CONGESTIVE HEART FAILURE (CHF)

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Heart Failure (HF)

- Imbalance between cardiac output (CO) and Tissue Demand.
- Progressive disease – gradually detoriating cardiac performance.
- May be due to Systolic, Diastolic or Both Dysfunction.
- Clinically manifested as à Decrease Cardiac output , poor systolic pumping, pulmonary congestion and oedema, breathlessness (Dyspnoea),peripheral oedema, decreased renal output,cardiac hypertrophy, cardiac remodelling and decreased Ejection Fraction (<35%).

Heart Failure (HF)

SYSTOLIC DYSFUNCTION

- Insufficient ventricular wall tension
- Poor ventricular pumping
- Poor ventricular ejection of blood
- Progressive dilatation of ventricles
- Further ventricular inefficiency (Laplace Equation)
- Wall Tension = Intraventricular pressure x ventricular radius
- Reduced Ejection Fraction (EF < 35%)

Heart Failure (HF)
SYSTOLIC DYSFUNCTION

Causes are :-

- Coronary Artery Disease (CAD)
- Myocardial Infarction (MI)
- Dilated cardiomyopathy
- Viral Myocarditis
- Atrial Fibrillation (AF)
- Valvular incompetency

Heart Failure (HF)

DIASTOLIC DYSFUNCTION

Thickened Ventricular Wall

Left Ventricular Hypertrophy (LVH)

Inadequate relaxation during diastole

Impaired ventricular filiing

Reduced stroke volume

Normal Ejection Fraction (EF>35%)

Heart Failure (HF)

DIASTOLIC DYSFUNCTION

- Causes are :-
- Persistent long lasting hypertension
- Ageing and Myocardial stiffening
- Aortic stenosis
- Hypertrophic cardiomyopathy
- A-V shunts
- Congenital Heart Disease (CHD)

Heart Failure (HF)

- Compensatory mechanisms (Initial Hemodynamic Benefits) to overcome reduced cardiac output are :-

(1) Increase stroke volume (by elevation of filling pressure) (Frank - Starling compensation)- Produces à venous engorgementà hepatic enlargementà peripheral oedemaà pulmonary congestionà dyspnoea à renal congestion à Oliguria.

Compensatory mechanisms

(2) Sympathetic tone augmentation:-

i) Beta-receptor mediated cardiac stimulation à cardiac myocyte apoptosis à Fibrotic changes.

ii) Alpha receptor mediated vasoconstriction à increases cardiac afterload à increases peripheral resistance à restricts cardiac output

Compensatory mechanisms

(3) Activation of Renin-Angiotensin System (RAS)à Raised Angiotensin II à Causes Vasoconstriction à LVH à myocardial remodelling à Cell Death à Fibrosis.

(4) Overproduction of Aldosterone à Na++ retentionà K+ loss à Fibroblast proliferation à Ventricular remodelling

Compensatory mechanisms

(5) Increased Endothelin Production à Reinforces vasoconstriction à Cardiac and vascular myocyte proliferation à Fibrotic changes.

(6) HF à Atrial & ventricular distension à releases natriuretic peptides (ANP & BNP) à opposes vasoconstriction and Na+ retention.

AIMS OF HF DRUG THERAPY

1) (a) Relief of congestive or low output symptoms

(b) Restoration of cardiac performance

© Treatment of acute decompensation

Achieved by :-

i) Inotropic drugs – Digoxin, Dobutamine, dopamine, Inamrinone, milrinone

ii) Diuretics – Furosemide, thiazides, metazolone

iii) RAS inhibitors – ACE-Is, ARBs

iv) Vasodilators – Hydralazine,nitrates, nitroprusside

v) B-blockers – Metoprolol, Nebivolol, carvedilol

vi) Synthetic BNP - Nesiritide

AIMS OF HF DRUG THERAPY

2) **(a) Arrest or Reversal of Disease progression**

(b) Prolongation of survival.

