Current Cardiovascular Pharmacology

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This Presentation is Approved for
1 CRCE Credit Hour

Learning Objectives

- Explain the actions, effects, indications, adverse effects, & precautions for agents from the following drug categories
  - Cardiotonic agents
  - Antidysrhythmic agents
  - Nitrates
  - Miscellaneous cardiovascular agents

Cardiotonic Agents

Epinephrine

- Actions
  - Alpha1: vasoconstriction
  - Beta1:
    - Chronotropic: heart rate
    - Inotropic: contractility
    - Dromotropic: conductivity
  - Beta2: smooth muscle relaxation
    - Bronchodilation
    - Vasodilation

- Effects
  - Increase systemic vascular resistance (SVR), blood pressure (BP), peripheral blood flow
  - Increase coronary & cerebral blood flow
  - Increase myocardial electrical activity → increased automaticity → increased HR
  - Increase myocardial contractility
  - Increase myocardial O₂ requirements

Epinephrine

- Indications
  - Resuscitation
  - Shock, including anaphylaxis
  - Severe asthma
Epinephrine

- **Routes**
  - Intravenous (IV)
  - Subcutaneous (SC)
  - Endotracheal tube (ETT) - double IV dosage

- **Adverse effects**
  - Hypertension
  - Myocardial infarction
  - Tachycardia
  - Peripheral tissue blood flow impairment (ischemia)

Norepinephrine (Levophed)

- **Actions:** alpha, beta1 adrenergic
- **Effects**
  - Increased SVR → increased BP
  - Increased HR
  - Positive inotropic

- **Indication:** neurogenic or septic shock

- **Adverse effects**
  - Myocardial hypoxia → infarction
  - Renal failure
  - Hypertension
  - Necrosis of exposed tissues
  - Peripheral ischemia

Dopamine

- **Actions:** alpha1, beta1 adrenergic, dopaminergic
- **Effects** (dose-dependent)
  - Low dose: Cerebral, renal, mesenteric vasodilation
  - Moderate dose: increase cardiac output
  - High dose: generalized vasoconstriction

- **Indications**
  - Hypotension (shock)
  - Decreased urinary output
Dopamine

- Adverse effects
  - Tachycardia
  - Renal necrosis
  - Peripheral tissue necrosis
  - Dysrhythmias

Vasopressin (Pitressin)

- Synthetic endogenous hormone: antidiuretic hormone
- Effects
  - Anti-diuresis
  - Vasoconstriction
  - Stimulation of ACTH release

FYI see links below for information on vasopressin

Vasopressin (Pitressin)

- Indications
  - Cardiac arrest
  - Shock
    - Septic
    - Hypovolemic
  - Diabetes insipidus: accompanies head trauma

Neosynephrine (Phenylephrine)

- Action: alpha adrenergic
- Effect: potent vasoconstrictor
- Indications
  - Non-hypovolemic shock
  - Mucosal edema: post-extubation?
  - Mucosal bleeding
  - Prolong action of local anesthetics
- Adverse effects: tissue ischemia

Dobutamine

- Actions: alpha, beta1, beta2 adrenergic
- Effects
  - Positive inotropic → increased cardiac output
  - Mild peripheral vasodilation → decreased PVR, SVR, increased coronary perfusion
  - Does NOT increase myocardial O₂
  - Combined with dopamine → maintain BP, without increasing PAP

Dobutamine

- Indications
  - Acute congestive heart failure (CHF)
  - Right ventricular failure
**Milrinone (Primacor)**

- **Action:** phosphodiesterase inhibitor
- **Effects**
  - Inotropic
  - Vasodilation

**Indications**
- Cardiomyopathy
- Congestive heart failure
- Pulmonary arterial hypertension (PAH)

**Digitalis Glycoside: Digoxin**

- **Action:** increased Ca++ in myocardium
- **Effects**
  - Positive inotropic
  - Negative dromotropic → depresses AV conduction

**Indication**
- Specific dysrhythmias
- Chronic CHF

**Adverse effects:** digitoxicity more likely with hypokalemia
- Multiple types of dysrhythmias
- Agitation
- Nausea & vomiting

**Antidysrhythmic Agents**
Atropine
- Action: parasympatholytic
- Effects (cardiac)
  - Increased SA node automaticity → increased HR
  - Increased AV node conductivity
- Indications
  - Bradycardia
  - Heart block
  - Asystole: may be worth a try
- Routes
  - IV
  - Instillation through ETT
- Side effects: tachycardia

Lidocaine
- Action: sodium channel blocker
- Effects
  - Decreased automaticity
  - Decreased conductivity
  - Increased threshold for fibrillation
- Indications: rapid ventricular dysrhythmias
- Routes
  - ETT administration → double dose
  - IV
- Adverse effects
  - Psychoses, seizures
  - Decreased contractility
  - Heart block: asystole
  - Increased threshold for defibrillation
  - Lethal if given for heart block with escape beats

