Retrospective Review of Pulmonary Hypertension Medication Transitions Within a Large Health Care System

Ming Yang, PharmD, Frank Spexarth, RPh, Eric Roberts, MD, Dianne Zwicke, MD
Aurora Health Care, Milwaukee, WI
Max.Yang@aah.org

Problem
The inherent need for medication transitions for patients with pulmonary arterial hypertension (PAH) and paucity of available primary literature drives the impetus for development and evaluation of proprietary transition protocols.

Background
A wide variety medications are available for the treatment of PAH. Due to nuances between medications even within a certain medication class, there is the need for medication transitions when managing these patients.

Medication transitions are done to:
- Minimize adverse drug reactions
- Optimize disease management
- Change route of administration
- Improve quality of life by facilitating ease of therapy

Transitions between medications comes with risks such as prostacyclin excess, insufficiency, and patient desensitization.

Objective
To assess the efficacy and safety of current PAH medication transition practices and protocols at our institution.

Methods
- Retrospective, observational, single-center study of PAH patients at St. Luke’s Medical Center in Milwaukee, WI
- Included adult PAH patients transitioned between PAH medications from January 2016 through December 2019
- Patients identified via pulmonary hypertension clinic records
- All patients transitioned based on institutional protocol references.
- Protocols included transitioned at least six patients
- Data collected included baseline demographics, baseline and post-transition hemodynamics, acute transition safety and efficacy, and six-month safety.
- Composite primary efficacy outcome: transition success, defined as transition to new medication without worsening of disease, new intolerable side effects at first follow-up, increased escalation of care or death within 1 month.
- Primary safety outcome was escalation of care

Results
- 73 patients comprised the final cohort
- 7 unique transition protocols evaluated
- 69 successful transitions (94.5%) and 4 complications
- 67 patients (91.8%) acutely achieved planned target dose
- Four complications occurred including:
  - 2 requiring escalation of care
  - 1 intolerable side effect requiring discontinuation
  - 1 death during the transition admission unrelated to medication transition
- 21 patients (28.8%) experienced prostacyclin excess
- 7 patients (9.6%) experienced prostacyclin insufficiency

Table 1 continued. Baseline Demographics

<table>
<thead>
<tr>
<th>Demographics (n=73)</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>49 (67.1%)</td>
</tr>
<tr>
<td>Age (years), median</td>
<td>62 (21.49)</td>
</tr>
<tr>
<td>Weight (kg), median</td>
<td>89 (40-140)</td>
</tr>
<tr>
<td>BMI (kg/m^2), median</td>
<td>31.59 (15.48-56.79)</td>
</tr>
<tr>
<td>Patients with baseline oxygen use</td>
<td>52 (71.2%)</td>
</tr>
</tbody>
</table>

Baseline Functional Class
- Functional Class 11 (13.1%)
- Functional Class 20 (27.4%)
- Functional Class 35 (47.9%)
- Functional Class 415 (20.5%)

Success
69 (94.5%)

Reason for transition complication
- Transformed to new medication
73 (100.0%)
- Without worsening of disease
72 (98.6%)
- Without intolerable side effect requiring discontinuation
72 (98.6%)
- Without escalation of care
71 (97.3%)
- Without death in 1 month
72 (98.6%)

Target dose achieved acutely
67 (91.8%)

Prostacyclin excess during transition
21 (28.8%)

Prostacyclin insufficiency during transition
7 (9.6%)

Dosing protocol adjustment required
15 (20.5%)

Dosing protocol adjustment required
15 (20.5%)

Functional class maintained at first follow-up visit
70 (95.9%)

Long Term Outcomes
- Number (Name of parameter)
- Death in 1 month
1 (1.4%)
- Lung transplant or balloon septostomy in 6 months
0 (0%)

Table 2 continued. Results

<table>
<thead>
<tr>
<th>Group (n=73)</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>64 (87.7%)</td>
</tr>
<tr>
<td>Group 2</td>
<td>16 (22.7%)</td>
</tr>
<tr>
<td>Group 3</td>
<td>1 (1.4%)</td>
</tr>
</tbody>
</table>

Concomitant PAH medications
- No concomitant medications
21 (28.8%)
- Prostacyclin + Nitric Oxide Pathway (tadalafil, sildenafil, riociguat)
36 (49.3%)
- Prostacyclin + Endothelin Receptor Antagonist (ambrisentan, bosentan, macitentan)
9 (12.3%)
- Triple therapy
11 (15.1%)

Clinical classification of pulmonary hypertension.

Echocardiography

Table 2. Periprocedural Hemodynamics

<table>
<thead>
<tr>
<th>PH Markers (n=73)</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Minute Walk Distance (m)</td>
<td></td>
</tr>
<tr>
<td>Pre (n=51)</td>
<td>350 (45-658)</td>
</tr>
<tr>
<td>(n=58)</td>
<td>417 (150-658)</td>
</tr>
<tr>
<td>Post (n=58)</td>
<td>441 (152-639)</td>
</tr>
</tbody>
</table>

Patients PAH MDK above or with <30% decrease in MDK
-- 28 (73.7%)

ECHO Parameters

<table>
<thead>
<tr>
<th>Pre (n=73)</th>
<th>Post (n=73)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline and repeat PAP (mmHg), median</td>
<td>41 (28-133)</td>
</tr>
<tr>
<td>Baseline and repeat TAPSE (mmHg), median</td>
<td>20 (10-33)</td>
</tr>
<tr>
<td>Repeat PASP below baseline or &lt;10% increase from baseline</td>
<td>18 (15.9%)</td>
</tr>
<tr>
<td>Repeat TAPSE above baseline or &gt;10% decrease from baseline</td>
<td>48 (72.2%)</td>
</tr>
</tbody>
</table>

RHC Parameters

<table>
<thead>
<tr>
<th>Pre (n=63)</th>
<th>Post (n=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline and repeat mPAP (mmHg), median</td>
<td>47 (21-74)</td>
</tr>
<tr>
<td>Baseline and repeat PVR (wood units), median</td>
<td>7.25 (2.24-4.91)</td>
</tr>
<tr>
<td>Baseline and repeat CI by thermometry L/min/m^2, median</td>
<td>2.81 (1.16-6.11)</td>
</tr>
<tr>
<td>Baseline and repeat CI by Fick L/min/m^2, median</td>
<td>2.18 (1.16-3.5)</td>
</tr>
</tbody>
</table>

REFERENCES