INPATIENT USE OF PARENTERAL PROSTACYCLINS IN AN ACADEMIC MEDICAL CENTER

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Objectives

• Describe the use of parenteral prostacyclin analogs (PPAs) in pulmonary arterial hypertension
• Review potential errors associated with PPAs in the inpatient setting
• Outline an academic medical center's process for use of PPAs in hospitalized patients
# Pulmonary hypertension (PH)

<table>
<thead>
<tr>
<th>Group</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pulmonary arterial hypertension (PAH)</td>
</tr>
<tr>
<td>2</td>
<td>PH due to left heart disease</td>
</tr>
<tr>
<td>3</td>
<td>PH due to lung disease/hypoxia</td>
</tr>
<tr>
<td>4</td>
<td>Chronic thromboembolic PH (CTEPH)</td>
</tr>
<tr>
<td>5</td>
<td>PH with unclear or multifactorial mechanism</td>
</tr>
</tbody>
</table>

**WHO FC***

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Ordinary physical activity does not cause undue dyspnea/fatigue, chest pain, or near syncope</td>
</tr>
<tr>
<td>II</td>
<td>Ordinary physical activity causes undue dyspnea/fatigue, chest pain, or near syncope</td>
</tr>
<tr>
<td>III</td>
<td>Marked limitation of physical activity</td>
</tr>
<tr>
<td>IV</td>
<td>Unable to carry out any physical activity without symptoms of right heart failure</td>
</tr>
</tbody>
</table>

*World Health Organization Functional Class*
Pulmonary arterial hypertension (PAH)

• “…progressive, incurable disease of the small pulmonary arteries characterized by vascular cell proliferation, aberrant remodeling, and thrombosis in situ.”

  • Estimates up to 50,000 to 100,000
  • 15,000 to 25,000 diagnosed and treated

N Eng J Med 2004; 351:1655-1665
J Am Coll Cardiol. 2004;43:13S-24S
Pulmonary arterial hypertension (PAH)

- Multifactorial pathophysiology
  - Vascular smooth muscle dysfunction
  - **Endothelial dysfunction**
    - Increased endothelin-1 and thromboxane A\textsubscript{2}
    - **Decreased prostacyclin** and nitric oxide (NO)
  - Adventitial changes
  - Prothrombotic abnormalities

- Causes
  - Idiopathic
  - Heritable
  - Drug/toxin-induced
  - Associated (HIV, connective tissue disease, portal hypertension, chronic hemolytic anemia)
Medical management of PAH

Parenteral prostacyclin analogs (PPAs)

- Indicated in WHO-FC III and IV PAH
- Several products and dosage forms available

<table>
<thead>
<tr>
<th>Dosage Forms</th>
<th>Treprostinil</th>
<th>Epoprostenol</th>
<th>Iloprost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>Orenitram®</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intravenous</td>
<td>Remodulin®</td>
<td>Flolan®</td>
<td>Veletri®</td>
</tr>
<tr>
<td>Subcutaneous</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhaled</td>
<td>Tyvaso®</td>
<td></td>
<td>Ventavis®</td>
</tr>
</tbody>
</table>

HIGH ALERT MEDICATION

Complex therapies that require close attention to detail in all steps of the medication use process
Relevant medication errors

- Medication not prepared as exact total volume
- Incorrect dispense based on infusion device
- Patient without therapy (epoprostenol) for 2 hours due to loss of central intravenous access and delayed placement of new line
- Medication dispensed from central pharmacy and wasted
- Medication prepared in incorrect/incompatible diluent
Relevant medication errors

- Medication orders not placed for admitted patient taken to procedural area
- Medication prepared in cassette for home infusion device without air removed (potential for pump error)
- Incorrect programming of hospital IV pump
  - Dose (mcg/kg/min)
  - Dose (ml/hour)
  - Dosing weight
  - Total volume
Active learning assessment

Which of the following statements regarding PPAs is true?

a. PPAs are indicated in patients with PAH and symptoms consistent with WHO-FC III or IV

b. PPAs improve symptoms in PAH by increasing endogenous endothelin-1 (ET) production

c. PPA dosing weight should be monitored and updated monthly

d. PPAs are readily compatible with multiple diluents for administration
Medication use process

- Ordering
- Preparation
- Dispensing
- Administration
- Monitoring
Medication use process

- **Ordering**
  - Unique dosing (ng/kg/min)
  - Specific dosing weight
  - Specialty Pharmacy contact

- **Preparation**
  - Specialty infusion devices
  - Final volume for infusion (exact)
  - Expiration of prepared product
  - Selection of diluent
Medication use process

