Pharmacotherapy in ACLS

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Pharmacotherapy in ACLS

• Lecture Objectives
  1. Know the ACLS algorithms for VF/pulseless VT, bradycardia, and tachycardia with a pulse.
  2. Given a patient scenario, be able to chose the appropriate medication(s) based on the algorithm recommendation.

Readings

Required
• Pharmacotherapy Text Chapter 12: Page 171-183.

Suggested
• ACC/AHA 2005 Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care.
  – Part 7.2: Management of Cardiac Arrest (pp:IV-58 to IV-66).
  – Part 7.3: Management of Symptomatic Bradycardia and Tachycardia (pp:IV-67 to IV-77).

Clinical Presentation

• Symptoms
  – Anxiety, change in MS, unconscious
  – Cold, clammy extremities
  – Dyspnea, SOB, no respiration
  – Chest pain
  – Diaphoresis
  – Nausea/vomiting

• Signs
  – Hypotension
  – Tachycardia, bradycardia, irregular, no pulse
  – Cyanosis
  – Hypothermia
  – Distant or absent heart and lung sounds

PULSELESS ARREST

Ventricular Tachycardia (pulseless)
Ventricular Fibrillation
Asystole
Pulseless Electrical Activity (PEA)
EPINEPHRINE

- Alpha and beta receptor agonist
  - Increases myocardial and cerebral perfusion pressure during CPR
  - Increases systemic arteriolar vasoconstriction
  - Increases aortic diastolic pressure
- Increases Heart Rate
- Increases Force of Contraction
- Increases Myocardial Oxygen Demand

EPINEPHRINE

- Bolus dose
  - 1mg IV bolus every 3-5 minutes
  - 10ml of 1:10,000 solution
  - Follow each dose with 20ml IV flush
- High dose epinephrine (up to 0.2mg/kg)
  - Literature does not support efficacy
  - May be needed if beta-blocker or CCB overdose

VASOPRESSIN

- Coronary and renal vasoconstriction
- Increased systemic vascular resistance
  - Increases myocardial and cerebral blood flow during CPR
  - Increases aortic diastolic pressure
**VASOPRESSIN**

Cardiac arrest patients randomized to VP 40 units IV or EPI 1mg IV.
EPI administered q3-5 min if no return of pulse.

<table>
<thead>
<tr>
<th></th>
<th>VP(n=104)</th>
<th>EPI(n=96)</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Additional EPI</td>
<td>87%</td>
<td>81%</td>
<td></td>
</tr>
<tr>
<td>Survival 1hr post arrest</td>
<td>39%</td>
<td>35%</td>
<td>0.66</td>
</tr>
<tr>
<td>H discharge</td>
<td>12%</td>
<td>14%</td>
<td>0.67</td>
</tr>
<tr>
<td>Tachyarrhythmias</td>
<td>10%</td>
<td>8%</td>
<td>0.75</td>
</tr>
</tbody>
</table>

Out of hospital arrest randomized to VP 40 units IV x 2 or EPI 1mg IV x 2.
Additional EPI as needed.

<table>
<thead>
<tr>
<th></th>
<th>VP (n=589)</th>
<th>EPI (597)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>H admission*</td>
<td>36.3%</td>
<td>31.2%</td>
<td>0.06</td>
</tr>
<tr>
<td>H discharge*</td>
<td>9.9%</td>
<td>9.9%</td>
<td>0.99</td>
</tr>
<tr>
<td>Additional EPI*</td>
<td>63.3%</td>
<td>60.1%</td>
<td></td>
</tr>
<tr>
<td>H admission*</td>
<td>25.7%</td>
<td>16.4%</td>
<td>0.002</td>
</tr>
<tr>
<td>H discharge*</td>
<td>6.2%</td>
<td>1.7%</td>
<td>0.002</td>
</tr>
</tbody>
</table>

*Subset with asystole SS more H admission and discharge with VP vs. EPI, but no improvement in neurologically intact survival.

**VASOPRESSIN**

• 40 units IV push x 1 dose as a substitute for the first or second EPI dose.

• If no response after 5-10 minutes, return to epinephrine dosing.

**Vasopressin vs. Epinephrine**

• Metabolic acidosis may blunt epinephrine effects, but not vasopressin.

