Avoiding the Infusion Confusion: The Safe Use of Infused Prostacyclins

Speakers:

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Disclosures

• Laura Duvall: no financial interests to disclose
• Rebekah Hanson: Speakers Bureau (United Therapeutics)

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Learning Objectives

At the conclusion of this activity, the participant will be able to:

1. Describe the process for evaluating safety risks at a participant's site of practice and summarize major challenges associated with infused prostacyclins

2. Provide tips for evaluating medication regimens including drug-drug interactions, drug-disease interactions, and ongoing safe-use monitoring

3. Describe strategies to improve management of infused prostacyclins during transitions in care through collaboration and communication

4. Evaluate how to develop resources, training, and competencies for safe management of infused prostacyclins to minimize risks
Speaker Background

• Laura Duvall:
  – Internal Medicine/PAH Specialty Practice Pharmacist, The Ohio State University Wexner Medical Center

• Rebekah Hanson:
  – Clinical Pharmacist for PAH Program and Specialty Pharmacy Services at UI Health
  – Previously Clinical Supervisor of the PAH Specialty Team at a major SP
Infused Prostacyclin Characteristics

- Infused medication
- Unique devices and associated supplies
- Complex dosing
  - Titrated in ng/kg/min using dosing weight
  - Narrow dosing spectrum
  - Highly individualized
- Often administered in specialty area’s
- Profound, potentially lethal, effects when under- or over-dosed
- Individualized drug properties and pharmacokinetics
- Used in small patient populations

*High risk, error prone medication*
National Survey of Prostacyclin Administration Errors

- Survey administered to PAH care providers
- 68% of respondents reported a serious error
- 29% serious AE/9 deaths
- Error rate independent of home vs. hospital pump
- Reported errors included:
  - Flushing of the central line
  - Patient received wrong cassette
  - Pump stopped and not restarted
  - Pump programmed incorrectly
  - Calculation or concentration error
  - Wrong dosing weight
  - Over or under shoot line dead space with epoprostenol
  - Concentrated IV on micro-infusion bolused

Kingman MS et al. J Heart Lung Transplant 2010;29:841–6
Audience Poll

When infused prostacyclin patients are admitted to your hospital center, you:

• Leave patients on their own pump
• Transition patients to a hospital CADD pump
• Transition patients to a regular hospital infusion pump

Do you keep backup prostacyclin cassettes (or bags) on the nursing unit?

• Yes
• No

Has your hospital/center EVER experienced one or more potentially serious errors related to an infused prostacyclin?

• Yes
• No

Kingman MS et al. J Heart Lung Transplant 2010;29:841–6
Patient Case 1

- 54 yo female admitted to CCU on Flolan 28 ng/kg/min administered via CADD Legacy pump
- On admission, infusion was switched to hospital pump (hospital did not stock CADD Legacy) and also changed to q8hr bag changes
- Mixed concentration was reduced from 3mg/100ml to 0.5ml/100ml and rate was adjusted to deliver current dose
- First bag hooked up and pump rate was initiated
- Within minutes the patient began experiencing anxiety, flushing, nausea, and sinus tachycardia

→ Discovered that more concentrated solution in the line was not aspirated and she was inadvertently bolused ←
Patient Case 2

- 34 year old female initiated on treprostinil IV during acute visit. Initiated on CADD Legacy infusion pump
- Pt had been titrated to dose of 18 ng/kg/min
- Further dose increases required more concentrated mixed concentration and reduction in rate
- Order for new concentration entered in the EMR at 5pm, delivered to the unit for next cassette change following morning
- After a few hours, the patient began experiencing nausea, headache, and became hypotensive

→ Discovered that the new infusion rate was not programmed into the pump ←
Patient Case 3

• 52 yo female on existing therapy with treprostinil SC on CADD MS3 infusion pump, admitted for acute DVT: Also ESRD on HD TIW.
• The patient seen by PAH coordinator during admission for evaluation of subcutaneous site, the patient had just returned from 4hr HD session
• Nurse went to assess infusion pump and found it underneath the patient and the screen was blank

➔Discovered on review of pump history, occlusion alarm occurred and went unheard during HD, depleting the battery and shutting the pump off. The pump had been off for a few hours ➜
Reason’s Model of Accident Causation

- Hazards or Unsafe Acts
- Latent Conditions
- Lapse or Slip (Action Failure)
- Organization and Workplace

Missing or failed defenses
Causes of Medication Administration Errors

• 54% of studies evaluating causes of MAE in hospitals most commonly identified “slips and lapses” ¹
• Active failure due to inadequate knowledge of drug or the patient is a common cause of hospital prescribing errors ²
• Most common cause of IV MAE’s in hospitals are “slips and lapses” ³
• Frequency of self administered MAE’s is estimated to be 19 - 59%⁴
• Non-oral routes, non traditional schedules, and special instructions increase medication regimen complexity⁵