Amiodarone (Cordarone)
- Action: multiple ion channel blocker
- Effects
  - Decreased AV conduction
  - Decreased sinus node function
- Indications: dysrhythmias
- Adverse effects (circulatory)
  - Hypotension
  - Bradycardia
- Adverse effects (pulmonary): occurs over days-years of treatment
  - Pulmonary oxygen toxicity
  - Interstitial pneumonitis
  - Pulmonary infiltrates
  - Organizing pneumonia ± bronchiolitis obliterans (BOOP)
  - Pulmonary fibrosis
FYI see links below for article on amiodarone toxicity
Amiodarone (Cordarone)
- Adverse effects (pulmonary)
  - A-C membrane permeability edema with or without ARDS
  - Alveolar hemorrhage
  - Bronchospasm
  - Laryngeal edema
  - Anaphylactic shock
  - Pleural effusion
  - Pleural / pericardial thickening

Dronedarone (Multaq)
- Indication - atrial fibrillation / flutter
- Contraindications
  - Severe heart failure
  - Liver disease
- Less effective than amiodarone
- Fewer adverse effects
- Hepatotoxic
- More expensive than amiodarone, but reduces hospitalization for AF
  FYI see links below for article on dronedarone

Beta Adrenergic Blockers
- Action: beta1 blockade
- Effects
  - Decreased HR
  - Decreased vascular resistance
  - Decreased contractility
  - Decreased conductivity
  - Decreased myocardial O$_2$ consumption

Beta Adrenergic Blockers
- Indications
  - Angina
  - Hypertension
  - Post-MI
  - Inhibit ventricular response to atrial flutter, fibrillation

Beta Adrenergic Blockers
- Side effects
  - Hypotension
  - CHF
  - Bronchospasm: non-selective agents

Beta Adrenergic Blockers
- Agents
  - Propanolol (non-selective)
  - Atenolol
  - Metoprolol
  - Sotalol (Betapace): non-selective
  - Esmolol: short duration of action
  - Nadolol (Corgard): non-selective
  - Sotalol (Betapace)
Calcium Channel Blockers

- **Action:** block entry of Ca++ to myocardium
- **Indications**
  - Angina
  - Dysrhythmias, e.g. PSVT
  - Hypertension

Calcium Channel Blockers

- **Agents**
  - Verapamil (Calan, Isoptan)
  - Diltiazem (Cardizem)
  - Amlodipine (Norvasc)

Magnesium Sulfate

- **Action:** replacement for depletion of Mg++
  - Malnourishment
  - Alcoholism
- **Effects**
  - Reverses torsades des pointes
  - Relaxes bronchial smooth muscle
  - Relaxes uterine muscle

Magnesium Sulfate

- **Indications**
  - Hypomagnesemia
  - Torsades des points VT
  - Status asthmaticus
  - Pre-eclampsia / eclampsia
- **Adverse effects:** minimal

Sodium Nitroprusside (Nipride)

- **Effects:** vasodilation, arterial & venous
- **Indications**
  - Hypertensive emergency
  - LV failure

Nitrates
Sodium Nitroprusside (Nipride)

- Adverse effects:
  - Cyanide poisoning
  - Hypotension
- Precaution: avoid exposure of agent to light

Nitroprlycerine

- Effect: decreased SVR → decreased afterload & preload
- Side effects: hypotension, headache
- Indication: angina pectoris, AMI
- Preparations: sublingual tablets, IV, patches

Miscellaneous Agents

Nitroglycerine

- Effect: decreased SVR → decreased afterload & preload
- Side effects: hypotension, headache
- Indication: angina pectoris, AMI
- Preparations: sublingual tablets, IV, patches

Nesiritide (Natrecor)

- Synthetic recombinant brain natriuretic peptide (BNP)
  - Potent vasodilator
  - Rapid reduction in PCWP
- FDA approval in 2001
- Indication
  - Severe decompensated CHF
  - Dyspnea at rest or minimal activity

FYI see links below for article on nesiritide

Angiotensin Converting Enzyme (ACE) Inhibitors

- Action: block conversion of angiotensin I to angiotensin II
- Effect: vasodilation
- Indications
  - Hypertension
  - Heart failure
- Side effect: chronic, dry cough
Angiotensin Converting Enzyme (ACE) Inhibitors

- Side effects
  - Chronic, dry cough
  - Angioedema: airway obstruction

FYI see links below for info on ACE inhibitors

ACE Inhibitors

- Agents
  - Lisinopril (Zestril, Prinivil)
  - Ramipril (Altace)
  - Enalapril (Vasotec)
  - Benazepril (Lotensin)
  - Captopril (Capoten)

Summary & Review

- Cardiotonic agents: simulatory cardiovascular effects
  - Epinephrine
  - Norepinephrine
  - Dopamine
  - Dobutamine
  - Milrinone
  - Vasopressin
  - Digitalis

Summary & Review

- Antidysrhythmic agents
  - Atropine
  - Lidocaine
  - Amiodarone
  - Beta adrenergic blockers
  - Calcium channel blockers
  - Magnesium sulfate

Summary & Review

- Nitrates: vasodilators
  - Sodium nitroprusside
  - Nitroglycerine

- Miscellaneous agents
  - Nesiritide: vasodilator for severe CHF
  - ACE inhibitors: antihypertensive