Kansas
Department of Health and Environment

Beta Ketothiolase Deficiency
Information for Health Professional

Beta ketothiolase deficiency (BKT) is an organic acid disorder that results from an inability to process the amino acid isoleucine.

✓ Clinical Symptoms

Symptoms usually begin around one year of age. Individuals with beta ketothiolase deficiency are at an increased risk of developing metabolic crises, particularly after fasting, illness/infection, or high protein intake. Metabolic crises can cause the following symptoms: lethargy, feeding difficulties, ketosis, fever, diarrhea, vomiting, metabolic acidosis, hypoglycemia, coma, and death. Long-term effects in untreated individuals include cardiomegaly, prolonged QT interval, neutropenia, thrombocytopenia, failure to thrive, abnormal muscle tone, ataxia, and intellectual disabilities.

✓ Incidence

Beta ketothiolase deficiency occurs in less than 1 in 100,000 births.

✓ Genetics of beta ketothiolase deficiency

Mutations in the ACAT1 gene cause beta ketothiolase deficiency. Mutations in this gene reduce or eliminate the activity of the enzyme mitochondrial acetoacetyl-CoA thiolase. This enzyme is necessary to process isoleucine. When an affected individual consumes proteins and fats, toxic byproducts accumulate in the body causing the symptoms of this condition and resulting in ketoacidosis.

✓ How do people inherit beta ketothiolase deficiency?

Beta ketothiolase deficiency is inherited in an 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 beta ketothiolase deficiency, 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 beta ketothiolase deficiency is critical to normal growth and development. L-carnitine supplementations may be beneficial. During a metabolic crisis, glucose and bicarbonate via IV may be necessary. Individuals should avoid fasting. Some children may need a low-protein diet. Urine tests to check ketone levels are periodically needed.

✓ Screening Methodology

Newborn screening for beta ketothiolase deficiency utilizes tandem mass spectrometry. Elevated C5-OH (3-hydroxyisovaleryl carnitine) indicates the possibility of beta ketothiolase deficiency. False positive and false negative results are possible with this screen

✓ What to do After Receiving Presumptive Positive BKT 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 analysis and other labs on the baby.**
4) **Call KS Newborn Screening Program at 785-291-3363 with questions about results.**
5) **Report clinical findings to the Newborn Screening Program at 785-291-3363.**
6) **Same birth siblings (twins, triplets) of infants diagnosed with BKT should be re-screened; additional testing of these siblings also may be indicated.**
7) **Consider testing older siblings. Some individuals may be affected, but show no symptoms of the condition.**

✓ Confirmation of Diagnosis

The diagnosis of beta ketothiolase deficiency is confirmed through urine organic acid analysis and plasma acylcarnitine analysis.

✓ Communication of Results to Parents

If a baby has a presumptive positive beta ketothiolase deficiency 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 BKT deficiency, the following points should be conveyed to parents:

- ***Parents should understand that treatment for beta ketothiolase deficiency will be lifelong.***
- ***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 includes pediatrics and a metabolic specialist.***
- ***Genetic counseling 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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