No IV, No Problem!
Practical Approaches to Alternative Routes of Administration

Objectives
• Evaluate the need for alternative routes of drug administration
• Utilize proper technique and identify medications appropriate for intranasal administration
• Evaluate the risks and benefits with drug administration via intraosseous route
• Recommend appropriate medications, doses, and techniques for endotracheal tube administration
• Recommend appropriate techniques, fluids, and adjunctive agents for hypodermoclysis

Feeling the Need for Speed!
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Does your ED and/or institution provide access to alternate routes of medication administration other than IV for emergent meds/fluids?

☐ Yes
☐ No
☐ I don’t know
☐ Working on it...

What alternate routes are utilized for emergent med/IV administration at your institution/ED?

☐ Intraosseous
☐ Intranasal
☐ Subcutaneous
☐ Endotracheal

Establishment of Vascular Access
• Vascular Access
  • Considered a standard of emergency care
  • Both pre-hospital and acute hospital settings
  • One of the most common procedures ordered in an Emergency Department (ED)
  • Reported top selected procedure of 2009 ED visits
  • High priority procedure for critically ill and unstable patients
  • Success rate and time to vascular access is crucial to optimal resuscitation of the most critical patients
Access Time Expectations

- Average time necessary for peripheral IV cannulation is 2.5-13 minutes
- Average time necessary for “difficult access” is as much as 30 minutes
- Goal for time to vascular access in emergent/urgent situations: Immediately!

Common Needs for Emergent Vascular Access

- Prompt resuscitation
- Reliable delivery of emergent/urgent medications, electrolytes, nutrition, and fluids
- Route for contrast needed in diagnostic imaging
- Blood tests for monitoring and diagnostic purposes
- Monitoring of hemodynamics

Difficult Venous Access (DVA)

- Definition
  - Multiple attempts and/or special interventions are anticipated or required to achieve and maintain peripheral venous access
- Emergent Intravenous Access Failure
  - Failure rate of 10-40%
  - One of the major limitations of out-of-hospital resuscitation
- Pediatric patients
  - Number of attempts in pediatric patients ranges from 1-10
  - Average child required 2.2 sticks to achieve venous access
  - Average time for venous access can range 10-33 minutes

Risk Factors for DVA

<table>
<thead>
<tr>
<th>Illness/Injury Related</th>
<th>Illness/Injury Related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute conditions</td>
<td>Chronic conditions</td>
</tr>
<tr>
<td>Multiple injuries/trauma patient</td>
<td>Diabetic patients</td>
</tr>
<tr>
<td>Dehydration/Hypotension</td>
<td>Tumors</td>
</tr>
<tr>
<td>Sepsis, Septic Shock</td>
<td>Vascular pathologies</td>
</tr>
<tr>
<td>Burns</td>
<td>Dermatologic abnormalities</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>Sickle cell disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk Factors for DVA</th>
<th>Effects of DVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illness/Injury Related</td>
<td>Patient related effects</td>
</tr>
<tr>
<td>Acute conditions</td>
<td>Increased on-scene times</td>
</tr>
<tr>
<td>Multiple injuries/trauma patient</td>
<td>Multiple needlesticks</td>
</tr>
<tr>
<td>Dehydration/Hypotension</td>
<td>Delayed IV fluid support</td>
</tr>
<tr>
<td>Sepsis, Septic Shock</td>
<td>Delayed medication delivery</td>
</tr>
<tr>
<td>Burns</td>
<td>Delay in diagnosis and initiation of treatment</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>Increased frustration and productivity loss of ED staff</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>Other complications</td>
</tr>
</tbody>
</table>

Risk Factors for DVA

<table>
<thead>
<tr>
<th>Treatment-Related</th>
<th>Illness/Injury Related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long term or repeated intravenous treatments</td>
<td>Acute conditions</td>
</tr>
<tr>
<td>Chemotherapy patients</td>
<td>Multiple injuries/trauma patient</td>
</tr>
<tr>
<td>Steroid therapy</td>
<td>Dehydration/Hypotension</td>
</tr>
<tr>
<td>Long term IV antibiotics</td>
<td>Sepsis, Septic Shock</td>
</tr>
<tr>
<td>Shunts</td>
<td>Burns</td>
</tr>
<tr>
<td>Fistulas</td>
<td>Peripheral edema</td>
</tr>
</tbody>
</table>
Effects of DVA

