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Case report

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### A case report on Amlodipine induced pedal edema-pitting type

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#### ABSTRACT

Amlodipine is a 4<sup>th</sup> generation dihydropyridine calcium channel blocker which is permitted for the treatment of essential hypertension and angina pectoris. The main mechanism of calcium channel blockers are blocks the voltage sensitive L-type calcium channels by binding to alpha-1 subunit, so prevent the entry of calcium in to the cells finally no excitation-contraction coupling in the heart and vascular smooth muscles. It is absorbed slowly after oral administration. But its bioavailability is high. It has a longer duration of action than nifedipine. It dilates both peripheral as well as coronary vessels. It is an alternative anti-hypertensive drug for patients with Nifedipine induced pedal edema. This drug is expected to produce a more incidence of pedal oedema, as compared to Nifedipine and other calcium channel blockers, based on the limited data available from clinical trials. The common adverse effects of Amlodipine are nausea, abdominal pain, vomiting, dry mouth, constipation, gingival hypertrophy, dizziness, heartburn, photosensitivity, headache, light headedness and insomnia. We report a case of Amlodipine induced pedal edema.

**Keywords:** Amlodipine, CCBs, CVA, pedal oedema, ADR analysis.

#### INTRODUCTION

Amlodipine is a 1,4-dihydropyridine derivative Calcium channel blocker, which is structurally linked to Felodipine, Nifedipine, and Nimodipine. Distinct other presently available CCBs in the dihydropyridine class, amlodipine have a longer duration of action<sup>1</sup>. Among the variety of ADRs, peripheral oedema (swelling of the hands and Feet) may inflict a change in drug treatment during Amlodipine therapy. This ADR is establish to be dose dependent, with incidence of 1.8 10.8% On a dose between 2.5 to 10 mg, daily<sup>2</sup>. Pedal edema, is a

frequent adverse effect of L-type calcium channel blocker (CCB) and can sometime progress to Anasarca<sup>3</sup>. CCB usually well-known to cause pedal edema are amlodipine, felodipine, diltiazem, nifedipine, manidipine, isradipine, lacidipine, lercanidipine and nisoldipine<sup>3,4</sup>. Amlodipine is a 4<sup>th</sup> generation dihydropyridine CCB permitted for the treatment of hypertension with efficacy and safety that is comparable to nifedipine. It is a distinctive L-type Ca<sup>2+</sup> channel blocker with an inhibitory action on the sympathetic N-type Ca<sup>2+</sup> channels. It has a slow onset but the long lasting action<sup>5</sup>. It was introduced in the market, with a claimed lead over

Amlodipine<sup>6</sup>. therapy with amlodipine resulted in complete resolution of clonidine induced Oedema in all the cases without major degeneration of hypertension or tachycardia and thus it has been suggested as an alternative anti-hypertensive for patients with clonidine induced pedal edema. We report an inaccessible case of amlodipine induced pedal edema. Even though, it was a relatively mild and no serious adverse effect, it can lead to reduced drug compliance or complete discontinuation of therapy.

### CASE REPORT

A 52 years male patient was admitted in ICU with the chief complaints of weakness of both right upper and lower limbs, vomiting and history of tongue bite present. He was known smoker and alcoholic since 20 years, known case of CVA since 1 year under the medication and hypertensive patient since 9 years. General examination of the patient on day-1 he was semiconscious and incoherent, but on day-4 patient was conscious and responded to painful stimuli. His vitals were: B.P-180/100 mm of hg, P.R-84 bpm, CNS- right hemi paralysis present, P/A-soft, CVS-

