ResQTrial Community Consultation
Presentation - Whatcom County

Resuscitating the Heart and Saving the Brain
“Devices and Techniques”

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Disclosure Statement

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69 yr Old Male

- Hx of Afib and sleep apnea
- Wife awoke to find in resp distress
- Shortly went into cardiac arrest
- EMS BLS arrived and AED defib
- ALS arrived, second defib, intubation
- In ED not waking, ST/T wave only
- ED Cooling started

69 yr Old Male

- Cooled 24 hrs at 33°C
- Awoke 48 hrs, first words, “that you Marv”
- EP study and AICD placed
- 6 month follow up MRS 0.5

Case of 45 yr Old Male

- Crossing at US Canadian Border
- Left car to use BR
- Found in Cardiac Arrest, CPR then Delayed CPR and AED by EMS ROSC by ALS
- Cooling in ED and beyond
- Cath Lab 99% RCA opened
- 3 days post cooling awake
- 6 month follow up MRS 0.5

Case of 51 Year-Old Male

- 51 year-old male seen down in field by passerby
  - Police called for welfare check
- Patient found unconscious and unresponsive
  - CPR by PD, EMS called
  - Downtime BEFORE CPR up to 25 minutes
- EMS CPR, defib, transport
- Cath Lab — RCA narrowing without lesion
- Patient remained comatose; Cooled for 24 hrs
- Discharged with baseline neurologic function
- Lost to long-term follow-up
Objective:
- Describe the current status of CPR and cardiac arrest resuscitation
- Discuss the use of new modalities to improve efficacy of CPR
- Present current results for ResQ Trial and Therapeutic Hypothermia

Cardiac Arrest
What do we know?

Current CPR’s effectiveness is poor...
Forward blood flow during CPR is less than 25% of normal.

Cardiac Arrest

Each year:
- United States: 255,000 out-of-hospital cardiac arrests
- Whatcom County area: about 300 out-of-hospital

Treatment of cardiac arrest:
- Unsatisfactory
- Outcome from cardiac arrest:
  - Dismal
- Survival rate in Whatcom County:
  - 16-18% transported to hospital
  - 100 patients in V-fib
  - 12% discharged from the hospital (approx. 3 out of 25 patients in V-fib)
- Long term survival in large cities = 1-2%
  - Kellerman: 3,400 unsuccessful pre-hospital arrests 6.47% survived to D/C
Why CPR Works…

Blood flow during CPR is due to:

- Direct compression of heart between the sternum and spine
- Alteration of intra thoracic pressure from chest compression and relaxation
- New mantra “pump hard pump fast”

Cardiac Arrest Research

Human studies

- Use of an Impedance Threshold Device (ITD) with S-CPR improves short-term survival
- Use of an ITD improves blood pressure among victims who receive S-CPR

Cardiac Arrest Research

Human studies

- Active Compression Decompression-CPR (ACD) improves survival
- Use of an ITD improves blood pressure and survival among victims who receive ACD-CPR

Cardiac Arrest Research

Information to date is encouraging BUT…

Unknown if improved blood flow with ACD-CPR + ITD results in improved outcome after cardiac arrest.

Res Q Trial:

Evaluate outcome in victims of cardiac arrest treated with:

- S-CPR
- ACD-CPR + ITD

Results of resuscitation efforts and short and long-term outcomes will be compared

Research Question:

- Does adding an ITD to ACD-CPR improve outcome?

Six Sites across US, NIH-NHLBI Funded

ResQPump®

- Performs active compression decompression CPR (ACD-CPR)

  - Same as standard CPR (S-CPR):
    - Actively compresses the chest
  
  - Different from standard CPR (S-CPR):
    - Actively decompresses the chest, assists in augmenting negative intrathoracic pressure, diastolic filling
ResQPOD™

Impedance Threshold Device (ITD)
- Prevents passive air entry during decompression cycle (diastolic) of CPR,
- Prolonging negative ITP
- Augments cardiac filling and CO
- Timing light

ITD in Respiratory Circuit

Endotracheal
Advanced life support

Facemask
Basic life support

Study Subject Inclusion

- Adult cardiac arrest patients
  - 18 years old or greater
  - Non-traumatic
  - Out-of-hospital
- Treated by EMS personnel with CPR

Study Endpoints

- Return of pulse
- Survival to one hour
- Survival to hospital admission
- Survival to 24 hours
- Survival to hospital discharge
- Survival to 30, 90 & 365 days
- Neurologic recovery at hospital discharge, 30 days, 90 days & 1 year
- Quality of life at 1 year
- Complication rates

New Recommendation from AHA on Post Resuscitative Care*

If we are going to save more lives... We have to be more facile with post-resuscitation care, in particular--cerebral resuscitation

Neuronal Viability

- Viability is flow dependant & regional

  - Functional loss as flow decreases:
    - Normal >60 ml/100 gm/min
    - Protein synthesis <55 ml/100 gm/min
    - Anaerobic glycolysis <35 ml/100 gm/min
    - Neurotransmitter release <20 ml/100 gm/min
    - Anoxic depolarization <15 ml/100 gm/min

