Can the block help the beat?
Beta blockers for ventricular fibrillation

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Learning Objectives

1. Describe the presentation and management of ventricular fibrillation (VF)
2. Identify the potential cellular benefit of beta blockers during VF
3. Evaluate the evidence regarding beta blockers in VF
4. Formulate a recommendation based on the available literature
I. Ventricular Fibrillation (VF)

A. Introduction \textsuperscript{1,2}

1. High-frequency and asynchronous contraction of the ventricles resulting in no cardiac output or blood pressure

2. Almost always fatal
   i. Approximately 92\% of out-of-hospital cardiac arrest die
   ii. Tends to deteriorate into asystole over time

3. Most common arrhythmia in cardiac arrest

4. The initial rhythm in 65-85\% of cardiac arrest patients

B. Epidemiology \textsuperscript{2,3,4}

1. VF accounts for approximately 100,000 deaths each year in the US

2. The incidence in the US is 0.1-0.2\%

C. Characteristics \textsuperscript{5,6}

1. Disorganized and totally random activation of ventricle

2. Electrical wavelet activity from multiple wandering locations

Figure 1. VF conduction\textsuperscript{6}

http://www.washingtonhra.com

D. Presentation

1. VF patients all have similar presentations
   i. Hemodynamic collapse
   ii. Lack of blood pressure
   iii. Absent heart sounds
   iv. Apnea or agonal breathing

2. Primary vs secondary \textsuperscript{7}
   i. Primary
      a. Independent of myocardial infarction damage
   ii. Secondary
      a. Associated with heart failure or underlying cardiac issues
Figure 2. Sinus rhythm evolving into VF on ECG

E. Risk Factors

1. Prior heart disease
   i. Myocardial infarction (13.6/1000 person-years)
   ii. Heart failure (21.9/1000 person-years)

2. Premature ventricular contractions

3. Coronary artery disease

4. Family history of cardiac arrest
   i. 2-fold increase with first degree relative

II. Management

A. Advanced cardiac life support (ACLS) overview (see Appendix A. for algorithm)

1. Builds on basic life support (BLS)
   i. Activation of emergency response system
   ii. High quality cardiopulmonary resuscitation (CPR)
   iii. Early defibrillation
      a. First line treatment for VF and ventricular tachycardia
      b. Only rhythm-specific therapy proven to increase survival
      c. Biphasic (120-200 joules) or monophasic (360 joules)

2. ACLS team
   i. Leader
   ii. Compressions
   iii. Airway
   iv. Vitals and defibrillation
   v. Access and medication
   vi. Recorder

3. Airway management

4. Ventilation
   i. Bag-mask ventilation

5. Medications
   i. Help to facilitate and maintain spontaneous rhythm
   ii. Increased rates of return of spontaneous circulation (ROSC)

6. Treat reversible causes
   i. H & T’s
Table 1. Reversible causes of cardiac arrest

<table>
<thead>
<tr>
<th>Reversible cause</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypovolemia</td>
<td>Fluids</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>Ventilation (advances airway)</td>
</tr>
<tr>
<td>Hydrogen ion (acidosis)</td>
<td>Ventilation, Sodium bicarbonate IV</td>
</tr>
<tr>
<td>Hypo-/hyperkalemia</td>
<td>Potassium / Sodium bicarbonate IV, Glucose + Insulin, Calcium IV</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>Warming measures</td>
</tr>
<tr>
<td>Tension pneumothorax</td>
<td>Needle decompression</td>
</tr>
<tr>
<td>Tamponade</td>
<td>Pericardiocentesis</td>
</tr>
<tr>
<td>Toxins</td>
<td>Antidote or Reversing agent</td>
</tr>
<tr>
<td>Thrombosis, pulmonary</td>
<td>Fibrinolytic treatment</td>
</tr>
<tr>
<td>Thrombosis, cardiac</td>
<td>Percutaneous Coronary Intervention (PCI)</td>
</tr>
</tbody>
</table>