S<sub>1</sub>S<sub>2</sub><sup>+</sup>, and his laboratory investigations were found to be Hb-8 gm %, RBS-72 mgs/dl, CT-Brain-multiple cell necrosis present. So based on subjective and objective evaluation patient was diagnosed as a recurrent CVA. On day-1 the patient was treated with following medications- Oral anti-platelet drugs (ecospirin 150mg OD, clopidogrel-75mg OD), Oral hypo-lipidemic drug (atorvastatin 40 mg od), parenteral anti-biotic (ceftriaxone 1gm iv bd), parenteral anti-ulcerative drug (pantoprazole 40 mg iv bd), parenteral antiemetic (domperidone 10mg tid), IV Fluids and physiotherapy. No fresh complaints on day-2, so patient was continued with the same medications, additionally added T. Amlodipine 5mg, this treatment was continued for 7 days. From 2<sup>nd</sup> day to 6<sup>th</sup> day patient was gradually developed pitting type of pedal edema, shown in figure:1. This edema was mainly due to the T. Amlodipine. The common ADR's of Amlodipine is headache and edema. On day-7 we intimated the condition of the patient to the doctor about the drug and doctor dechallenged the drug after that patient was recovered from the edema. So based on these results the patient had developed pedal oedema due to the T. Amlodipine.



**Figure 1: Amlodipine induced pitting type pedal edema.**

### ADR analysis

After collecting the past and current medication history from the patient it was suspected that the patient had developed drug induced Edema. After analyzing the ADR profiles of all the drugs, it was found that the most suspected drug for producing oedema was Amlodipine. We have further analysed to establish the relationship between the drug and the

observed ADRs, through causality assessment by using naranjo's scale, WHO-UMC ADR assessing scale as well as Karch and lasagna scale, results were shown in Table 01. We have also assessed the severity, predictability, and preventability as a part of management through Modified Hartwig and Siegel severity scale, Schumock and Thornton Preventability Scale.

### ADR Management

Generally, management of ADR includes withdrawal/suspension, dose reduction of suspected

drug and administration of supportive therapy. Here in this case report the suspected drug amlodipine was discontinued.

### ADR analysis

**Table 1: causality assessment of suspected ADRs**

Suspected drug And Reaction(ADR)	Naranjos scale	WHO-probability scale	Karch& Lasagnas scale
Amlodipine induced pedal edema	Possible	Probable	Probable

**SEVERITY:-**Moderate level 4

**PREDICTABILITY:-**UN predictable

**PREVENTABILITY:-** Probably preventable

### DISCUSSION

Amlodipine is a 1:1 mixture of S and R enantiomers. different studies on the racemic mixture of (R) and (S)isomers, have exposed that the S isomer of Amlodipine has a better pharmacological effect Than the R isomers. the S (-) isomer being 1000 times additional potent than the R (+) isomer<sup>6</sup>. Frequent adverse effects reported with Amlodipine are nausea, abdominal pain, vomiting, dry mouth, constipation, gingival hypertrophy, dizziness, heartburn, photosensitivity, headache, light headedness and insomnia. hardly ever, hot flushes, palpitations, ECG abnormalities, chest pain, atrioventricular block, hypersensitivity reactions, frequent urination and elevated liver enzyme<sup>7</sup>. Amlodipine has been recently suggested to result in complete declaration of nefidipine induced oedema and has been suggested as an alternative antihypertensive for patients with amlodipine induced pedal oedema. On the other hand, the opposing our case presented with bilateral pitting type pedal edema with Amlodipine treatment<sup>8</sup>. The mechanism of amlodipine induced adverse effect is unknown. But, number of mechanisms has been postulated for CCBs induced pedal oedema including inhibition of pre-capillary vasoconstriction through arteriolar dilatation and consequently, promoting interstitial edema. CCBs are well-known to origin

pedal edema. This ADR has "probable" causal relationship with Amlodipine as assessed by Naranjos scale and WHO-UMC<sup>9</sup>. The usual move toward to patients with CCBs induced pedal oedema involves cessation of therapy and substitution with an alternative antihypertensive and thiazide diuretic or angiotensin receptor blockers (ARBs), angiotensin converting enzyme inhibitor (ACEI), as was accepted in our case. A combination therapy of diuretic, CCB, ARBs are common in clinical practice in such cases<sup>9</sup>. furthermore, the present case report grass another important message for the practicing physicians, that not at all be first and last to prescribe any new drug.

### CONCLUSION

The involvement of pedal oedema due to Amlodipine in this case, so physicians have a responsibility to closely Monitoring the patients condition during the administration of drug like Aamlodipine, which do not have enough safety and efficacy data. Since our explanation are based on only case reports. In this case report, the conventional practice to prescribe ARBs, thiazide diuretic or ACEI should be carried Until larger clinical trial chains the function of Amlodipine in such conditions.

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