Achieved By :-

i) ACE Inhibitors, ARBs

ii) Beta – Blockers

iii) Aldosterone antagonist – Spironolactone, Eplerenone

iv) Neprilysin inhibitors - Sacubitril

CHF classification

NYHA Functional Classification (New York Heart association)

1. **Class I**
2. **Class II**
3. **Class III**
4. **Class IV**

Class I

Functional capacity:

- Ø Pt. with cardiac disease but without resulting limitation of physical activity

- Ø Ordinary activity does not cause undue fatigue, palpitation, dyspnoea or anginal pain

Objective assessment

- Ø No objective evidence of cardio vascular disease

Class II

Functional capacity:

- Pt. with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest.

- Ordinary physical activity result in fatigue,palpitations,dyspnoea or anginal pain

Objective assessment

- Objective evidence of minimal cardiovascular disease

Class III

Functional capacity

- Pt. with cardiac disease resulting in marked limitation of physical activity. Comfortable at rest.

- Less than ordinary activity causes fatigue, palpitations, dyspnoea or anginal pain.

Objective assessment

- Objective evidence of moderately severe cardiovascular disease

Class IV

Functional capacity:

- Ø Pt. with cardiovascular disease resulting in inability to carry on any physical activity with out discomfort. Symptoms of anginal pain or heart failure may be present even at rest.

- Ø If any physical activity is under taken , discomfort is increased.

Objective assessment

- Ø Evidence of severe cardiovascular disease

CLASSIFICATION

1. Cardiac glycosides
- Digoxin, digitoxin
2. ACEIs :
- Enalapril , Lisinopril, Ramipril etc
3. Diuretics :
- Frusemide, Amiloride, HCTZ

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Hp1 Hp pc, 01-01-200

4. PDE III inhibitors
- Amrinone, Milrinone etc

5. Direct vasodilators
- Nitroprusside , Hydralazine etc

6. Others :
- Dobutamine, Xamoterol, Prazosin etc

CARDIAC GLYCOSIDES

1. Digitalis purpura (Leaf) : Digitoxin
2. Digitalis Lanata (Leaf) : Digoxin, Digitoxin
3. Strophanthus- Gratus (Seed) : Strophanthus- G (Quabain)

4. William Withering showed the use of Digitalis in the treatment of Heart Failure.

Chemistry : A glycoside consists of

1. **An aglycone ring- (Steroid nucleus with an attached Lactone ring)**

2. **Attached With Sugar moieties**

ACTIONS OF DIGITALIS IN CHF

1. HEART :

a) Direct action by inhibiting Na+ K+ - ATPase

b) Indirect action by stimulating Vagus nerve (Vagomimetic effect).

ACTIONS OF DIGITALIS IN CHF

(a) Myocardium Contractility :-

- +ve Inotropic Effect (↑ Force of Contraction of Heart)
- Complete emptying of ventricles during systoles --- ↑ COP
- ↓ Pulmonary congestion and systemic venous pressure
- ↓ Oxygen requirement of myocardium by reducing diastolic size of the heart and muscle fibres.

- Digitalised heart do more work for the same energy.

- Hence, Digitalis is more “Çardiotonïc”

b) Heart Rate : ↓

- Marked in CHF
- Improved circulation restores the diminished vagal tone
- Abolishes symph. overactivity
- Stimulates vagal centre
- Sensitize SA node to Ach
- Sensitize baroreceptors
- Direct anti-adrenergic action on SA & AV nodes

c) Conduction :

- A-V conduction prolonged

d) ECG:

- ↓amp or inversion of T- wave
- ↑ P-R interval
- Shortening of Q-T interval
- Depression of S-T segment

e) Excitability:

- ↑ at low, depressed at high doses

f) ERP :

