Test Definition: HYOX

Hyperoxaluria Panel, U

Overview

Useful For

Distinguishing between primary and secondary hyperoxaluria

Distinguishing between primary hyperoxaluria types 1, 2, and 3

Genetics Test Information

Primary hyperoxalurias (PH), classified into types 1, 2, and 3, are genetic disorders of oxalate metabolism characterized by increased urinary excretion of oxalic acid and kidney stone formation.

Secondary hyperoxaluria is an acquired condition resulting from either increased intake of dietary oxalate or altered intestinal oxalate absorption.

Highlights

A diagnostic workup in an individual with hyperoxaluria demonstrates increased concentration of oxalate in urinary metabolite screening. If glycolate, glycerate, or 4-hydroxy-2-oxoglutarate is present, a primary hyperoxaluria is indicated.

Each type is distinguished from the others based on the urine profile.

Testing Algorithm

See Hyperoxaluria Diagnostic Algorithm in Special Instructions.

Special Instructions

- Hyperoxaluria Diagnostic Algorithm

Method Name

GasChromatography-MassSpectrometry(GC-MS)

NY State Available

Yes

Specimen

Specimen Type

Urine

Specimen Required

Supplies: Urine Tubes, 10 mL (T068)

Container/Tube: Plastic, 10-mL urine tube

Specimen Volume: 10 mL

Collection Instructions:

1. Have patient void the first-morning specimen, then **collect specimen within 2 hours of first-morning void.**

2. No preservative.

3. Immediately freeze specimen.

Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

-Inborn Errors of Metabolism Test Request (T798)

-Renal Diagnostics Test Request (T830)

Specimen Minimum Volume

1.1 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Urine	Frozen (preferred)	90 days	
	Refrigerated	14 days	

Clinical and Interpretive

Clinical Information

Increased urinary oxalate frequently leads to renal stone formation and renal insufficiency. Identifying the cause of hyperoxaluria has important implications in therapy, management and prognosis.

Hyperoxalurias are classified as primary and secondary. Primary hyperoxaluria is an inherited disorder of oxalate metabolism while secondary hyperoxaluria is an acquired condition resulting from either increased intake of dietary oxalate or altered intestinal oxalate absorption. Primary hyperoxalurias are classified into types 1, 2, and 3.

Hyperoxaluria type 1 (PH1) is an autosomal recessive disorder resulting in a deficiency of peroxisomal alanine: glyoxylate aminotransferase due to variants in the *AGXT* gene. It is characterized by increased urinary oxalic, glyoxylic, and glycolic acids. PH1 is the most common type with manifestations that include deposition of calcium oxalate in the kidneys (nephrolithiasis, nephrocalcinosis), and end-stage renal disease. Calcium oxalate deposits can be further deposited in other tissues such as the heart and eyes, and lead to a variety of additional symptoms. Age of onset is variable with a small percentage of patients presenting in the first year of life with failure to thrive, nephrocalcinosis, and metabolic acidosis. Approximately half of affected individuals show manifestations of PH1 in late childhood or early adolescence, and the remainder present in adulthood with recurrent renal stones. Some individuals with PH1 respond to supplemental pyridoxine therapy.

Hyperoxaluria type 2 (PH 2) is due to a defect in *GRHPR* gene resulting in a deficiency of the enzyme hydroxypyruvate reductase. PH2 is inherited in an autosomal recessive manner and is identified by an increase in urinary oxalic and glyceric acids. Like PH1, PH2 is characterized by deposition of calcium oxalate in the kidneys (nephrolithiasis, nephrocalcinosis), and end-stage renal disease. Most individuals have symptoms of PH2 during

childhood, and it is thought that PH2 is less common than PH1.

Hyperoxaluria type 3 (PH3), due to recessive variants in *HOGA1* (formerly *DHDPSL*), occurs in a small percentage of individuals with primary hyperoxaluria. *HOGA1* encodes a mitochondrial 4-hydroxy-2-oxoglutarate aldolase that catalyzes the 4th step in the hydroxyproline pathway. PH3 is characterized biochemically by increased urinary excretion of oxalate and 4-hydroxy-2-oxoglutarate (HOG). As with PH types 1 and 2, PH type 3 is characterized by calcium-oxalate deposition in the kidneys or kidney stone formation. Most individuals with PH3 have early onset disease with recurrent kidney stones and urinary tract infections as common symptoms. End-stage renal disease is not a characteristic of PH3. Of note, individuals with heterozygous variants in *HOGA1* can have variable and intermittent elevations of urine oxalate.

