Comorbidities and complications in adults with pyruvate kinase deficiency


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BACKGROUND

Pyruvate kinase (PK) deficiency is a rare congenital disorder caused by autosomal recessive mutations in the PKLR gene.

- A glycolytic defect caused reduced adenosine triphosphate (ATP) levels and leads to hemolytic anemia.
- A previously published analysis characterized the rates of comorbidities and complications among 254 pediatric and adult patients with PK deficiency.

OBJECTIVES

The objectives of this study were to:

- Compare rates of comorbidities and complications between adults with PK deficiency and the general population.
- Assess the impact of transfusion frequency on the prevalence of comorbidities and complications in adults with PK deficiency.

METHODS

Data sources:

- The PK Deficiency Natural History Study (NHS): Longitudinal cohort study that evaluated 254 patients with genetic confirmation of PK deficiency at 31 centers in six countries from June 2014 through April 2017.
- US-based IBM MarketScan® claims databases:
  - Inpatient, outpatient, and prescription drug claims for many conditions, a gradient is seen across PK deficiency on the MarketScan® cohort.
- For many conditions, a gradient is seen across PK deficiency on the MarketScan® cohort.
- To minimize the risk of understating the occurrence of comorbidities and complications, comparisons were limited to certain conditions, and three different analytical approaches were used:
  - A focus on chronic conditions that require ongoing management and thus are likely to appear in claims data regardless of diagnosis date (osteoporosis, liver cirrhosis, and pulmonary hypertension).
  - Mortality for which the "current status" was reported in both datasets; medications (anticoagulants, prophylactic antibiotics, antidepressants, and antianxiety) were considered high indicators of comorbidities and complications.
  - A narrowing of the observation window for the PK deficiency population to be aligned with the average 8-year observation window for the general population, with a focus on conditions for which a diagnosis procedure/data was available in the PK Deficiency NHS cohort.

RESULTS

Table 1. Transition status and demographics of the PK deficiency cohort (N=122)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ERT (n=1)</th>
<th>NRT (n=4)</th>
<th>NT (n=21)</th>
<th>Burden of disease vs NRT</th>
<th>Burden of disease vs NT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, %</td>
<td>30 (48.2)</td>
<td>17 (67.7)</td>
<td>16 (76.2)</td>
<td>0.383 vs NRT</td>
<td>0.395 vs NT</td>
</tr>
<tr>
<td>Age, mean (SD), years</td>
<td>34.2 (11.0)</td>
<td>35.8 (14.7)</td>
<td>37.2 (18.3)</td>
<td>0.033 vs NRT</td>
<td>0.033 vs NT</td>
</tr>
<tr>
<td>White, %</td>
<td>83 (69.0)</td>
<td>30 (100)</td>
<td>27 (100)</td>
<td>&gt;0.999 vs NRT</td>
<td>&gt;0.999 vs NT</td>
</tr>
<tr>
<td>Hispanic or Latino, %</td>
<td>2 (1.1)</td>
<td>1 (3.3)</td>
<td>1 (3.7)</td>
<td>&gt;0.999 vs NRT</td>
<td>&gt;0.999 vs NT</td>
</tr>
<tr>
<td>Genotype, %</td>
<td>2 (1.1)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>&gt;0.999 vs NRT</td>
<td>&gt;0.999 vs NT</td>
</tr>
<tr>
<td>Anemia (Hb&lt;74g/L)</td>
<td>20 (2.0)</td>
<td>4 (13.3)</td>
<td>3 (11.1)</td>
<td>0.085 vs NRT</td>
<td>0.003 vs NT</td>
</tr>
<tr>
<td>Mioasemia</td>
<td>21 (22.3)</td>
<td>14 (46.7)</td>
<td>19 (70.4)</td>
<td>0.003 vs NRT</td>
<td>0.003 vs NT</td>
</tr>
<tr>
<td>Non-mioasemia</td>
<td>11 (11.0)</td>
<td>8 (26.7)</td>
<td>6 (10.9)</td>
<td>0.003 vs NRT</td>
<td>0.003 vs NT</td>
</tr>
<tr>
<td>Non-mioasemia</td>
<td>18 (18.0)</td>
<td>12 (38.7)</td>
<td>0 (0.0)</td>
<td>0.003 vs NRT</td>
<td>0.003 vs NT</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (1.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>&gt;0.999 vs NRT</td>
<td>&gt;0.999 vs NT</td>
</tr>
</tbody>
</table>

DISCLOSURES

The PK Deficiency NHS and this analysis were funded by Agios Pharmaceuticals, Inc.

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CONCLUSIONS

- Patients with PK deficiency, regardless of transfusion status, have higher rates of selected comorbidities and complications than age- and gender-matched individuals from the general population.
- For many conditions, a gradient is seen across PK deficiency transfusion cohorts, with the highest rates observed for ERT patients.
- Even patients with PK deficiency who have never been transfused are at increased risk of complications of the disease and its treatment.

Competencies and complications in adults with pyruvate kinase deficiency

Figure 1. Adults with PK deficiency had higher lifetime rates of pulmonary hypertension, osteoporosis, and liver cirrhosis.

Figure 2. Adults with PK deficiency had higher rates of splenectomy, cholecystectomy, and gallstones over the preceding 8 years.

Figure 3. Rates of many complications varied by transfusion cohort.

- No significant differences were found for bone enlargement/dissection, seizures, thyroïd disease, arthrythmia, congestive heart failure, and leg ulcers.

Table 1. Transition status and demographics of the PK deficiency cohort (N=122)

Comparisons with the general population

- Patients with PK deficiency had higher rates of splenectomy, cholecystectomy, and gallstones over the preceding 8 years.

Conclusions

- For conditions for which fair and balanced comparisons with the general population could not be made, we show the lifetime prevalence rates just for the PK deficiency cohort, stratified by transfusion cohort (Figure 4).

- Rates of current prophylactic antibiotic and anticoagulant use were also significantly higher among patients with PK deficiency (not shown).
- There were no differences in rates of antidepressant and anti-anxiety medication use.

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