Stayin’ Alive: Updates in ACLS and Post-Cardiac Arrest Management

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Disclosure

I have nothing to disclose concerning possible financial or personal relationships with commercial entities (or their competitors) that may be referenced in this presentation.
Objectives

• Review fundamentals in management of adult cardiac arrest, focusing on changes in the 2015 ACLS guidelines

• Discuss evidence utilizing vasopressin during cardiac arrest leading to its removal from the ACLS algorithm

• Evaluate alteplase administration during cardiac arrest caused by suspected or confirmed pulmonary embolism

• Assess benefits and risks associated with sodium bicarbonate use during cardiac arrest given the recent drug shortage

• Discuss changes to targeted temperature management post-cardiac arrest and pharmacologic considerations during cooling
Cardiac Arrest

- **Sudden cessation of cardiac activity where the victim becomes unresponsive, with no normal breathing and no signs of circulation**

- 2016 statistics
  - Out-of-hospital cardiac arrest (OHCA)
    - Incidence: 350,000
    - Survival to discharge: 12%
  - In-hospital cardiac arrest (IHCA)
    - Incidence: 209,000
    - Survival to discharge: 24.8%

http://www.cpr.heart.org/AHAECC/CPRAndECC/General/UCM_477263_Cardiac-Arrest-Statistics.jsp
Adult Cardiac Arrest Algorithm

1. Start CPR
   - Give oxygen
   - Attach monitor/defibrillator

2. Rhythm shockable?
   - Yes
   - Shock

3. VF/pVT
   - CPR 2 min
     - IV/O access

4. Shock
   - CPR 2 min
     - Epinephrine every 3-5 min
     - Consider advanced airway, capnography

5. Rhythm shockable?
   - Yes
   - Shock

6. CPR 2 min
   - Epinephrine every 3-5 min
   - Consider advanced airway, capnography

7. Rhythm shockable?
   - Yes
   - Shock

8. CPR 2 min
   - Amiodarone
   - Treat reversible causes

9. Asystole/PEA

10. CPR 2 min
    - IV/O access
    - Epinephrine every 3-5 min
    - Consider advanced airway, capnography

11. Rhythm shockable?
    - Yes
    - CPR 2 min
      - Treat reversible causes

12. CPR 2 min
    - If no signs of return of spontaneous circulation (ROSC), go to 10 or 11
    - If ROSC, go to Post-Cardiac Arrest Care

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Adult Cardiac Arrest Algorithm

1. Start CPR
   - Give oxygen
   - Attach monitor/defibrillator

2. Rhythm shockable?
   - Yes, proceed to next step
   - No, go to 9

3. VF/VT

4. CPR 2 min
   - IV/Io access

5. Rhythm shockable?
   - Yes, go to 4
   - No, go to 10

6. CPR 2 min
   - Epinephrine every 3-5 min
   - Consider advanced airway, capnography

7. Rhythm shockable?
   - Yes, go to 6
   - No, go to 8

8. CPR 2 min
   - Amiodarone
   - Treat reversible causes

9. Augistole/PEA

10. CPR 2 min
    - IV/Io access
    - Epinephrine every 3-5 min
    - Consider advanced airway, capnography

11. Rhythm shockable?
    - Yes, go to 10
    - No, go to 12

12. CPR 2 min
    - Treat reversible causes

Go to 5 or 7

If no signs of return of spontaneous circulation (ROSC), go to 10 or 11
If ROSC, go to Post-Cardiac Arrest Care
Treat Reversible Causes

**H’s**
- Hypovolemia
- Hypoxemia
- Hydrogen ion (acidosis)
- Hypo-/hyperkalemia
- Hypothermia

**T’s**
- Tension pneumothorax
- Tamponade (cardiac)
- Toxins
- Thrombosis (pulmonary)
- Thrombosis (coronary)

High-Quality Evidence?