- Central Venous Catheterization
  - Common alternative approach when venous access establishment has failed
  - Associated consequences
    - Delayed time to establishment
    - Venous thrombosis
    - Arterial puncture
    - Associated bloodstream infections
    - Pneumothorax

Effects of DVA

- Central Venous Catheterization
  - Associated bloodstream infections
    - As high as 20% mortality rate
    - Costly – up to $56,000 per episode
    - May add 7-14 days to a hospital stay
  - Institute of Health Improvement
    - Reduction of central line infections initiative to reduce patient harm in healthcare settings

Effects of DVA

- 2012 Prospective Cohort Study
  - Objective
    - Estimate the incidence of intravenous access difficulty (IVAD) and its associated delays in an urban ED
  - Methods
    - Recorded the time from the initial skin puncture to IV line establishment
  - Results
    - 125 patients enrolled, 107 had an IV placed in ED
    - Incidence and delays associated with IVAD were as follows
      - None: 61%/1min
      - Mild: 11%/5 min
      - Moderate: 23%/15 min
      - Severe: 5%/120 min

Effects of DVA

- Healthcare Worker Effects
  - Needle-free drug delivery
    - Addresses concerns over bloodborne pathogens
    - Broader scope of healthcare workers can deliver drugs by other routes vs. having to access a vein
    - Reduces cost associated with needlestick injury
    - Reduces time spent reporting needlestick injuries
    - Reduces the amount of time off work secondary to a needlestick injury

Management of DVA

- Technique chosen will depend on urgency of case
  - ACLS guidelines
  - Emergency Nursing Resource Guideline
    - Ultrasound-guided IV access
    - Intraosseus vascular access
    - Subcutaneous rehydration therapy
    - Warming
    - Alternative methods

Barriers to Management of DVA

- Inadequate availability of staff
- Lack of available expertise
- Limited access to or training in advanced technologies that facilitate peripheral venous access
Alternative Routes: Need for Options

• Rapid establishment of vascular access is more important than the site of access
• The need for availability of alternative routes
• Immediate vascular access required
• DVA situations
• Mass casualties
• Delay or prevent central line placement
• Hospital protocols that limit the number of IV establishment attempts
• Decrease in occupational exposures
• “The Perfect Storm” scenarios...

Alternative Routes: The Need for Options

<table>
<thead>
<tr>
<th>Route</th>
<th>Fluids</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraosseous</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Transmucosal (inc. Intransal)</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Subcutaneous</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Inhalation (inc. Endotracheal)</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

What are examples of risk factors for DVA?

- Dark skin
- IV drug abuse patients
- Dehydration
- All of the above

Key Takeaways

• Alternate routes of administration is essential to deliver urgent/emergent medications in DVA situations
• Identification for risk factors for DVA is key in the preparation for utilizing alternate routes of administration

A Sarah Case

No IV Access, Get MAD!

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PGY1 Residency Program Director
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**Why Intranasal (IN)?**

**Safety**
- Needleless
- Pain-free
- No sterile technique needed
- Patient tolerated

**Efficacy**
- Transmucosal drug absorption
- Nose-to-brain pathway
- Relatively rapid onset of action

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**Variability IN Drug Absorption**

**Drug**
- Formulation
- Physicochemical properties

**Patient**
- Transepithelial passage
- Drug degradation & elimination
- Other

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**Physicochemical Drug Properties**

- Molecular weight
  - Rapid absorption: < 300 Da
  - Slow absorption: >1000 Da
- Hydrophilicity vs lipophilicity
  - Lipophilic = transcellular
  - Hydrophilic = paracellular > transcellular
- Degree of ionization

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**Mechanism of IN Drug Absorption**


Image from: [http://care.americanrhinologic.org/sinus_anatomy](http://care.americanrhinologic.org/sinus_anatomy)

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**Drug Formulation**

- Volume less than 200 µL to avoid runoff
- Concentrated, potent drug
- ≥ 10 µm in diameter to ensure adsorption
- Viscosity indirectly related to size of spray
- 30° angle of drug administration demonstrated 90% deposition efficiency

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**Transepithelial Passage**

- Must overcome mucus barrier on epithelium
- Mucociliary clearance:
  - Biphasic
  - Transcellular vs. paracellular passage
- Nasal blood flow

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Degradation and Elimination

• Means of elimination:
  • Sneezing
  • Run-off
  • Difficulty in penetration epithelial cells and tight junctions
  • Nasal first-pass effect: enzymes, efflux proteins

