertensive drugs. 40 patients were on monotherapy with amlodipine. 12 patients with amlodipine and ACE inhibitor. 6 patients were with amlodipine and beta- blocker. 4 Patients were with amlodipine and thiazide diuretics. All of them had ankle edema.

Baseline parameter such as ankle edema, pulse rate, blood pressure, body weight and bilateral ankle circumference were recorded. Amlodipine was stopped and with replaced by cilnidipine 10 mg/20mg for 5 mg/10 mg of amlodipine as an efficacy equivalent dose. All patients were followed up for 6 weeks. Relevant parameters were again recorded for all the patients.

RESULT:

Male 50 patients.

Female 12patients.

Age group 52-64 years.

Duration of treatment with amlodipine 5 mg 52 patients, 10 mg 10 patients at the time of inclusion was 10-12 months. Follow up for 6 weeks, revealed complete clinical resolution of ankle edema with significant reduction of body weight. The blood pressure and pulse rate were well controlled.

Comparison of clinical parameters at the time of enrolment and after 6 weeks of observation.

Parameters	Start	End	P. Value
Pulse rate (bpm)	76.4 + 5.76	76.4 + 6.72	1.000
Mean peripheral BP (mmHg)	106.76 + 4.38	108.45 + 6.85	0.1043
Body weight (Kg)	66.6 + 8.66	62.6 + 4.45	<.0001
Ankle circumference(R) cm	25.0 + 1.56	23.6 + 2.22	<.0001
Ankle circumference (L) cm	25.1 + 1.68	23.7 + 1.9	<.0001

DISCUSSION:

Following is the postulated mechanism for CCB induced ankle edema:

1. In normal individual pre capillary vasoconstriction in response to venous congestion protects the capillary bed from increased blood pressure, thus restricts hydrostatic filtration of fluid into the interstitium. L-type CCBs like amlodipine directly inhibit pre-capillary constriction and causes arteriolar dilatations and thus leads to intestinal edema.⁵
2. Capillary hypertension due to dilatation of pre-capillary resistance vessels by L-type CCBs sparing post capillary vascular tone leading to capillary hypertension and promotes fluid filtration into the interstitium.⁶

3. Increased microvascular permeability which causes extravasations of plasma protein and water into the interstitial space.^{7,8}

Action of Cilnidipine: It is a dual blockade of L-type and N-type Ca⁺⁺ Channels. L-type Ca⁺⁺ channel blockade inhibits pre-capillary vasoconstriction leading vasodilatation such as amlodipine.⁹

N-type Ca⁺⁺ channel blockade disrupts outflow of sympathetic nervous system, leading to further vasodilatation by lowering plasma catecholamine. This twin action result vasodilatation of both pre & post capillary resistance vessels and prevent hyper filtration of fluid into the interstitium.¹⁰

Reno protection Effect: Cilnidipine reduces sympathetic outflow as well as the afferent vasodilatory effect which attenuates glomerular hyper filtration and thus act as renal protector.^{11,12,13,14,15}

Reduction of capillary hyper filtration in the peripheral systemic circulation appears due to the aforesaid mechanism.

By blockade of both L-type and N-type Ca⁺⁺ channels by cilnidipine and maintaining the local vasoconstrictor effect which prevents excess fluid filtration into the tissue and thus prevent ankle edema with adequate blood pressure control.

CONCLUSION: Cilnidipine is a novel and unique, effective CCB (L-type and N-type) which is an alternative antihypertensive medication in those groups of patient having CCB (L-type) such as amlodipine induced ankle edema.

This is a small study. Further studies are required to elucidate the other various mechanisms of action of cilnidipine which are responsible for the absence of ankle edema along with adequate blood pressure control.

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