3. BMJ Open 2015;5:e005948
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# Applying Risk Assessment Concepts to Infused Prostacyclins

## Risk Assessment for Infused Prostacyclins

<table>
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<tr>
<th>ISMP Key Element</th>
<th>Risk Assessment Questions</th>
<th>Identified Problems</th>
<th>Possible Interventions</th>
<th>Follow up Responsibilities</th>
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</thead>
</table>
| I Patient Information | - How is critical patient information obtained including infusion details and comprehensive medication history?  
- How are patients managed during pregnancy?  
- How are patients managed during acute deterioration?  
- How are comorbidities assessed?  
- How are patient specific factors identified including cognitive ability, health literacy, language, depression, dementia, limitations, and special populations? |                      |                        |                           |
| II Drug Information      | - How is updated and accurate drug information disseminated?  
- What drug references are available for infused prostacyclins?  
- Who is responsible for titrations and dose adjustments?  
- How is critical drug property and dilution requirement information verified?  
- How is staff alerted to medication related problems, such as side effects or drug interactions, in real-time?  
- What computer or automatic alerts are available?  
- How are high risk/high alert medications managed?  
- What are the independent checks and process steps that must occur with these medications? |                      |                        |                           |
| III Communication of Drug Orders | - Who is responsible for verification of information with the specialty pharmacy?  
- What is the process for contacting the specialty pharmacy?  
- Do electronic orders contain the necessary infusion information, unique to the drug?  
- How are orders communicated during transitions in care?  
- How are current patient specific infusion orders documented and how to key personnel access these orders?  
- How are the IT/Team members notified of admissions, discharges, or any changes in orders?  
- How are post-discharge orders communicated? |                      |                        |                           |
| IV Labeling and Packaging | - How are mixed cassettes or bags labeled? What necessary information is included on the label?  
- How are they differentiated based on drug? |                      |                        |                           |
## Potential Prostacyclin Drug Interactions

### Anti-Hypertensives
- **Common:**
  - CCB’s
  - Beta-blockers
  - ACE-Inhibitors
  - ARB’s
  - Diuretics
  - Other PAH Drugs
- **Less Common:**
  - TCA’s
  - MAO-I
  - Alpha-blockers

### Anti-Platelet/Anti-Coagulants
- **Common:**
  - Warfarin
  - Heparin
  - LMWH
  - Factor Xa inhibitors
  - DTI
  - NSAIDs
  - Dipyridamole
  - ADP-receptor inhibitors
  - Thrombolytics
  - SSRI’s
  - Kinase inhibitors
- **Less Common:**
  - Ephedra
  - Ma Huang
  - Cocaine

### Sympathomimetics
- **Common:**
  - Pseudoephedrine
  - Phenylephrine
  - Methylphenidate
  - Lisdexamfetamine
- **Less Common:**
  - Ephedra
  - Ma Huang
  - Cocaine

### Treprostinil: CYP2C8
- **Inhibitors:**
  - Gemfibrozil
  - Montelukast
  - Zafirlukast
  - Teriflunomide
  - Trimethoprim
  - Glitazones
- **Inducers**
  - Rifampin
Important Co-Morbidities to Consider

- Liver or renal impairment
- Congestive heart failure
- Depression
- Cognitive impairment
- Substance abuse disorder
- Dexterity/mobility impairment
- Significant hypotension
- Immunosuppression
Ongoing Monitoring

- Regular follow up and support is critical
- Ongoing safe-use monitoring
- Medication access
- Infection surveillance
- Medication changes and transitions in care (TOC)
Infused Prostacyclin Personal Medication Guide

Complete the information before leaving the hospital. The PAH nurse or pharmacist will help you complete the sections.

Make sure you understand the purpose of everything included in this guide before leaving.

Make a copy and share this guide with your family members or other people that help take care of you.

Keep this guide with you and bring it to all of your doctor’s appointments.

It’s important to keep this guide updated. The PAH nurse or pharmacist will help you keep it updated regularly.

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### MY IMPORTANT CONTACT INFORMATION

<table>
<thead>
<tr>
<th>MY INFORMATION</th>
<th>MY EMERGENCY CONTACT PERSON</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name:</td>
<td>Name:</td>
</tr>
<tr>
<td>Birthday:</td>
<td>Phone number:</td>
</tr>
<tr>
<td>Preferred hospital:</td>
<td>Phone number:</td>
</tr>
<tr>
<td></td>
<td>Email:</td>
</tr>
<tr>
<td></td>
<td>Relationship:</td>
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### MY MEDICAL CONTACTS

If I am having a medical emergency I should dial 911 for immediate assistance (see appendix for examples of medical emergencies, urgent issues and non-urgent concerns)

<table>
<thead>
<tr>
<th>Name:</th>
<th>Phone number:</th>
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</table>

If I am having a serious health problem or urgent infusion related problem I should call