Patient Factors

Mucosal Health
• Dysfunction in mucociliary clearance: CF
• Rhinosinusitis
• Radiation to head/nasal cavity
• Cigarette smoking

Drug Interactions
• Vasoconstrictors: phenylephrine, oxymetazoline
• Considered relative contraindications

Patient Factors

Mucosal Health
• Dysfunction in mucociliary clearance: CF
• Rhinosinusitis
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• Cigarette smoking

Drug Interactions
• Vasoconstrictors: phenylephrine, oxymetazoline
• Considered relative contraindications

Types of IN Devices

Nose Drops
Atomizers
Aerosol
Syringe and Cotton Ball

Ideal Conditions for IN Drug Administration

Lipophilic drug
< 1000 Da
Relatively healthy nasal mucosa

Atomization
• Delivers small drug particles to nasal mucosa
• Rapid administration
• No regard for positioning
• Devices available:
  • Mucosal Atomization Device (MAD)
  • Accuspray Nasal Spray
  • Kurve Controlled Particle Dispersion

DDAVP Drops
DDAVP Spray
• Delivered posteriorly
• Rapid clearance
• Immediate swallowing
• Delivered anteriorly
• Slow nasopharynx clearance
• 2-3 fold increase in relative bioavailability

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**Ketamine Spray vs. Drops**

- 34 uncooperative children with ASA Grade 1 requiring dental treatment
- Patient acceptance: $p<0.0001$
- Onset of sedation: $p<0.05$
- Recovery time: $p<0.05$

**Pharmacokinetic (PK) Study of Haloperidol in Healthy Adults**

<table>
<thead>
<tr>
<th>Dose: haloperidol 2.5 mg</th>
<th>Log P= 3.2, MW 370 Da</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (min)</td>
<td>Half-life (hrs)</td>
</tr>
<tr>
<td>16.3</td>
<td>17.1</td>
</tr>
<tr>
<td>[15.0]</td>
<td>[15.0]</td>
</tr>
</tbody>
</table>

*Musosal Atomization Device not used

**Midazolam PK Study**

<table>
<thead>
<tr>
<th>Midazolam</th>
<th>IN</th>
<th>IV</th>
<th>IM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioavailability (%)</td>
<td>72.5</td>
<td>100%</td>
<td>93%</td>
</tr>
<tr>
<td>Tmax (mins)</td>
<td>10.3</td>
<td>12.4</td>
<td>29.2</td>
</tr>
</tbody>
</table>

- Sedative properties: IV > IN > IM
- Adverse effects:
  - Nasal irritation
  - Taste disturbance
  - Eye watering
  - Dizziness
  - No severe e.g., respiratory depression

**New Therapeutic Uses of IN Drugs**

<table>
<thead>
<tr>
<th>Patient Population &amp; Indications</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatrics &amp; adults</td>
<td>• Opioids</td>
</tr>
<tr>
<td>Life-threatening situations</td>
<td>• Fentanyl</td>
</tr>
<tr>
<td>Seizures</td>
<td>• Sedative</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>• Benzodiazepines</td>
</tr>
<tr>
<td>Analgesia</td>
<td>• Ketamine</td>
</tr>
<tr>
<td>Opioid overdose</td>
<td>• Other</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>• Narxone</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>• Lidocaine</td>
</tr>
</tbody>
</table>

*Considered off-label use of medications!

**IN Midazolam**

- Anxiolytic and treatment of seizure
- Properties:
  - $\log P = 2.5$, MW = 326 Da
  - Tmax: 5 < 10 mins
  - Usual dose: 0.2 mg/kg (max 10 mg)
- Adverse Effects:
  - Nasal irritation
  - Dysgeusia, nausea, vomiting, salivation
  - Visual and gait disturbances

**EMS Treatment of Peds Seizures**

- **IN midazolam**
  - Median seizure time: 11 mins
- **PR diazepam**
  - Median seizure time: 30 mins
  - Repeat seizure in ED
  - ED intubation
  - Other seizure meds
  - Hospital admission
  - PICU admission
Treatments of Acute Peds Seizures at Home

**IN Midazolam**
- Dose: 0.2 mg/kg (max 10mg) x 1
- Median time to seizure cessation: 3 mins
- Median total seizure time: 10.5 mins
- Easier to administer
- No difference in adverse drug effects