- **Atrial usually ↓**
- **A-V node & bundle of His ↑**
- **Ventricles ↓**

MOA of DIGITALIS

Binds & inhibits Na+ / K+ /ATPase

↓

Progressive accumulation of iNa+

↓

Increases Intracellular Na^+

↓

Decreases extrusion of Ca2+ via Na+/Ca2+ exchanger

↓

Entry of Ca2+ into cardiac cell via L-Type Ca2+ channels during action potential

↓

Increases iCa2+

↓

Increases Ca2+ uptake & storage in SR

↓

Increases Releases more Ca^{2+} from SR

↓

↑ E-C coupling

↓

+ve inotropic action

↓

Increases Cardiac Output

ACTIONS(CONT)

2. Blood vessels :

CHF : ↓ in per. Resistance

Normal : no sig. action

3. Kidney :

- Diuresis

4. CNS:

- activation higher dose
- Confusion, Blurring of vision, disorientation

ADRs

1. Non- cardiac :

- G.I.T : A,N,V, abd pain, Diarrhoea
- Vision :
  - . Colour vision disturbance
  - . White vision
  - . Blurred vision
  - . Photophobia
  - . Diplopia , Scotomata

ADR (Contd)

CNS :

Headache , fatigue, malaise, drowsiness, neuralgic pain, confusion, delirium, disorientation, altered mood, restlessness

- **Others :**
  Gynaecomastia

(Digitalis – ADR)

2. Cardiac :

- Any types of arrhythmia, Ventricular premature beats
- Pulsus bigeminy , VES, VT, VF, A-V block , bradycardia , AF,AFI, atrial extrasystoles

Factors affecting Digitalis toxicity

- Age :- Elders due to poor renal & hepatic Fns
- Route : IV Digitalization more risk
- Hypokalaemia,
- Hypomagnesaemia,
- Hypothyroidism,
- Hypoxia,
- Hypercalaemia,
- Hyperthyroidism,
- Renal failure,
- Myocarditis

Treatment of cardiac toxicity

1. Stop Digitalis, pot. loosing diuretic (Thiazides, loop Diuretics)
2. Tachyarrhythmias : KCl I.V or orally
3. Vent. arrhy : IV lignocaine

   (i) Rapid onset, short duration

   (ii) Action fades on stopping infusion

   (iii) No action on AV node – Does not intensify AV block

1. SV arrhy : IV or oral propranolol
2. AV block / brady :- Atropine, Cardiac Pacemaker
3. Digibind (digoxin antibodies) :- In Severe Digitalis Toxicity → Neutralizes circulating digoxin & rapidly reverses the toxicity.

THERAPEUTIC USES OF DIGITALIS

1. CHF :

- Low out put failure due to AFI
- Beneficial Effects are due to :-+ve Inotropic Effect
- Venous system
- Kidney
- (NOT EFFECTIVE IN HIGH OUTPUT FAILURE due to severe anaemia, thyrotoxicosis, AV shunt).

2. Cardiac arrhythmias

(i) AFl : Atria beat at a rate of 350-600/min.

Digitalis → Direct & Indirect (Vagomimetic) action on AV node.→ Increases ERP, decreases conduction velocity → depresses AV node→ decreases ventricular rate. Propranolol, Verapamil use in AFl.

(ii)AF:- Atria beats at rate of 300/min.

Digitalis → Depresses AV conduction → Controls Ventricular rate.

(iii) PSVT (Paroxysmal Supraventricular Tachycardia) :- HR is 140-220/min.

Digoxin → not suitable due to slower onset, but useful in PSVT with Heart Failure. Terminates arrhythmias by increasing vagal tone.

