Antiarrhythmic Pharmacology: Important Practice Implications

NTI 2014
Session A75M403

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Welcome to NTI 2014
We are going to have a great session and a wonderful week!
Methodology

Electrical Conduction Pathway

- SA Node
- Interatrial pathways
- AV Node
- Bundle of His
- AV Junction
- Right and Left Bundle Branches
- Anterior and Posterior Fascicles
- Purkinje Fibers
WAVES and COMPLEXES

- **P wave**: atrial depolarization
- **QRS**: ventricular depolarization
- **T wave**: ventricular repolarization
- **PR interval**: AV conduction time
- **QRS width**: intraventricular conduction time
- **ST Segment**: entire ventricular depolarization
- **QT interval**: used to reflect ventricular repolarization time

Understanding the Origin of Arrhythmias

- **Disorder of impulse initiation**
  - Abnormal automaticity
    - Enhanced
    - Abnormal
  - Triggered mechanism: disturbance in recovery or repolarization (less common)
    - Early or delayed after depolarizations

- **Disorder of impulse conduction**
  - Reentrant Circuit (*Most common*)
Causes of Arrhythmias: Abnormal Impulse Initiation

- Ectopic focus in paroxysmal atrial fib (near pulmonary veins)
- Ectopic focus in VT from ischemia or electrolyte abnormalities

However, Re-entry is the more common mechanism.
Examples of Reentrant Tachycardias: Atrial

Examples of Reentrant Tachycardias: SVTs
Reentry in Monomorphic VT

- **Speed Sinus Rate:**
  - Atropine
  - Epinephrine

- **Slow Sinus Rate:**
  - Beta blockers
  - Ca++ blockers
  - Digoxin

- **Speed AV Conduction:**
  - Atropine

- **Slow AV Conduction:**
  - Beta blockers
  - Ca++ blockers
  - Adenosine
  - Digoxin

- **Suppress Atrial Arrhythmia:**
  - Amodarone
  - Dofetilide
  - Flecainide
  - Ibutilide
  - Procainamide
  - Propafenone
  - Sotalol

- **Slow or Block Accessory Pathway:**
  - **Amodarone**
  - Flecainide
  - Procainamide
  - Propafenone
  - Sotalol

- **Suppress Ventricular Arrhythmia:**
  - Amodarone
  - Beta Blockers
  - Lidocaine
  - Magnesium
  - Procainamide
  - Sotalol
The Electronics

Action Potential of Cardiac Cells

- Phase 0: Rapid depolarization – Sodium Influx (beginning of QRS complex)
- Phase 1: Brief, rapid initiation of repolarization

The Electronics

- Phase 2: Slowing of the repolarization – Calcium Influx – correlates with ST segment
- Phase 3: Sudden acceleration in the rate of repolarization - Potassium Efflux – Correlates with T wave
- Phase 4: Resting membrane potential
Antiarrhythmic Medications Effecting the Action Potential

- **Class I** – Fast sodium channel blockers
  - IA: Quinidine, Procainamide, Disopyramide
  - IB: Lidocaine, Mexiletine, Tocainide
  - IC: Flecainide, Propafenone
- **Class III** – Potassium channel blockers
  - Amiodarone, Dronedarone, Ibutilide, Dofetilide, Sotalol
- **Class IV** – Calcium channel blockers
  - Verapamil, Diltiazem

Class I
Slow conduction (widen QRS).
Some prolongation of refractory period (prolong QT interval).

Class III
Marked prolongation of refractory period (prolong QT interval).
Effects of Class 1 Antiarrhythmics

- All Class 1 antiarrhythmics by definition block the fast sodium channel
  - Different drugs do this to a different degree
  - IC > IA > IB

- Blocking of the fast sodium channel interferes with rapid depolarization and decreases conduction velocity
  - This will increases the duration of the cardiac action potential
  - Note: This effect is seen in the action potential of the purkinje fibers but not in the action potential of the nodal tissue

Benefits of Reducing Rate and Degree of Depolarization

- Decrease in conduction velocity in non-nodal tissue is called negative dromotropy.

