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A CASE REPORT ON AMLODIPINE INDUCED PEDAL OEDEMA

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ABSTRACT
Amlodipine is a 4th 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 an nifedipine. It dilates both peripheral as well as coronary vessels. It is an alternative anti-hypertensive drug for patients with Nifedipine induced pedal oedema. This drug is expected to produce a more incidence of pedal oedema, as compared to Nefidipine 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 oedema.

KEYWORDS: Amlodipine, CCBs, CVA, pedal oedema, ADR analysis.

INTRODUCTION
Amlodipine is a 1,4dihydropyridinederivative Calcium channel blocker, which is structurally linked to Felodipine, Nifedipine and Nimodipine. Distinct other presently available CCBs in the dihydropyridine class, amlodipine has a longer duration of action.[1] Among a variety of ADRs, peripheral oedema (swelling of the hands and Feet) may inflict a change in drug treatment during Amlodipine theraphy. This ADR is established to be dose dependent, with incidence of 1.8 10.8% On a dose between 2.5 to 10 mg, daily.[2] Pedal oedema, is a frequent adverse effect of L-type calcium channel blocker (CCB) and can sometime progress to Anasarca.[3] CCB usually well-known to cause pedal edema are amlodipine, felodipine, diltiazem, nifedipine, manidipine, isradipine, lacidipine, lercanidipine and nisoldipine[3,4]. Amlodipine is a 4th generation dihydropyridine CCB permitted for the treatment of hypertension with efficacy and safety that is comparable to nifidipine. It is a distinctive L-type Ca 2+ channel blocker with an inhibitory action on the sympathetic N-type Ca 2+ channels. It has a slow onset but the longlasting action.[5] It was introduced in the market, with a claimed lead over Amlodipine.[6] therapy with amlodipine resulted in complete resolution of clonidipine 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 cilnidipine induced pedal oedema. 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.

CASEREPORT
A 48 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 in the past 15 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_1S_2 $^+$, 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 (ecosprin150mg od, clopidogrel-75mg od), Oral hypo-lipidemic drug (atorvaststin 40 mg od), parentral anti-biotic (ceftriaxone 1gm iv bd), parentral anti-ulcerative drug (pantoprazole 40 mg iv bd), parentral 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 2nd day to 6th 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 oedema. So, based on these results the patient had developed pedal oedema due to the T. Amlodipine.

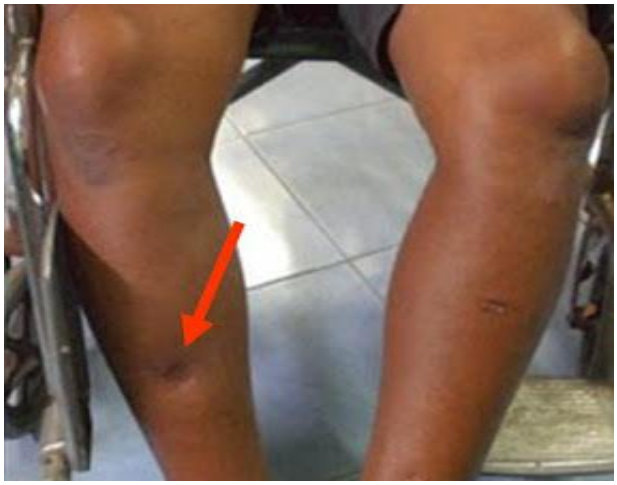

Figure 1: Amlodipine induced pitting pedal edema.

ADR analysis

After collecting the past and current medication history from the patient it was suspected that the patient had developed drug induced Oedema. 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 severityscale, SchumockAnd 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.[6] frequent adverse effects reported with Amlodipine are nausea, abdominal pain, vomiting, dry mouth, constipation, gingival hypertrophy, dizziness, heartburn, photosensitivity, headache, lightheadedness and insomnia. hardly ever, hot flushes, palpitations, ECG abnormalities, chest pain, atrioventricular block, hypersensitivity reactions, frequent urination and elevated liver enzyme.[7] 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.[8] 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.[9] The usual move toward to patients with CCBs induced pedal oedema involves cessation of therapy and substitution with an alternativeantihypertensive 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.[9] furthermore, the present case report grass another important message for thepracticing 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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