PREPARATIONS

Digoxin :

0.25mg tab

0.5mg / 2ml amp inj

Digitoxin :

0.1mg tab

DIURETICS IN CHF

- **Loop Diuretics :** Furosemide, Bumetanide, Torsemide
- **Aldosterone Antagonists :** Spirinolactone, Eplerenone

LOOP DIURETICS IN CHF

- Furosemide, Bumetanide
- Used in all cases of symptomatic CHF treatment with diuretics
- **DOC** because :-
- i) Increases Salt and water excretion
- ii) Decreases Plasma volume & Oedema
- iii) IV Furosemide Mobilizes oedematic fluid from pulmonary circulation to systemic circulation à relieves pulmonary congestion & oedema à relieves Dyspnoea (Breathlessness)
- iv) Have natriuretic activityà decreases preload à decreases venous pressure à decreases circulating volume à remove peripheral oedema & Pul. Congestion à Increases cardiac performance
- v) Only improve symptoms & not disease

LOOP DIURETICS IN CHF

- **Precautions to be observed with Diuretics** :-
- i) Use cautiously
- Ii) Avoid excessive diuretics
- Iii) Causes Dehydration, electrolyte imbalances
- Hypokalaemia à predisposes to digitalis toxicity (Closely monitor CHF patients)
- Use Thiazides when lesser degree of diuresis is required to treat CHF patients.

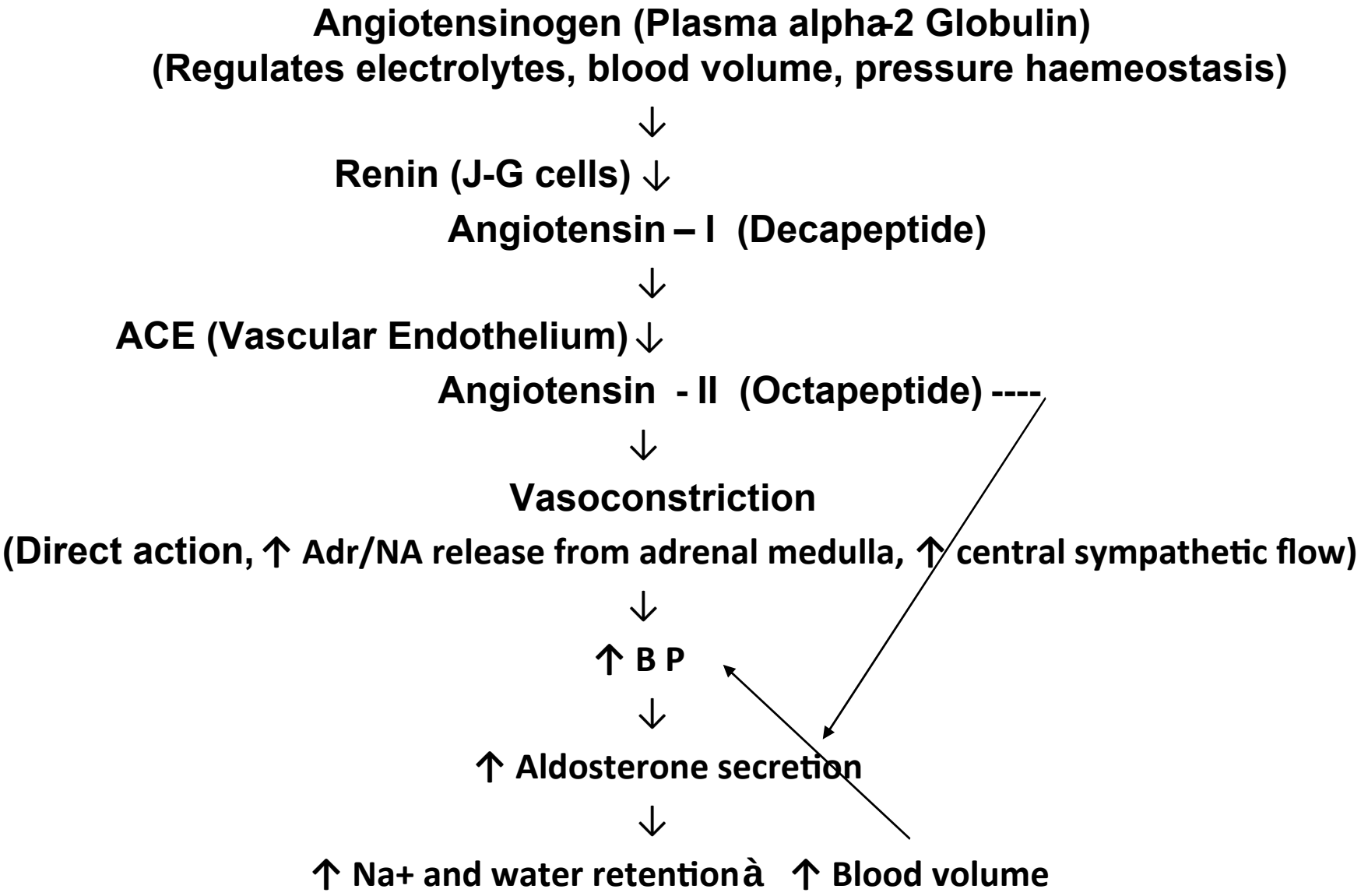
ALDOSTERONE ANTAGONISTS DIURETICS IN CHF