- This is suppresses reentrant tachycardias because reentrant tachycardias are caused by abnormal conduction.
Effects of Class 1 Antiarrhythmics

• In addition to blocking the fast sodium channel (Phase 0)
  – some class I agents also block the potassium channel (Phase 3)
• Potassium channel blockade directly affects the duration of the cardiac action potential and the effective refractory period.
• Benefits and disadvantages of effecting refractory period
  – Beneficial in reentrant tachycardias
  – Can increase risk for Torsades
• Different drugs do this to a different degree
  – IA (increase refractory period) > IC (no effect) > IB (decrease refractory period)

Effects of Class 1 Antiarrhythmics

Depression of Automaticity
• Can suppress abnormal automaticity
• Not related to sodium channel effect
• Mechanism not fully understood

Anticholinergic Effect
• Strong inhibitors of vagal activity
• Offsets some of benefit (i.e. an increase ventricular rate during the treatment of atrial arrhythmias)
• Can increase SA rate and conduction through the AV node
Class I A Antiarrhythmics

| Action Potential | • Depresses Phase 0 of Action Potential; Inhibits influx of sodium in the fast channel of the cardiac cell membrane  
|• Also blocks Phase 3 of the Action Potential (blocks potassium efflux)  
| | Actions | • Slows conduction velocity (including over accessory pathways)  
|• Increases the recovery period after repolarization; Effective refractory period prolonged; slightly prolongs QT (greatest effect of all Class 1 antiarrhythmics)  
|• Can have anticholinergic effect  
|• Decreases automaticity, excitability  
|• Can have a negative inotropic effect  
| Cautions | See individual drugs  
| Uses | Atrial fib / flutter  
| Ventricular tachycardia  
| Drugs | Quinidine  
| Procaainamide (Pronestyl)  
| Disopyramide (Norpace)  

Class I A Antiarrhythmics

| Quinidine | Effective antimalarial agent (S.E. cinchonism (blurred vision, tinnitus, headache, psychosis); cramping and nausea)  
| • Anticholinergic effects - increase ventricular rate in A fib / flutter  
| Enhances digoxin toxicity  
| Procaainamide (Pronestyl) | Anticholinergic effects less pronounced  
| Indications: Stable monomorphic or polymorphic VT with preserved ventricular function  
| Can be used along with class IC drugs in WPW tachycardias  
| S.E. – Lupus like syndrome  
| Disopyramide (Norpace) | Significant anticholinergic effects (limits uses)  
| Significant negative inotropic effect  
| IV form not approved in US. (Has been used to convert atrial arrhythmias).  
| **Only used for suppression of life threatening ventricular arrhythmias** |
Class I B Antiarrhythmics

**Action Potential**
- Blocks Phase 0 of Action Potential; inhibits influx of sodium the fast channel of cardiac cell membrane (least suppression of the sodium channel of all three groups of Class 1 drugs).
- Does not block Phase III of the cardiac action potential

**Actions**
- Slows conduction velocity (the least of class I antiarrhythmics)
- Actually decreases refractory period
- Suppresses automaticity but not in the SA node
- Suppresses spontaneous depolarization in the ventricle
- Acts preferentially on ischemic tissue
- No anticholinergic properties

**Cautions**
- Heavily metabolized in liver; toxicity manifested neurologically

**Uses**
- Acceptable for stable monomorphic or polymorphic VT (Acceptable for impaired ventricular function)
- Not for prophylaxis of arrhythmias post infarction

**Drugs**
- Lidocaine; Mexiletine (Mexitil); Tocainide (Tonocard)

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**Chart based on Lidocaine:**

<table>
<thead>
<tr>
<th>Class I B Antiarrhythmics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lidocaine</strong></td>
</tr>
<tr>
<td>Parenteral administration only; Can give via E-Tube during code</td>
</tr>
<tr>
<td>Amiodorone considered first for pulseless ventricular tachycardia or ventricular fibrillation</td>
</tr>
<tr>
<td><strong>Good efficacy in ischemic tissue</strong></td>
</tr>
<tr>
<td>CNS: Effects confusion, numbness or tingling of lips or tongue, blurred vision</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Mexiletine (Mexitil)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Orally active lidocaine analog</td>
</tr>
<tr>
<td>Used in treatment of life threatening ventricular arrhythmias (good efficacy in ischemic tissue)</td>
</tr>
<tr>
<td>Also used to treat diabetic neuropathy pain</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Tocainide (Tonocard)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Orally active lidocaine analog</td>
</tr>
<tr>
<td>Tablets were discontinued in US 12/31/2003</td>
</tr>
<tr>
<td>Potential fatal hematological side effect of agranulocytosis; can also cause pulmonary fibrosis</td>
</tr>
</tbody>
</table>
### Class I C Antiarrhythmics