• Beta receptor stimulation by epinephrine can increase myocardial oxygen demand. Vasopressin does not stimulate beta receptors.

**VT/VF**

Indications

– Pulseless VT/VF

– PMVT and wide complex VT

– Stable VT if cardioversion fails

**Amiodarone**

• Indications

– Pulseless VT/VF

– PMVT and wide complex VT

– Stable VT if cardioversion fails
Amiodarone vs. Lidocaine
Dorian et al. NEJM 2002; 346:884-90
• Double blind-controlled trial with block randomization
Out of hospital arrest.
Resistant to 3 shocks, 1 dose EPI, 4th shock, or recurrent VF after defibrillation.
• Medications
Amiodarone 5mg/kg bolus, MR with 2.5mg/kg.
Lidocaine 1.5mg/kg bolus, MR with 1.5 mg/kg.

Amiodarone vs. Lidocaine
Dorian et al. NEJM 2002; 346:884-90
• Survival to discharge
  | Amiodarone | Lidocaine |
  | 9/41 (21.9%) | 5/20 (25%) p=0.34 |
• Treatment for bradycardia or dysrhythmias
  | Amiodarone | Lidocaine |
  | Atropine 24% | 23% |
  | Dopamine 7% | 4% |
  | Open label lidocaine 6% | 6% |

Amiodarone vs. Placebo
Kudenchuk et al. NEJM 1999;341:871-8
• Out of Hospital Cardiac arrest-shock
• Shock refractory VT/VF
• Amiodarone 300mg in 20ml D5W or PL

Amiodarone
• Cardiac Arrest
  300mg IV push, repeat in 3-5 mins. at half dose (150mg)
• Infusion (Wide Complex Tachycardia)
  – Rapid: 150 mg IV over 10mins, repeat as needed
  – Slow: 360 mg IV over 6 hrs (1mg/min)
  – Maintenance: 540 mg IV over 18 hrs (0.5mg/min)
• Maximum dose 2.2 gm in 24 hours
**LIDOCAINE**

- Significant ventricular ectopy.
- VT/VF that persists after defibrillation/epinephrine or vasopressin.
- Ventricular tachycardia with a pulse.
- Wide-complex tachycardia of uncertain origin.
- Post-MI ventricular arrhythmias.

**VF/Pulseless VT**
- 1-1.5 mg/kg initial
- Repeat dose at 0.5-0.75 mg/kg in 5-10 minutes
- Maximum total dose = 3 mg/kg
- Only bolus therapy is used in cardiac arrest

**Continuous infusion**
- Mix 1 gram of lidocaine in 250 ml or 2 grams in 500 ml
- Infusion rate 1-4 mg/min
  - After 1 mg/kg bolus, drip 2 mg/min
  - After 1 1/2 - 2 mg/kg, drip 3 mg/min
  - After 2 1/2 - 3 mg/kg, drip 4 mg/min
- Because Lidocaine is metabolized in the liver, the infusion rate should be reduced by 50% in:
  - Hepatic dysfunction
  - >70 years of age
  - Decreased cardiac output
    - Shock
    - Acute MI
    - Congestive Heart Failure

**In patients with a pulse, a second IV bolus is recommended 10 min. after the initial lidocaine bolus to prevent subtherapeutic lidocaine levels.**

**Pharmacokinetics**
**LIDOCAINE**

- Dizziness
- Drowsiness
- Mild Agitation
- Slurred Speech
- Hearing Impairment
- Disorientation & Confusion
- Muscle Twitching/Seizures
- Respiratory Arrest

**Precautions**

- Lidocaine may be LETHAL in a bradycardia with a ventricular escape rhythm.
  - Second degree AV Block Type II
  - Third degree AV Block with a wide QRS
  - Idioventricular rhythm

**MAGNESIUM SULFATE**

- Torsades de Pointes
- Cardiac arrest with known or suspected hypomagnesemia
- Refractory VF

**Cardiac Arrest:**
- 1-2 grams (2-4ml of 50% solution) diluted in 10ml D5W IV push
- Torsades with a pulse:
  - Loading dose of 1-2 grams mixed in 50-100ml of D5W and administered over 5-60 minutes
  - Followed with 0.5 - 1.0 g/h up to 24 hours

