
بسم الله الرحمن الرحيم

THERAPEUTIC USES of Sympathomimetics (adrenergic drugs)

By

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Therapeutic uses;

➢CVS;

- **Acute hypotension;**
  - **Identification of the *cause* & its treatment.**
  - Supportive measures --- ***recumbent position & adequate I/V fluid.***
  - ***Sympathomimetic drugs;***
    - **Direct acting α agonist (Phenylephrine…ephedrine)----** in hypotensive emergency to preserve the cerebral, coronary and renal blood flow.
- **Chronic orthostatic hypotension;**
  - **α_1 agonist: Midodrine** (Orally active α_1 agonist), **Phenylephrine or ephedrine.**

- **Spinal shock (neurogenic shock);**
  - phenylephrine, **ephedrine** --- By inhalation or parenteral route.
    - ✓ Duration of action 15-60 minutes.
- **Cardiogenic shock and AHF;**
  - **+ve** ionotropic agents such as **Dopamine, dobutamine & dopexamine.** Drugs of choice in Cardiogenic shock.
  - **Dobutamine;**
    - Relatively selective β1 agonist.
    - No effect on dopamine receptors.
    - Increases cardiac output with limited vasodilation activity and reflex tachycardia.
    - I/V infusion because of its short half life (t ½ = 2 minutes).
  - **Dopamine** (D_1, β1, α (large dose);
    - Low doses ---- Dopaminergic receptors (D_1 --- renal, coronary & splanchnic Blood Vessels).
    - Moderate dose --- β1 agonist activity --- ↑ in contraction and cardiac output.
    - High doses --- α_1 receptors in Blood Vessels causing vasoconstriction -- ↑ TPR --- ↑ systolic and diastolic blood pressure.

- **Dopexamine;**
  - An analogue of dopamine.
  - Activates β 2 + D 1+ D2.
  - Vasodilatation of splanchnic and renal vessels.
  - Weak ionotropic.

Anaphylaxis;

- What is the drug of choice in Anaphylaxis?
- **Adrenaline;**
  - **Physiological antagonism of mediators of anaphylaxis.**
  - **Dose & Route of administration of adrenaline;**
    - 0.3 to 0.5 ml of 1:1000 solution S/C, I/M.
    - For a severe reaction repeated doses at an interval of 5-20 minutes.
    - Absorption by S/C route is unpredictable in hypotensive patient.
    - **i/v infusion** with impaired cardiovascular function (shock) 2 ml diluted 1;10,000 at 5-10 minutes interval.

- **Anaphylaxis –Secondary therapy;**
  - The adrenaline is supplemented with
    - **Glucocorticoids and antihistamines.**
    - **I/V fluids** - normal saline for replacement of intravascular volume due to postcapillary venular leakage.

- **Route of administration of adrenaline;**
  - Can Adrenaline be given as I/V bolus? **Yes or No**
  - Adrenaline should never be given as I/V bolus **except during CPR** of cardiac arrest.
  - Why? To avoid **fatal cardiac arrhythmias.**
- **IV isoproterenol** and **adrenaline**.
  - To **restore cardiac activity** in **Cardiac arrest** during CPR.
  - Temporary emergency management of **complete heart block.**
  - Electronic pacemakers are both safe and more effective.
- **Which type of shock is made worse by vasoconstrictors?**
  - **Shock due to septicemia or myocardial infarction,** because sympathetic discharge is usually already increased.

To reduce regional blood flow; (via vasoconstriction);

- Alpha receptor activation;
- To achieve hemostasis **(epistaxis).**
  - **Epinephrine in nasal packs for epistaxis.**
    - Cocaine (hemostatic effect + local anesthesia).
- To **reduce diffusion of local anesthetics** away form administration site.
  - Epinephrine 1:200,000
  - Norepinephrine, phenylepherine, and other α agonist may be used.
- To achieve **hemostasis in surgery** by **local application.**
  - For facial, oral, and nasopharyngeal surgery.

Nasal decongestants; (α receptor activation)

- **To reduce mucous membrane congestion;**
  - To reduce the discomfort of hay fever, common cold.
  - May cause **Rebound hyperemia.**
  - **Regular use for long periods should be avoided.**
    - Impaired ciliary function.
    - Atrophic rhinitis.
    - Anosmia.
  - Imadazoline compounds
    - Xylometazoline ------0.1 % nasal drops
    - Oxymetazoline ----- 0.05 % nasal drops
    - Naphazoline --------0.1 % nasal drops
  - Phenylepherine
  - Pseudoephedrine

Bronchial asthma and COPD;

To treat bronchospasm;

