CONGENITAL HYPOTHYROIDISM

Congenital hypothyroidism (CH) is caused by a deficiency of thyroxine (T4), a hormone produced by the thyroid gland. Thyroxine is critically important to brain development in the infant. If left untreated, CH will result in permanent mental retardation and growth failure. If detected and treated early with hormone replacement medication, infants with CH will grow normally and have normal intelligence. The earlier the treatment, the better the long term outlook. However, newborns with CH often appear completely normal up to three months of age. Therefore, newborn screening can be the only way to know early if an infant has congenital hypothyroidism.

Screening

As of July 1, 2009, the Utah Newborn Screening Program is using a primary TSH (thyroid stimulating hormone) to screen for CH. Prior to this time, a primary T4 (thyroxine) was used.

TSH values of <1 or > 40.0 μU/mL are considered to be abnormal. If the TSH is abnormal, the T4 level is also measured. T4 levels of ≤ 4.0 μg/dL are considered to be abnormal. The specimen is reported out as an abnormal newborn screen suggestive of CH when the TSH value is greater than 40.0 μU/mL (> 40.0 μU/mL) or when the TSH is less than 1 (<1 μU/mL) <u>and</u> the T4 value is less than or equal to 4.0 μg/dL (≤ 4.0 μg/dL).

Typically, in a newborn with congenital hypothyroidism and an intact pituitary-hypothalmic feedback mechanism, the T4 remains decreased and the TSH increased. A TSH of > 230 μU/mL represents a critical screening value. Decreased T4 levels are often seen in sick infants and should be closely monitored. Newborn screening can detect congenital hypothyroidism with a high degree of accuracy. However, remain alert to clinical symptoms in older infants despite normal newborn screening results.

Clinical Signs and Symptoms

Infants with CH often appear healthy. They may have a large posterior and/or anterior fontanelle, facial myxedema, large protruding tongue, hoarse cry, hypothermia, lethargy, prolonged jaundice, delayed stooling and constipation, feeding difficulties with poor suck and abdominal distention with vomiting. The most frequent clinical sign of hypothyroidism is poor linear growth in the face of adequate weight gain. Hypothyroidism from congenital malformations of the thyroid gland, enzymatic abnormalities and other causes can present in the weeks and months after birth.

Frequency

Congenital hypothyroidism occurs in 1:3,000-4,000 births. Most cases of CH are sporadic, occurring in families without a family history. Approximately 15 to 20 percent of cases are inherited. Most CH is permanent, caused by either failure of normal formation of the thyroid gland or failure of proper production of thyroxine. Mothers who have hypothyroidism may pass TSH receptor blocking antibodies through the placenta, causing temporary hypothyroidism in the infant.

Treatment

Thyroxine is replaced by administration of synthetic levothyroxine. Newborns need relatively large doses (10-15 mcg/kg/day) as compared with older children and adults. Levothyroxine is a tablet that can be crushed or dissolved in a small amount of water and placed in the infant's mouth. Liquid preparations are not stable and should never be used. Soy formulas and iron preparations interfere with levothyroxine absorption. Levothyroxine administration should be separated from soy formula or iron by at least one hour. Decreased absorption due to soy formula can be compensated for by adjusting dosages. If formula is changed from a cow's milk based formula to a soy formula, thyroid levels should be repeated in 2-4 weeks and the dose adjusted as indicated by the levels.

Essential Steps for Diagnosis and Treatment

Follow-up all abnormal newborn screening results with clinical evaluation. If any doubt exists obtain serum free T4 and serum TSH levels. The Utah Newborn Screening Program recommends confirmatory laboratory testing (serum free T4 and serum TSH) for an infant when the screening specimen result is a TSH > 230 μU/mL or the first and second specimens are abnormal or the second specimen is abnormal.

1. Contact family for immediate examination of the infant and evaluation of her/his clinical condition.
2. Initiate lab work: IMMEDIATE serum free T4 and serum TSH levels. The results determine action:

TSH Result	Possible Causes	Action
Elevated	Primary Hypothyroidism Maternal Antibodies Maternal Medications -PTU	- Begin thyroid hormone replacement therapy for a low serum free T4 and an elevated serum TSH. - Serial monitoring of hormone levels.
Decreased	Pituitary-Hypothalamic Disorder (Secondary Hypothyroidism)	- Begin thyroid hormone replacement therapy for a low serum free T4 and a low serum TSH. - Serial monitoring of hormone levels. - Further studies may be necessary.
Normal	False positive screen TBG Deficiency Iodine Exposure Non-thyroidal illness (prematurity) Mild Primary Hypothyroidism Central Hypothyroidism Normal	-Further studies may be necessary for diagnosis. -Normal serum TSH and low serum free T4 require further evaluation. Contact pediatric endocrinologist

3. Consult with a pediatric endocrinologist as soon as possible for further guidance regarding additional testing that may be indicated and assistance with management of the infant.

Pediatric Endocrinologists Available for Consultation

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