B. ACLS Medication<sup>10</sup>

1. Epinephrine
   i. Endogenous catecholamine with both alpha and beta activity
   ii. 1 mg IV push every 3-5 minutes
   iii. Primary benefit is alpha receptor stimulation (vasoconstriction)
       a. Increase coronary and cerebral perfusion pressure
       b. Found to improve ROSC
   iv. Controversial effects with epinephrine
       a. Increased demand and decreased oxygen

2. Vasopressin
   i. Nonadrenergic peripheral vasoconstrictor
      a. V<sub>1</sub> receptor activation
   ii. 40 units IV push for 1 dose
      a. To replace 1<sup>st</sup> or 2<sup>nd</sup> epinephrine dose
      b. No difference in outcomes verses epinephrine
   iii. Not affected by pH variation

3. Amiodarone
   i. Antiarrhythmic agent
      a. Potassium, sodium, and calcium channel blocker
      b. Alpha and beta adrenergic blocking properties
   ii. VF unresponsive to CPR, defibrillation, and vasopressor therapy
   iii. 300 mg IV push
      a. Repeat 150 mg if needed
   iv. Termination of arrhythmias are improved

4. Lidocaine
   i. Class Ib antiarrhythmic
      a. Sodium channel blocker
   ii. 1-1.5 mg/kg IV
      a. Repeat 0.5-0.75 mg/kg if needed
   iii. No proven short- or long-term efficacy
      a. Consider if amiodarone not available
III. Cardiac action potential

**Figure 3. Cardiac electrophysiology**

<table>
<thead>
<tr>
<th>Phase 0</th>
<th>Depolarization - Rapid Na+ channels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>Peak-L-type Ca**++** channels</td>
</tr>
<tr>
<td>Phase 2</td>
<td>Plateau- Rectifier K+ channels</td>
</tr>
<tr>
<td>Phase 3</td>
<td>Repolarization- Ca**++** channels close</td>
</tr>
<tr>
<td>Phase 4</td>
<td>Resting membrane potential</td>
</tr>
</tbody>
</table>

IV. Catecholamine effects on myocardium

A. Catecholamines

1. Bind to G-protein coupled adrenergic receptors
   i. Intracellular enzyme activation
      a. Cardiac and/or vascular response

**Figure 4. Intracellular mechanism of action of catecholamines**

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http://www.cvpharmacology.com
B. Positive effects
   1. Essential for maintaining cardiovascular system
   2. “Fight-or-flight” response
   3. Life saving effects in hypotension and decreased cardiac output

C. Detrimental effects
   1. Calcium overload
      i. Hallmark of persistent catecholamine exposure
      ii. Change in mitochondrial membrane permeability
      iii. Sarcoplasmic reticulum dilation
   2. Oxidative stress
      i. Hydrogen peroxide formation through catecholamine deamination
      ii. Superoxide anion radical formation
      iii. Aminochrome accumulation
         a. Coronary vasoconstriction
   3. Mitochondrial dysfunction
      i. Opening of mitochondrial permeability transition pore

Figure 5. Effects of sustained catecholamine exposure
V. Bench Research
   A. Mann et al used cultures of adult cardiac muscle cells to evaluate norepinephrine
      1. Determining norepinephrine's effects on cardiac myocytes in vitro
         i. Cultured cells treated with adrenergic agonist, antagonist, chelating and calcium
            channel blocking agents
         ii. Only lowest concentration producing effect reported
         iii. Response based on spontaneous beating

