MEDIBEATS
The Medical Bulletin

Drug Corner

ACE INHIBITORS

ACE inhibitors have been shown to have the broadest impact of any drug in CVS medicine. ACE Inhibitors not only have become the cornerstone of the treatment of heart failure, but increasingly also play a major role in hypertension and in cardiovascular protection. ACE INHIBITORS give both primary and secondary protection from CVS disease thereby interrupting the vicious circle

ACE Inhibitors are efficacious with better adverse effect profile, patient compliance and have these advantages

1. No postural hypotension or rebound hypertension

2. Reverse LVH and increase wall to lumen ratio in blood vessels.

3. No effect on electrolytes or metabolism

4. They are cardio-protective , safe in bronchial asthma, DM, IHD, CHF and PVD

5. Prevent secondary hyperaldosteronism and T2DM

6. More effective in younger Patients i.e. less than 55 yrs

7. Better quality of life as compared to other antihypertensive patients

BASIC ASPECTS:

ACE inhibitors are mixed vasodilators thereby decreasing preload and afterload. This leads to decrease both in systolic and diastolic pressure which further decreases myocardial hypertrophy and fibrosis.

The coronary arteries are also dilated with increase in endothelial function and releasing nitric oxide. This leads to decreased oxidative stress.

ACE inhibitors decreases intraglomerular pressure, protein leak, glomerular growth and fibrosis and also it decreases sodium reabsorption

It also decreases the aldosterone formation thereby decreasing sodium and water retention.

On coagulation system it decreases fibrinogen levels and tissue plasminogen factors.

INDICATIONS FOR ACE INHIBITORS

1. Heart failure

2. Hypertension

3. AMI

4. NEPHROPATHY BOTH diabetic and non diabetic

5. T2DM lessens new microalbuminuria and LV hypertrophy

6. CV protection in specified doses (ramipril, perindopril)

HYPERTENSION:

ACE inhibitors are superior to other agents in the treatment of HTN as they improve QOL and are well accepted with other co morbid conditions also

PREFERRED IN	REASON
Diabetes Mellitus	Slow the development and progress of diabetic glomerulopathy and diabetic glomerulosclerosis
Renal disease	Slows the development of glomerulopathy
IHD AND LVH	Improves ventricular function and reduce morbidity and mortality
USED IN COMBINATION	REASON
WITH DIURETICS	ENHANCE THE efficacy of diuretics and a small dose of diuretic increases the significant improvement in the antihypertensive efficacy of ACE inhibitors

Cardiac failure:

ACE inhibitors reduce both the preload and afterload and useful in all grades of heart failure. Preload is reduced because of reduced circulatory volume due to natriuresis and diuresis hence reducing venomotor tone and reduced venous return. Afterload is reduced due to reduced PVR but there is no reflex increase in sympathetic activity. It also reverses Ventricular remodeling, fibrosis and apoptosis.

Acute MI:

ACE inhibitors should be administered immediately after MI particularly in HTN and DM patients as it prevents remodeling. It should be administered lifelong , severe hypotension being only the contraindication.

CHRONIC RENAL FAILURE (PROGRESSIVE):

These agents protect the renal damage by reduced BP, dilatation of renal efferent arterioles, prevention of mesangial cell growth and production of matrix induced by A II

DIABETIC NEPHROPATHY:

They reduce nephropathy, reduce microalbuminuria, improve endothelial function and reduce cardiovascular complication They are superior in reducing the CVS complications They also reduce the rate of MI, stroke and death.

SCLERODERMA CRISIS:

is a condition which is fatal and rare but has shown improvement by the use of Captopril . The ultimate outcome remains unaffected.

ADVERSE EFFECTS: ACE inhibitors do not produce serious side effects and they do not affect the level of calcium or uric acid.

ADR	**REASON**
DRY BRASSAY COUGH	Due to accumulation of bradykinin occurs as early as one week or delayed up to few months of continuous treatment and subsides thereafter REMEDY Reassurance If not tolerated change to ARB
SKIN RASHES	WITH Captopril due to sulfa group usually subsides by itself occasionally requiring ANTIHISTAMINES
HYPOTENSION	In patients having high plasma renin activity or sodium depleted **First dose hypotension is common with captopril and fosinopril BUT CARE HAS TO BE TAKEN TO ADMINISTER LOW DOSE AND AT NIGHT**
HYPERKALEMIA	Common due to potassium supplementation, use of potassium sparing diuretics , NSAIDs, beta blockers or potassium rich foods and renal dysfunction
ANGIONEUROTIC EDEMA	NOT DOSE RELATED. Discontinue the drug immediately, administer Adrenaline, antihistaminics and corticosteroids. ANGIOEDEMA OF INTESTINES may occur leading vomiting, watery diarrhea and pain abdomen
PROTEINURIA	RARE. however ACE inhibitors provide protection against proteinuria due to diabetic nephropathy
ACUTE RENAL FAILURE	IF THERE IS Na loss or volume depletion there is increased aldosterone and Ang II formation as a compensatory mechanism . when ACE inhibitors are used they block this leading to renal failure. More so in RENAL ARTERY STENOSIS, HEART FAILURE OR DEHYDRATION **BUT REVERSIBLE IF ADEQUATE MEASURES ARE TAKEN**
DURING PREGNANCY	OLIGOHYDRAMNIOS, pulmonary hypoplasia, growth retardation and anuria **THE FOETOPATHIC EFFECT IF PARTLY DUE TO FETAL HYPOTENSION** **ONCE PREGNANCY CONFIRMED REPLACE BY A SAFER ANTIHYPERTENSIVE METHYLDOPA OR AMLODIPINE**

DRUG INTERACTIONS:

ACEI	K + sparing diuretics	Hyperkalemia
ACEI	Lithium & Digoxin	Their plasma levels may increase
ACEI	Antacids	Bioavailability of ACEI is decreased
ACEI	NSAIDS like aspirin and Indomethacin	Anti-hypertensive action of ACEI is reduced
ACEI	Allopurinol	Hypersensitivity to allopurinol may be enhanced

CONTRAINDICATED:

Pregnancy – all trimesters

Severe renal failure (caution if creatinine >2.5-3 mg/dl

Hyperkalemia requires caution or cessation

Bilateral renal artery stenosis or equivalent lesions

Preexisting hypotension

Severe aortic stenosis or obstructive cardiomyopathy

Allergy or hypersensitivity reactions

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