<table>
<thead>
<tr>
<th>Action Potential</th>
<th>Potent inhibition of fast sodium channel; decrease in maximal rate of phase 0 depolarization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actions</td>
<td>Slow His-Purkinge conduction and cause QRS widening; QT intervals are also usually prolonged; No effect on refractory period</td>
</tr>
<tr>
<td>Cautions</td>
<td>Proarrhythmic effects</td>
</tr>
<tr>
<td>Uses</td>
<td>Life threatening ventricular arrhythmias; Conversion to SR (Flecainide)</td>
</tr>
<tr>
<td>Drugs</td>
<td>Flecainide (Tambocor); Moricizine (Ethmozine); Propafenone (Rhythmol)</td>
</tr>
</tbody>
</table>

#### Flecainide (Tambocor)
- Not a first line agent for ventricular arrhythmias
- Will slow conduction over accessory pathways in WPW tachycardias
- **Used in atrial fibrillation (pill in the pocket)**
- CAST Trial: propensity for fatal proarrhythmic effects
- Not used post MI or with depressed LV function

#### Moricizine (Ethmozine)
- CAST studies: Reserved for life threatening ventricular arrhythmias
- Has properties of class I B also

#### Propafenone (Rhythmol)
- Used in supraventricular arrhythmias and life threatening ventricular arrhythmias
- Also has small beta blocking actions and calcium channel blocking effects that can worsen HF
- **Must be initiated in hospital setting to monitor ECG in structural heart disease**
A Closer Look at Antiarrhythmics

**Beta blockers**
- Depresses SA node automaticity
- Increases refractory period of atrial and AV junctional tissue to slow conduction
- Inhibits sympathetic activity
- “lol” medications
- Sotalol (Class II and III)

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![Diagram of Autonomic Nervous System with Beta Blockers](image-url)
### Cardiovascular Indications for Beta Blockers

- Hypertension
- Angina
- MI / Post Infarction
- Heart failure
- Aortic Dissection
- Hypertrophic cardiomyopathy

- Supraventricular arrhythmias
- Ventricular arrhythmias
- Congenital Long QT
- Digitalis induced ventricular arrhythmias

### Polymorphic VT with normal QT:

- Seen frequently in ischemic conditions
  - Think revascularization
  - Think beta blockers
**Beta Blockers**

- **Nonselective: Block both Beta 1 and Beta 2**
  - Propranolol (Inderal)
  - Timolol (Blocadren)
  - Nandolol (Corgard)
  - Sotolol (Betapace)
  - Carvedilol (Coreg) (also alpha blockade)

- **Cardio selective: Block Beta 1**
  - Acebutolol (Sectral)
  - Metoprolol (Lopressor)
  - Atenolol (Tenormin)
  - Esmolol (Breviblock)
  - Bisoprolol (Z Beta)
  - Nebivolol (Bystol) (also nitric oxide vasodilatory properties)

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**Class III Antiarrhythmics**

<table>
<thead>
<tr>
<th>Action Potential</th>
<th>Inhibits potassium ion fluxes during phase II and III of the action potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actions</td>
<td>Directly on myocardium to delay repolarization (prolongs QT); prolongs effective refractory period in all cardiac tissue; By definition act only on repolarization phase and should not impact conduction</td>
</tr>
<tr>
<td>Cautions</td>
<td>Proarrhythmic Effects (amiodarone less)</td>
</tr>
<tr>
<td>Uses</td>
<td>Drug dependent</td>
</tr>
</tbody>
</table>
| Drugs            | Amiodarone (Pacerone, Cordorone)  
Dronedarone (Multaq)  
Ibutilide (Corvert) – pure class III  
Dofetilide (Tikosyn) – pure class III  
Sotalol (Betapace) |
Class III Antiarrhythmics

| Amiodarone (ARREST Trial) | Approved for life threatening refractory ventricular arrhythmias; considered before lidocaine in pulseless VT or V fib; considered ahead of lidocaine for stable VT with impaired cardiac function; expanded to atrial and ventricular arrhythmias, conversion and maintenance of atrial fibr

**Survival to hospital admission improved 29%**

**Use in atrial fibrillation is off label**

- Slows conduction in accessory pathways
- Originally marketed as anti-anginal (potent vasodilator)
- Relaxes smooth and cardiac muscle, reduces afterload and preload (well tolerated in heart failure and cardiomyopathy)
- **Proarrhythmias less frequent**
- Is also a weak sodium channel blocker, also has effects similar to class II and IV, also has anticholinergic properties