- Dispensing
  - Special precautions (in-line filter, light protect)
  - Replacement supply/drug waste
  - Delivery of medication to bedside at requested time

- Administration
  - IV access
  - Programming/management of infusion device
  - Second check for high-alert medication
Medication use process

- Monitoring
  - Adverse effects (management)/dose titration
  - Replacement supply
UC Health

- University of Cincinnati Medical Center (UCMC)
- West Chester Hospital
- Daniel Drake Center
- UC Health Surgical Hospital
- UC Physicians
University of Cincinnati Medical Center

- Designated as a Center of Comprehensive Care for PAH by the Pulmonary Hypertension Association (PHA)
  - 36 PPA patients managed
  - 12 new starts in 2015

Criteria 4.8

- Must have a pharmacy with immediate access to parenteral prostacyclin analogues
- Pharmacy staff must be proficient with preparation of prostacyclin analogue infusions
Patient admissions

- Therapy initiation
- PAH-related
- Medication therapy
- IV access
- Other disease-related process
- Outpatient imaging
Health system update – PPA use

- Epic order set updates
  - Physician
  - Pharmacists
- Continuation of patients’ home infusion devices
- UC Health Guidelines
- UCMC Standard Operating Procedure (SOP)
Physician order set update

- Nursing orders
- Bedside assessment of medical equipment
  - Patient’s ability to manage infusion device
  - Date and time of last medication change
- Admission to restricted units
  - ICU
  - Medical stepdown
  - Cardiac stepdown
- Inpatient consult to pharmacy
Nursing orders

- Dedicated central line is required for infusion
- Not compatible with other medications or dextrose-containing fluids
- Line for **VELETRI** infusion should not be flushed or used for phlebotomy
- Medication should be changed based on infusion rate and product expiration
- Change IV tubing with each medication supply change
- Call inpatient pharmacy if assistance is needed
Inpatient consult to pharmacy

- Review/re-assessment of date and time of last medication supply change
- Review of physician assessment of patient’s ability to continue to use home infusion device
- Inspection of home infusion device
  - Release of hospital responsibility
- Verification of dosing parameters with specialty pharmacy
- Placement of order using pharmacy order set
Active learning assessment

In which of the following ways are pharmacist involved in the medication use process with PPAs?

a. Ordering  
b. Preparation  
c. Dispensing  
d. Administration  
e. Monitoring  
f. All of the above
Additional pharmacist responsibilities

- Emergency line management
- Transition of parenteral supply if necessary
- Device management
Home infusion devices

CADD-Legacy® 1

Crono 5® (Crono Five®)

CADD-MS®3
# Home infusion devices

<table>
<thead>
<tr>
<th></th>
<th>CADD-MS®3</th>
<th>CADD-Legacy® 1</th>
<th>Crono 5® (Crono Five®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epoprostenol (Flolan®)</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Epoprostenol (Veletri®)</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Treprostinil (Remodulin®)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
Health system guidelines

• Medication – ordering, administration, and preparation
  • Parenteral epoprostenol, treprostinil
  • Oral treprostinil
• Use of patients’ medical devices during inpatient stay
• Conversion of therapy if needed
• Line maintenance (more updates to come)
• Specialty Pharmacy information
Medical center standard operating procedure

- General Information
- Ordering
  - Inpatient Consult to Pharmacy
- Order verification
  - Second, independent double check
- Dispensing
  - Hospital drug supply
  - Infusion device and expiration of prepared product
  - Instructions for syringes/cassettes for infusion devices
  - Prepare as exact labeled concentration
  - Additional dispensing instructions (filter tubing, light protect, cold pack)
EMR updates

• Pharmacy order sets
  • Restricted ordering (pharmacists only)
  • Medication records
    • Dose (ng/kg/min)
    • Dosing weight (restricted to order-specific)
    • Diluent
    • Rate is automatically calculated

• Label changes
  • Drug and diluent volume
  • Total volume
  • Device for infusion
  • Expiration of prepared product
Education

• Nursing (regular/ongoing)
  • ICU, stepdown
  • ED, OR/PACU
• Pulmonary fellows (annual/ongoing)
• Admitting physicians
• Pharmacy
Conclusions

• PPA use is increasing with increased incidence of PAH
• The complexity of prostacyclin therapy warrants high attention during all parts of the medication use process.
• Pharmacists should be involved in all steps of the process to ensure safe and optimal use of these medications
• Education and references should be standardized and repeated at regular intervals
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