**PR Diazepam**
- Dose: 0.3-0.5 mg/kg (max 20mg) x 1
- Median time to seizure cessation: 4.3 mins
- Median total seizure time: 12.5 mins

*Statistically significant

IN Fentanyl
- Analgesia
- Properties:
  - log P = 4.05, MW = 336 Da
  - Tmax = 5 – 15 mins
- Dosing:
  - 1.7 mcg/kg (1 – 2 mcg/kg)
- Adverse Effects:
  - Epistaxis, dysgeusia, nasal irritation

IN Ketamine
- Sedation and analgesia
- Properties:
  - log P = 2.9, MW = 237 Da
- Dosing: not established in peds
  - 0.5 – 9 mg/kg have been studied
  - 5 mg/kg (usual)
- Adverse effects:
  - Nasal irritation
  - Emergence phenomena

IN Ketamine (INK)
- Analgesia in adults (moderate to severe pain)
  - Sub-dissociative dose: 0.7 – 1 mg/kg
  - Only 56% efficacious (N=72)
- Analgesia in ≥ 6 years old (moderate-severe pain)
  - 0.5 to 0.75 mg/kg
  - 88% treatment success (N=40)
- Procedural sedation in peds
  - Dose: 3 – 6 mg/kg (5 mg/kg)

IN Naloxone
- Opioid reversal
- Properties:
  - log P = 2.09, MW = 327 Da
  - Tmax = 6 – 9 mins
- Usual dosing: 2 mg
- Adverse effects:
  - Nasal irritation
Saved by the Nose: Bystander IN Naloxone Study

- 385 bystanders over 15 months
- Opioid use: 24.1 out of 30 days
- Overdose Kits
  - Instructions: 1 mg/nostril; may repeat x 1
  - 2 Luer-lock, prefilled syringes with naloxone 2mg/2mL
  - Mucosal atomization device (MAD)
- Results: 50 participants reported overdose
  - 74 successful reversals
  - Participants used multiple kits

To get MAD or not to get MAD

**Pros**
- Easy to use without regard to patient position
  - Upright vs supine
  - Healthcare vs. lay personnel
  - Relatively inexpensive

**Cons**
- One size-fits all
- Single-use only
- Cumulatively expensive

How to Use the MAD Device

- Obtain and prepare all supplies.
  - Drug
  - 3 mL syringe and needle
  - Atomization device
- Calculate the dose needed.
- Draw up the volume needed.
  - Add 0.1 mL to account for “dead space.”
- Remove needle and replace with atomization device using Luer-lock system.
- Monitor the patient.

Key Takeaways

- Ideal conditions for IN administration
  - Lipophilic drug with MW less than 300 Da
  - Relatively healthy nasal mucosa
  - Concentrated drug; volume up to 1 mL
- Administration technique
  - 30° angle towards middle nasal turbinates
- Safety:
  - Monitor for severe adverse effects e.g., respiratory depression
  - Counsel the patient on possible burning sensation and discomfort
Appendix: IN Dosing Table

<table>
<thead>
<tr>
<th>Indication</th>
<th>Drug</th>
<th>Dose</th>
<th>Factors to Consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesia</td>
<td>Fentanyl</td>
<td>1.5 – 2 mcg/kg</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Re-dose in 15 mins</td>
</tr>
<tr>
<td>Anxiolysis</td>
<td>Midazolam</td>
<td>0.4 – 0.5 mg/kg (max 10 mg)</td>
<td>Burning sensation for 30 seconds</td>
</tr>
<tr>
<td>Seizures</td>
<td>Midazolam</td>
<td>0.2 mg/kg (max 10 mg)</td>
<td>Provide airway support</td>
</tr>
<tr>
<td>NG Insertion</td>
<td>Lidocaine 4%</td>
<td>0.5 – 1 mL, 1.5 mL</td>
<td>In addition to pharyngeal and topical lidocaine 2% jelly</td>
</tr>
<tr>
<td>Opioid Reversal</td>
<td>Naloxone</td>
<td>2 mg</td>
<td>Avoid using less concentrated 0.4 mg/mL vial</td>
</tr>
<tr>
<td>Sedation</td>
<td>Ketamine</td>
<td>5 mg/kg (peds) (0.5 – 9 mg/kg have been studied)</td>
<td>Monitor for emergence phenomena, HTN</td>
</tr>
</tbody>
</table>

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**No IV Access? Get the IO!**

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Detroit Receiving Hospital  
Detroit, MI

**What is the first line alternative access according the ACLS recommendations?**

- Endotracheal
- Central venous catheter
- Intraosseous
- Intramuscular

**Current Recommendations**

- **ACLS¹**
  - "It is reasonable for providers to establish IO access if IV access is not readily available (Class IIa, LOE C).”

