

Cilnidipine Induced Ankle Edema: A Rare Adverse Event

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ABSTRACT

Cilnidipine is a 4th generation dihydropyridine calcium channel blocker that is used in essential hypertension. Unlike amlodipine, cilnidipine rarely causes ankle edema. Therefore, cilnidipine is often

used as an alternative drug in patients with amlodipine-induced ankle edema. However, we report a case of cilnidipine induced ankle edema.

Keywords: Cilnidipine; Calcium Channel Blocker; Amlodipine; Essential Hypertension

INTRODUCTION

Cilnidipine, a 4th generation dihydropyridine calcium channel blocker (CCB), is approved for the treatment of essential hypertension in many countries. Unlike other CCBs (such as amlodipine, nifedipine, felodipine, isradipine, diltiazem, manidipine and nisoldipine) that often cause ankle edema, cilnidipine rarely causes ankle edema [1, 2]. Due to this difference in side-effect profile, cilnidipine is often used to replace CCB in patients that experience ankle edema. In one study [3], therapy with cilnidipine resulted in complete resolution of amlodipine-induced edema without a difference in blood pressure when compared to amlodipine. The mechanism of this difference in adverse effect is unknown. We report a case of cilnidipine induced ankle edema. The side effect of this drug although relatively rare, can lead to reduced drug compliance or drug discontinuation [1,3].

CASE REPORT

A 38-year old female presented to medical outpatient department of Guru Nanak Dev Hospital, Amritsar with complaints of headache, and decreased sleep. Her blood pressure was 158/88 mm of Hg in the right arm while she was sitting. Her clinical examination was otherwise unremarkable. Her laboratory investigations were normal. Her fundoscopic examination was normal. She was diagnosed with uncomplicated hypertension (stage 1) as per JNC 7 guidelines. She was advised to start cilnidipine 5 mg once daily with salt restriction and lifestyle

management. She presented to medical outpatient department after 3 weeks for follow up. At follow up, her blood pressure was 130/90 mm of Hg and she was asymptomatic. She was continued on cilnidipine 5 mg once daily but she presented with bilateral pitting ankle edema after the 6th week of the drug therapy. A repeat thorough clinical examination was normal. Laboratory investigations revealed no abnormality. X-ray chest was normal. T3, T4 and thyroid stimulating hormone and serum uric acid were normal. Electrocardiography and 2D-echocardiography were normal. Ultrasonography abdomen revealed no abnormality. On the basis of normal clinical examination and high degree of suspicion, the patient was instructed to stop cilnidipine and was started on olmesartan 20 mg once daily. The ankle edema disappeared completely on the 12th day after stopping cilnidipine with good control of blood pressure. Thus the patient on cilnidipine, developed ankle edema after 6 weeks of therapy which disappeared completely on discontinuation of drug.

DISCUSSION

Cilnidipine is a 1,4- DHP CCB that suppresses the influx of calcium ions via L-type and N-type calcium channels, thus reducing the blood pressure through vascular smooth muscle relaxation and arterial dilatation [4, 5]. It is used as an antihypertensive agent with a long duration of action that allows once-daily dosing. When administered to the patients with essential hypertension, cilnidipine suppresses cardiac

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sympathetic over activity and an increase of heart rate with blood pressure reduction [6]. Both amlodipine and cilnidipine have shown equal efficacy in reducing blood pressure in hypertensive individuals. But cilnidipine being N-type and L-type CCB, is associated with lower incidence of pedal edema compared to only L-type channel blocker, amlodipine. CCBs with an N-type channel blocking effect may dilate the venules through sympathetic nerves distributed to these vessels. Hence cilnidipine has a lesser incidence of pedal edema compared with the other CCBs which act only on L-type calcium channels. But in our case, cilnidipine use produced ankle edema which is a rare manifestation. In one study there was a significant difference in the incidence of pedal edema between amlodipine and cilnidipine group ($P < 0.05$), but no significant difference was found in the antihypertensive efficacy of amlodipine and cilnidipine ($P > 0.05$) [4].

Common adverse effects reported with cilnidipine are nausea, vomiting, abdominal pain, constipation, dry mouth, heartburn, headache, gingival hypertrophy, and insomnia. Rarely, palpitations and elevated liver enzymes can be seen. Cilnidipine has been recently used to alleviate CCB-induced bilateral ankle edema which is a common side effect of amlodipine but not of cilnidipine.

Cilnidipine is an effective and well-tolerated alternative antihypertensive in patients with amlodipine-induced edema. But if present, it is of importance and all physicians treating hypertension should think of this adverse event.

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