• Few randomized controlled human trials in cardiac arrest
  • Retrospective
  • Animal subjects
  • Case reports/series
  • Expert consensus

• **Cornerstone of therapy**: high-quality CPR and early defibrillation
  • ≥ 2 inches, 100-120 compressions/min
  • Allow complete chest recoil
  • Minimize interruptions

Vasopressin removed from the Adult Cardiac Arrest Algorithm

Prognostication during CPR based on exhaled CO2 measurements

Bundle treatment of steroids, vasopressin, and epinephrine may provide some benefit in treating IHCA

In cardiac arrest with non-shockable rhythm, the early provision of epinephrine is suggested
Overview

- Vasopressin removal from ACLS algorithm
- Alteplase in cardiac arrest due to PE
- Sodium bicarbonate
- Targeted temperature management
Epinephrine vs. Vasopressin

• Epinephrine: alpha-adrenergic effects
  • Increase coronary perfusion pressure
  • Cerebral perfusion pressure
  • Dose: 1 mg IV/IO q 3-5 min

• Vasopressin: non-adrenergic peripheral vasoconstrictor
  • Coronary and renal vasoconstriction
  • Dose: 40 units IV/IO x 1
  • Cost: 20 unit vial – $135

Why Vasopressin?

- Large release after cardiac arrest
  - Higher the endogenous concentration, greater chances of return of spontaneous circulation (ROSC)

- Long duration cardiac arrest
  - Severe hypoxia and acidosis
  - Vasopressin seems to be more effective than epinephrine in achieving ROSC

- Animal studies suggest vasopressin is associated with better vital organ perfusion and resuscitation rates than epinephrine for cardiac arrest

## Conflicting Data…

<table>
<thead>
<tr>
<th>Trial</th>
<th>Patient Population</th>
<th>Intervention</th>
<th>Outcomes (Epi vs. Vaso)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized comparison of epinephrine and vasopressin in patients with out-of-hospital ventricular fibrillation¹</td>
<td>N = 40</td>
<td>Epinephrine 1 mg (n = 20) OR vasopressin 40 units (n = 20) as initial therapy</td>
<td>Survival to admission: 35% vs. 70% (p = 0.06)</td>
</tr>
<tr>
<td></td>
<td>VF OHCA refractory to defibrillation</td>
<td></td>
<td>Survival at 24 hr: 20% vs. 60% (p = 0.02)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Survival to discharge: 15% vs. 40% (p = 0.16)</td>
</tr>
<tr>
<td>Vasopressin versus epinephrine for in-hospital cardiac arrest: a randomized controlled trial²</td>
<td>N = 200</td>
<td>Epinephrine 1 mg (n = 96) OR vasopressin 40 units (n = 104) as initial therapy</td>
<td>Survival to discharge: 14% vs. 12% (p = 0.67)</td>
</tr>
<tr>
<td></td>
<td>IHCA of any initial rhythm</td>
<td></td>
<td>Survival at 1 hr: 35% vs. 39% (p = 0.66)</td>
</tr>
<tr>
<td>A comparison of vasopressin and epinephrine for out-of-hospital cardiopulmonary resuscitation³</td>
<td>N = 1186</td>
<td>Epinephrine 1 mg (n = 597) OR vasopressin 40 units (n = 589)</td>
<td>Survival to admission: 31.2% vs. 36.3% (p = 0.06)</td>
</tr>
<tr>
<td></td>
<td>OHCA of any initial rhythm</td>
<td></td>
<td>Survival to discharge: 9.9% vs. 9.9% (p = 0.99)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Asystole</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Survival to admission: 20.3% vs. 29.0% (p = 0.02)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Survival to discharge: 1.5% vs. 4.7% (p = 0.04)</td>
</tr>
</tbody>
</table>


VF = ventricular fibrillation
Multicenter, randomized controlled trial of adults with out-of-hospital cardiac arrest

