Pharmacology of Antiarrhythmics and Vasoactive Substances

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Objectives

- Overview of Antiarrhythmic and Vasoactive Medications
  - actions
  - pharmacokinetics
  - indications
  - dosing and Administration
  - adverse effects
- Classification of Antiarrhythmics
- Cardiac Arrest Medications
Antiarrhythmic Classification

- **Class I - Fast Channel Blockers**
  - *Ia - Quinidine, Disopyramide, Procainamide*
  - *Ib - Lidocaine, Phenytoin, Mexilitine, Tocainide*
  - *Ic - Ecainide, Flecainide, Propafenone, Indecainide, Moricizine*
Antiarrhythmic Classification

- **Class II - Beta Blockers**
  - Propanolol, Acebutolol, Atenolol, Betaxolol, Bisoprolol, Esmolol, Labetalol, Metoprolol, Nadolol, Oxprenolol, Penbutolol, Pindolol, Sotalol, Timolol
Antiarrhythmic Classification

- **Class III**
  - Bretylium, Amiodarone, Sotalol

- **Class IV - Calcium Channel Blockers**
  - Verapamil, Diltiazem

- **Unclassified - Digoxin, Adenosine, Mg**
Procainamide - Actions

- **Suppresses automaticity**
  - decreasing the rate and amplitude of phase 4 diastolic depolarization
  - prolongs action potential duration
  - reduces the speed of impulse conduction
  - suppresses fibrillatory activity in the atria and ventricles

- **Dose dependant anticholinergic activity**
Procainamide - Actions

- **Negative Inotrope**
  - more pronounced in ischemic myocardium

- **Hypotension in high doses**
  - vasodilatation of peripheral vasculature
Procainamide - Pharmacokinetics

- **Onset**
  - 5 - 10 minutes IV
  - 15 - 60 minutes IM

- **Half Life**
  - 2.5 to 4.7 hrs in normal renal function
  - increased in CHF, Renal Failure

- **Metabolized to N-acetyl Procainamide**
  - NAPA
**Procainamide - Indications**

- **Ventricular arrhythmias**
  - Stable Ventricular Tachycardia
  - Premature Ventricular Contractions
  - Ventricular Fibrillation / Pulseless VT

- **Supraventricular tachyarrhythmias**
  - PSVT, PAT, paroxysmal AV junctional
  - Atrial flutter and fibrillation
Procainamide - Contraindications

- AV block
  - Second or third degree
- Long QT interval
- Torsade de pointes
- Caution
  - SLE, CHF, hepatic or renal disease
**Procainamide - Administration**

-Continuous infusion safer than bolus
-Infusion of 20 - 30 mg/min until
  - control of arrhythmia
  - hypotension
  - QRS widens by > 50%
  - QT interval prolongation
  - Total of 17 mg/kg has been administered
Once ectopy is suppressed

- maintenance drip of 1 to 4 mg/min

Lower doses for CHF and renal failure
**Procainamide - Adverse Effects**

- **Myocardial Depression**
  - prolonged QRS, QT, AV conduction, VF and Torsade de pointes

- **Hypotension**
  - High doses or rapidly administered

- **Hypersensitivity**
  - angioedema, bronchoconstriction, vascular collapse, febrile episodes, respiratory arrest

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Lidocaine - Actions

Class IB antiarrhythmic

- blocks fast sodium channels
- decreases slope of phase 4
- decreased automaticity in the His-purkinje system
- action potential duration and effective refractory period of His-purkinje increased
- Acts preferentially on ischemic tissue
Lidocaine - Actions

Continued

- Causes little or no effect on AV conduction
- Elevates v-fib threshold
- Suppresses ventricular ectopy
- Negligible effect
  - autonomic nervous system
  - myocardial contractility
  - peripheral vascular tone
Lidocaine - Pharmacokinetics

- **Onset of Action**
  - 30 to 60 seconds IV
  - 10 minutes IM

- **Bolus administration necessary**
  - Infusion alone will not reach therapeutic levels for 30 min to several hrs.