Amiodarone Dosing

- **Life-threatening ventricular arrhythmias**
  - Rapid loading infusion 150 mg administered at a rate of 15 mg/minute (over 10 minutes); initial infusion rate should not exceed 30 mg/minute
  - The slow loading phase is 360 mg at a rate of 1 mg/minute (over 6 hours)
  - First maintenance phase of the infusion is 540 mg at a rate of 0.5 mg/minute (over 18 hours).
  - After the first 24 hours, maintenance infusion rate of 0.5 mg/minute should be continued; the rate of the maintenance infusion may be increased to achieve effective arrhythmia suppression.
  - In the event of breakthrough episodes supplemental infusions of 150 mg administered at a rate of 15 mg/minute (over 10 minutes) may be given.

- **For cardiac arrest secondary to pulseless ventricular tachycardia or ventricular fibrillation**
  - Initial adult loading dose is 300 mg (diluted in 20–30 mL of a compatible IV solution) given as a single dose, rapid IV
More on Amiodarone

- Peripheral IV concentration not to exceed 2mg/ml
- Oral administration = GI symptoms

Potential Extra Cardiac Effects

<table>
<thead>
<tr>
<th>Pulmonary toxicity without initial symptoms / Potentially lethal interstitial pneumonitis /</th>
<th>Photosensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatotoxicity</td>
<td>Corneal micro deposits</td>
</tr>
<tr>
<td></td>
<td>Optic neuropathy / neuritis</td>
</tr>
<tr>
<td></td>
<td>Thyroid dysfunction</td>
</tr>
</tbody>
</table>

Toxic side effects increase with length of use and increased dose
### Inpatient Dosing Regimes in Atrial Fibrillation

**Cardioversion**
- PO - 1.2 to 1.8 g/day in divided doses until 10g total – then 200mg to 400mg daily for maintenance
- Or: PO 400mg TID x 5 to 7 days, then 400mg daily x 1 month, then 200mg daily

**Post Op Prevention**
- Post op: PO 400mg BID for up to 7 days
- Or: Start 7 days preoperatively 600mg PO per day and convert to 200mg per day until hospital discharge
- Or: IV – 1000mg/24 hours x 2 days

*Note: Amiodarone use in atrial fibrillation is off label.*

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**HOT OFF THE PRESS**

New 2014 Atrial Fibrillation Guidelines

**CHANGE IN RECOMMENDATION REGARDING AMIODARONE FOR PATIENTS WITH PRE-EXCITATION**
• Lethal Outcome After Intravenous Administration of Amiodarone in Patient with Atrial Fibrillation and Ventricular Preexcitation
  • MUJOVIĆ NEBOJŠA M.D.¹,
  • SIMIĆ DRAGAN M.D.¹,
  • ANTONJEVIĆ NEBOJŠA M.D.¹ and
  • ALEMPUEVIĆ TAMARA M.D.²

• Journal of Cardiovascular Electrophysiology
  • Volume 22, Issue 9, pages 1077–1078, September 2011

• Article first published online: 18 FEB 2011
• DOI: 10.1111/j.1540-8167.2011.02013.x

WPW and Atrial Fibrillation

• Mechanism of Action
  – Development of Atrial Fibrillation in WPW
    • 10-32% of patients
  – Refractory period of accessory pathway
### Class III Antiarrhythmics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibutilide (Corvert)</td>
<td>Indicated for rapid conversion of atrial fib or flutter to sinus rhythm; IV use only; also facilitated cardioversion (Don’t convert atrial fib or flutter of duration without anticoagulation) Rather than blocking outward potassium currents – promotes influx of sodium through slow inward sodium channel</td>
</tr>
<tr>
<td>Dofetilide (Tykosin)</td>
<td>More “pure” class III agent Conversion to and maintenance of SR in A fib and flutter Reserved for very symptomatic patients, monitored 3 days in hospital Widens the QT; cannot be given with many other drugs (prolong QT or inhibit metabolism or elimination); no negative inotropic effects, neutral effect on mortality from arrhythmias post MI and in in HF, can be used in this population to prevent worsening HF from atrial fib</td>
</tr>
</tbody>
</table>

### CLINICAL PEARL

ALWAYS check potassium level prior to use of ibutilide—potassium level should be in high normal range.
Simultaneous 2-lead ECG (leads II and V1) showing initiation and termination of torsade de pointes in patient in AF after ibutilide infusion.


