Succinylacetone, Quantitative, Urine – Tyrosinemia Type 1

Tyrosinemia type 1, also known as fumarylacetoacetate hydrolase (FAH) deficiency or hepatorenal tyrosinemia, is a rare but severe genetic disorder. Urine organic acid and plasma amino acid measurements are the recommended initial tests for the evaluation of suspected tyrosinemia type 1. Urine succinylacetone measurement is useful in diagnosis and may be ordered concurrently with organic acids. Urine succinylacetone measurements may also be useful to monitor tyrosinemia treatment.

Disease Overview

Tyrosinemia type 1 is caused by a mutation in the FAH gene and exhibits autosomal recessive inheritance. The FAH gene encodes FAH, an enzyme involved in the metabolic pathway of phenylalanine and tyrosine. Tyrosinemia type 1 generally presents in early infancy. If untreated, symptoms include renal tubular dysfunction with hypophosphatemic rickets, poor feeding, vomiting, hepatosplenomegaly, and porphyria-like neurological crisis. Late onset symptoms include growth retardation, bruising, hepatomegaly, cirrhosis, and increased risk for hepatocellular carcinoma. FAH deficiency results in a buildup of tyrosine (can be normal on newborn screen), fumarylacetoacetate, maleylacetoacetate, and succinylacetone (the pathognomonic finding for tyrosinemia type 1). Succinylacetone is also mildly elevated in maleylacetoacetate isomerase deficiency, which is characterized by a milder phenotype.

Test Interpretation

Results

Urine succinylacetone is measured in millimole per mole of creatinine (mmol/mol CRT).

<table>
<thead>
<tr>
<th>Succinylacetone Concentration</th>
<th>Interpretation</th>
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<tbody>
<tr>
<td>Elevated (&gt;0.300 mmol/mol CRT)</td>
<td>Expected result in untreated patients with tyrosinemia type 1 or maleylacetoacetate isomerase deficiency</td>
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<tr>
<td>Normal (0.000-0.300 mmol/mol CRT)</td>
<td>Expected result in patients with normal FAH function or patients on therapy</td>
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Limitations

Succinylacetone testing cannot be used to determine carrier status.

Related Tests

**Organic Acids, Urine 0098389**

**Method**: Gas Chromatography-Mass Spectrometry (GC-MS)

**Amino Acids Quantitative by LC-MS/MS, Plasma 2009389**

**Method**: Quantitative Liquid Chromatography-Tandem Mass Spectrometry