- **PALS²**
  - "IO access is a rapid, safe, effective, and acceptable route for vascular access in children, and it is useful as the initial vascular access in cases of cardiac arrest (Class I, LOE C).”

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When to Consider IO

- Cardiac or respiratory arrest
- Shock, including sepsis
- Respiratory distress (need RSI)
- Multitrauma patients
- Status epilepticus

Why IO?

- Quick access
- Reliability
- Safety
- Laboratory studies

<table>
<thead>
<tr>
<th>Access Type</th>
<th>Average Time (min)</th>
<th>1st Attempt Success Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral IV</td>
<td>3.6</td>
<td>73.7 %</td>
</tr>
<tr>
<td>Central IV</td>
<td>15.6</td>
<td>20 %</td>
</tr>
<tr>
<td>Intraosseous</td>
<td>1.5</td>
<td>80.6 %</td>
</tr>
</tbody>
</table>

Intraosseous Success Rates

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>IO Site(s)</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glaeser, et al. Ann Emerg Med 1990;21:1109-1110</td>
<td>Pediatric (n=152) and adults (n=113)</td>
<td>Proximal tibia</td>
<td>76% overall success rate 12% infiltration</td>
</tr>
<tr>
<td>Roda, et al. Ann Emerg Med 2011;58:509-516</td>
<td>Cardiac arrest adults (n = 182)</td>
<td>Tibial (n = 64) Humeral (n = 51) Periheal IV (n = 67)</td>
<td>First attempt success 91% tibia 51% humeral 43% peripheral IV</td>
</tr>
<tr>
<td>Glaeser, et al. Ann Emerg Med 1990;21:1109-1110</td>
<td>Adults (n = 34) and pediatrics (n = 5)</td>
<td>Unknown</td>
<td>84% first attempt success 97% second attempt success</td>
</tr>
</tbody>
</table>

Laboratory Studies

- Serum chemical analysis
  - Na+, Cl-, BUN/Scr, Mg, Phos, Total Ca++, bicarb
  - Albumin, bilirubin, total protein
  - K+, glucose, lactate
  - Hgb/ Hct
  - Blood gas analysis
  - Blood typing

Drugs Delivery of IO

- Dogs (n=21)
  - Distal femur (14G)
  - Femoral vein (16G)
  - Peripheral IV (16G)
- Drugs
  - Epinephrine 0.01 mg/kg
  - Bicarb 1 mEq/kg
  - CaCl 10 mg/kg
  - Lidocaine 1 mg/kg
  - D50W 0.25 mg/kg
- IO = IV = CVC

Contraindications

- Bone with a fracture
- Recent history of orthopedic surgeries
- Extremity with vascular injury
- Active infection
- Recent IO access attempt
- History of prior sternotomy (for sternal site)
Intraosseous Anatomy

IO Insertion Sites

What type of intraosseous device do you have at your hospital?

- EZ-IO®
- BIG®
- FAST1®
- Manual needles

Manual Needles

Approved Sites for IO Needles

<table>
<thead>
<tr>
<th>Device</th>
<th>Pediatric</th>
<th>Adult</th>
<th>Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manual</td>
<td>✔</td>
<td>✔</td>
<td>Sternum, humeral head, distal radius and ulna, ilium, femur, proximal and distal tibia, including malleoli</td>
</tr>
<tr>
<td>FAST®</td>
<td>✔</td>
<td>✔</td>
<td>For sternal use only in ≥ 12 years old</td>
</tr>
<tr>
<td>BIG®</td>
<td>✔</td>
<td>✔</td>
<td>Proximal humerus in adults, proximal tibia in both adults and children</td>
</tr>
<tr>
<td>EZ-IO®</td>
<td>✔</td>
<td>✔</td>
<td>Proximal and distal tibia, humeral head</td>
</tr>
</tbody>
</table>
Verification of Proper Placement

- Firm placement
- Aspiration of bone marrow (?)
- Easy to flush
- Ultrasound to identify misplaced needles

55 y/o M with out-of-hospital cardiac arrest
IO placed into the proximal tibia
20 min resuscitation
Echo: dilatation of right ventricle and a collapsed left ventricle
Suspected PE – tPA given

48 hours later

Complications

- Extravasation
- Soft tissue necrosis
- Compartment syndrome
- Cellulitis / skin abscesses
- Osteomyelitis
- Bone injury
- Embolic complications

Depot Effect

- Drug remain in medullary cavity
- Lower serum peak concentration
- Longer time to peak concentration
- Drugs (animal models)
  - Phenytoin
  - Vancomycin
  - Ceftriaxone
  - Tobramycin

How Fast Can You Infuse?

