Alternative Routes of Administration

When PO is NOT an Option

Presented by: Zachary T. Hopkins, PharmD
Outline

• Medication Delivery Routes and Necessity
• Inhaled Antibiotics for Cystic Fibrosis
• New Inhaled Antibiotics
• What to Expect for Inhaled Antibiotics
• Feeding Tubes
• Medication Administration Considerations
• PLO Gels
• Questions?
• References
Medication Delivery Routes

• Oral
• IM
• IV
• IR
• Transdermal
• Inhalation
• PLO
• Feeding Tubes
Medication Delivery Routes

- Oral
- IM
- IV
- IR
- Transdermal
- Inhalation
- PLO
- Feeding Tubes
Why Are Alternative Routes Necessary?

- Dysphagia
  - Treatment-related
  - Disease-related
- Failure to Thrive
- Physical Deformity
- Safety Concerns
- Ease of Administration
- Targeted Administration
Inhaled Antibiotics
Inhaled Antibiotics (IA) for Cystic Fibrosis (CF)

• Use began in 1940’s for chronic airway infections
  • Aerosolized version of parenteral medications
    • Significant bronchial irritation/spasm
    • Added preservatives and non-physiologic chemical composition

• First FDA approval of IA in 1997
  • Tobramycin for inhalation for treatment of chronic Pseudomonas aeruginosa in CF patients

• Maximization of medication delivery in the airway

• Local Adverse Effects of IA’s
  • Bronchoconstriction/spasm, altered taste, dysphonia and throat irritation

• Reduction in systemic Adverse Effects of antibiotic treatment
  • Rare oto- and nephro-toxicity

Source 1: Ann Am Thorac Soc
## IA’s Currently Used in Clinical Practice

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Disease Indications</th>
<th>Formulation</th>
<th>Recommended Dose / Frequency</th>
<th>Delivery Device</th>
<th>Cost (AWP)</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approved Use</td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Aztreonam</td>
<td>Cayston</td>
<td>CF, ventilator-associated pneumonia</td>
<td>Inhalation solution</td>
<td>75 mg nebulized three times a day</td>
<td>Altera eFlow nebulizer</td>
<td>$7900 (75mg, 84mL)</td>
<td>Wheezing</td>
</tr>
<tr>
<td></td>
<td>Colomycin</td>
<td>CF; ventilator-associated pneumonia</td>
<td>Powder dissolved in saline</td>
<td>1–2 million units (75–150 mg) nebulized twice a day</td>
<td>Jet or ultrasonic nebulizer</td>
<td>$34 (150mg)</td>
<td>Cough, Bronchospasm, Throat irritation</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>TOBI Podhaler</td>
<td>CF</td>
<td>Inhalation solution (5-ml ampule containing 300 mg tobramycin and sodium chloride, pH 6.0)</td>
<td>300 mg nebulized twice a day</td>
<td>PARI LC PLUS jet nebulizer</td>
<td>$130 (300mg/5mL)</td>
<td>Tinnitus, Dysphonia, Bronchospasm, Hearing loss</td>
</tr>
<tr>
<td></td>
<td>TOBI</td>
<td>CF</td>
<td>Inhalation solution (4-ml ampule containing 300 mg tobramycin and sodium chloride, pH 5.0)</td>
<td>300 mg nebulized twice a day</td>
<td>PARI LC PLUS jet nebulizer</td>
<td>$122 (300mg/4mL)</td>
<td>Tinnitus, Dysphonia, Bronchospasm, Hearing loss</td>
</tr>
</tbody>
</table>

