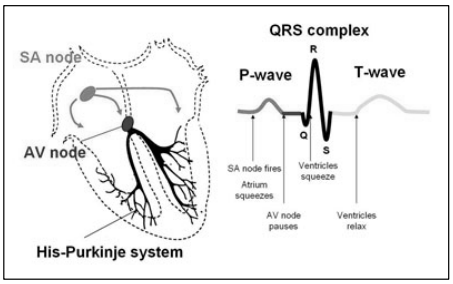
ARRHYTHMIAS

Raed Abughazaleh, PharmD, BCPS
PHAR 551: Pharmacotherapy I
Birzeit University

Background



Background

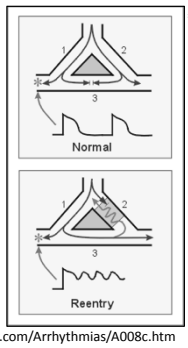
- Automaticity
  - SA: 60-100 bpm, AV: 40-60 bpm, ventricle: 30-40 bpm
  - If SA slows below 60 bpm other tissue with automaticity may take over
- Ventricular action potential: phases 0-4
- EKG: P, QRS, T, QT-interval, QT_c, PR-interval
- Refractory period: absolute vs. relative

Background

- Cardiac arrhythmias are the result of abnormality in signal origination, conduction, or both
- Signal origination:
  - SA automaticity: tachycardia, bradycardia
  - Automaticity is controlled by: SNS, pSNS, hypoxia, ventricular stretch, electrolytes (K^+, Mg^+)
  - Atrial automaticity problems: sinus tachycardia, bradycardia, AF, etc.
  - Ventricular automaticity problems: VT, VF, etc.

Background

- Signal conduction (Re-entry Model)
  - Requires two pathways, unidirectional block, slow conduction in the other pathway
  - Premature impulse blocked by fast path in refractory, passes through slow pathway, reenters retrograde
  - Reentrant impulse may excite surrounding tissue at faster rate than SA node → tachyarrhythmia



*

*Klabunde RE. Cardiovascular Physiology. http://cvphysiology.com/Arrhythmias/A008c.htm

Vaughan Williams Classification

- I: Na Channel blockers, inhibit automaticity and slow conduction
  - IA: Intermediate potency in slowing conduction
  - IB: lowest potency
  - IC: greatest potency
- II: Beta-Blockers
- III: Inhibit ventricular repolarization, i.e. prolong refractoriness
- IV: NDHP CCBs

STUDENTS-HUB.com Uploaded By: anonymous

Supraventricular Arrhythmias: Sinus Bradycardia

- SA rate < 60 bpm
- Can cause dizziness, syncope, fatigue, etc.
- Common amongst some athletes; non-pathologic
- Can be caused by: nodal blocking Rx, pSNS agonists, hypothyroidism, myocardial ischemia, hyperkalemia
- Sick sinus syndrome: idiopathic sinus bradycardia

Supraventricular Arrhythmias: Sinus Bradycardia

- Treatment is indicated if symptomatic after no reversible causes detected
- Pacemaker if needs Rx, i.e. βB, or sick sinus syndrome
- 1st line: Atropine 0.5 mg IV q3-5 min PRN as bridge to pacing
- 2nd line: Dopamine, epinephrine

Supraventricular Arrhythmias: AV Block

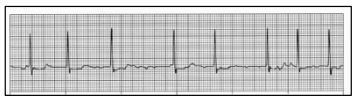
- 1st Degree: prolonged PR interval
- 2nd Degree: Blocks every 3rd or 4th impulse
- 3rd Degree: Complete block/dissociation
- Symptoms similar to sinus bradycardia
- Treat like sinus bradycardia if symptomatic w/ o reversible cause

Supraventricular Arrhythmias: AF/Atrial Flutter Atrial Fibrillation

- High association with morbidity and mortality
- Often caused by atrial hypertrophy
- Risk factors: HTN, HF, CAD
- "AF begets AF"
- Paroxysmal vs. persistent vs. permanent
- Risk of ischemic stroke: 5% per year, AF causes 1/6 strokes, with risk 7x higher than non-AF pts
- Increases risk for cardiomyopathy 2/2 tachycardia

Supraventricular Arrhythmias: AF/Atrial Flutter Atrial Fibrillation

- "Irregularly irregular"- chaos on ECG
- Ventricular response is 120-180 bpm with irregular pulse- much slower than atrial rate
- Caused by multiple reentrant loops



Supraventricular Arrhythmias: AF/Atrial Flutter Atrial Flutter

- Rapid (270-330 bpm) but regular atrial rhythm with regular ventricular response (1:1, 2:1,..)
- Sawtooth ECG pattern
- Caused by single reentrant loop
- Often intermixes with episodes of AF
- Lower risk for stroke than AF but similar management with possibility of ablation