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>IO Site(s)</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Humeral: PB 153 vs. No PB 84 mL/min No difference between sites</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Distal tibia: PB 3.8 vs. no PB 2.07 mL/min</td>
</tr>
</tbody>
</table>

PB = Pressure bags
Drug Administration Pearls

- Minimize pain
- Lidocaine (preservative free)
- Medication / fluid infusions
- Pressure bags
- Infusion pumps
- Standard intravenous doses
- Flush with saline between medications

54 y.o. male with septic shock currently on norepinephrine and vasopressin

PMH: ESRD with recent infected graft (MRSA)

In the ED
- 20 G, right hand
- ultrasound guided lines (x 4)

In the ICU
- permacath (x 2)

Patient remains hypotensive & requires norepinephrine

What about IO?

Key Takeaways

- Get the IO kits ready!
- Lidocaine to minimize pain
- Pressure bags for faster infusions
- Standard IV medications dosing
- Watch for EXTRAVASATION!

Medications Given via IO

- ACLS medications
  - Adenosine
  - Amiodarone
  - Atropine
  - Calcium salts
  - Epinephrine
  - Lidocaine
  - Naloxone
  - Sodium bicarbonate
  - Vasopressin
- RSI medications
  - Etomidate
  - Thiopental
  - Rocuronium
  - Succinyllcholine
  - Vercuronium
  - Resuscitation fluids
  - Albumin
  - Blood products
  - Dextrose solutions
  - Saline, Lactated ringers

Medications Given via IO

- Vasopressors
  - Dobutamine
  - Dopamine
  - Norepinephrine
- Analgesics & Sedatives
  - Diazepam
  - Midazolam
  - Fentanyl
  - Morphine
- Antibiotics
  - Penicillin
  - Ampicillin
  - Cefotaxime
  - Vancomycin
- Miscellaneous
  - Phenytoin
  - Tenecteplase
  - Heparin
  - Insulin
  - Furosemide

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Case - It Could Happen

- Code Blue called
- 68 y.o. diabetic patient recently admitted for pneumonia
- Found on floor V.Fib arrest
- IV ripped out in fall
- CPR in progress, defibrillated 2x, anesthesia intubating
- Patient well-known to unit and requires IV access
- Only IO kit is locked in the ED 10 minutes away
- 3rd year medical resident running code is requesting amiodarone

What would we recommend to our resident about route of administration?

- Wait until we can get an IV
- Wait until we can get an IO
- Use the ETT tube

Current Recommendations

- PALS
  - "Vascular access (IO or IV) is the preferred method for drug delivery during CPR, but if it is not possible, lipid-soluble drugs, ...can be administered via an endotracheal tube."
- ACLS
  - "If IV or IO access cannot be established, epinephrine, vasopressin, and lidocaine may be administered by the endotracheal route during cardiac arrest (Class IIB, LOE B)."

What medication would we recommend to our resident?

- Give amiodarone via ETT
- Give epinephrine via ETT
- Give lidocaine via ETT

Medications for ET Administration

- Naloxone
- Atropine
- Vasopressin
- Epinephrine
- Lidocaine

Administration

- Volume
  - Peds 5ml/Adults 10ml
- Diluent
  - Sterile water may improve absorption of epinephrine/lidocaine
  - 0.9% Saline may not decrease PaO₂ as much as sterile water
**Administration**

- **Direct instillation vs. Endobronchial Tube**
  - Endobronchial tube administration may increase absorption
  - LMA administration may further decrease absorption

- **Ventilation Post Administration**
  - 5-10 positive pressure ventilations immediately post administration

**What dose of medication would we recommend to our resident?**

- Give epinephrine 1mg ETT
- Give epinephrine 3mg ETT

**Dosing**

- Optimal dosing is unknown via ETT
  - **ACLS**
    - Recommend 2-2.5x the IV dose
    - Equipotent epinephrine dose 3-10x IV in animals
  - **PALS**
    - Double or triple dose of lidocaine, naloxone, atropine
    - Give a 10-fold increase dose of epinephrine