Table 2. Induction of spontaneous cardiac myocyte beating

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Beating of myocytes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0</td>
</tr>
<tr>
<td>$10^{-6}$ M norepinephrine</td>
<td>20.9 ± 2.5</td>
</tr>
<tr>
<td>$10^{-5}$ M dideoxyadenosine + norepinephrine</td>
<td>0</td>
</tr>
<tr>
<td>$10^{-6}$ M forskolin</td>
<td>12.5 ± 4.1</td>
</tr>
<tr>
<td>$10^{-3}$ M dibutyryl cyclic AMP</td>
<td>20.5 ± 4.6</td>
</tr>
<tr>
<td>$10^{-3}$ M ethylene glycol tetraacetic acid (EGTA) + norepinephrine</td>
<td>0</td>
</tr>
<tr>
<td>$10^{-6}$ M verapamil + norepinephrine</td>
<td>0</td>
</tr>
<tr>
<td>$10^{-2}$ M cobalt + norepinephrine</td>
<td>0</td>
</tr>
<tr>
<td>$10^{-5}$ M lidocaine + norepinephrine</td>
<td>20.2 ± 3.4</td>
</tr>
<tr>
<td>$10^{-5}$ M tetrodotoxin + norepinephrine</td>
<td>20.8 ± 3.1</td>
</tr>
<tr>
<td>$10^{-3}$ M dibutyryl cyclic AMP + $10^{-6}$ verapamil</td>
<td>0</td>
</tr>
</tbody>
</table>

See appendix B for mechanisms

iv. Results
   a. Response blocked by removing calcium or blocking slow calcium channels

2. Effects of norepinephrine on cAMP levels within stimulated cells
   i. Cultured cells pretreated with propranolol or normal medium
   ii. Stimulation with norepinephrine for 1,5,15, and 30 minutes
   iii. Radioimmunoassay measured cAMP

Figure 6. cAMP levels with norepinephrine stimulation
iv. Results
   a. 4 fold increase in cAMP with norepinephrine stimulation
   b. Propranolol blunted cAMP elevation
v. Beta blockers decrease cAMP levels, causing decreased calcium release

3. Effects of norepinephrine stimulation on calcium concentrations
   i. Cultured cells pretreated with propranolol, normal medium alone, or EGTA
   ii. Calcium concentrations measured directly with tetracarboxylate calcium indicator fura-2
      a. Emission of fluorescence measured

Figure 7. Calcium concentrations after norepinephrine stimulation

iii. Results
   a. Propranolol and EGTA significantly reduced calcium concentrations
iv. Beta blockers and chelating agents decrease calcium concentrations, limiting the overall effects norepinephrine

VI. Animal Studies 15-17
   1. To determine if short-acting beta1-selective blockade during CPR will improve initial and post-resuscitation survival
   2. Esmolol group (n=9): 300µg/kg bolus
   3. Placebo group (n=9)
   4. Methods
      i. VF induced and left untreated for 6 minutes
      ii. Resuscitation
         a. Precordial compressions and mechanical ventilation
         b. Defibrillation attempted up to 3 times
         c. Esmolol injected 2 minutes after precordial compression into right atrium
      iii. ROSC: supraventricular rhythm with MAP 60 mmHg for 5 minute
5. ROSC
   i. Esmolol 9/9 vs placebo 5/9 (p<0.05)
6. Postresuscitation survival prolonged in esmolol group (50 vs 20 hours)(p<0.05)

1. Assess whether beta blockade will improve initial cardiopulmonary resuscitation success in piglets
2. Group A (n=10): placebo (saline) + epinephrine
3. Group B (n=10): atenolol + epinephrine
4. Methods
   i. VF was induced
   ii. Arrhythmia confirmed by electrocardiography and sudden drop in MAP
   iii. After induction of VF, mechanical ventilation was stopped and left untreated for 8 minutes
   iv. Resuscitation procedure
      a. 100% oxygen and study drugs
      b. Mechanical chest compressions for 2 minutes
      c. Defibrillation attempted after 2 minutes
      d. Maximum of three cycles
   v. End points: asystole, ROSC, or VF after 3 failed defibrillations
5. 4 animals in group A had ROSC, 9 in group B had ROSC (p< 0.05)

Table 3. Different parameter before defibrillation and ROSC after defibrillation

<table>
<thead>
<tr>
<th></th>
<th>Epi + Placebo (n=10)</th>
<th>Epi + Atenolol (n=10)</th>
<th>p&lt;0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP 2 minutes post drug administration</td>
<td>73 ± 11</td>
<td>90.5 ± 11.3</td>
<td></td>
</tr>
<tr>
<td>DBP 2 minutes post drug administration</td>
<td>32 ± 4.5</td>
<td>49.1 ± 6.9</td>
<td></td>
</tr>
<tr>
<td>CPP</td>
<td>19 ± 7.0</td>
<td>27.7 ± 5.3</td>
<td></td>
</tr>
<tr>
<td>ROSC</td>
<td>4</td>
<td>9</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>ROSC First Defibrillation</td>
<td>4</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>ROSC Second Defibrillation</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

