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A REVIEW ON AMLODIPINE USED IN TREATMENT OF HEART DISEASES

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Abstract: Amlodipine is Oral Dihydropyridine calcium channel blocker. Compare to nifedipine and other medication in the dihydropyridine class, amlodipine has the longest halflife at 30 t0 50 hrs. The benefit of such a long half-life is the ability to have once daily –dosing. Amlodipine is available as amlodipine besylate, which was initially approved in 1987 by the FDA. This activity reviews the indications, content indicators, activity, adverse events, and other key elements of amlodipine in the clinical setting as related to the essential points needed by members of an interprofessional term managing the care of patients rom amlodine therapy. Amlodipine is used in the treatment of heart disease and angina pectoris.

I. INTRODUCTION

Amlodipine is belong to the group of calcium channel blockers , there are some newer calcium channel blockers such as felodipine, dihydropyridine and nisoldipine.

They have advanced vascular selectivity and longer duration of action. They bind to target receptors in a slow and carryon pattern producing a smooth onset of action with a 24 hour control of blood pressure.

The Amlodipine is commonly used in the treatment of heart diseases such as hypertension and angina.

Amlodipine plays an important role in apoptosis. It is also used in the treatment of cerebrovascular stroke,breast cancer and leukemia.[1]

Calcium-channel blockers (CCBs), comprise three Distinct subgroups: benzothiazepines

(e.g. diltiazem),Dihydropyridines (e.g. amlodipine, nifedipine) and Phenylalkylamines (e.g. verapamil).[20]

II. Objectives

- Identify the uses and indication of amlodipine, both approved and off-label.
- Describe tha MOA of amlodipine.
- Summarize the adverse drug reaction of amlodipine.
- Outline inter-professional term strategies for improving care-coordination and communication to advance the knowledge on amlodipine and improve outomes.

FORMULATION OF AMLODIPINE :-

The formulation of amlodipine may contains its various salts like mesylate and besylate. Amlodipine besylate is the derivative of amlodipine used to prepare its various dosage form.[1][3]

The salts of amlodipine affects the physicochemical properties of the drug as the besylate salt is known to have well solubility than amlodipine alone.

There are some newer salts compared with amlodipine besylate for their pharmacokinetics.It was observed that all new salts were show bioequivalent and similar pharmacokinetic properties to those of Amlodipine besylate.[1] [4]

TABLETS:-

Amlodipine is available in tablet dosage form in once daily doses of 5 and 10mg.

It is orally administrated in besylate form. It is better absorbed after oral administration and has bioavailability near about 60 – 65% .[5]

Amlodipine is a photosensitive drug and has been made to formulate tablets by photo protection to the active drug.

These tablets were exposed to different radiation like UVA and UVB for 8 hour to determine photoprotective effect of the coating material. [6]

TOPICAL FORMULATION :-

Gel :- Gel formulations containing dexamethasone(0.3%) and ADB(0.5%) have been formulated using carboxymethyl cellulose sodium as gelling agent , alone (laurocapram) as penetration enhancer and propylene glycol as solvent and humectant.The gels were studied for drug penetration on flap tissues through excised rat skin .[1]