*Source 1: Ann Am Thorac Soc  
Source 5: Lexicomp Online®*
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</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>N/A</td>
<td>Nontuberculous mycobacteria</td>
<td>Injectable solution diluted with saline</td>
<td>250 mg nebulized daily (up to 500 mg twice a day if tolerated)</td>
<td>Jet nebulizer</td>
<td>$8 (500mg/2mL)</td>
<td>Hearing Loss, Vertigo, Dysphonia, Nephrotoxicity, Shortness of breath, Cough, Abnormal taste, Bronchospasm</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>Fungizone</td>
<td>Post-transplant fungal prophylaxis or treatment</td>
<td>Injectable solution diluted with sterile water</td>
<td>Prophylaxis: 25 mg daily for 4 d then weekly for 7 wk</td>
<td>Jet nebulizer</td>
<td>$45 (50mg)</td>
<td>Shortness of breath, Cough, Abnormal taste, Bronchospasm</td>
</tr>
<tr>
<td></td>
<td>Abelcet</td>
<td>Post-transplant fungal prophylaxis or treatment</td>
<td>Liposomal solution</td>
<td>Prophylaxis: 50 mg daily for 4 d then weekly for 7 wk</td>
<td>Jet nebulizer</td>
<td>$240 (5mg/mL, 20mL)</td>
<td>Cough, Abnormal taste, Bronchospasm</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>Fortaz</td>
<td>Ventilator-associated pneumonia; CF (Burkholderia cepacia infection)</td>
<td>Injectable solution diluted with saline</td>
<td>Ventilator-associated pneumonia: 15 mg/kg nebulized every 3 h for 8 d</td>
<td>Jet nebulizer</td>
<td>$15 (1g) $30 (2g)</td>
<td>Eosinophilia, Increased ALT</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>N/A</td>
<td>Non-CF bronchiectasis</td>
<td>Injectable solution diluted with saline</td>
<td>80 mg nebulized twice a day</td>
<td>Porta-Neb Ventstream jet nebulizer</td>
<td>$1.30 (40mg/mL)</td>
<td>Bronchospasm, Unpleasant taste, Tinnitus, Dysphonia, Bronchospasm, Hearing loss</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>N/A</td>
<td>CF</td>
<td>Injectable solution diluted with saline</td>
<td>80 mg nebulized twice a day</td>
<td>Jet nebulizer</td>
<td>$2.40 (80mg/2mL)</td>
<td></td>
</tr>
</tbody>
</table>

Source 1: Ann Am Thorac Soc  
Source 5: Lexicomp Online®
IA’s for CF Continued: What’s in the Pipeline?

<table>
<thead>
<tr>
<th>Anti-Infective</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>To Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled Tobramycin</td>
<td></td>
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<tr>
<td>Azithromycin</td>
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<tr>
<td>Cayston®</td>
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<tr>
<td>TIP (TOBI Inhaled Powder)</td>
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<tr>
<td>Levofloxacin (Inhaled)</td>
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<tr>
<td>Arikace®</td>
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<tr>
<td>AeroVanc®</td>
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</tr>
</tbody>
</table>

Source 1: Ann Am Thorac Soc
IA’s for CF Continued: What’s in the Pipeline?

• *Streptococcus pneumoniae*
  • levofloxacin inhalation solution (MP-376, Aeroquin; Aptalis)

• Nontuberculous Mycobacteria (NTM)
  • liposomal amikacin (Arikayce; Insmed)

• Chronic mycobacterial infections
  • liposomal amikacin (Arikayce; Insmed)

• *Pseudomonas aeruginosa*
  • fosfomycin/tobramycin for inhalation (FTI; Gilead)

• Methicillin-resistant *Staphylococcus aureus (MRSA)*
  • inhaled vancomycin (AeroVanc; Savara)

Source 1: Ann Am Thorac Soc
IA’s: What to Expect

• Additional Controlled Trials
  • Expanded indications outside of CF Treatment
    • Current RCT’s: non-CF bronchiectasis, vent-associated pneumonia, COPD, mycobacterial disease and post lung transplant
  • Recurring/chronic infections
  • Treatment/prevention of resistant organisms
    • Continuous vs intermittent therapy
  • Dosage, Duration of Treatment

• New Technology in Delivery Devices
  • Movement away from Nebulizers
  • Dry Powder Inhalations
  • Aerosolization devices

Source 1: Ann Am Thorac Soc
Feeding Tubes
Parenteral Feeding

Complete Bypass of the Gastric/Enteral System

1. Peripheral Parenteral Nutrition (PPN)
   • Peripheral Vein Placement (arm)
   • Short term nutrition supplementation

2. Total Parenteral Nutrition (TPN)
   • Central Vein Placement
   • Long term nutrition supplementation

Source 2: American Gastroenterological Association (AGA)
Enteral Feeding

- Percutaneous Endoscopic Gastrostomy (PEG/G-tube)/Jejunal (PEJ)
  - Inserted through the abdominal wall directly into the stomach/jejunum
  - Long term feeding (>1 month)
  - Invasive/surgical tube placement/removal
  - Complications: gastric leakage to peritoneal cavity, septic shock, death