STUDENTS-HUB.com Uploaded By: anonymous

Supraventricular Arrhythmias: AF/Atrial Flutter

- Symptoms of AF/Atrial Flutter: palpitations, dizziness, light-headedness, syncope
- Goals of therapy of AF/Atrial Flutter:
  - 1) stabilize pt with rate or rhythm CTL
  - 2) maintain rate or rhythm
  - 3) prevent stroke
- *Rate* Vs. Rhythm control
  - No mortality difference

Supraventricular Arrhythmias: AF/Atrial Flutter Acute Management

- Hemodynamically unstable
  - DCC
- Symptomatic but hemodynamically stable
  - Control ventricular rate (IV preferred)
    - First line: βBs, CCBs
    - Second line: digoxin, amiodarone
    - HF: Avoid IV NDHP CCBs, βBs
    - HoTN: digoxin, amiodarone preferred
    - Consider DCC if remains symptomatic

Supraventricular Arrhythmias: AF/Atrial Flutter Acute Management: Pharmacotherapy

- Digoxin
  - Target level 0.8-1.2 mg/dL
  - LD: 10-15 mcg/kg in normal renal fcn
    - 50%, then 25% 6h later, then 25% 6h later.
  - MD: 125 mcg/d, adjust per level
  - Does not cardiovert
  - Amiodarone increases level of digoxin
  - Reduce dose in renal dysfunction

Supraventricular Arrhythmias: AF/Atrial Flutter Acute Management: Pharmacotherapy

- Amiodarone
  - IV or PO loading of a total of 10g *oral equivalent*, then maintenance dose of 200-400 mg QD
  - Most effective amongst antiarrhythmics in conversion and maintenance of SR
  - Drug of choice in HF pts
  - AEs: HoTN, photosensitivity, pulmonary toxicity, hypothyroidism, liver toxicity, visual disturbances, slate blue skin discoloration
  - Drug Intxns: CYP450 and p-gp inhibitor; warfarin and digoxin levels
  - T½: ~50 days

Supraventricular Arrhythmias: AF/Atrial Flutter Non-Acute Management

- Consider cardioversion in select pts
  - If new onset and likely to convert to SR and remain in it; if no expectation to spontaneously convert; if not persistent or recurrent AF
  - DCC preferred over pharmacologic cardioversion
- ≤ 48h from AF/Atrial Flutter
  - Likely no atrial thrombus has formed
  - If DCC not an option or C/I or fails
    - No HF, normal EF: flecainide, propafenone amiodarone, dofetilide, ibutilide
    - HF, rEF: amiodarone, dofetilide

Supraventricular Arrhythmias: AF/Atrial Flutter Non-Acute Management

- > 48h from AF/Atrial Flutter
  - Likely to have formed atrial thrombus
  - Two options:
    1. Can obtain TEE to R/O thrombus, if negative can cardiovert per prior algorithm for ≤48h
    2. Anticoagulate x 3 wks, cardiovert, continue anticoagulation x4 wks post conversion
- If conversion not performed or unsuccessful then focus is on rate control with long-term anticoagulation for stroke prevention

STUDENTS-HUB.com Uploaded By: anonymous

Supraventricular Arrhythmias: AF/Atrial Flutter Pharmacologic Cardioversion

- No SHD
  - 1st line: single dose flecainide or propafenone
- SHD (valve dz, LVH, congenital, HF, rEF, etc.)
  - Amiodarone (dofetilide = 2nd line)
  - Avoid flecainide, propafenone, ibutilide 2/2 proarrhythmia risk

Supraventricular Arrhythmias: AF/Atrial Flutter Cardioversion Pharmacotherapy

- Dofetilide
  - High risk for Torsades
  - Requires hospitalization for initiation (PO)
- Ibutilide
  - IV injection of 1-2 mg for cardioversion
  - 2nd line to propafenone/flecainide if no SHD
- Propafenone
  - Single oral dose of 600 mg for cardioversion
- Flecainide
  - Single oral dose of 300 mg for cardioversion
- Dronedarone
  - C/I in NYHF II-IV 2/2 increased mortality

Supraventricular Arrhythmias: AF/Atrial Flutter Long-Term Management: Maintenance

1. Rhythm Maintenance/Episode Reduction
   - Generally not effective or lasting, many AEs and drug intxns
   - Consider only in pts with paroxysmal AF who remain symptomatic in spite of maximal rate control regimen
   - Class Ic or III antiarrhythmics are preferred
     - Class III are first line (amiodarone, dofetilide, dronedarone, ibutilide, sotalol)
     - Class Ic are last line (flecainide, propafenone)

Supraventricular Arrhythmias: AF/Atrial Flutter Long-Term Management: Maintenance

- Rate Maintenance (oral Rx)
  - Goal is HR < 100 bpm or reduction of HR by >20% with symptom relief
  - No HF, normal EF:
    1. NDHP CCBs or βB
    2. Add digoxin
    3. Add amiodarone
  - HF, rEF:
    1. βB
    2. Add digoxin
    3. Add amiodarone

Supraventricular Arrhythmias: AF/Atrial Flutter Long-Term Management: Anticoagulation