- May 1, 2004 – April 30, 2006
- Epinephrine 1 mg + vasopressin 40 units vs. epinephrine 1 mg + placebo
  - Repeat if ROSC not restored within 3 min
  - Epinephrine thereafter
- **Primary Endpoint:** survival to hospital admission
- **Secondary Endpoints:** ROSC, survival to hospital discharge, good neurologic recovery, 1-year survival

Results

- Baseline characteristics similar between both groups
  - Exception: male sex (75.4% vs. 71.7%, $p = 0.03$)
- Witnessed cardiac arrest were more likely to survive to hospital admission (23.2% vs. 14.4%, $p < 0.001$)
- BLS $\leq 8$ min and ACLS $\leq 12$ min higher rate of survival to admission (38.3% vs. 20.5%, $p = 0.001$)

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Results

• Post hoc subgroup analysis evaluating combination vs. epinephrine alone on rate of survival to discharge
  • Ventricular fibrillation: 6.8% vs. 10.3%, NS
  • Asystole: 1.3% vs. 1.0%, NS
  • PEA: 0.0% vs. 5.8%, p = 0.02

• Authors’ Conclusions: Lack of superiority on outcomes suggests it may be futile to add vasopressin to epinephrine during ACLS for OHCA
Updated 2015 Recommendation

• Vasopressin offers no advantage as a substitute for epinephrine in cardiac arrest (Class IIb, LOE B-R)

• Vasopressin in combination with epinephrine offers no advantage as a substitute for standard-dose epinephrine in cardiac arrest (Class IIb, LOE B-R)

Overview

- Vasopressin removal from the ACLS algorithm
- Alteplase in cardiac arrest due to PE
- Sodium bicarbonate
- Targeted temperature management
Acute Pulmonary Embolism

- Submassive vs. massive PE
  - Fulminant PE
- Less than 5% progress to cardiac arrest
  - Mortality: 65-90%
  - May occur within hours of symptom onset
  - Most common rhythm: PEA
- Variable, non-specific signs and symptoms
  - May lead to delayed diagnosis

Acute Pulmonary Embolism

- Obstruction to blood flow
- Increase in RV afterload
- Dilation, hypokinesis
  - Tricuspid regurgitation
  - Intraventricular septal deviation
  - Ventricular failure

- Reduced cardiac output
  - Cardiogenic shock
  - Cardiac arrest

Treatment Options

- Fibrinolysis
- Surgical pulmonary embolectomy
- Pharmacomechanical catheter-directed therapy
Fibrinolysis
Alteplase

• Mechanism: convert plasminogen to plasmin, leading to degradation of the fibrin matrix within a thrombus
  • During CPR: improved microcirculatory reperfusion and hemodynamic stability
• Duration of action: ~80% cleared in 10 min; fibrinolytic activity persists for ~1 hour post-infusion
• Only selective thrombolytic agent FDA approved for PE
• Cost
  • Alteplase 50 mg vial: $3988
  • Alteplase 100 mg vial: $7976

## Thrombolytics in ACLS

<table>
<thead>
<tr>
<th>Trial</th>
<th>Patient Population</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy and safety of thrombolytic therapy after initially unsuccessful cardiopulmonary resuscitation: a prospective clinical trial&lt;sup&gt;1&lt;/sup&gt;</td>
<td>N = 40 study drugs N = 50 historical control OHCA where ROSC not achieved in 15 min</td>
<td>rt-PA 50 mg + heparin 5000 units vs. control</td>
<td>ROSC: 68% vs. 44% (p = 0.026) Admitted: 58% vs. 30% (p = 0.009) No difference in bleeding complications, 24 hr survival, or hospital discharge</td>
</tr>
<tr>
<td>Tissue plasminogen activator in cardiac arrest with pulseless electrical activity&lt;sup&gt;2&lt;/sup&gt;</td>
<td>N = 117 t-PA N = 116 placebo OHCA (undifferentiated) with initial rhythm of PEA</td>
<td>t-PA 100 mg over 15 min vs. placebo</td>
<td>Survival to discharge: 0.9% vs. 0.0% (p = 0.99) No difference in ROSC, survival to admission, hemorrhage Avg 32.1 min from CPR to t-PA Only 1 case with confirmed PE</td>
</tr>
<tr>
<td>Thrombolysis during resuscitation for out-of-hospital cardiac arrest&lt;sup&gt;3&lt;/sup&gt; (TROICA Trial)</td>
<td>N = 525 in each group OHCA</td>
<td>Tenecteplase vs. placebo</td>
<td>30-day survival: 14.7% vs. 17.0% (p = 0.36) No difference in ROSC, hospital admission or discharge More intracranial hemorrhage in tenecteplase (2.7% vs. 0.4%, p = 0.006)</td>
</tr>
</tbody>
</table>

