Corticosterone methylxoximase deficiency

Corticosterone methylxoximase deficiency, also known as aldosterone synthase deficiency, is a disorder characterized by excessive amounts of sodium released in the urine (salt wasting), along with insufficient release of potassium in the urine, usually beginning in the first few weeks of life. This imbalance leads to low levels of sodium and high levels of potassium in the blood (hyponatremia and hyperkalemia, respectively). Individuals with corticosterone methylxoximase deficiency can also have high levels of acid in the blood (metabolic acidosis).

The hyponatremia, hyperkalemia, and metabolic acidosis associated with corticosterone methylxoximase deficiency can cause nausea, vomiting, dehydration, low blood pressure, extreme tiredness (fatigue), and muscle weakness. Affected infants often experience failure to thrive, which means they do not gain weight and grow at the expected rate. Severe cases of corticosterone methylxoximase deficiency can result in seizures and coma and can be life-threatening. However, affected individuals who survive infancy generally have a normal life expectancy, and the signs and symptoms of the disorder typically become milder or disappear by adulthood.

Frequency

Corticosterone methylxoximase deficiency is a rare disorder; its prevalence is unknown. Researchers have described two types of the condition: Type I is more common in the Amish population of Lancaster, Pennsylvania, while type II is more common in people of Iranian Jewish ancestry. The two types have similar signs and symptoms but can be distinguished by laboratory testing.

Causes

Mutations in the CYP11B2 gene cause corticosterone methylxoximase deficiency. This gene provides instructions for making an enzyme called aldosterone synthase. The aldosterone synthase enzyme is found in the adrenal glands, which are located on top of the kidneys.

Aldosterone synthase helps produce a hormone called aldosterone. Aldosterone regulates blood pressure by maintaining proper salt and fluid levels in the body. The aldosterone synthase enzyme is involved in a series of three chemical reactions that produce aldosterone from other (precursor) molecules: the conversion of 11-deoxycorticosterone to corticosterone, the conversion of corticosterone to 18-hydroxycorticosterone, and the conversion of 18-hydroxycorticosterone to aldosterone.

The CYP11B2 gene mutations that cause corticosterone methylxoximase deficiency lead to insufficient production of aldosterone, which impairs the kidneys' ability to reabsorb salt (sodium chloride or NaCl) into the blood and release potassium in the urine. As a
result, excessive amounts of salt in the form of charged atoms (ions) of sodium (Na\(^+\)) and chlorine (Cl\(^-\)) leave the body in the urine, while not enough potassium is released. The resulting imbalance of ions in the body underlies the signs and symptoms of corticosterone methyloxidase deficiency.

**Inheritance Pattern**

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

**Other Names for This Condition**

- 18-hydroxylase deficiency
- 18-oxidase deficiency
- aldosterone deficiency
- aldosterone deficiency due to deficiency of steroid 18-hydroxylase
- aldosterone deficiency due to deficiency of steroid 18-oxidase
- aldosterone synthase deficiency
- CMO deficiency
- congenital hypoaldosteronism
- corticosterone 18-monooxygenase deficiency
- corticosterone methyl oxidase deficiency
- familial hyperreninemic hypoaldosteronism
- steroid 18-hydroxylase deficiency
- steroid 18-oxidase deficiency
- Visser-Cost syndrome

**Diagnosis & Management**

**Genetic Testing Information**

- What is genetic testing? [primer/testing/genetictesting](https://www.ncbi.nlm.nih.gov/gtr/conditions/CN074214/)
Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22corticosterone+methyloxidase+deficiency%22+OR+%22Hypoaldosteronism%22

Other Diagnosis and Management Resources

- MedlinePlus Encyclopedia: Aldosterone
  https://medlineplus.gov/ency/article/003704.htm
- MedlinePlus Encyclopedia: Potassium Test
  https://medlineplus.gov/ency/article/003484.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Aldosterone
  https://medlineplus.gov/ency/article/003704.htm
- Encyclopedia: High Potassium Levels
  https://medlineplus.gov/ency/article/001179.htm
- Encyclopedia: Hyponatremia
  https://medlineplus.gov/ency/article/000394.htm
- Encyclopedia: Potassium Test
  https://medlineplus.gov/ency/article/003484.htm
- Health Topic: Adrenal Gland Disorders
  https://medlineplus.gov/adrenalglanddisorders.html
- Health Topic: Fluid and Electrolyte Balance
  https://medlineplus.gov/fluidandelectrolytebalance.html

Genetic and Rare Diseases Information Center

- Hypoaldosteronism
  https://rarediseases.info.nih.gov/diseases/2874/hypoaldosteronism

Educational Resources

- Jewish Genetic Disease Consortium
  https://www.jewishgeneticdiseases.org/diseases/corticosterone-methyloxidase-deficiency/
- MalaCards: corticosterone methyloxidase deficiency
  https://www.malacards.org/card/corticosterone_methyloxidase_deficiency
• Orphanet: Familial hypoaldosteronism
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=427

• You and Your Hormones: Aldosterone
  http://www.yourhormones.info/hormones/aldosterone.aspx

Patient Support and Advocacy Resources

• National Adrenal Diseases Foundation
  https://www.nadf.us/

Scientific Articles on PubMed

• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28corticosterone+methyloxidase+deficiency%29+OR+%28aldosterone+synthase+deficiency%29+OR+%28corticosterone+methyl+oxidase+deficiency%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

• CORTICOSTERONE METHYLOXIDASE TYPE I DEFICIENCY
  http://omim.org/entry/203400

• CORTICOSTERONE METHYLOXIDASE TYPE II DEFICIENCY
  http://omim.org/entry/610600

Sources for This Summary


  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16733367
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/8481357
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15134805

Reprinted from Genetics Home Reference:

Reviewed: November 2013
Published: May 14, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services