Secondary hyperoxalurias are due to hyperabsorption of oxalate (enteric hyperoxaluria); total parenteral nutrition in premature infants; ingestion of oxalate, ascorbic acid, or ethylene glycol; or pyridoxine deficiency, and may respond to appropriate therapy.

A diagnostic workup in an individual with hyperoxaluria demonstrates increased concentration of oxalate in urinary metabolite screening. If glycolate, glycerate, or HOG is present, a primary hyperoxaluria is indicated. Additional analyses can include molecular testing for PH1 (AGXTZ / *AGXT* Gene, Full Gene Analysis), PH2 (GRHPZ / *GRHPR* Gene, Full Gene Analysis, Varies), or PH3 (*HOGA1* sequencing).

Reference Values

REPORTING/INTERPRETING RESULTS

Reference Intervals (Normal Ranges):

GLYCOLATE

< or =17 years: < or =75 mg/g creatinine

> or =18 years: < or =50 mg/g creatinine

GLYCERATE

< or =31 days: < or =75 mg/g creatinine

32 days - 4 years: < or =125 mg/g creatinine

5 - 10 years: < or =55 mg/g creatinine

> or =11 years: < or =25 mg/g creatinine

OXALATE

< or =6 months: < or =400 mg/g creatinine

7 months - 1 year: < or =300 mg/g creatinine

2 - 6 years: < or =150 mg/g creatinine

7 - 10 years: < or =100 mg/g creatinine

> or =11 years: < or =75 mg/g creatinine

4-HYDROXY-2-OXOGLUTARATE (HOG)

< or =10 mg/g creatinine

Interpretation

Increased concentrations of oxalate and glycolate indicate type 1 hyperoxaluria.

Increased concentrations of oxalate and glycerate indicate type 2 hyperoxaluria.

Increased concentrations of oxalate and 4-hydroxy-2-oxoglutarate indicate type 3 hyperoxaluria.

Increased concentrations of oxalate with normal concentrations of glycolate, glycerate, and 4-hydroxy-2-oxoglutarate indicate secondary hyperoxaluria.

Cautions

Ascorbic acid (vitamin C) will falsely elevate oxalic acid results.

Clinical Reference

1. Bhasin B, Urekli HM, Atta MG: Primary and secondary hyperoxaluria: Understanding the enigma. World J Nephrol 2015;4(2):235-244 doi: 10.5527/wjn.v4.i2.235

2. Danpure CJ: Primary Hyperoxaluria. In The Online Metabolic and Molecular Bases of Inherited Disease. Edited by D Valle, AL Beaudet, B Vogelstein, et al. New York. McGraw-Hill. Accessed August 26 2015. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225543281&bookid=2709&Resultclick=2

3. Byrd DJ, Latta K: Hyperoxaluria. In Physician's Guide to the Laboratory Diagnosis of Metabolic Disease. Edited by N Blau, ED Chapman. Hall Medical, 1996, pp 377-390

4. Fraser AD: Importance of glycolic acid analysis in ethylene glycol poisoning. Clin Chem 1998;44(8):1769

5. Beck BB, Baasner A, Buescher A, et al: Novel findings in patients with primary hyperoxaluria type III and implications for advanced molecular testing strategies. Eur J Hum Genet 2013;21:162-172

Performance

Method Description

Urine samples corresponding to 0.25 mg of creatinine (not to exceed 1 mL of urine) are oximated by reaction with methoxyamine hydrochloride to stabilize one of the target analytes, 4-hydroxy-2-oxoglutaric (HOG). The urine is then acidified and extracted with ethyl acetate:isopropanol. After evaporation, the dry residue is silylated with BSTFA/1%TMCS:pyridine and analyzed by capillary gas chromatography/mass spectrometry (GC/MS). (Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Thursday; 8 a.m.

Analytic Time

14 days

Specimen Retention Time

2 months

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

82542

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
HYOX	Hyperoxaluria Panel, U	53710-0

Result ID	Test Result Name	Result LOINC Value
50592	Glycolate	13751-3
50593	Glycerate	13749-7
50594	Oxalate	13483-3
38049	4-hydroxy-2-oxoglutarate	13678-8
29982	Interpretation	59462-2
29984	Reviewed By	18771-6