Class III Antiarrhythmics

| Sotalol (Betapace<sup>R</sup>) (Betapace<sup>AF</sup>) | Used in atrial arrhythmias and life threatening ventricular arrhythmias
Indicated for stable monomorphic VT or Polymorphic VT with normal QT in ACLS protocol
Non selective beta blocking agent with class III properties
**Significant class III effects are only seen at doses > 160 mg**
Proarrhythmic potential (prolonged QT)
More effective in preventing reoccurring arrhythmias than several other drugs |
Newer Antiarrhythmic

• Dronedarone (Multaq)
  – Rejected by FDA 2006
  – Approved by FDA 2009
  – Decreases hospitalizations in atrial fibrillation
    • Not permanent atrial fibrillation
  – Proposed safer alternative to amiodarone in terms of extra cardiac side effects
    • Iodine content

Dronedarone

• Similar to amiodarone without iodine component and less fat soluble
• Class III antiarrhythmic (K+ channel blocker) with effects from all four classes
• Less effective than amiodarone at maintaining sinus rhythm but also less toxic
• Elimination half-life 13-19 hours
• Has both rate and rhythm control effects but is primarily indicated for rhythm control
• May reduce incidence of stroke (mechanism uncertain)
Dronedarone (ATHENA)

- Approved for maintenance of sinus rhythm in patients with history of paroxysmal or persistent AF or flutter with EF > 35% who are in sinus rhythm or will be cardioverted
- Dose: 400 mg PO bid with meals (no grapefruit juice)
- **Contraindicated in patients with NYHA Class IV HF or NYHA Class II-III HF with recent decompensation requiring hospitalization or referral to a specialized HF clinic**
  - > twofold increase in mortality in HF patients
- Side Effects
  - GI, skin disorders
  - Can prolong QTc but low risk of Torsades
  - Increases serum creatinine
  - Interferes with digoxin metabolism
  
  **Concern: LIVER Dysfunction:** 1/2011

ACCF/AHA/HRS Atrial Fibrillation Guidelines

**Class II A Recommendation:**

Dronedarone is reasonable to decrease the need for hospitalization for cardiovascular events in patients with paroxysmal AF or after conversion of persistent AF. Dronedarone can be initiated during outpatient therapy *(Level of Evidence: B)*

Reduces risk of recurrent atrial fibrillation after cardioversion by 25%
ACCF/AHA/HRS Atrial Fibrillation Guidelines

Class III Recommendation:
Dronedarone should not be administered to patients with class IV heart failure or patients who have had an episode of decompensated heart failure in the past 4 weeks, especially if they have depressed left ventricular function (left ventricular ejection fraction 35%)

(Level of Evidence: B)
More on Dronederone

• PALLAS Trial
  – Dronederone in permanent atrial fibrillation
  – Stopped early due to adverse outcomes in dronederone arm
  – Adverse outcomes were cardiovascular in nature and not hepatic in nature

Class IV Antiarrhythmics
Calcium Channel Blockers

• Phase II of Action Potential
  – Depresse automaticity in the SA and AV Junction
  – Increase the refractory period at the AV junction
  – Decrease contractility
  – Verapamil (SA Node), Cardizem (AV Node)
A Closer Look at Calcium Channel Blockers

**Note:** Not all calcium channel blockers are created equal: therefore not all calcium channel blockers have the same actions

<table>
<thead>
<tr>
<th></th>
<th>Verapamil</th>
<th>Dihydropyridines</th>
<th>Diltiazem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>▼▼</td>
<td>▲</td>
<td>▼</td>
</tr>
<tr>
<td>AV Nodal Conduction</td>
<td>▼▼</td>
<td>------</td>
<td>▼</td>
</tr>
<tr>
<td>Contractility</td>
<td>▼▼</td>
<td>▼</td>
<td>▼</td>
</tr>
<tr>
<td>Arterial Vasodilatation</td>
<td>▲▲</td>
<td>▲▲▲</td>
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Initiation in Outpatient Setting

- **Propafenone**
  - Absence of structural HD / SR
- **Flecainide**
  - Absence of structural HD / SR
- **Amiodarone**
  - Bradycardia biggest safety concern
  - Absence of conduction system disease
- **Sotalol**
  - In selected healthy patients