- $CHADS_2$ Score
  - Determines annual stroke risk 2/2 AF/Atrial Flutter
  - Determines need for anticoagulation
    - C: CHF, 1 point
    - H: HTN, 1 point
    - A: Age ≥ 75, 1 point
    - D: DM, 1 point
    - S: Stroke or TIA history, 2 points

0	1.9% per year
2	4% per year
4	8.5% per year
6	18.2% per year

  - 0: Low risk, no therapy or ASA 75-325/d
  - ≥ 1: intermediate-to-high risk, oral anticoagulation recommended with dabigatran over warfarin (INR 2-3)

Supraventricular Arrhythmias: AF/Atrial Flutter Anticoagulation Pharmacotherapy

- Warfarin
  - Starting dose ~5 mg/d, adjust to INR 2-3
  - Many drug intxn, substrate of CYP2C9
  - Major cause of serious bleeding in chronic use
- Dabigatran
  - Direct thrombin inhibitor
  - Preferred over warfarin per new guidelines in long-term prevention of stroke in non-valvular AF
  - Dose 150 mg BID (75 mg BID if CrCl 15-30 mL/min), C/I if CrCl < 15 mL/min.
  - No monitoring, rapid onset, fewer drug intxn
  - No antidote like warfarin

STUDENTS-HUB.com Uploaded By: anonymous

Supraventricular Arrhythmias: AF/Atrial Flutter Anticoagulation Pharmacotherapy

- Rivaroxaban, Apixaban
  - Factor Xa Inhibitor
  - Approved for stroke prevention in non-valvular AF
  - AHA/ASA: reasonable alternative to warfarin
  - No monitoring required
  - Rapid onset, no antidote

Supraventricular Arrhythmias: PSVT

- Also known as AV reentrant tachycardia
  - Reentry circuit involving AV node or vicinity
- Palpitations are main symptom
- Includes Wolff-Parkinson-White Syndrome
- Treatment:
  - Severe symptoms: DCC
  - Mild-moderate symptoms:
    1. Vagal maneuvers
    2. Pharmacotherapy (IV): adenosine, NDHP CCBs, βBs, digoxin, amiodarone
    3. Ablation

Supraventricular Arrhythmias: PSVT
Pharmacotherapy

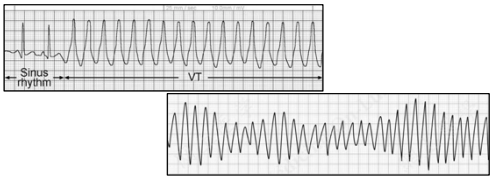
- Adenosine
  - Direct AV nodal inhibition
  - T½ = 10 sec
  - 6 mg IV rapid push followed by saline flush, follow with 12 mg if no response
  - Eliminates PSVT in majority of cases
  - AEs include flushing, chest tightness, AV block, sinus bradycardia

Ventricular Arrhythmias
Premature Ventricular Contractions (PVC)

- Non-life-threatening and usually asymptomatic
- Premature impulses originating from ventricles and causing contraction before complete filling
- Caused by excessive SNS activity and/or heart disease
- Common in healthy individuals, associated with increased risk for sudden cardiac death in pts with CAD or hx MI
- No treatment required in healthy individuals, otherwise βB in pts with CAD or hx of MI

Ventricular Arrhythmias
Ventricular Tachycardia (VT)

- ≥3 PVCs occurring at a rate > 100 bmp
- Sustained (>30 sec) vs Non-sustained (<30 sec)
- Monomorphic Vs. Polymorphic
- Etiology: CAD, MI, HF, lytes, Rx (ex. AADs)



Ventricular Arrhythmias
Ventricular Tachycardia (VT)

- Treatment:
  - Hemodynamically unstable with pulse: DCC
  - Pulseless VT: defibrillation
  - Hemodynamically stable:
    - Normal EF, no HF:
      - 1st line: procainamide infusion until VT resolves or AEs or max dose reached
      - 2nd line: add amiodarone bolus then infusion if needed
    - HF/rEF: amiodarone bolus + infusion if needed
  - Recurrent VT: consider ICD

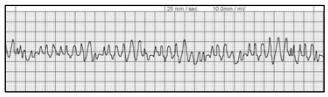
STUDENTS-HUB.com Uploaded By: anonymous

Ventricular Arrhythmias
Torsades de Pointes

- Polymorphic VT 2/2 delayed ventricular repolarization (prolonged QT interval)
- Can be caused by medications (abx, AADs, antipsychotics, methadone..)
- Usually other underlying risk factors must be present for Rx to cause Torsades
- Treatment:
  - Hemodynamically unstable: DCC then Mg/lytes
  - Stable pt: Mg 1-2g IV and replace low lytes

Ventricular Arrhythmias
Ventricular Fibrillation (VF)

- Electrical anarchy of ventricle resulting in no cardiac output and CV collapse
- Usual cause for sudden cardiac death
- Risk factors include MI and HF
- Treatment is defibrillation. Perform CPR. Administer ACLS drugs to facilitate defib.



STUDENTS-HUB.com Uploaded By: anonymous