# Thrombolytics in ACLS

<table>
<thead>
<tr>
<th>Objective</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
<th>Case 5</th>
<th>Case 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Demographics</td>
<td>Female 45 years old</td>
<td>Male 28 years old</td>
<td>Male 34 years old</td>
<td>Male 73 years old</td>
<td>Male 76 years old</td>
<td>Female 56 years old</td>
</tr>
<tr>
<td>Presenting rhythm</td>
<td>PEA</td>
<td>PEA</td>
<td>Asystole</td>
<td>PEA</td>
<td>Asystole</td>
<td>PEA</td>
</tr>
<tr>
<td>CPR Initiation</td>
<td>Immediate</td>
<td>After 5 min</td>
<td>After ≥ 10 min</td>
<td>Immediate</td>
<td>Immediate</td>
<td>Immediate</td>
</tr>
<tr>
<td>rt-PA delay</td>
<td>60 min</td>
<td>30 min</td>
<td>30 min</td>
<td>15 min</td>
<td>Immediate</td>
<td>15 min</td>
</tr>
<tr>
<td>rt-PA Regimen</td>
<td>50 mg bolus + 50 mg bolus after 30 min</td>
<td>50 mg bolus + 50 mg bolus after 30 min</td>
<td>50 mg bolus</td>
<td>50 mg bolus + 50 mg bolus after 30 min</td>
<td>50 mg bolus + 50 mg bolus after 30 min</td>
<td>50 mg bolus + 50 mg bolus after 30 min</td>
</tr>
<tr>
<td>Total CPR time</td>
<td>70 min</td>
<td>45 min</td>
<td>90 min</td>
<td>30 min</td>
<td>5 min</td>
<td>40 min</td>
</tr>
<tr>
<td>Post-CPR complications</td>
<td>Hemorrhage at injection sites</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Alive at 1 yr</td>
<td>Death</td>
<td>Death</td>
<td>Alive at 1 yr</td>
<td>Stroke at 1 yr</td>
<td>Alive at 6 mon</td>
</tr>
</tbody>
</table>

ROSC and survival to discharge: 4/6 (66.7%)
Mortality cases had no possibility of survival (carcinoma of the pancreas, CPR initiation > 10 min)
No fatal hemorrhages reported

UGIB = Upper gastrointestinal bleed

Thrombolytics in ACLS

• Do not delay thrombolytic therapy for confirmation when high clinical suspicion
  • Minimize time from collapse to administration of therapy
• Dosing options: 50 mg vs. 100 mg
• Continue resuscitation for at least 15-20 min if ROSC is not achieved

AHA ACLS Guideline Recommendations

In patients with cardiac arrest and without known PE, routine fibrinolytic treatment given during CPR shows no benefit and is not recommended (Class III, LOE A)

In patients with confirmed PE as the precipitant of cardiac arrest, thrombolysis, surgical embolectomy, and mechanical embolectomy are reasonable emergency treatment options (Class IIa, LOE C-LD)

Thrombolysis may be considered when cardiac arrest is suspected to be caused by PE (Class IIb, LOE C-LD)