6. Group A > group B postresuscitation heart rate (p<0.05)

1. Part 1: Assess the levels of myocardial interstitial catecholamines at baseline, during 8 minutes of VF, after defibrillation, and during reperfusion
   i. 8 mixed-breed pigs
   ii. Open chest with 2 microdialysis probes in lateral wall of LV
   iii. Catheters placed in aorta and coronary sinus (CS)
   iv. Interstitial fluid (ISF) from left ventricle collected
   v. VF induced and continued for 8 minutes
   vi. Defibrillation
vii. Results
   a. Significant increase in both norepinephrine and epinephrine during VF
   b. Aortic and CS levels do not correlate to ISF levels
      • Plasma levels peak earlier and higher
      • Decrease rapidly below ISF values
   c. Longer sustained levels in ISF (p<0.05)

2. Part 2: Determine the effects of short-acting beta blockade on catecholamine surge and survival
   i. Catheter placed at junction of superior vena cava and right atrium to measure coronary perfusion pressure and central venous pressure
   ii. 8 minutes of VF
   iii. External defibrillation
   iv. 1 mg/kg esmolol (n=8) or placebo (saline) (n=8) intravenously after defibrillation
v. ACLS performed in both groups
   a. Only epinephrine and dobutamine used

Table 4. Resuscitation data

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=8)</th>
<th>Esmolol (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival (p&lt;0.05)</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Mean number of shocks</td>
<td>10 ± 8</td>
<td>5 ± 4</td>
</tr>
<tr>
<td>Total CPR time (min)</td>
<td>27 ± 15</td>
<td>13 ± 7</td>
</tr>
<tr>
<td>Survivor CPR time (min)</td>
<td>9 ± 8</td>
<td>9 ± 7</td>
</tr>
<tr>
<td>Coronary perfusion pressure (mmHg)</td>
<td>15 ± 7</td>
<td>17 ± 7</td>
</tr>
<tr>
<td>Animals requiring dobutamine</td>
<td>1/3</td>
<td>2/7</td>
</tr>
</tbody>
</table>

vi. Esmolol improved ROSC

VII. Literature Review


Overview

Objective

To determine the efficacy of sympathetic blockade in treatment of electrical storm (ES) patients and compare their outcomes with ES patients treated according to ACLS guidelines

Trial Design

Retrospective observational analysis, non-randomized, non-blinded

Inclusion Criteria

- Recent myocardial infarct (MI) with ES.
  - ES: ≥20 ventricular tachycardia (VT)/VF episodes per day or ≥ 4 VT/VF episodes per hour
  - Recent MI: occurring within 72 hours to 3 months before the onset of ES

Exclusion Criteria

- Onset of MI was <72 hours
- Acute pulmonary edema
- Previous treatment with intravenous amiodarone
- Acute respiratory failure
- Acquired or congenital long QT syndrome
- Recent coronary revascularization (<1 week before the onset of ES)

Outcomes

- Termination of ES
- Determine short-term and long term effects of treatment

Interventions

Sympathetic blockade treatment within 1 hour after all ACLS antiarrhythmic medications were discontinued

Sympathetic blockade treatments:

- Left stellate ganglionic blockade
  - 10-20 mL 1% xylocaine injected millimeters anterior to lateral process of spine until Horner’s syndrome developed (miosis, partial ptosis)
  - Repeat with 10 mL 0.25% marcaine or xylocaine if needed
- Esmolol 300-500 mg/kg load followed by 25-50 mg/kg/min infusion
  - Infusion titrated every 5-10 minutes up to 250 mg/kg/min
- Propranolol 0.15 mg/kg followed by 3-5 mg dose every 6 hours
- ACLS Protocol
  - Lidocaine 1 mg/kg IV bolus was first antiarrhythmic