**ACLS/PALS Dosing Via ET**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult IV Dose</th>
<th>Adult ET Dose</th>
<th>Pediatric IV Dose</th>
<th>Pediatric ET Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naloxone</td>
<td>0.4-2 mg</td>
<td>0.8-5 mg</td>
<td>0.1 mg/kg</td>
<td>0.1-0.3 mg/kg</td>
</tr>
<tr>
<td>Atropine</td>
<td>1 mg</td>
<td>2-3 mg</td>
<td>0.02 mg/kg</td>
<td>0.04-0.06 mg/kg</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>40 units</td>
<td>40-100 units</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>1 mg</td>
<td>2-10 mg</td>
<td>0.03 mg/kg</td>
<td>0.1 mg/kg</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>100 mg</td>
<td>200-300 mg</td>
<td>1 mg/kg</td>
<td>1-3 mg/kg</td>
</tr>
</tbody>
</table>

**Medication Considerations**

- Epinephrine – Don’t be low on the dose
  - $\beta_2$ effects have caused transient hypotension

- Vasopressin- IV dose may be adequate via ET

- Lidocaine- only antiarrhythmic with data

- Dosing may be limited by availability

**ET Kinetic Considerations**

- Decrease pulmonary blood flow
  - Arrest <20% of normal

- Delayed onset of action
  - 1-2 min compared to IV

- Prolonged action with ROSC
  - Possible depot effect
Efficacy

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>3 year retrospective review</td>
<td>5 year retrospective review</td>
</tr>
<tr>
<td>Out-of-hospital arrest - Asystole</td>
<td>Out-of-hospital arrest - All rhythms</td>
</tr>
<tr>
<td>n=78 IV drugs, n=43 ET drugs</td>
<td>n=495 IV drugs, n=101 ET drug</td>
</tr>
<tr>
<td>Epinephrine/Atropine dose 2mg ET</td>
<td>Epinephrine/Atropine dose 2mg ET</td>
</tr>
<tr>
<td>ROSC 17% IV vs. 0% ET (p = 0.005)</td>
<td>ROSC 27% IV vs. 15% ET (p = 0.04)</td>
</tr>
<tr>
<td>No difference in survival to discharge</td>
<td>Survival to Discharge 5% IV vs. 0% ET (p = 0.03)</td>
</tr>
</tbody>
</table>

Key Takeaways

- IV/IO preferred
- ET route last resort
- Use high doses
- Use enough volume
- Don’t stress over diluent
- Hyperventilate briefly after drug given

Lost IV? Check Under the Skin

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Case

- 2 y.o. male
- 3 days of diarrhea, vomiting, and poor oral intake.
  - 1 wet diaper in the last 24 hours.
- Exam
  - fatigued
  - mucus membranes are dry
  - extremities are cool
  - capillary refill is prolonged (2 seconds)
- Ondansetron ODT given - continued vomiting
- ED RN’s unable to establish IV access after 1 attempt

What are the options?

- Repeat IV attempt – RN ultrasound guided, IV access team and IV rehydration?
- Nasogastric tube placement – oral rehydration?
- Subcutaneous administration of fluid?
- Intraosseous administration of fluid?

Background

- Hypodermoclysis
  - Administration of subcutaneous fluids - SQ hydration
  - Used historically 1930’s-50’s
  - Fell out of favor
  - Adverse case reports
  - Improved IV technology
  - Currently used in palliative care and new research in pediatrics
Indications
- Mild to moderate dehydration in pediatrics and adults unable/unwilling to tolerate oral rehydration and...
  - IV therapy not available
  - IV therapy failure/expected failure
  - No other needs for IV access
  - Facilitate IV access
- Equally effective as IV rehydration in these patients