  - Selectively vulnerable neuronal zones:
    - Hippocampus CA 1,4
    - Cerebral cortex 3-5
    - Cerebellar Purkinje cells

* Circulation published online Oct 23, 2008;
Neuronal Viability

- Penumbra
- Neurons functionally silent
- Energy metabolism is preserved
- Fundamentally salvageable
- Normal Neurons threatened
  - <15 ml/100 gm/min
  - CPP <30 mmHg
  - Cerebral venous PO₂ <20 torr

Post-Arrest Encephalopathy

- Restored quickly
  - Brain ATP depletion
  - Ion pumps
  - Tissue pH
- Perfusion failure
  - Vasodistention
  - Platelet aggregation
  - Pre-capillary cellular edema
  - Abnormal calcium ion fluxes
- Reperfusion / reoxygenation injury
- Extra cerebral organ dysfunction
- Post-arrest inflammatory process

Events Leading to Neuronal Death During Post-Ischemic Brain Reperfusion

Ischemia

- ATP depletion
- Cytosolic Ca²⁺
- Activated Phospholipases

Reperfusion

- Membrane Damage
- Lipo-Peroxidation
- \( \text{Fe}^{2+} \)
- Lipid Peroxidation

Cells unable to respond to injury and die

What Have We Tried?

- BRCT I: Thiopental coma → No Effect
- Calcium Channel blockers → No Effect
- BRCT II: Lidoflazine → No Effect
- Nimodipine / Helsinki → No Effect
- Tirilazad: Radical scavenger → No Effect
- Selfotel: Glutamate antagonist → No Effect
- PEG-SOD: No differences in phase III CHI → No Effect
- AMPA receptor antagonists → No Effect
- Lubeluzole → No Effect

What Can We Do About This?

- Prevent hypotension
  - Brief hypertensive to MAP of 130 mm/Hg at ROSC
    - Correlates with good outcome
    - Hypotension: Poor prognosis
    - Most patients with good recoveries do this on their own
    - Artificial increases may increase cardiac ischemia
- Prevent and treat hyperglycemia
  - ↑ initial glucose non-diabetic CVAs
  - 3.3 times more likely to die (Cape meta-analysis)
- Therapeutic hypothermia
Therapeutic Hypothermia

- Concept of reduced neuronal metabolic rate
- Presence of reduced O₂ delivery
- Allow neuronal recovery
- Allow reduction of free radicals and peroxidases

Hypothermia: Potential Mechanisms

- 6% ↓ in metabolic rate per 1°C reduction in brain temperature
- CMR declined to 50% after brain cooling to 32°C (CBF & CMR coupled)
- Blocks release of excitatory amino acid
- Reduces early calcium rise
- Reduces calpain specific and cytoskeletal damage
- Reduces enzymatic activity, apoptosis via reduced protein production

How Quickly?

- Ideally hypothermia should be initiated as soon as possible
- Delays of up to 2-6 hours may still be of benefit
- Sooner is always better!

How Long?

- Prolonged (~24 hr), mild hypothermia is beneficial
- Even if initiated hours after reperfusion

Therapeutic Window for Hypothermia Provides Clues to Biochemical Mechanisms

- Decreased temperature helpful
- Increased temperature harmful
- Neurons begin to die
- Asphyxial Cardiac Arrest

References:

Clinical Hypothermia

- The European group, 136 patients
  - VF arrest, comatose, stable hemodynamics
  - External cooling device
  - 8 hours = median time to target temp (32-34°C)
  - 14.4% of intervention did not reach target T°
  - Cooling continued for a mean of 24 hours
  - Good outcome = 55% vs. 39%

- Bernard S et al., Australia (77 patients)
  - External cooling, ice bags, initiated by EMS at ROSC (2 L iced saline)
  - 33.5°C within two hours ROSC cooled for 12 hours
  - Good outcome = 49% vs. 26%
  - New work suggests 4 L iced saline

Commercial Devices to Achieve Hypothermia

Arctic Sun 2000

- Functions in response to feedback from patient temperature probe
- Circulating water temperature is controlled between 4°C (39.2°F) and 42°C (107.6°F) to achieve preset target temp
- Temp range 33°C to 37°C (91.4°F to 98.6°F)
- Control algorithm changes the temperature of the water once patient approaches the target to minimize overshoot
- Precise control of temperature-can be used for days at a time
- Expensive can cause skin burns non reusable pads

Cincinnati Sub-Zero

- Similar characteristics to Arctic Sun system
- System & blanket less expensive, reusable same pt
- Non-gel system
- Head cover
- Appears effective
- Less total cost

ThermoSuit System (TSS)*

- TSS Operation
  - Enclose subject in disposable “ThermoSuit”
  - Activate pumping system to fill suit with water
  - Circulate water in direct contact with skin to induce convective heat exchange
  - Device and blanket expensive
  - No current data

* Investigational device.
Innercool Endovascular Temperature Therapy Systems

- Advanced heat exchange technology
- System components:
  - Controller
  - Heat exchange cassette
  - Heat exchange catheter
  - Temperature sensor
- Requires invasive lines
- More expensive than topical systems

Alsius Intravascular System

- Intravascular multi-lumen catheter
- Heat exchanger with temperature control
- Feed back system
- Improved patient access
- Requires invasive line
- More expensive than topical systems

What Should We Do Now?