CJStephenson 11
Repeated once and continuous infusion started at 1-4 mg/min for persistent VF
- Procainamide 100 mg bolus was given if no sinus rhythm every 5 minutes up to 500-1000 mg then 2-4 mg/min continuous infusion
- Procainamide alternative was bretylium tosylate 5 mg/kg every 5 minutes up to 25 mg/kg

Baseline Characteristics
- No significant differences in any variables

Table 5. Characteristics of sympathetic blockade vs ACLS groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Sympathetic blockade (n=27) group 1</th>
<th>ACLS (n=22) group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59 ± 11</td>
<td>56 ± 9</td>
</tr>
<tr>
<td>Men/women</td>
<td>23/4</td>
<td>19/3</td>
</tr>
<tr>
<td>Ejection Fraction (%)</td>
<td>31 ± 9</td>
<td>34 ± 6</td>
</tr>
<tr>
<td>Calcium antagonist</td>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>Onset of VF after MI (days)</td>
<td>12 ± 10</td>
<td>11 ± 12</td>
</tr>
<tr>
<td>K+ &lt;3.5</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

Primary Outcomes
- 1-week mortality rate, n=6 (22%) group 1 vs n=18 (82%) group 2 (p<0.0001)
- Overall survival to 1 year: 67% group 1 vs 5% group 2 (p<0.0001)

Figure 10. Kaplan-Meier survival cure of sympathetic blockade and ACLS group

Conclusion
- Sympathetic blockade along with amiodarone improves survival of ES

Strengths
- Standard ACLS vs sympathetic blockade
- Length of follow-up

Limitations
- Treatment was physician preference
- Retrospective, Non-blinded
- Sample size
- ACLS guidelines contained lidocaine which is no longer first line

### Overview

**Objective**
Evaluating the effects of landiolol on electrical storm (ES) refractory to class III antiarrhythmics.

**Trial Design**
Prospective, observational.

### Inclusion Criteria
- Patient had ES
  - ES: sustained VT/VF twice or more per hour or 3 times or more over 6 hours
  - Class III antiarrhythmics administered to all patients prior to inclusion
  - Difficult to treat following established guidelines
  - CPR, electric cardioversion, antiarrhythmic drugs

### Exclusion Criteria
- Cardiac arrest at time of arrival
- Antiarrhythmic drugs before arrival
- Renal failure (SCr >2.0 mg/dL)
- Hemodynamically stable VT

### Outcomes
- Inhibition of ES, survival, and discharge from hospital

### Interventions
- Landiolol initiated at 2.5µg/kg/min; starting maintenance 10-40µg/kg/min
  - Effects assessed 10 minutes after administration
  - Titration using doubling protocol (2.5-5-10-20 etc.)
  - Maximum dose of 80 µg/kg/min
- Severe bradycardia or hypotension in landiolol effective treatment patients
  - Temporal pacemaker or catecholamines were used as needed
  - Treatment was discontinued if landiolol treatment was difficult to maintain with supportive treatment
- Inhibition of ES
  - Completely resolved VT/VF for 12 hours after maintenance dose administered
  - Oral carvedilol or bisoprolol given concomitantly at 2.5 and 1.25 mg/day for landiolol responsive patients

### Results
- 42 patients admitted to critical care center
- All had ES and were difficult to treat following established guidelines
- 60% had ischemic heart disease
- 21 (50%) patients had an acute MI
- Mean left ventricular ejection fraction 39 ± 15%
- Killip class III and IV in 21(50%) patients
- Mean APACHE II score 19 ± 10
- Number of shocks was 5 ± 13
- 17(40%) patients had assisted circulation devices

### Primary Outcomes
- Landiolol inhibited ES in 33 (79%) patients

**Take Home Points**
- Sympathetic blockade had better outcomes than ACLS alone
- Unknown effects of sympathetic blockade without amiodarone
• 25 (60%) patients survived and were discharged
• Significant differences were found between survivors and non-survivors