- **Non selective agonists (β1 & β2 + α)** – Adrenaline, Isoprenaline.
- **beta selective agents** (isoproterenol) and
- **β2 selective drugs are as effective as and less toxic than the less selective agents.**
- **Short acting;**
  - Salbutamol(albuterol)
  - Pirbuterol
  - Terbutaline
- **Long acting ---- dose /12 hours;**
  - Salmeterol
  - Formeterol
    - Inhalor
    - Salmeterol has a delayed onset of action than formeterol

Ophthalmic uses;

- **Mydriatic agents;**
  - Phenylepherine
- **Decongestant** for minor allergic hyperemia of the conjunctiva.
- In localizing lesion in **Horner's syndrome**
  - **Postganglionic lesion;**
    - Indirectly acting sympathomimetic (cocaine, hydroxyamphetamine) will not dilate abnormally constricted pupil.
    - Pupil will dilate in response to directly acting phenylephrine.
  - **Preganglionic lesion;**
    - Normal response to both drugs.
- **Glaucoma;**
  - **Epinephrine and beta-blocking agents.**
    - **Epinephrine** Topical 1-2 % solution lowers intraocular pressure primarily by increasing aqueous flow.
  - **Dipivefrin** is a prodrug of **epinephrine.**
    - Enhanced penetration into the anterior chamber of the eye.
  - **Apraclonidine, Brimonidine are an alpha 2 agonists.**
    - lower intraocular pressure and is used after laser therapy.

Genitourinary applications;

- In the treatment of **stress incontinence.**
  - Oral sympathomimetic therapy is occasionally useful.
    - **Ephedrine or pseudoephedrine** may be tried.
- **Uterine relaxant;**
  - β 2 selective agents relax the pregnant uterus.
    - Ritodrine,
    - Isoxsuprine,
    - Salbutamol,
    - Terbutaline.

CNS applications;

- **Mood elevating (euphoriant)effect**: (drug abuse)
  - Amphetamine like sympathomimetics.
- **Treatment of narcolepsy;**
  - Alerting, sleep deferring action (Amphetamines).
- **Treatment of obesity (Anorectics);**
  - Appetite suppressing effect.
    - **Serotonergic agents;** (Serotonin reuptake inhibitor)
      - Fenfluramine
      - Dexfenfluramine (dextroisomer of fenfluramine)
    - **Noradrenergic/ serotonergic agent;**
      - Sibutramine; Inhibit the reuptake of both NA as well as 5-HT.
- **Attention –deficit hyperkinetic syndrome of** children. Amphetamines.

Toxicity of sympathomimetics

- **Excessive vasoconstriction;**
  - **Tissue necrosis** due to intense vasoconstriction may occur in fingers and toes following the use of **infiltration of local anaesthetics combined with adrenaline.**
  - **Marked elevation in BP** which may cause **cerebral hemorrhage or pulmonary edema.**
  - **Increased cardiac work** may **precipitate severe angina or MI.**
    - **Anginal pain** is readily induced by adrenaline in patients suffering from angina pectoris.
- **Cardiac arrhythmias,**
  - **Cardiac arrhythmias** are liable to occur if adrenaline is given during general anaesthesia with halothane.
  - **β stimulant drugs;**
    - **sinus tachycardia,**
    - **ventricular arrhythmias.**
  - **Special caution** is indicated in
    - Elderly patients,
    - Hypertension,
    - Coronary artery disease.

CNS toxicity;

- **Phenylisopropylamines** commonly cause
  - Restlessness, tremor, insomnia and anxiety
  - In very high doses paranoid sate may be induced.
- **Cocaine** may precipitate convulsions, cerebral hemorrhage, arrhythmias or MI.

Contraindications/drug interactions;

- Hypertension,
- Ischemic heart disease,
- Tachyarrhythmias,
- Peripheral vascular diseases,

- **Drug interactions;**
  - Halogenated general anaesthetics.
    - Hypercapnia and hypoxia have a potent aggravating effect.
  - Digoxin and tricyclic antidepressants.
  - Hyperthyroidism.

Special sympathomimetics;

Cocaine;

- Heavily abuse drug------ smoked, snorted, or injected.
- Local anesthetic.
- Peripheral sympathomimetic.
  - Inhibit reuptake of NA.
- Enters the CNS and produce amphetamine like effects, Shorter lasting and more intense.
- Inhibit dopamine reuptake into neuron in the "pleasure centers" of brain.

Tyramine;

- A normal by product of **tyrosine metabolism** in the body + fermented foods – cheese.
- Metabolized by MAO.
- Very high first pass effect when taken orally.
- An **indirect sympathomimetic** action caused by release of stored catecholamines (Actions similar to NA)
- **Patients on MAO inhibitors** ---effect of tyramine is greatly intensified ---- marked increased in BP.
  - **Eat pizza and die of hypertension.**


Thank You