- Nasogastric (NG) / Nasoduodenal (ND) / Nosojejunal (NJ)
  - Inserted through the nostril and into the stomach/duodenum/jejunum
  - Non-invasive, temporary, short-term feeding (<1 month)
  - Nasal Irritation upon insertion/removal
  - Complications: improper tube placement into lungs, pneumonia, death

Source 2: American Gastroenterological Association (AGA)
Enteral Tube Placement

Gastric feeding Indications:

• Requires normal or near-normal gastric and small bowel motility
• Adequate gastric anatomy to receive a gastric access tube
• Bolus feeding regimen

Post-pyloric feeding Indications:

• Gastroparesis, partial gastrectomy (not enough stomach for gastric access), partial or complete gastric outlet obstruction, pancreatitis and intolerance to gastric feeding
• Reduced risk of aspiration
• Duodenal
  • Pre-pancreas
• Jejunal
  • Post-pancreas – pancreatitis

Source 2: American Gastroenterological Association (AGA)
## Special Considerations to Drug Administration

<table>
<thead>
<tr>
<th>Medication</th>
<th>Administration Adjustment Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atovaquone</td>
<td>Administer with enteral feeding to increase absorption</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Dilute with NS/%5 Dex in divided total daily doses</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Higher doses required for enteral administration: 750 mg enterally ≈ 400 mg i.v. Hold feeding 1 hour pre &amp; 1 hour post administration</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Use crushed tablets with moderate fat content. Avoid use of solution due to plastic binding in the tube.</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>Do not crush ER tabs. Use IR equal daily dose Q6-8h</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>Hold nutrition 1 hour pre and 1 hour post admin. DR caps may be opened, but do not crush granules</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>Capsule preferred with “full meal”. Liquid preferred in concomitant PPI/H2RA</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>Do not crush DR caps. Mix packet granules with acidic medium (apple/orange juice), admin prior to ‘meal’, flush tube with acidic medium</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>Use IV if severe infection. Admin 1 hour pre or 2 hours post ‘meal’</td>
</tr>
</tbody>
</table>

Source 3: AJHP
## Special Considerations to Drug Administration

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<thead>
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<th>Administration Adjustment Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levothyroxine sodium</td>
<td>Use &lt;7 days, no adjustments. Use &gt;7 days, hold food 1 hour pre and post administration. Monitor thyroid function</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>Take 1 hour pre ‘meal’. Do not crush granules. May be suspended with bicarbonate or apple juice.</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td></td>
</tr>
<tr>
<td>Penicillin V</td>
<td>Hold feeding 1 hour pre or 2 hours post administration. Consider Amoxicillin</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Hold feeding 1 hour pre or 2 hours post administration. Divide daily dose into two administrations to minimize nutritional hold time</td>
</tr>
<tr>
<td>Sevelamer</td>
<td>Avoid use in enteral feeding if possible</td>
</tr>
<tr>
<td>Sucralfate</td>
<td>Avoid use in enteral feeding if possible. Consider PPI/H2RA</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Hold feeding 1 hour pre &amp; 1 hour post administration. Use of rapid release or solution is preferred.</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Hold feeding 1 hour pre &amp; 1 hour post administration. Avoid soy protein formulations. Monitor INR</td>
</tr>
</tbody>
</table>

Source: AJHP
PLO Gel

• PLO stands for Pluronic Lecithin Organogel and is a combination of oil and water that forms a thickened paste
• Lecithin component allows medication to cross all layers of skin
• Primary use has typically been for pain relief
• Application can occur at the intended source of discomfort (in the case of pain) OR on the inside of the wrist(s) for a generalized effect throughout the entire body system

Source 4: Northern Arizona Healthcare
Chemistry of PLO

Stage 1. Solubilization of Lecithin in Organic Media

Stage 2. Addition of Polar Additive

Stage 3. Spontaneous Formation of Organogel with Solubilized Guest Molecules

http://www.plo-gel.com/Main/plo-gel.php
## Commonly Compounded PLO Gels

<table>
<thead>
<tr>
<th>Medication</th>
<th>Targeted Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td>Nausea</td>
</tr>
<tr>
<td>Cyclobenzaprine</td>
<td>Muscle Spasm</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Pain (Neuropathic)</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Pain</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>Pain</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>Pain</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Anxiety</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>Motion Sickness / Nausea</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>Motion Sickness / Nausea</td>
</tr>
<tr>
<td>Testosterone</td>
<td>Hormone Replacement</td>
</tr>
</tbody>
</table>

Source 4: Northern Arizona Healthcare
Questions?
References