Outpatient Initiation

- Does not imply lack of monitoring
- Will be standard for new drug development
- Need to carefully dose and titrate

Future FDA Approval
# More on Antiarrhythmics in Atrial Fibrillation

<table>
<thead>
<tr>
<th>Class</th>
<th>Specific Medications</th>
<th>Purpose of Medication</th>
<th>Major Cardiac Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I A</td>
<td>Disopyramide</td>
<td>Rhythm Control</td>
<td>Torsade de pointes, HF</td>
</tr>
<tr>
<td>Class I B</td>
<td>Procainamide</td>
<td>Rhythm Control</td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td>Class I C</td>
<td>Quinidine</td>
<td>Rhythm Control</td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td></td>
<td>Not used in atrial</td>
<td>Rhythm Control</td>
<td>Ventricular tachycardia, HF, Atrial Flutter</td>
</tr>
<tr>
<td></td>
<td>fibrillation</td>
<td></td>
<td>* Organ toxicity</td>
</tr>
<tr>
<td></td>
<td>Flecainide</td>
<td>Rhythm Control</td>
<td>Torsade de pointes, HF</td>
</tr>
<tr>
<td></td>
<td>Propafenone</td>
<td>Rhythm Control</td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td>Class II</td>
<td>Beta Blockers</td>
<td>Rate Control</td>
<td>Torsade de pointes, HF, Beta blocker side effects</td>
</tr>
<tr>
<td>Class III</td>
<td>Amiodarone</td>
<td>Rhythm / Rate Control</td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td></td>
<td>Dronedarone</td>
<td>Rhythm Control</td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td></td>
<td>Dofetilide</td>
<td>Rhythm Control</td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td></td>
<td>Sotalol (Also contains beta blocker)</td>
<td>Rhythm Control (also controls rate)</td>
<td>Torsade de pointes, HF, Beta blocker side effects</td>
</tr>
<tr>
<td>Class IV</td>
<td>Calcium Channel Blockers</td>
<td>Rate Control</td>
<td></td>
</tr>
</tbody>
</table>
Medications Used to Maintain Sinus Rhythm in Patients with Atrial Fibrillation

- Amiodarone
- Disopyramide
- Dofetilide
- Dronedarone
- Flecainide
- Procainamide
- Propafenone
- Quinidine
- Sotalol
Pharmacological Considerations in Rate Control

• Calcium channel blockers versus beta blockers
  – All beta blockers and only two calcium channel blockers slow conduction through AV node

• Pros and Cons of Digoxin
  – Blood pressure effect
  – Heart rate control at rest versus exercise

• Pros and Cons of Amiodarone
  – Limiting use of other antiarrhythmics (terminal half-life elimination 40 to 55 days)
  – Use in heart failure
  – Least likely to cause Torsades de Pointes

ACCF/AHA/HRS Atrial Fibrillation Guidelines

Class IIb Recommendation:
Treatment to achieve strict control of heart rate (<80 bpm at rest and <110 bpm during a 6-minute walk) is not beneficial compared to achieving a resting heart rate <110 bpm in patients with persistent AF who have stable ventricular function (left ventricular ejection fraction >0.40) and no or acceptable symptoms related to the arrhythmia, though uncontrolled tachycardia can over time be associated with irreversible decline in ventricular performance (Level of Evidence: B)
New 2014 Guideline Update

A randomized trial suggested that a lenient (<110 bpm) rate control strategy was as effective as a strict strategy (<80 bpm) in patients with persistent/permanent AF. However, the writing committee still advocates for the latter (Class IIa), as the results of this single trial were not thought to be definitive.

Non-classified Antiarrhythmics

- **Adenosine**
  - Blocks conduction through AV Node
- **Atropine**
  - Parasympatholytic
- **Digitalis**
  - Cardiac Glycoside
Adenosine (Adenocard)

- Slows conduction through the AV Node
- Vasodilator
- Interrupts reentry pathways through the AV node and restores sinus rhythm
- Uses: Paroxysmal SVT, AVNRT, Drug stress testing
- Side Effects: Headache, arrhythmias (blocks), SOB, chest pressure

Adenosine

**Nursing Considerations:**
- Use cautiously in patients with asthma – could cause bronchospasm
- Onset IV: Immediate
- Peak: 10 sec
- Duration 20-30 **seconds**
- Dosing for conversion of arrhythmia:
  - 6mg IV rapid push
  - If no change within 1-2 minutes repeat with 12mg rapid push
  - Not indicated in WPW
Typical AV Nodal Re-entrant Tachycardia