If I have non-urgent medical questions I should call

If I am having a non-urgent infusion related concern I should call

### MY DOCTORS

<table>
<thead>
<tr>
<th>Name:</th>
<th>Phone number:</th>
<th>Clinic Name:</th>
<th>Location:</th>
<th>Reason for seeing:</th>
</tr>
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<tbody>
<tr>
<td>PAH Management</td>
<td></td>
<td>Primary Care</td>
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### MY PHARMACIES

<table>
<thead>
<tr>
<th>Specialty pharmacy for my infusion</th>
<th>Pharmacy Name:</th>
<th>Phone number:</th>
<th>Location:</th>
<th>Medication Managed:</th>
</tr>
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<tbody>
<tr>
<td>Specialty pharmacy for oral PAH meds</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Other pharmacies I use</td>
<td></td>
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Transitions of Care

• Patient safety is the #1 priority

• Each institution has to look at transitions of care in an individualized manner based on experience and resources

• Have a defined process in place
  – Policies and Procedures
  – Anticipate as many scenarios as possible
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Policy and Procedure

- Pumps
- Verifying prescription with medication supplier
- Dosing weight
- Discontinuation of therapy / dose changes
- RN double-check
- Restrictions
- Back up IV access, IV bag, pump
- Priming or “packing” the line
- Aspiration of lines
- Preparation of products
- Formulary products
- Procedural areas
- Education tools and requirements
Pumps

• When a patient is admitted to the hospital should they stay on their home pump or be transitioned to a hospital pump?

• Things to consider
  – Is the patient on a Crono-5 pump?
  – Nursing education regarding pumps
  – Physical and mental capacity of the patient
  – Distributor resources
  – Hospital resources
Verifying the Prescription

• Accredo
• CVS Caremark

• Confirm
  – Dosing weight
  – Dose
  – Concentration of medication
  – Mixing diluent
  – Home pump rate
    • CADD-1 – mL/day
    • CADD-MS3 – mL/hr

• Electronic Order Sets
Dosing Weight

• Dosing weight is the weight the patient was on the day that the prostacyclin therapy was initiated regardless how long ago that occurred.

• ALWAYS use dosing weight, NOT actual weight to calculate dosing parameters.
Discontinuation of Therapy and Dosing Changes

• Continuous Infusion Prostacyclin therapy is LIFELONG.

• Dose changes either purposeful or accidental WILL likely lead to side effects in the patient.
  – Nursing education
  – To treat or not to treat?
RN double check / Restrictions

• Double check helps to prevent errors
  – It takes a village!
• Physician restrictions
• Location restrictions
  – Staff education
Back up IV access, IV bag, pump

- Epoprostenol – half life ~ 4 minutes
- Treprostinil – half life ~ 4 hours

- Especially with EPO – best to be proactive and prepared for any worst case scenario
When TO prime

- Concentration changes
- New line (PIV or CVC)

When NOT TO prime

- Routine IV bag changes (same conc.)
- Routine transition from home supply to hospital supply (same conc.)
Aspiration of IV lines

• When TO aspirate
  
  – If the prostacyclin line is not going to be used for prostacyclin administration anymore for any reason
  
  – If prostacyclin cannot be aspirated out of the line
    – the line MUST be labeled “do not use” and must be removed from the patient
Preparation of Intravenous Prostacyclins

• Minimizing errors in the IV room
  – Store medication in isolated location
    • Veletri® away from Flolan®
    • Single concentration for IV Treprostinil prep, 1mg/mL
  – Prepare Veletri vs. Flolan vs. Remodulin at different specified times during the day
  – Stickers / Colored baggies
  – Portless tubing/filters
  – Pharmacist log sheet
  – Nothing else in the hood during preparation
    • RPh check prior to injection into empty bag (in hood)
Preparation of Subcutaneous Prostacyclin Pump Refills

• Prepared in a separate hood / different room

• Medication supply kept in a defined location, away from IV room supply
  – 2.5mg/mL, 5mg/mL, 10mg/mL

• Prepared in pump syringe for patient
Formulary Product Selection

• Veletri® AND Flolan®?

• Treprostinil Consignment Program?
Procedural areas

• PAH trained anesthesiologists
• PAH trained ancillary staff to accompany patient
• Home vs. Hospital pumps when patients are sedated

• Planning ahead for pump compatibility issues in MRI
Education Tools and Requirements

• How do you go about developing resources, training and competencies in your institution?

• Successful management tools
  – Make education a priority
  – Appoint a core team of practitioners
    • Varying backgrounds/education
  – Enforce “competency” as a requirement of all practitioners caring for the PAH patient population
    • Computer-based learning
    • Hands-on Skills Assessments
  – Quarterly learning opportunities for staff
  – New hire training
    • Pharmacy residents, Pulm/Cardio fellows, Nursing orientation
Obtaining CME/CE Credit

• If you would like to receive continuing education credit for this activity, please visit:

http://pha.cds.pesgce.com
Supplemental Materials

• Supplemental materials discussed in this session can be accessed at:
  – www.pahshare.com
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