- Prevent hyperthermia
- Early induction of permissive hypothermia
  - ? Prehospital iced saline
  - ED iced saline
  - Continue in ED, Cath Lab, ICU
- Goal of 32-34° C
- Maintain for 24 hrs

What Else?

- Relaxing doses of paralytics
- Sedate with benzodiazepines/barbituates
- Seizure prophylaxis phenytoin/lorazepam if necessary

Other Considerations

- HCT around 30-35%
- Normalize electrolytes
- Serum Osm 280-330 mOsm/L
- Elevated head 30 degrees

Therapeutic Hypothermia at SJH

- Process and implementation
- Patient scenario
- Challenges
- Successes and the future
Small group of ED and ICU individuals collaborate to start program – persistence pays off!

- Bernard Article

- Contacts for protocols: not much out there
- Observed active re-warming of post-arrest patients
  - Both ED and ICU
- 2006: Hypothermia protocol(s) based on research protocols from University of Chicago, Australia, UK and Netherlands
  - Processes for ED, cath lab and ICU outlined
  - Staff education began

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- Needing new cooling equipment
- Vendor contacts
- Surface vs. endovascular
- Continued focus on door to balloon time
  - CV outcomes
- Protocols and order sets updated
  - Sedation
  - Analgesia
  - Neuromuscular blockade
- CBT
  - Staff awareness and education
  - Monitoring techniques
- Intensivist process in the works

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- Tests of change with each patient
- Early days were very labor intensive and temperatures labile

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- Refined the process to include paralytics and the CSZ B-III system
Patient Scenario

- Passive cooling at the scene
- Inclusion vs. exclusion criteria- when to decide “non-responsive”
  - Making the commitment
  - Sedation, paralytic and cool saline in the ED
  - Rx responds to cath codes
  - ED staff place B-III wraps if they have time
  - CVC continues cooling, paralytic and sedation
  - Cooling may be suspended (but patient NOT re-warmed) if refractory hypotension or bleeding
  - Target start time 6 hours
  - Will probably decrease with research

Patient Scenario: ICU

- B-III, sedation, paralytic, BIS, TOF if needed
- ? Seizures
- Maintain target temp x 24 hours then allow passive re-warming
- Active re-warming after 4 hours if not 36 degrees
- Stop paralytic (and then sedation) at 36 degrees
- May not awaken right away
  - BIS indicates wakefulness if little anoxic injury

Challenges....

- Reluctant commitment to sedation and paralytic
  - No complications seen so far
  - Early: unable to get patient cool/stay cool
  - Wanting to cool everyone–exclusion criteria
  - Patients with unknown/long down time
  - Seizures

Success....

- ED and cath lab staff quick to “buy in”
  - Page NTL if they think a patient is a candidate and it hasn’t been addressed or is delayed
  - CSZ very responsive with product development and support
  - 24 hour immediate pharmacy support
  - Pulmonologists agreed to manage patients
  - RN’s more adept with B-III and monitoring devices
  - Very few complications- bleeding, use of paralytics
  - Family agreement/teaching
  - Several amazing patient recoveries

Cardiac Arrest Data 2002-2006

Whatcom County Prior to ResQ Trial

- Annual average resuscitation rate 22% ROSC all rhythms (~220-270 worked CA per year)
- None cooled
- Discharge rate 9%, unknown MRS*

Whatcom County EMS Dispatch to Cardiac Arrests: 1/1/06-2/28/09

- 350 Cardiac Arrests
- 140 transported with ROSC (95 VF/VT; 45 PEA/Asystoli)
- We cooled 130 of the 140 patients

* Mean Rankin Score (score of 2 carries out daily activity, 1 minimal deficit, 0 normal)
Whatcom County EMS Dispatch to Cardiac Arrests: 1/1/06-2/28/08

48 were discharged; 39 of 48 had been cooled

Of the 48, 36 had VF/VT; 12 were PEA/Asystole

42 (88%) patients had a MRS of ≤ 2 or less

MRS = Mean Rankin Score; PEA = pulseless electrical activity
VF = ventricular fibrillation; VT = ventricular tachycardia

Wayne M et al. Unpublished data.

Future....Is more rapid cooling better?
Are there drugs to help us? (Neurotensin)

- Who else should we cool?
  - Stroke, TBI, trauma, sepsis, neonatal encephalopathy
  - Ongoing research

L'Her A et al. Crit Care Med. 2006;34.

Questions?