Kansas
Department of Health and Environment

Tyrosinemia Type 1
Information for Health Professionals

Tyrosinemia type 1 is an amino acid disorder in which the enzyme fumarylacetoacetase (FAH) is missing or is not functioning correctly. This leads to a buildup of tyrosine and succinylacetone in the body, causing health problems including liver and kidney disease.

✓ Clinical Symptoms

There are two forms of tyrosinemia type 1; the common form in which symptoms develop in infants and the less common "chronic" form that develops in children and adults.

In the common form, symptoms develop within the first few months of life and may include diarrhea, bloody stools, failure to thrive, vomiting, lethargy, irritability, and a "cabbage-like" odor to the skin or urine. If untreated, liver problems such as hepatomegaly, jaundice, easy bleeding/bruising, and swelling of the legs/abdomen are common. Kidney problems can cause rickets and delays in walking. Without treatment, liver and kidney problems usually lead to death. Periodic episodes of pain/weakness (particularly in the legs), tachycardia, breathing problems, seizures, and coma may occur.

Both forms of tyrosinemia type 1 can lead to hepatocellular carcinoma.

✓ Incidence

Tyrosinemia type 1 occurs in less than 1 out of every 100,000 births. The incidence is increased in individuals with a French-Canadian background, particularly if they are from the Saguenay Lac Saint-Jean region of Quebec.

✓ Genetics of tyrosinemia type 1

Mutations in the FAH gene cause tyrosinemia type 1. Mutations in this gene reduce or eliminate the activity of the enzyme fumarylacetoacetate hydrolase which prevents the metabolism of tyrosine and phenylalanine. Fumarylacetoacetate accumulates and is converted into succinylacetone, which leads to elevated tyrosine levels and causes liver toxicity.

✓ How do people inherit tyrosinemia type 1?

Tyrosinemia type 1 is inherited an in autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition. Each pregnancy between carrier parents has a 25% chance of producing a child affected with tyrosinemia type 1, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Immediate diagnosis and treatment of tyrosinemia type 1 in the neonatal period is critical to normal development and survival. Treatment can prevent liver, kidney, and neurological symptoms if started immediately. Individuals should follow a life-long low-tyrosine and phenylalanine diet, which generally requires medical formulas and foods. Liver and kidney damage can be prevented with the medication nitisinone (NTBC). NTBC also stops neurological crises. This medication increases the level of tyrosine in patients, making adherence to the diet crucial. Regular blood and urine tests are needed to check amino acid levels, succinylacetone and nitisinone levels, and liver and kidney function. Liver transplantation is the only proven curative treatment.

✓ Screening Methodology

Primary newborn screening for tyrosinemia type 1 utilizes tandem mass spectrometry to determine the levels of Succinylacetone (SUAC). Elevated SUAC indicates the possibility of tyrosinemia type 1. False positives and false negatives are possible with this screen.

✓ What to do After Receiving Presumptive Positive TYR 1 Screening Results

1) **The clinician should immediately check on the clinical status of the baby.**
2) **Consultation with a metabolic specialist is essential.**
3) **The specialist may request urine organic acid or plasma amino acid analysis on baby.**
4) **Call KS Newborn Screening Program at 785-291-3363 with questions about results.**
5) **Report Clinical Findings to Newborn Screening Program at 785-291-3363.**
6) **Same birth siblings (twins, triplets) of infants diagnosed with TYR 1 should be re-screened; additional testing of these siblings also may be indicated.**

✓ Confirmation of Diagnosis

The diagnosis of tyrosinemia type 1 is confirmed through urine or plasma analysis revealing elevated succinylacetone or its metabolites. A lack of fumarylacetoacetase activity in lymphocytes or fibroblasts also confirms the diagnosis.

✓ Communication of Results to Parents

If a baby has a presumptive positive tyrosinemia type 1 newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with tyrosinemia type 1, the following points should be conveyed to the parents:

- ***Parents should understand that treatment for tyrosinemia type 1 will be life-long.***
- ***Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include the following specialties: pediatrics, metabolic disease specialist, dietician, hematologist, and hepatologist or gastroenterologist.***
- ***Periodic blood and urine analysis is needed.***
- ***Genetic counseling services may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation, contact:

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