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, Tocaininde*
  - *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*

Procainamide - Administration

- *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*

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*
  - *Supresses 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*

Beta Blockers - Actions

- *Block effects of catacholamines 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*

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*