**Table 6. Significant differences between survivors and non-survivors**

<table>
<thead>
<tr>
<th></th>
<th>Survivors (n=25)</th>
<th>Non-survivors (n=17)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60 ± 16</td>
<td>72 ± 11</td>
<td>0.01</td>
</tr>
<tr>
<td>Acute MI</td>
<td>8 (32%)</td>
<td>13 (76%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Killip class (I/II/III/IV)</td>
<td>16/1/0/8</td>
<td>4/0/2/11</td>
<td>0.02</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>15 ± 9</td>
<td>24 ± 11</td>
<td>0.01</td>
</tr>
<tr>
<td>pH</td>
<td>7.3 ± 0.1</td>
<td>7.2 ± 0.2</td>
<td>0.007</td>
</tr>
<tr>
<td>Hypertension</td>
<td>16 (64%)</td>
<td>16 (94%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Assisted circulation device</td>
<td>5 (20%)</td>
<td>9 (53%)</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>IABP*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Intra-aortic balloon pump

- Mean duration of landiolol treatment was 29 ± 31 hours
- Mean dose was 7.5 ± 12.2 µg/kg/min
- Landiolol reduced heart rate (HR) (p<0.0001)
- No changes noted in blood pressure (BP)
- 21 (64%) patients received carvedilol and 12 (36%) received bisoprolol

**Conclusion**

When class III antiarrhythmics are ineffective landiolol should be considered for possible ES refractory to antiarrhythmics.

**Strengths**

- Landiolol used after traditional standards of care failed
- Initiated landiolol at very low dose
- Specific reassessment period after administration
- Clinical features used for evaluation

**Limitations**

- Lack of control
- Differences in baseline characteristics between survivors and non-survivors
- Sample size
- Treatment for patients experiencing MI was only noted for 1 patient

**Take Home Points**

- Landiolol was effective at inhibiting ES in the majority of patients
- Non-survivors had significantly different clinical feature than survivors

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**Driver BE et al. Use of esmolol after failure or standard cardiopulmonary resuscitation to treat patients with refractory ventricular fibrillation. Resuscitation. 2014;85:1337-1341.**

**Overview**

**Objective**

To compare the outcomes of patients who received esmolol to those who did not receive esmolol during refractory ventricular fibrillation.

**Trial Design**

Retrospective observational analysis, non-randomized, non-blinded

**Inclusion Criteria**

- Initial rhythm was VF or VT
- Cardiac arrest (CA) in the emergency department (ED) or had CA pre-hospital and remained in arrest upon ED arrival
- Received at least 3 defibrillation attempts, 300 mg of amiodarone, and 3 mg of adrenaline

**Exclusion Criteria**

- Received esmolol before CA or after sustained ROSC

**Outcomes**

Not defined
Data collected
• Pre-hospital and ED rhythms
• Medications administered
• CA management
• Presence of ST-elevation myocardial infarction (STEMI)
• Timing of ROSC
• Patient outcomes

Definitions
• Temporary ROSC - non-fleeting return of restored circulation lasting more than 30 s, but less than 20 min
• Sustained ROSC - 20 min of spontaneous circulation without recurrence of CA

Interventions
Esmolol 500 mcg/kg load followed by infusion at 0-100 mcg/kg/min

Results

Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Esmolol (n=6)</th>
<th>No esmolol (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>54.5</td>
<td>56</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>6 (100)</td>
<td>18 (94.7)</td>
</tr>
<tr>
<td>Initial rhythm VF(%)</td>
<td>5 (83.3)</td>
<td>18 (94.7)</td>
</tr>
<tr>
<td>Witnessed arrest (%)</td>
<td>5 (83.8)</td>
<td>16 (84.2)</td>
</tr>
<tr>
<td>Bystander CPR (%)</td>
<td>3/4 (75)</td>
<td>14/18 (77.8)</td>
</tr>
<tr>
<td>Time from call to EMS arrival (min)</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Total pre-hospital time (min)(IQR)</td>
<td>25 (18,29)</td>
<td>42 (25.5, 51)</td>
</tr>
</tbody>
</table>