AV Nodal Reentrant Tachycardia (Typical)

- Most common supraventricular tachycardia
- Least likely to be life threatening
- **Narrow QRS has no visible P waves**
  - Simultaneous depolarization
- Or, P waves are so close to QRS they look like part of it (pseudo R waves in V1 and pseudo R waves in inferior leads)
AVNRT

AVNRT: Conversion with Adenosine
Adenosine to Diagnose as Opposed to Convert

Adenosine to Diagnose
Antegrade Conduction over Accessory Pathway

Drugs that slow conduction over accessory pathway:
- Amiodarone
- Procainamide
- Flecainide
- Sotalol
- Propofenone

Arrhythmias of WPW (AVRT or CMT)

Orthodromic SVT

Antidromic SVT

Atrial fibrillation
Example of WPW Atrial Fib
(antegrade conduction via accessory pathway)
Atropine

- Parasympatholytic drug
- Can only work where there are available parasympatholytic fibers
- Parasympathetic fibers exist in SA node, throughout atria, and in AV node
- Therefore atropine is effective for:
  - SB
  - Second degree type one block where the physiological problem is in the AV node.

Wenckebach (2\textsuperscript{nd} Degree Type I)

- Progressive lengthening of the PR interval (problem in the AV node)
- Normal QRS width (no problem in the His Perkinge System)
Atropine

- Atropine will not work when the block is below the level of the AV node (meaning the block is in the His Perkinje system)
  - Second degree type two block
  - Complete heart block with ventricular escape rhythm

Both of these examples:
1. One P wave at a time fails to conduct
2. There is a fixed PR interval – no problem in the AV node
3. There is a wider than normal QRS – problem in the His Perkinje System
**Digoxin**

- Inhibits the NA+ and K+ membrane pump ▼
- Increase in intracellular Na+ ▼
- Enhances the Na+ and Ca++ exchange ▼
- Leads to ▲ in intracellular Ca++ ▼
- ▲ inotropic activity

- Digoxin decreases sympathetic outflow and decreases renin production
  - Beneficial in heart failure

**Digoxin**

- Increases vagal activity
- Digoxin decreases conduction velocity through the AV node
  - HOWEVER: Sympathetic stimulation easily overrides the inhibitory effects of digoxin on AV node conduction
  - Calcium channel blockers are replacing digoxin as agent for rate control in atrial arrhythmias
  - Remains good option in acute setting when blood pressure is marginal
  - Digoxin no better than placebo in converting atrial fibrillation to sinus rhythm
  - The conduction velocity increases in the atria, but decreases in the AV node.
  - Automaticity is also increased, in the atria, AV node, Purkinje fibers and ventricles.
Digoxin

• Indications
  – HF
  – Atrial arrhythmias (older indication)
    • Still an option when BP is a concern

• Contraindication / cautions
  – Acute MI
  – Ventricular arrhythmias, HB, Sick Sinus Syndrome
  – Obstructive Hypertrophic Cardiomyopathy
  – Electrolyte abnormalities
    • Hypokalemia increases risk of toxicity
    • Hypocalcemia decreases sensitivity to digoxin
    • Don’t give IV calcium if digoxin toxic

Digoxin

• Has a narrow therapeutic range
• Toxicity may occur at therapeutic levels
• Lower doses now routinely used 0.125 mg daily
• Amiodarone increases serum digoxin concentration (digoxin doses must be reduced if starting amiodarone)
• Multiple other medication interactions
• Dialysis is not effective with digoxin toxicity because of high tissue binding of digoxin
More About Digoxin Toxicity

- EKG Changes with Toxicity
  - Increased automaticity with impaired conduction is common (example: PAT with AV Block)

- Other Signs and Symptoms of Toxicity
  - N & V, HA, Confusion
  - Visual disturbances: halos, change in color perception

More on Ventricular Arrhythmias
**Arrhythmias with ACS: ACC/AHA**

- **V-fib early in ACS**
  - Increase hospital mortality
  - No increase in long term mortality
- **Lidocaine prophylaxis**
  - Decrease V-fib
  - Increase mortality
- **Beta-blockers prophylaxis**
  - Decrease V-fib
- **Correction of potassium and magnesium**