- **(Spirinolactone, Eplerenone)**
- **Role of Aldosterone in CHF :-**
- Increase Angiotensin II production à Increases Aldosterone plasma levels à Increase Sodium & water retention à Increases blood volume à Increases BP à worsens progression of CHF disease symptoms
- Has direct and indirect effects
- A) Expansion of ECF volume à Increases cardiac preload
- B) Fibroblast proliferation à Fibrotic changes in myocardium à worsens systolic dysfunction à causes cardiac remodelling
- C) Hypokalaemia, hypomagnaesemia à increases the risk of ventricular arrhythmias & sudden cardiac death

ALDOSTERONE ANTAGONISTS DIURETICS IN CHF

- Role of Aldosterone Antagonists in CHF (**Spirinolactone, Eplerenone)**
- Antagonises all above effects à Indicated as Add-on – Therapy to ACE-Is/ARBs + other drugs in moderate to severe CHF
- Retards disease progression à Reduces episodes of decompensation, death due to CHF / sudden cardiac death
- Use lower dose of Aldosterone antagonists (12.5 – 25 mg / Day) to avoid Hyperkalaemia due to concurrent use of ACE-Is / ARBs
- Help restoration of diuretic response to furosemide when refractoriness have developed
- Slow onset à But significant prognosis benefit
- C/I in renal insufficiency (risk of hyperkalaemia)
- Causes Gynaecomastia in Males (Monitor spironolactone level)

Renin Aldosterone Angiotensin System (RAAS)



Consequences of↑ Aldosterone – II Levels in CHF Patients

i) **Severe vasoconstriction** à ↑ BP

ii) **↑ Aldosterone secretion à** ↑ Na+ & water retention à ↑ Blood volume à ↑ BP à ↑ Peripheral oedema

iii) **Promotes movement of fluid from vascular to extra vascular compartment**

iv) **Chronically induces :-**

(a) Hypertrophy, Hyperplasia, ↑ intracellular matrix production

(b) Volume overload, ↑ tpr à Hypertrophy & cardiac remodelling (abnormal distribution of body muscle mass)

(c) Vessel wall & intimal thickness à Ventricular hypertrophy à Fibrosis à progressive cardiac myocyte death (Apopstosis) à Fibrotic transformation à CHF à ↑ Morbidity & Mortality

ROLE OF ACE -Is in CHF

- Causes both arteriolar & venodilation in CHF
- Reduces Preload & Afterload
- ↓ right arterial pressure, ↓ pulmonary capillary wedge pressure, ↓ systemic vascular resistance, ↓ systolic wall stress à ↓ systemic BP
- ↑stroke volume à ↑ COP à ↓ HR à Diuresis initially
- Inhibits ANG-II & Aldosterone production à ↑ Na= & water excretion à improve renal perfusion à ↓ Cardiac work
- Enhances exercise capacity of CHF pts
- Retards progression of Left ventricular systolic dysfunction
- Produces regression of Left ventricular Hypertrophy
- Prevents cardiac remodeling

ROLE OF ACE -Is in CHF (contd..)