Overview

- Vasopressin removal from ACLS algorithm
- Alteplase in cardiac arrest due to PE
- Sodium bicarbonate
- Targeted temperature management
Sodium Bicarbonate

• Tissue acidosis occurs during severe ischemia seen in cardiac arrest
  • Rapid accumulation of CO\textsubscript{2}
  • Slow accumulation of lactic acid
• Until 1986, sodium bicarbonate (buffer therapy) was an integral component of ACLS
  • Lack of benefit and possibly deleterious effects
  • Compressions and hyperventilation sufficient
• 50 mEq/ 50 mL = 1 ampule

Theoretical Disadvantages

- Reduce systemic vascular resistance
- Extracellular alkalosis $\rightarrow$ shift in oxyhemoglobin saturation curve $\rightarrow$ inhibit oxygen release
- Hypernatremia
- Excess CO2 causing intracellular acidosis
- Exacerbate central venous acidosis and inactivate catecholamines

• Prospective, randomized, double-blind study in OHCA refractory to defibrillation

• Early administration of empirical (1 mEq/kg) sodium bicarbonate (n = 420) vs. placebo (n = 372)
  • Brief (< 5 min), moderate (5-15 min), and prolonged (>15 min) down time

• **Primary outcome**: survival to admission 13.9% vs. 13.8%, p = 0.199
  • Prolonged (> 15 min) down time: 32.8% vs. 15.4%, p = 0.007

• **Conclusions**: early administration of sodium bicarbonate has no effect on overall outcome in OHCA
Sodium Bicarbonate: When to use it?

AHA ACLS Guideline Recommendations
Routine use of sodium bicarbonate is not recommended for patients with cardiac arrest (Class III, LOE B)

Pre-existing metabolic acidosis
Hyperkalemia
Overdose causing QRS ≥ 120 msec

Overview

- Vasopressin removal from ACLS algorithm
- Alteplase in cardiac arrest due to PE
- Sodium bicarbonate
- Targeted temperature management
Post-Cardiac Arrest Syndrome

- Poor prognosis despite achieving ROSC
  - 12% of out-of-hospital arrests survive to discharge
  - 24.8% of in-hospital arrests survive to discharge
- ~80% of patients remain comatose for more than an hour post-resuscitation
  - Secondary brain injury
  - Myocardial dysfunction
  - Systemic ischemia
  - Consequences of the disorder that caused the arrest
  - Ongoing inflammation and injury
Cardiac Arrest

No Blood Flow/O₂ Deprivation → Ischemic Injury

Coagulopathy/Toxic Metabolites

ROSC

• Myocardial dysfunction
  • “Stunning”

• Hyperemic macro-circulation
• Excitotoxicity
• Disrupted Ca²⁺ homeostasis
• Free radical formation
• Activation of apoptosis

• Ischemic metabolites
• Poor O₂ delivery
• ↑Immune & coagulation cascade

Targeted Temperature Management

- Reduction in cerebral metabolic rate
- Reduction in oxygen demand and ATP consumption
- Inhibition of glutamate release
- Decreased lipid peroxidation
- Decreased cerebral edema and intracranial pressure
- Preservation of blood brain barrier
- Inhibition of apoptosis
- Decreased inflammation and cytokine release
- Decrease free radical reactions

### Landmark Trials Assessing Therapeutic Hypothermia

<table>
<thead>
<tr>
<th>Trial</th>
<th>Patient Population</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest¹ | N = 138 (hypothermia)  
N = 137 (normothermia)  
RCT of comatose patients with ROSC after OHCA due to ventricular fibrillation | Therapeutic hypothermia (32-34°C) over 24 hr vs. normothermia | Favorable neurologic (CPC 1 or 2) outcome at 6 months: 55% vs. 39%, p = 0.009  
Mortality at 6 months: 41% vs. 55%, p = 0.02  
Complications within 7 days: no difference |
| Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia² | N = 43 (hypothermia)  
N = 34 (normothermia)  
RCT of comatose patients with ROSC after OHCA due to ventricular fibrillation | Therapeutic hypothermia 33°C within 2 hr of ROSC for 12 hr vs. normothermia | Survival to hospital discharge with sufficient neurologic function: 49% vs. 26%, p = 0.046  
OR 5.25 (1.47-18.76; p = 0.011)  
No difference in frequency of adverse events |