**Overdose**

- Signs and symptoms of magnesium overdose include:
  - Hypotension
  - Flushing, sweating
  - Bradycardia, AV block
  - Decreased respiration rate
  - Drowsiness, decreasing level of consciousness
  - Diminished reflexes or muscle weakness, flaccid paralysis

- Physiological antagonism
  - Electrical opposition at site of action
- Elemental calcium 100-200 mg IV push or infusion over 10 min
  - Calcium gluconate 10% -- 9 mg/mL (0.45 mEq/mL)
  - Calcium chloride 10% -- 27 mg/mL (1.36 mg/mL)
Asystole

Pulseless Electrical Activity

ATROPINE

- Blocks vagally mediated parasympathetic (cholinergic) actions on the heart
  - Increases rate of sinus node discharge
  - Improves AV conduction
  - Increases blood pressure
  - May restore cardiac rhythm in asystole and bradycardic pulseless electrical activity (PEA)

ATROPINE

- Indications in ACLS*
  - Asystole
  - Pulseless Electrical Activity (PEA)
    - If PEA rate is slow

*No randomized controlled trials to support

ATROPINE

- Asystole, Bradycardic PEA:
  - 1.0mg rapid IV bolus every 3-5 minutes
  - Maximum 0.04mg/kg (3mg)
  - 3mg given IV is a fully vagolytic dose in most patients
**Atropine**

- Doses of less than 0.5mg may further slow heart rate
- Excessive doses may result in tachycardia
- May exacerbate ischemia or induce VT or VF
  - Use with caution in acute MI

**Summary of Pulseless Arrest**

- **BLS, CPR, Oxygen, Monitor/defibrillator**
- **Shockable rhythm-VF/VT-YES**
  - Shock-CPR-shock-CPR
  - EPI 1mg q3-5 min or VP 40 units x 1, then EPI
  - CPR-Shock-CPR
  - Consider Antiarrhythmics
    - Amiodarone or Lidocaine
    - Magnesium for Torsades de pointes

**Summary of Pulseless Arrest**

- **BLS, CPR, Oxygen, Monitor/defibrillator**
- **Shockable rhythm-Asystole/PEA-NO**
  - CPR
  - EPI 1mg q3-5 min or VP 40 units x 1, then EPI
  - Atropine 1mg IV q5 min x 3
  - Shockable rhythm-YES-VF/VT algorithm
    - NO-continue with EPI and Atropine as above.

**Bradyarrhythmia**
ATROPINE

- Symptomatic Bradycardia:
  - 0.5-1.0 mg rapid IV bolus every 3-5 minutes
  - Maximum 0.03-0.04mg/kg (2-3mg)
  - If unresponsive to atropine, consider
    - Epinephrine
    - Dopamine

EPINEPHRINE

Bradycardia Infusion

- Mix 1mg of 1:1000 in 500ml bag of normal saline
- Start at 1mcg/min and titrate to desired response (2-10mcg/min)

DOPAMINE

- Dopamine 400mg/D5W250ml
  - Start at 2 mcg/kg/min, titrate to 10 mcg/kg/min
  - Predominant beta-adrenergic stimulating properties
    - Increased myocardial contractility
    - Increase in heart rate
    - Increased cardiac output

LIDOCAINE

Precautions

- If the heart rate is less than 60 bpm, do not treat ventricular ectopy! Treat the Bradycardia First.
Bradycardia

**Summary**

- ABC
- Adequate perfusion?
  - Increase HR as needed.
- Reminders.

Tachycardia with Pulse

- Narrow Complex (QRS < 0.12 sec)
  - Sinus tachycardia
  - Atrial fibrillation/flutter
  - AV node reentry
  - Accessory pathway-mediated tachycardia
  - Atrial tachycardia (ectopic or reentry)
  - Multifocal atrial tachycardia
  - Junctional tachycardia
- Wide Complex (QRS ≥ 0.12 sec)
  - Ventricular tachycardia
  - SVT with Aberrancy
  - Pre-excited tachycardia
ADENOSINE
• Decreases SA and AV node activity.
• Can interrupt reentrant pathways through the AV node.
• Direct effect on supraventricular tissue.
• Will not convert AF, A flutter, ventricular arrhythmias
  – But may produce AV or retrograde block that may clarify the diagnosis.