PHYSICOCHEMICAL PROPERTIES OF AMLODIPINE BESYLATE : STRUCTURE OF AMLODIPINE BESYLATE :-

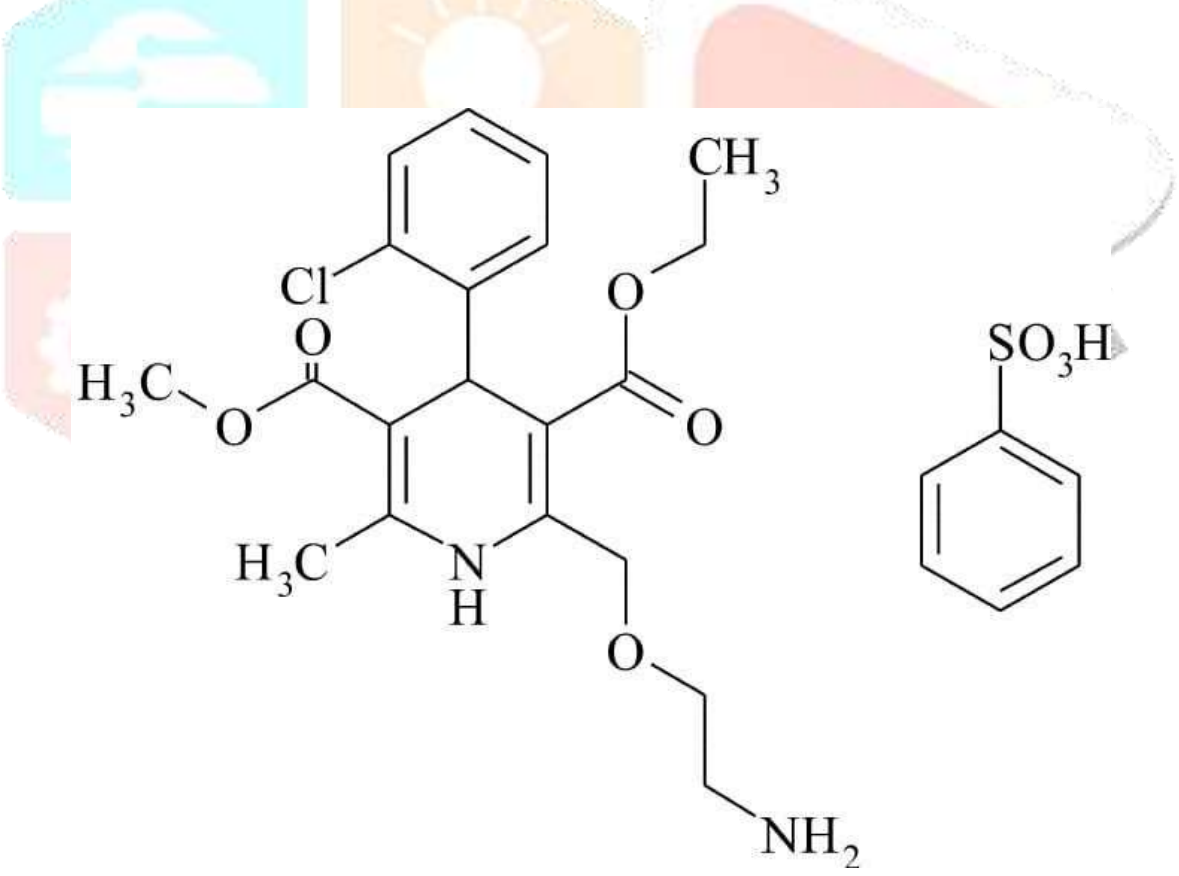

Fig . No . 1: Amlodipine besylate [11]

Solubility

1) It is slightly soluble in water .
2) Sparingly soluble in ethanol.
3) It is freely soluble in methanol.[8]

COLOUR :-

1) It is white powder.

MECHANISM OF ACTION :-

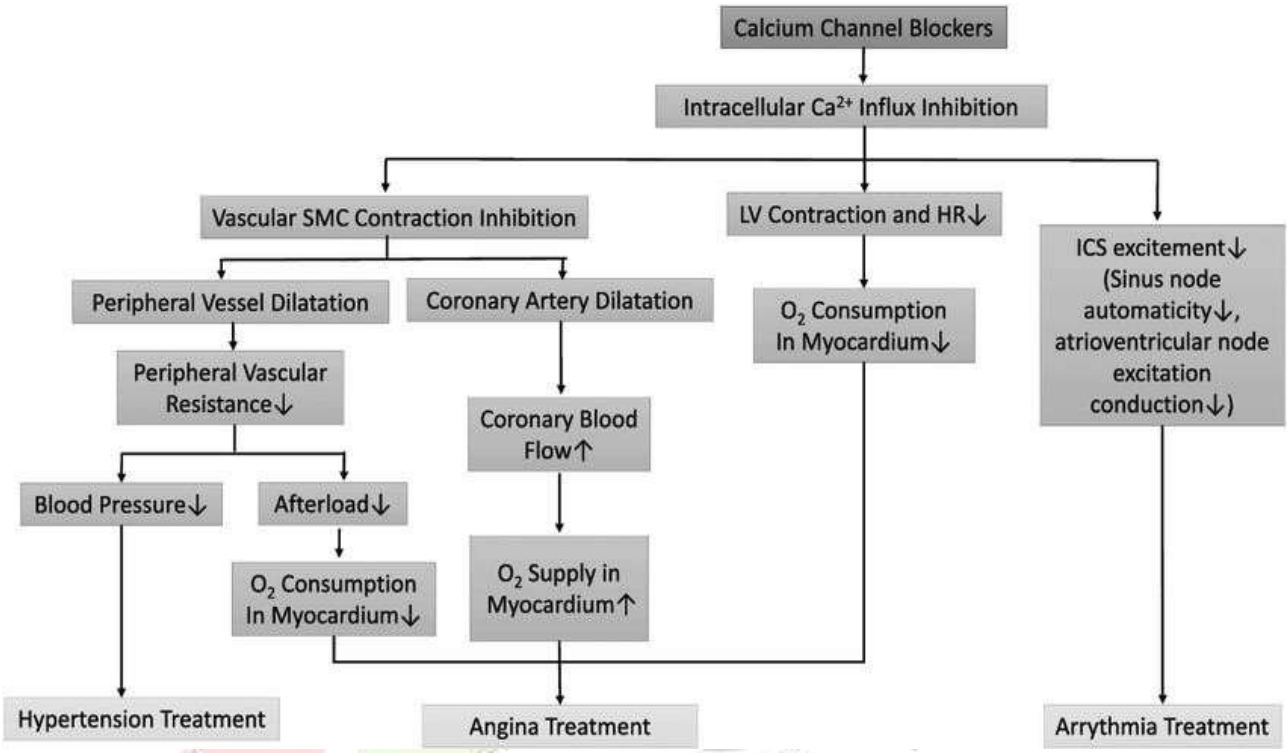

Fig. No. 2 : Mechanism of action of calcium channel blockers [12]