**2010 AHA ACLS Guideline Recommendations**

Comatose adult patients with ROSC after out-of-hospital VF cardiac arrest should be cooled to 32-34°C for 12-24 hours

Considerations for comatose adult patients with ROSC after in-hospital cardiac arrest of any initial rhythm or after out-of-hospital cardiac arrest with an initial rhythm of PEA or asystole

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Multicenter, randomized controlled trial of adults who remain unconscious (GCS ≤ 8) after ROSC from out-of-hospital cardiac arrest of presumed cardiac cause

- November 2010 – January 2013

- Targeted temperature management 33°C vs. 36°C for 24 hr

- **Primary Endpoint**: all-cause mortality

- **Secondary Endpoints**: composite of poor neurologic function or death at 6 months

TTM Trial: Results

**Adverse Events**

- ≥1 serious adverse event: 93% vs. 90%, p = 0.09
- Hypokalemia: 19% vs. 13%, p = 0.02
- Shivering: 30% vs. 34%, p = 0.20

**Figure 1. Body Temperature during the Intervention Period.**

**Table 2. Outcomes.**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>33°C Group</th>
<th>36°C Group</th>
<th>Hazard Ratio or Risk Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome: deaths at end of trial</td>
<td>235/473 (50)</td>
<td>225/466 (48)</td>
<td>1.06 (0.89–1.28)</td>
<td>0.51</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurologic function at follow-up†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPC of 3–5</td>
<td>251/469 (54)</td>
<td>242/464 (52)</td>
<td>1.02 (0.88–1.16)</td>
<td>0.78</td>
</tr>
<tr>
<td>Modified Rankin scale score of 4–6</td>
<td>245/469 (52)</td>
<td>239/464 (52)</td>
<td>1.01 (0.89–1.14)</td>
<td>0.87</td>
</tr>
<tr>
<td>Deaths at 180 days</td>
<td>226/473 (48)</td>
<td>220/466 (47)</td>
<td>1.01 (0.87–1.15)</td>
<td>0.92</td>
</tr>
</tbody>
</table>

TTM Trial: Conclusions

• No significant differences between 33°C and 36°C in overall mortality or composite of poor neurologic function or death at 180 days

• No difference in harm

• Hypothermia influences all organ systems, any potential benefits should be balanced with possible side effects

2015 AHA ACLS Guideline Recommendations
Comatose (i.e., lack of meaningful response to verbal commands) adult patients with ROSC after cardiac arrest should have TTM (Class I)
Select and maintain a constant temperature between 32°C and 36°C during TTM (Class I)

Recommend against the routine pre-hospital cooling of patients after ROSC with rapid infusion of cold intravenous fluids (Class III: no benefit)

Physiologic Effects of Cooling

**Cardiovascular**
- Tachycardia (induction)
- Bradycardia
- Hypertension/Hypotension
- Dysrhythmias (≤ 32°C)
- ↑ Mixed oxygenation values

**Musculoskeletal**
- Shivering

**Hematologic**
- Impaired plt aggregation
- ↑ Clotting times
- ↓ WBC

**Genitourinary/GI**
- ↑ Urine Output
- ↑ Electrolyte loss
- ↓ CrCl
- ↓ Motility

**Neurologic**
- ↓ Cerebral metabolic demands
- ↓ ICP
- ↓ Inflammation/damage

**Metabolic**
- ↓ Metabolic demands
- ↓ CO₂ production
- ↓ O₂ consumption

**Endocrine**
- ↓ Insulin production
- ↓ Insulin sensitivity

Altered Pharmacokinetics and Pharmacodynamics

- Temperature-dependent enzyme-mediated reactions
  - Decrease in rate of drug metabolism by the liver
  - Reduction in drug clearance
- Temperature affect response to drugs
  - Blunted effects of drugs
  - Changes in volume of distribution
- Careful monitoring to assess for toxicity and efficacy