- Prolongs survival of CHF pts of all grades (Class I to IV)
- Decrease episodes of decompensation, MI, sudden death
- Sustains beneficial effects with chronic therapy
- Improves Haemodynamic functions
- Long term benefits of AVC-Is accrue from withdrawal of ANG II – mediated ventricular hypertrophy, cardiac remodelling, accelerated cardiac myocyte apoptosis & fibrosis
- Indirect benefits occurs due to :-

(i) Reduction in sympathetic activation

(ii) Decrease in Aldosterone levels

(iii) Finally, improves NYHA Functional class in most CHF pts.

Sympathomimetic Inotropics

- (Dobutamine, Dopamine)
- Have Beta-adrenergic & dopaminergic (DA) agonistic action
- Have +ve inotropic action (↑ force & contraction of cardiac muscles)
- Have Vasodilator property at low dose
- (**Hence, above properties help combat emergency pump failure in CHF)**

DOBUTAMINE

- Dose :- 2-8 mcg/kg/min IV infusion
- Selective B-1 agonist
- Prominent inotropic action
- IV infusion for acute CHF with MI, cardiac surgery to tide crisis in advanced decompensated CHF
- Does not raise (But lowers) systemic resistance à Preferred in HF

DOPAMINE

- Dose :- 5-10 mcg/kg/min by IV infusion
- Low Dose :- (< 5mcg/kg/min) IV infusion à selectively stimulates DA1 receptors of renal blood vessels à renal vasodilatation à Increases renal perfusion à Increases GFR à Restores diuretic response to Furosemide in refractory CHF
- Intermediate dose :- (5-10 mcg/kg/min) stimulates B-1 adrenoceptors of heart à produces +ve inotropic & chronotropic effectà useful in cardiogenic shock
- Long term chronic use of Dopamine à produces tolerance & increases cardiotoxic potential à Therefore, not used in management of CHF for long term.

Beta –Blockers in CHF

Role of Beta-adrenoceptor stimulation in Pathophysiology of Heart Failure

- Excessive & chronic sympathetic stimulation contributes to :

(a) Tachycardiaà ↑ Oxygen demand à ↑ infarct size à ↑ propensity of cardiac remodeling

(b) ↑ RAAS activation à ↑Ventricular hypertrophy à ↑ apoptosis à ↑ Fibrosis à Cardiac remodeling

(c) Leads to Myocyte hypertrophy à Apoptosis à Cardiac dilatation à Ventricular wall thinning

(d) ↑ Production of cardiac cytokines (TNF-α , Interlukines) à induces cardiac myocytes hypertrophy à apopstosis à alteration in intracellular matrix à Fibrosis à Ventricular wall stiffness

Role of Beta –Blockers in CHF

Benefits of Beta-Blockers Therapy in HF

(i) B-Blockers used in daily dose range are Carvedilol (12.5-25 mg/d), Metoprolol (10-100 mg/d), Bisoprolol (1.25 – 10 mg/d) & Nebivolol (1.25 mg/d).

(ii) Reduces excessive sympathetic stimulation of heart

(iii) Improves cardiac function, antagonizes ventricular wall stress enhancing (ventricles hypertrophy), inhibits apoptosis promotion & prevents pathological cardiac remodeling in HF.

(iv) Improves left ventricular ejection fraction, improves cardiac performance, reduces mortality and prevents cardiac sudden death due to anti arrhythmic property.

(v) Lowers plasma markers of acivation of sympatheic system, RAAS and endothelin-I.