ADENOSINE
• Narrow QRS Tachycardia (PSVT)
• Effective in terminating those due to reentry involving the AV or Sinus node

ADENOSINE
• 6mg rapid IV bolus over 1-3 seconds.
  – Follow with 20ml saline flush.
  – Elevate extremity.
• If no response in 1-2 minutes, administer 12mg over 1-3 seconds.
• May repeat 12mg dose once in 1-2 minutes.

ADENOSINE
• Short half-life
  – Each dose should be administered rapidly over 1-3 seconds
• Follow with Saline flush 20 ml
• Repeat dose may be administered in 1-2 minutes

ADENOSINE
• Side effects common but transient and usually resolve within 1-2 minutes:
  – Flushing Lightheadedness
  – Nausea Asystole/bradycardia
  – Headache Ventricular ectopy
  – Dyspnea
  – Hypotension
  – Chest pressure

ADENOSINE
• Methylxanthines (caffeine, theophylline)
  – Block adenosine receptor
  – Higher doses of adenosine needed
• Carbamazepine (Tegretol)
  – Higher degrees of heart block may occur
• Dipyridamole
  – Blocks adenosine uptake-potentiates effect
Calcium Channel Blockers

- SVT recurrence after conversion with adenosine.
- SVT conversion fails with adenosine.

Beta-Adrenergic Blockers

Metoprolol (β1)
- 5mg slow IV (over 2-5 minutes) repeat every 5 minutes as tolerated to 15mg total.
- Follow with 50 mg twice daily x 2, then 100mg twice daily.

Propranolol (β1 AND β2)
- 0.1mg/kg total dose slow IV push (1mg/min).
- Divided into three doses administered at 2-3 minute intervals.
- Repeat after 2 minutes if necessary.

Calcium Channel Blockers

- Verapamil
  - 2.5 to 5.0 mg slow IV bolus over 2 min (3min in elderly)
  - May repeat with 5-10mg in 15-30min (max. 20mg)
    - If no response and the blood pressure remains normal or elevated

- Diltiazem
  - 0.25mg/kg (20mg) IV over 2 minutes
  - If needed, follow in 15 minutes with 0.35mg/kg (25mg) IV over 2 min
  - Maintenance infusion of 5-15 mg/hr
  - Titrate to heart rate watch blood pressure

Beta-Adrenergic Blockers

Atenolol (β1)
- 5mg slowly IV over 5 minutes
- After 10 minutes may repeat 5mg dose IV over 5 minutes

Esmolol (t½ 2-9 minutes) (β1)
- 0.5mg/kg slow IV (over 1min )
- Infusion at 0.05mg/kg/min
- Maximum 0.3mg/kg/min
- May repeat loading dose before infusion rate increases.

Wolff-Parkinson-White Syndrome

- AV node blocking drugs can cause paradoxical increase ventricular response
- Amiodarone
- Avoid
  - calcium channel blockers
  - beta-blockers
  - digoxin
  - adenosine
Tachycardia with Pulse

Summary

- ABC, EKG, cause
- Is patient stable
  - No-synchronized cardioversion
  - Yes
    - Narrow or wide QRS?
    - Regular or irregular
    - Pharmacotherapy based on results

When to administer meds:

- Meds should be administered during CPR

CPR-RHYTHM CHECK-CPR (WHILE MEDS ADMINISTERED AND DEFIBRILLATOR CHARGED)-SHOCK

- Designed to minimize interruption in chest compressions.

Tracheal Drug Administration

- Several medications may be administered via the tracheal tube,
  - Epinephrine 2-2.5 times IV dose
  - Atropine 2-2.5 times IV dose
  - Lidocaine 2-2.5 times IV dose
  - Vasopressin SAME as IV dose
- Catheter tip beyond ETT, stop CPR, spray solution quickly down ETT, several quick insufflations, resume CPR.
ACLS Pulseless Arrest Algorithm.

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Figure 1. Bradycardia Algorithm.
Figure 2. ACLS Tachycardia Algorithm.