- **First pass metabolism**
  - No PO form
Lidocaine - Pharmacokinetics

- **Half-Life (elimination)**
  - 80 to 108 minutes
    - healthy patients
  - 7 hrs
    - in patients with CHF, liver disease

- **Therapeutic Levels**
  - 1.5 to 6 ug/ml
  - >5 ug/ml may cause CNS toxicity
Lidocaine - Indications

- **Drug of Choice**
  - ventricular arrhythmias
  - ventricular ectopy
    - frequent multifocal PVC’s (>6/min)
    - PVC couplets, salvos
    - long runs of VT
    - Not used for chronic PVC’s when asymptomatic

- **Prophylactic use**
  - No longer recommended
Lidocaine - Administration

- **Initial Dose IV**
  - **Ventricular Ectopy**
    - 1 mg/kg bolus
    - additional doses of 0.5 mg/kg q 5-10 min
  - **Ventricular Fibrillation**
    - 1.5 mg/kg

- **Total Dose IV**
  - 3 mg/kg
Lidocaine - Administration

- **Endotracheal**
  - If IV not available
  - 2 to 2 1/2 times the dose diluted to total volume of 10 cc’s

- **IM**
  - 300 mg of 10% solution, deltoid vastus lateralis
  - Auto- injectors available
Lidocaine - Adverse Effects

- **CNS side effects**
- **Abrupt change in mental status**
- **Plasma levels greater than 9 ug/ml**
  - psychosis, seizures, respiratory depression
- **Contraindicated**
  - SA or AV blocks
  - Known hypersensitivity

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Beta Blockers - Actions

- Block effects of catecholamines on Beta receptors
- Selective Beta blockers
  - metoprolol
  - acebutolol
  - atenolol
  - esmolol
  - metoprolol
**Beta Blockers - Actions**

- **Negative**
  - **Chronotropic**
    - slows sinus rate
    - depresses AV conduction
    - Decreases cardiac output
  - **Inotropic**
- **Vasodilatation**
Beta Blockers - Pharmacokinetics

- **Onset**
  - rapid - within 1 minute IV

- **Half Life**
  - 1 to 26 hours
  - Excretion is renal and GI

- **Dose adjustment necessary for renal failure for some beta blockers**
Beta Blockers - Administration

- Metoprolol
  - 5 mg IV push
  - selective B1
  - Half life of 3-7 hrs

- Esmolol
  - ultra-short half life of 9 minutes
  - 25-50 ug/kg/min
  - load of 500 ug/kg not necessary
Beta Blockers - Adverse Effects

- **Similar for most Beta blockers**
  - nausea, vomiting, light headedness, mental depression, bradycardia, hypotension, bronchospasm

- **Contraindicated**
  - > first degree heart block
  - CHF or cardiogenic shock
  - Caution with calcium channel blockers
Bretylium - Actions

- **Class III**
- **Biphasic Effects**
  - Norepinephrine release
    - effects last 20 minutes
  - Blocks release of norepinephrine
    - 45 to 60 minutes after administration
  - Affects phase 3 (repolarization) prolongs refractoriness - antifibrillatory
Bretylium - Indications

- **VF**
  - refractory VF, after epinephrine, lidocaine

- **VT**
  - refractory VT with a pulse, after lidocaine and procainamide

- **Wide Complex Tachycardia Unknown**
  - after lidocaine and adenosine
Bretylium - Administration

- **VF or Pulseless VT**
  - 5 mg/kg rapid IV push
  - repeat at 10 mg/kg in 15 to 30 minutes
  - maximum is 35 mg/kg

- **VT / ventricular arrhythmias**
  - 5 - 10 mg.kg over 8 to 10 minutes

- **Maintenance of 1-2 mg/min**
**Diltiazem - Actions**

- **Class IV - Calcium Channel Blocker**
  - decreases conduction velocity in diseased tissue
  - prolongs refractory period in AV node
  - slows discharge from SA node
  - minimal effect on normal tissue
  - Interrupts reentrant pathway in PSVT
Diltiazem - Indications

- **Rapid Conversion of PSVT**
  - as effective as adenosine and verapamil

- **Slowing of rate in A-Fib or A-flutter**

- **Hypertension**
**Diltiazem - Administration**

- **PSVT, A-fib, A-flutter**
  - .25 mg/kg (average 20 mg) over 2 minutes
  - Second bolus of .35 mg/kg

- **Maintenance Infusion**
  - 5-15 mg/hr
Diltiazem - Adverse Effects

- **Cardiovascular**
  - angina, bradycardia, asystole, CHF, AV block, BBB, flushing, hypotension

- **Non-cardiovascular**
  - headache, dizziness, constipation, rash
Adenosine - Actions

- **Endogenous Nucleoside**
  - produced by dephosphorylation of ATP

- **Negative Chronotropic effects on SA and AV node**
  - Does not alter accessory pathways
  - blockade of the AV node
  - potent vasodilator - no effects due to metabolism