Role of Beta –Blockers in CHF

Benefits of Beta-Blockers Therapy in HF

CARVEDILOL :-

i) 3rd Generation B- Blocker à inhibits B1 & B2 as well as alpha-1 adrenoceptors (vasodilator)

ii) Carvedilol & its metabolites have anti-oxidant effect

iii) Exhibits anti-inflammatory, anti-RAAS & anti-apoptotic properties

iv) Hence, **Carvedilol** à known as '**Multiple action Neurohumoral antagonist)**

v) ↑Left Ventricular Ejection Fraction (LVEF), Slows disease progression

vi) Reduces both hospitalization & mortality

Role of Beta –Blockers in CHF

Benefits of Beta-Blockers Therapy in HF

vii)Recommended for all patients with HF without significant hypotension, pulmonary congestion or AV blockade

viii) **Adverse effects of Carvedilol** are :-

Bradycardia, Worsening of HF, Dizziness, Light Headedness by vasodilatation, Fall in BP.

GUIDELINES FOR USING B-BLOCKERS in HF

- B-Blockers preferred are Carvedilol (α +β blocker),& β1 blockers (Metoprolol, Bisoprolol & Nebivolol).
- Preferred in selected cases of dilated cardiomyopathy with systolic dysfunction, NYHA class II & III (mild to moderate)
- Avoided in severe decompensated heart failure, asymptomatic left ventricular dysfunction and acute HF.
- Start treatment with low dose and increase gradually (titrated upwards) to maximum (target) dose as per the response for maximum benefit. Benificial effect is gradual and occurs after 4-8 weeks of treatment.
- Abrupt withdrawal should be avoided as it may worsens HF, precipitate ischaemia or MI or ventricular arrhythmias in IHD patients.
- Discontinue treatment if acute failure develops during treatment.

Phosphodiesterase -3 (PDE3) inhibitors

- Inamrinone(amrinone), Milrinone, Levosimendon
- Called ‘Inodilators’ (produces both positive inotropic and peripheral vasodilator effects)
- Selectively inhibits PDE-3 enzyme in heart & blood vessels à inhibits intracellular degradation of cAMP à ↑ myocardial cAMP levels & transmembrane influx of Ca2+.
- Decreases both preload & afterload on heart à decreases systemic vascular resistance.
- Avoided in patients with hypotension because they produces vasodilatation.
- Both are used in Loading dose initially followed by i.v. infusion. Both are unstable in Dextrose solution.

Phosphodiesterase -3 (PDE3) inhibitors

- **Inamrinone (amrinone) :-**
- In CHF à IV amrinone OOA is 5Min, DOA is 2-3 Hrs, Elimination t1/2 is 2-4 Hrs
- It ↑cardiac index, left ventricular ejection fraction, decreases peripheral vascular resistance, CVP, left ventricular end diastolic volume & pressure accompanied by tachycardia & slight fall in BP.
- 0.5 mg/kg bolus injection followed by 5-10 mcg/kg/min i.v. infusion. (Max. 10 mg/kg in 24 hrs)
- S/Es :-Thrombocytopenia, liver damage, arrhythmias.
- Uses :-
- As an adjuvant therapy for short term i.v. use in severe & refractory CHF with conventional drugs like diuretics, digitalis & vasodilators

Phosphodiesterase -3 (PDE3) inhibitors

- **Milrinone :-**
- Similar as Amrinone. But more selective PDE3 inhibitor & 10 times more potent, fewer side effects than amrinone. Is shorter acting. T1/2 is 40-80 min
- Increases myocardial contraction, increases cardiac output,& reduces peripheral vascular resistance due to vasodilatation.
- Dose : Loading dose of i.v. 50 mcg/kg followed by i.v. infusion 0.25 – 1 mcg /kg/min.
- Uses ;-
- Emergency control of HF or before transplantation
- Short term management of advanced/severe/acute HF
- S/Es ;- rarely Thrombocytopenia, arrhythmias on prolonged use causing increase mortality.

Phosphodiesterase -3 (PDE3) inhibitors

Levosimendon :-

- Is Inodilator
- Inhibits PDE3 à increases cAMP levels
- Acts by sensitizing cardiac muscle to action of Ca2+
- Activates ATP sensitive K+ channel in vascular smooth muscles
- Useful in severe heart failure and shock
- Used as i.v. infusion preceded by i.v.loading dose.

