17 Disorders of Glycerol Metabolism

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17.1 Introduction

Disorders of glycerol metabolism include complex glycerol kinase deficiency (cGKD), isolated glycerol kinase deficiency (iGKD), and glycerol intolerance syndrome (GIS) (McCabe 2001a; Dipple and McCabe 2003). Glycerol kinase deficiency (GKD), both complex and isolated, is due to deletions or mutations of the glycerol kinase (GK) gene on Xp21. GIS is less well defined and some cases are due to fructose-1,6-diphosphatase (FDP) deficiency (McCabe 2001a; Dipple and McCabe 2003; Beatty et al. 2000). The treatment of acute crises includes intravenous glucose and supportive care (McCabe 2001a). The mainstay of long-term treatment remains a low-fat diet and avoidance of fasting. With cGKD, there can be associated Duchenne muscular dystrophy, adrenal hypoplasia, congenital and mental retardation; therefore, these associated diseases must be recognized and treated, especially the adrenal insufficiency (McCabe 2001a, b; Dipple and McCabe 2003; Vilain 2001). Patients with iGKD are at risk for insulin resistance, glucose intolerance, and type II diabetes mellitus (Gaudet et al. 2000), so individuals with iGKD should be monitored carefully for diabetes. Patients with GIS must avoid glycerol, especially in intravenous infusions (McCabe 2001a). In addition, some patients with GIS have FDP deficiency, and this must be identified and treated appropriately (McCabe 2001a; Beatty et al. 2000). Unfortunately, because disorders of glycerol metabolism are such rare and presumably underdiagnosed diseases, many patients go untreated, and we therefore do not know the efficacy of treatment (Fig. 17.1).
Avoid fasting
Low fat diet
IV glucose for crises

Avoid glycerol
IV glucose for crises

Monitor for insulin resistance and diabetes

Evaluate for DMD, adrenal insufficiency and developmental delay

Avoid fructose

Fig. 17.1. Management if disorders of glycerol metabolism

17.2 Nomenclature

<table>
<thead>
<tr>
<th>No.</th>
<th>Disorder (symbol)</th>
<th>Definitions/comment</th>
<th>Gene symbol</th>
<th>OMIM No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>17.1</td>
<td>Glycerol kinase deficiency (GKD)</td>
<td>Includes complex GKD (disorder 17.1.1) and isolated GKD (disorder 17.1.2 and 17.1.3)</td>
<td>GK</td>
<td>307030</td>
</tr>
<tr>
<td>17.1.1</td>
<td>Complex glycerol kinase deficiency (cGKD)</td>
<td>GKD as part of a contiguous gene syndrome</td>
<td>GK, NROB1, DMD</td>
<td>307030, 300200, 310200</td>
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<tr>
<td>17.1.2</td>
<td>Isolated glycerol kinase deficiency (iGKD)</td>
<td>Juvenile, symptomatic form</td>
<td>GK</td>
<td>307030</td>
</tr>
<tr>
<td>17.1.3</td>
<td>Isolated glycerol kinase deficiency (iGKD)</td>
<td>Adult onset, benign form</td>
<td>GK</td>
<td>307030</td>
</tr>
</tbody>
</table>

Adapted from Dipple and McCabe 2003

17.3 Treatment

- **17.1 Glycerol kinase deficiency**
  - 17.1.1 Complex
  - 17.1.2 Isolated symptomatic (juvenile)
  - 17.1.3 Isolated benign (adult)