Adenosine - Pharmacokinetics

- **Onset**
  - 30 seconds

- **Duration**
  - 60 to 90 seconds

- **Half-life**
  - less than 7 seconds
Adenosine - Indications

- Emergency management of PSVT
  - involving the AV node
- Diagnostic
  - Wide complex tachycardia of uncertain origin
  - detection of accessory pathways
Adenosine - Administration

- 6 mg Rapid IV push (over 1-2 seconds)
  - most proximal port
  - followed by 20 ml saline flush
  - elevate the extremity after bolus

- Repeat Dosing
  - 12 mg rapid IV push if heart rate not decreased in 2 minutes
Adenosine - Adverse Effects

- **Minor and well tolerated**
  - less than 1 minute
  - dyspnea, cough, syncope, vertigo, parasthesias

- **Higher doses**
  - Dipyramidole
  - Carbamazepine
  - Asthmatics, excessive coffee drinkers
Magnesium - Actions

- **Directly**
  - Na, K+, ATPase pump

- **Indirectly**
  - calcium channel blocking activity

- **Effects**
  - Increases membrane potential
  - prolongs AV conduction
  - Corrects hypomagnesemia/hypokalemia
Magnesium - Indications

- Intractable VF/VT
- Torsade de pointes
- May be useful
  - PVC’s, MAT, PSVT, digoxin toxicity
Magnesium - Administration

- **IV Loading dose**
  - 1 to 2 grams in 50-100 cc of D5W over 1 to 2 minutes

- **Acute MI**
  - 8 to 12 grams per day in acute MI
Vasoactive Medications

- Epinephrine
- Dopamine
- Norepinephrine
- Atropine
- Nitroglycerin
Epinephrine - Overview

- **Nonselective alpha and beta agonist**
  - increased heart rate, SVR, ventricular contractility

- **Onset**
  - 1 to 2 minutes

- **Duration of action**
  - 2 to 10 minutes
Epinephrine - Continued

- **Indications**
  - Cardiac Arrest
  - Bronchospasm
  - Anaphylaxis / hypersensitivity reactions

- **Administration**
  - Cardiac Arrest
    - 1 mg IV push every 3 - 5 minutes
    - escalating and high dose options
Epinephrine - Continued

- Endotracheal
  - 2 to 2.5 the IV dose diluted to 10 cc

- Adverse Effects
  - may increase myocardial oxygen consumption
Dopamine - Overview

- **Actions**
  - acts on dopaminergic, alpha and beta receptors

- **Low Dose**
  - dilatation of renal, mesenteric, coronary, and intracerebral vascular beds
  - improves organ perfusion and increases urine output
Dopamine - Continued

- **Moderate Dose 2 - 10 ug/kg/min**
  - mostly beta effects
    - inotropic, chronotropic on heart
    - increased cardiac output

- **High Dose >10 ug/kg/min**
  - Alpha effects predominate
    - increased peripheral resistance
    - decreased blood flow to kidney
Norepinephrine - Overview

- Endogenous Catacholamine
  - powerful alpha agonist
  - potent vasoconstrictor

- Onset
  - 1 to 3 minutes

- Indications
  - severe hypotension refractory to fluids and other pressor agents

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Norepinephrine - Continued

- **Specific Uses**
  - Septic Shock
  - refractory hypotension due to AMI

- **Dosing**
  - 0.5 to 1 ug/kg/min
    - increase by 1 to 2 ug/kg/min every 3-5 min
    - goal is systolic BP of 80 to 100
Norepinephrine - Continued

- Adverse Effects
  - ventricular irritability
  - cardiac depression
  - decreased renal blood flow
  - reflex bradycardia
  - acute hypertension
    - MAOI, TCA’s
  - Extravasation necrosis
    - pentolamine 5-10 mg/10 cc subcutaneous
Atropine Overview

- **Antimuscarinic Agent**
  - *parasympatholytic / vagolytic*
    - increases SA node automaticity by blocking vagus nerve

- **Indications**
  - hemodynamically unstable bradycardias
  - PEA, Asystole, bradyasystolic rhythms
  - anticholinergic properties
Atropine Continued

- **Dose**
  - 0.5 to 1 mg IV

- **Endotracheal**
  - 1 to 2 mg IV (10 cc volume)

- **Adverse effects**
  - increased MVO2
  - undesirable tachycardia
  - precipitate ventricular arrhythmias
Summary

- Pharmacology of antiarrhythmic and vasoactive medications
  - Actions
  - Pharmacokinetics
  - Indications
  - Administration
  - Adverse Effects