Patient Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Esmolol (n=6)</th>
<th>No esmolol (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total ED CPR time (min)</td>
<td>39.5</td>
<td>16</td>
</tr>
<tr>
<td>Total CPR time (min)</td>
<td>63</td>
<td>57</td>
</tr>
<tr>
<td>Temporary ROSC (%)</td>
<td>4 (66.7)</td>
<td>8 (42.1)</td>
</tr>
<tr>
<td>Sustained ROSC (%)</td>
<td>4 (66.7)</td>
<td>6 (31.6)</td>
</tr>
<tr>
<td>STEMI (%)</td>
<td>3/5 (60)</td>
<td>1/7 (14.3)</td>
</tr>
<tr>
<td>Emergency cardiac catheterization from ED (%)</td>
<td>5 (83.3)</td>
<td>3 (15.8)</td>
</tr>
<tr>
<td>Survival to ICU admission (%)</td>
<td>4 (66.7)</td>
<td>6 (31.6)</td>
</tr>
<tr>
<td>Therapeutic hypothermia (%)</td>
<td>4 (66.7)</td>
<td>5 (26.3)</td>
</tr>
<tr>
<td>Survival to hospital discharge (%)</td>
<td>3 (50)</td>
<td>3 (15.8)</td>
</tr>
<tr>
<td>Survival to discharge with good neurologic outcome (%)</td>
<td>3 (50)</td>
<td>2 (10.5)</td>
</tr>
</tbody>
</table>

Conclusion

Author’s Conclusion
• Prospective studies of beta-blockers in CA are warranted
• Beta-blockers should be considered in patients with RVF once standard therapy has been performed

Strengths
• Inclusion criteria defined exact number of defibrillations and doses of medications needed
• Therapeutic hypothermia and catheterization was reported

Limitations
• Retrospective
• Sample size
• Non-blinded, non-randomized

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• Different rates of therapeutic hypothermia and catheterization between the groups
• Descriptive statistics

Take Home Points
• Improvement in mortality was seen with esmolol although not significant
• The different rates of therapeutic hypothermia and catheterization may have effected the survival rate
• Favorable neurologic outcomes are possible with prolonged CPR

VIII. Summary of evidence
  A. Bench research
     1. Demonstrates the effects of norepinephrine on cardiac myocytes
     2. Use of a beta blocker, calcium channel blocker, or calcium chelator decrease the response to norepinephrine
  B. Animal studies
     1. Use of beta blockers improved ROSC and postresuscitation survival
     2. Quantified the levels of catecholamines during VF and CPR in various compartments
  C. Literature
     1. Beta blockers along with antiarrhythmic medication has a positive effect on ROSC in patients with prolonged or recurrent VF
     2. Beta blockers alone have not been studied in the setting of VF

IX. Conclusion
  A. Limited evidence for beta blockers in VF
  B. Current evidence suggests the beta blockers may benefit patient refractory to the current established guidelines.
  C. Recommendations
     1. Beta blockers may be considered after antiarrhythmic administration and all reversible causes have been ruled out.
        i. After ACLS performed
        ii. Continued VF
        iii. Esmolol 500 mcg/kg followed by 25-50 mcg/kg/min
References


Appendix B. Mechanism of action

<table>
<thead>
<tr>
<th>Dideoxyadenosine</th>
<th>Adenylate cyclase inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forskolin</td>
<td>Direct action stimulates adenylate cyclase</td>
</tr>
<tr>
<td>Dibutyryl cAMP</td>
<td>cAMP analog</td>
</tr>
<tr>
<td>Ethylene glycol tetraacetic acid (EGTA)</td>
<td>Chelating agent</td>
</tr>
<tr>
<td>Cobalt</td>
<td>Depresses oxygen uptake by the mitochondria</td>
</tr>
<tr>
<td>Tetrodotoxin</td>
<td>Block the pore of the Na⁺ channel</td>
</tr>
<tr>
<td>Verapamil</td>
<td>Non-dihydropyridine calcium channel blocker</td>
</tr>
</tbody>
</table>