Normally, vascular smooth muscle contraction initiates when calcium enters the cell via voltage-dependent L-type calcium channels. The calcium binds to intracellular calmodulin, which binds to and activates myosin light-chain kinase (MLCK). MLCK is responsible for the phosphorylation of myosin light-chain, ultimately leading to muscle contraction and vasoconstriction. The vascular smooth muscle contraction becomes further amplified by calcium-induced calcium release from the sarcoplasmic reticulum. This sequence of events leads to a decreased vascular cross-sectional area, increased vascular resistance, and increased blood pressure.

Amlodipine works by blocking the voltage-dependent L-type calcium channels, thereby inhibiting the initial influx of calcium. Reduced intracellular calcium leads to decreased vascular smooth muscle contractility, increased smooth muscle relaxation, and resultant vasodilation. Additionally, amlodipine has been shown to improve vascular endothelial function in hypertensive patients. In summary, amlodipine decreases blood pressure by inducing smooth muscle relaxation and vasodilatation.

Amlodipine's role in relieving stable angina is due to the lowering of afterload secondary to its vasodilatory and antihypertensive properties. Reducing afterload leads to lowering myocardial oxygen demand at any level of exertion as the heart does not need to work as hard to pump blood into the systemic circulation. Amlodipine also alleviates Prinzmetal or variant angina by blocking coronary spasms and restoring blood flow in the coronary arteries.

Raynaud phenomenon (RP) is an excessive vascular response to cold temperature, manifested clinically by color changes of the distal skin of the digits and toes, nose, and earlobes. Amlodipine induces smooth muscle relaxation and is an effective short-term treatment for patients with Raynaud's phenomenon.

ACE inhibitors(ACE-I)/angiotensin receptor blockers(ARBs) are the initial treatment of choice for diabetic nephropathy. However, clinical trials have shown that combined antihypertensive therapy with either amlodipine plus an ARBs/ACE-I plus exerts a greater antiproteinuric effect in patients with type 2 diabetic nephropathy.[13]

USES OF AMLODIPINE:-

1. It is used in treatment of Hypertension.
2. It is used in treatment of angina pectoris.
3. It prevent the future heart stroke.
4. It is used to prevent the chest pain caused due to heart diseas
5. It is use for lowering high blood pressure. [8]

ADVERSE EFFECTS:-

1. Amlodipine can cause heart failure .[8]
2. Amlodipine can cause peripheral edema.[13]
3. It causes constipation. [13]

Efficacy and Safety:-

The vital sign monitoring and physical examinations were performed at every visit, and the inflexibility of adverse events . and their association With study medicines were assessed by the investigator using WHO Adverse Response Terminology (WHO- ART; 2009 2nd quarter interpretation). The sitting in- clinic BP was measured using automatic BP examiner (Verge-70801T, Omron Corporation, Kyoto, Japan) at the . original webbing, the end of the run-in treatment period previous .to randomization, and after 4 and 8 weeks of double-eyeless . treatment. The BP,palpitation rate, and body temperature were measured. The BP was recorded as the mean of three con- secutive measures.The primary efficacity endpoints were assessed after 8 weeks of treatment. The primary efficacity endpoint was the change in sitDBP from birth to Week 8 between the study medicines and the comparator . The secondary Efficacity endpoints were the change in sitDBP . From birth to Week 4 (Visit 3) with the study medicine versus the comparator, the changes in sitSBP from birth to Weeks 4 and 8 with the study medicine versus the comparator, .the control rate (rate of subjects who achieved the target sitDBP, mmHg at Weeks 4 and 8), and response rate . (rate of subjects with a drop in sitDBP$ 10 mmHg or a mean sitDBP, mmHg, or both at Weeks 4 and 8) .

The safety variables included adverse events, vital signs, height, weight,and Resting 12- lead electrocardiography, as well as casket and clinical laboratory test (hematology, blood chemistry, and urinalysis).The adverse events were Assessed and recorded in the case report form. Adverse Events being after randomization were assessed separately to determine whether they were associated with the Study medicine or comparator (S- amlodipine besylate or telmisartan) taken by the subjects during the treatment period, or if they were caused by any beginning complaint or S-amlodipine 2.5 mg monotherapy. The adverse events were farther assessed to determine their clinical significance. [14]

CONCLUSION:-

Amlodipine should be consider as highly effective in treatment of hypertension and angina pectoris . Amlodipine is an excellent first-line choice among the myriad options of antihypertensive agents.

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