**Monomorphic VT: ACC/AHA**

- **DC cardioversion with sedation if unstable**
- **IV procainamide**
  - Stable VT
  - Caution with CHF or severe LV dysfunction
- **IV amiodarone**
  - Hemodynamically unstable
  - Refractory to shock
- **TTVP for pace termination**
- **Lidocaine if ischemia**
- **Class III: Calcium channel blockers in wide complex of unknown origin; especially if myocardial dysfunction**
Repetitive Monomorphic VT: ACC/AHA

- IV amiodarone, beta-blocker, procainamide
- Generally idiopathic VT – RV outflow tract
  - May be provoked by exercise
  - Beta-blockers or calcium channel blockers may be effective
  - Ablation is successful treatment option

Polymorphic VT: ACC / AHA

- DC cardioversion with sedation when unstable
- IV beta-blockers if ischemia suspected
  - Improve mortality
- IV amiodarone in absence of abnormal repolarization
- Urgent angiography to exclude ischemia
- Lidocaine may be reasonable if ischemia suspected
Incessant VT – VT Storm: ACC/AHA

- **Class I**
  - Revascularization and beta-blocker
  - Followed by IV amiodarone or procainamide

- **Class IIa**
  - IV amiodarone or procainamide followed by VT ablation
  - Important to understand substrate to target treatment

Clinical Pearls for Ventricular Arrhythmias

- V-fib seldom is seldom preceded by warning arrhythmias
  - Prophylactic lidocaine not indicated
- R on T PVCs are typically only important first 24 hours of myocardial infarction
- Bigeminy may need treated if cardiac output effected
- Ventricular ectopy (as infrequent as 15% burden) can result in heart failure
Clinical Pearls for Ventricular Arrhythmias

• Potential reversible causes
  – Hypokalemia: K < 3.2 mEq/L (cause or result)
  – Magnesium < 1.5 mEq/dL
  – Ischemia
  – Use of inotropic agents

Patients Not Requiring Antiarrhythmics

• Because of proarrhythmias or exacerbations of existing arrhythmias antiarrhythmic therapy not indicated for:
  – Asymptomatic atrial ectopy and unsustained SVT
  – Asymptomatic ventricular ectopy without runs of VT
  – Simple ventricular ectopy in AMI with no hemodynamic compromise
  – Asymptomatic unsustained VT with no structural heart disease
  – Asymptomatic WPW without known SVT
  – Mildly symptomatic simple atrial or ventricular ectopy
General Considerations for SCD

• CPR / AED
• Use of IV amiodarone in recurrent ventricular tachyarrhythmias after maximal shock
• Address reversible causes:
  • Hypoxia
  • Electrolyte abnormalities
  • Mechanical factors
  • Volume depletion

Antiarrhythmic Therapy in Ventricular Arrhythmias and Sudden Death

♥ Beta Blockers
  ✓ Suppresses ventricular arrhythmias
  ✓ Reduces incidence of SCD

♥ Amiodarone
  ✓ Suppresses ventricular arrhythmias
  ✓ No definite survival benefit
  ✓ Complex drug interactions and many adverse side effects

♥ Sotalol
  ✓ Suppresses ventricular arrhythmias
  ✓ No definite survival benefit
  ✓ More pro-arrhythmic than amiodarone

• Antiarrhythmics (excluding beta blockers) not used as primary therapy for prevention

• Patients with VT who do not meet criteria for ICD
  • Beta-blocker first line
  • Amiodarone or sotalol if not effective

• Patients with ICD with recurrent VT
  • Sotalol or
  • Combination of amiodarone and beta-blocker
Automatic Implantable Cardioverter Defibrillators

ICD Functions

- ATP-Anti tachycardia Pacing
  - Tiered Antiarrhythmic Therapies

2014
ICD Functions

- **Cardioversion Shock**
  - Delivers shocks from 0.1 to 30 joules synchronized on the R wave

- **Defibrillating Shock**
  - Delivers high energy (20-34 joules) unsynchronized shock for VF
A Final Thought

Impact every patient and family on their journey and provide safe passage by meeting them where they are, connecting with them in a meaningful way, and delivering care with wisdom and intention.

- Karen

Nurses Make a Difference

THANK YOU!!!

Enjoy NTI!

BE THE BEST THAT YOU CAN BE EVERY DAY. YOUR PATIENTS ARE COUNTING ON IT!

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Final slides will be available at www.cardionursing.com next week