Vasopressin Antagonists in HF

- **Conivaptan (IV), Tolvaptan (Oral)**
- In acute heart failure (HF with acute decompensation)à develops Hyponatraemia due to increase activity of vasopressin.

- Vasopressin antagonists are found to be effective in above cases, but lacks long term benefits in terms of decreasing mortality.

- **Tolvaptan:-**
- Orally effective, non-peptide, selective V2 receptor antagonist.
- More suitable for HF with hyponatraemia.
- Also used in SIADH (Syndrome of Inappropriate ADH secretion by correcting water retention & hyponatraemia.
- Provides short term benefits in HF by excretion ofwater,restores Na+ level & relief in dyspnoea.
- **Dose :-** Oral 15-30 mg OD

Parenteral Vasodilators

- **Sodium nitroprusside, Hydralazine, Glyceryl trinitrate (GTN) & Natriuretic peptides**

1) Sodium Nitroprusside :-

* Is a potent vasodilator,Both venodilator & arteriodilator

* Reduces both preload (ventricular filling pressure à reduces oedema) and afterload (systemic peripheral vascular resistance à increases cardiac output)

* Useful in severe decompensated HF (Acute HF)

* Also used for rapid control of severe hypertension

2) Hydralazine :-

* Is a vasodilator, produces arterio dilatation only.

*Used with GTN in acute HF

3) GTN :- Potent venodilatation--. Reduces preload (low dose), reduces afterload & peripheral resistance (high dose)

Parenteral Vasodilators in HF

Natriuretic Peptides

1) Arterial natriuretic peptides **(ANP)**, Brain natriuretic peptides **(BNP)** & C-type natriuretic peptides are endogeneous hormones à have potent natriuretic, diuretic & vasodilator properties.

2) **BNP** is secreted by ventricular cardiac myocytes

Increase circulating level of BNP in HF overcome effect of angiotensin & NA by producing natriuresis, diuresis & vasodilatation.

3) Increase levels of BNP in HF patients are used for diagnostic as well as prognostic purpose.

4) Example ;- **Nesiritide**

Nesiritide

- Is a recombinant human brain natriuretic peptide (BNP).
- Has natriuretic, diuretic,vasodilator effect with short term infusion
- Dilates both capacitance and resistance vessels (↑cGMP levels)
- Eliminated by intracellular proteolysis & dose adjustment not needed in renal dysfunction
- Reduces ventricular filling pressure à Relieves dyspnoea à useful in acute decompensated HF à has short term benefit
- Less chances of arterial & ventricular arrhythmias à useful in relieving dyspnoea in refractory cases HF with risk of arrhythmia
- Prolonged use à lead to potential fatal renal damage & avoided if SBP < 90 mmHg as it causes hypotension which is reversible on discontinuation of drug (t1/2 is 18 min).
- Dose :- Loading dose 2 mcg/kg i.v. followed by iv infusion of 0.01 mcg /kg/min..Max 0.03 mcg/kg/min.

DRUGS FOR ACUTE HF

- Emergency treatment with parenteral drugs. Patient is hospitalized

1) Diuretics :-

Loop Diuretics (Furosemide IV) alone or in combination with Dopamine and Milrinone.

2) Parenteral vasodilators :-

Sodium nitroprisside, hydralazine, glyceryl trinitrate or Nisertitide

3) Inotropic drugs :-

Dobutamine, Dopamine, Milrinone

DRUGS USED IN CHRONIC HF

- Drugs used by oral route mainly

1) **Diuretics :** Furosemide, Thiazides, Spirinolactone

2) Vasodilators : ACE inhibitors, ARBs, Organic nitrates (Isosorbide dinitrate) & GTN, Hydralazine, CCBs (Amlodipine)

3) B- blockers : Carvedilol, Metoprolol, Bisoprolol, Nebivolol

4) Cardiac Glycosides : Digitalis

T H A N K Y O U

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