Pharmacologic Considerations during TTM

• Sedation
  • Midazolam: metabolized by CYP3A4 and 3A5
    • 5-fold increase in plasma concentrations and 100-fold decrease in systemic clearance in < 35°C
  • Propofol: metabolized by CYP2B6
    • Increased concentrations by 30% during hypothermia (34°C vs. 37°C)

• Analgesia
  • Fentanyl: metabolized by CYP3A4
    • Plasma concentrations 2-fold higher and clearance decreased 3.7-fold during hypothermia
  • Morphine: metabolized by hepatic glucuronidation
    • Reduced affinity at the μ-receptor as temperature decreased
Pharmacologic Considerations during TTM

• Electrolyte management
  • Monitor K⁺, Mg²⁺, PO₄⁻ closely
    • Renal tubule dysfunction
    • Electrolyte shifts intra-/extracellular

• Glycemic management
  • Decreased insulin production and receptor sensitivity
  • Increased glycemic variability is associated with increased mortality
  • Hyperglycemia during induction and maintenance
  • Hypoglycemia during rewarming
Summary

- The 2015 AHA ACLS Guidelines contain several important updates including the removal of vasopressin from the cardiac arrest algorithm.

- Thrombolytic administration should be considered when there is confirmed or high suspicion of pulmonary embolism causing cardiac arrest.

- Evidence of sodium bicarbonate in ACLS does not show benefit and should not be routinely used.

- Comatose patients successfully resuscitated should undergo targeted temperature management (32-36°C), with careful monitoring of medication therapy due to altered pharmacologic properties during cooling.
Assessment Question #1

Why was vasopressin removed from the arrest algorithm in the 2015 ACLS Guidelines?

a) Epinephrine was shown to be superior to vasopressin in achieving ROSC and survival to hospital discharge in two large randomized controlled trials

b) Vasopressin is associated with worse vital organ perfusion in animal models during cardiac arrest

c) Vasopressin as a substitute to or in combination with epinephrine has shown no additional benefit and is considered futile to administer during cardiac arrest

d) The exponential increase in cost of vasopressin caused the AHA to remove it from the algorithm
Assessment Question #2

AM is a 55 year-old female admitted to the Surgical ICU with left tibia/fibula fractures and multiple rib fractures after a high-velocity motor vehicle collision. Seven days into her admission, she was diagnosed with a DVT and began therapeutic anticoagulation. The next day, her condition deteriorated and she became unresponsive and found to be in a PEA arrest. CPR began immediately, and a member of the cardiac arrest team asks, “Should we give t-PA?”

What is an appropriate response?

a) Alteplase should be given immediately and administered over 2 hours while continuing CPR

b) Alteplase should be administered immediately as a bolus and chest compressions should continue for at least 15-20 minutes or until ROSC achieved

c) Alteplase should be administered as a bolus after 15-20 minutes of unsuccessful CPR

d) Alteplase should not be administered given the high risk of life threatening hemorrhage
Assessment Question #3

Which of the following is an appropriate pharmacologic consideration for a patient receiving targeted temperature management of 34°C?

a) Fentanyl and midazolam infusion rates should be increased given the rapid clearance of both drugs during hypothermia

b) Frequent glucose monitoring and subsequent insulin administration is necessary given the risk for hyperglycemia during hypothermia

c) TTM can cause increased affinity of drugs such as morphine to the receptors, causing increased potency

d) Drugs metabolized via CYP450 enzymes are the safest to use during TTM as these are temperature independent enzymatic reactions
Stayin’ Alive: Updates in ACLS and Post-Cardiac Arrest Management

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