Efficacy Hypodermoclysis - Adult

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Sex</th>
<th>Q IV</th>
<th>Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>O'Keefe/ et al.</td>
<td>Hospitalized Elderly Mild Dehydration</td>
<td>30</td>
<td>30</td>
<td>RCT 1.5%/day 48 hours</td>
<td>No difference in serum urea (P=0.5) or creatinine (P=0.5)</td>
</tr>
<tr>
<td>Sleisak et al.</td>
<td>Hospitalized Elderly Mild/Mod Dehydration</td>
<td>48</td>
<td>48</td>
<td>RCT 1.5%/day 6 days</td>
<td>No difference in routes in discomfort, cardiac failure, hyponatremia, local side effects, or improvement in ADL performance (P=0.25, P=0.68, P=1.0, P=1.0, P=0.74)</td>
</tr>
<tr>
<td>Duermo et al.</td>
<td>Hospitalized Elderly Mild/Mod Dehydration</td>
<td>34</td>
<td>33</td>
<td>RCT 1.5%/day 72 hours</td>
<td>No difference in routes in post-hydration serum urea, creatinine, osmolality (P=0.96, P=0.80, P=0.43)</td>
</tr>
</tbody>
</table>

Challiner et al.
Acute Stroke
Unable to Take Oral Fluids
60/60
RCT 1.5%/day 72 hours
No difference in post-hydration osmolality (P=0.12)

Efficacy Hypodermoclysis - Pediatrics

- Infuse-PEDS2
- Randomized non-inferiority study
- Children 1 month – 10 years, n=148
- Compare IV and hyaluronidase (HDASE) facilitated SQ hydration
- 20 ml/kg isotonic fluids over 1 hour then as needed

Hyaluronidase (HDASE)

- Products
  - Hylenex- recombinant human
  - Vitrase- ovine derived
- Mechanism
  - Enzymatic hydrolysis of hyaluronic acid
  - Increased permeability of SQ tissue
- Dosing - Clysis
  - 100-200 units- typically 150 units
- Duration
  - 24-48 hours

- Adverse reactions
  - <0.01% risk of allergic reaction
- Benefits
  - 3-4x increased rate of SQ fluid administration
  - Comparable to IV infusions
  - Increased rate of absorption?
  - Radiolabeled NSS faster - no difference at 1hr
  - Decreased pain scores?
  - 5.8 on 100mm VAS with HDASE
  - 9.6 on 100mm VAS w/o HDASE (p < 0.002)

Compare
• Hylenex
• Vitrase
• Hyaluronidase
• Hypodermoclysis
• Oral hydration
Hypodermoclysis

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No IV</td>
<td>• Cannot provide more than 3L/24 hours</td>
</tr>
<tr>
<td>• Less staff time to place</td>
<td>• Limited choice of IVF</td>
</tr>
<tr>
<td>• Decreased needle sticks</td>
<td>• Systemic absorption delayed</td>
</tr>
<tr>
<td>• Extremities free</td>
<td>• Decreased cost</td>
</tr>
<tr>
<td>• Less pain</td>
<td>• Extremities free</td>
</tr>
<tr>
<td>• Decreased cost</td>
<td>• Less pain</td>
</tr>
<tr>
<td>• Site lasts 24-48 hours</td>
<td>• Decreased cost</td>
</tr>
</tbody>
</table>

Sites

- Abdomen
- Scapula
  - Interscapular area best for children
- Thigh
- Upper chest

Fluids

- Recommended
  - Lactated Ringers, 0.9% Saline
- Pediatrics and Adults
- Also used
  - D_{5}W, D_{3}NS, D_{3.1}/2NS, 1/2NS
- Acidic pH of dextrose solutions may cause more discomfort
- Potassium up to 30meq/L tolerated in adults
- Hypertonic and electrolyte free fluid not recommended
- Fluid/electrolyte shifts

Technique

1. Prepare site as for IV
2. Pinch skin
3. Insert 24-25g angiocath or butterfly at 30-45 degree angle
4. Check for lack of blood return
5. Inject hyaluronidase if desired
6. Prop catheter with gauze
7. Secure with occlusive dressing
8. Start infusion and titrate slowly to desired rate

Adverse reactions

- Common
  - Edema - 9-14%
  - Erythema - 9-14%
  - Inflammation - 3-5%
  - Pain - 3-5%
- Rare
  - Cellulitis
  - Abcesses
Subcutaneous hydration is appropriate for which of the following?

- Mild Dehydration
- Moderate Dehydration
- Severe Dehydration

Hyaluronidase facilitates more rapid administration of subcutaneous fluids.

- True
- False

Key Takeaways

- Subcutaneous fluid administration offers advantages for rehydration in certain clinical situations for both adults and pediatrics
- Hyaluronidase increases the rate of fluid delivery
- Isotonic solutions are recommended – LR is better tolerated

No IV, No Problem!
Practical Approaches to Alternative Routes of Administration