MCG PEDIATRIC PODCAST

A medical education resource produced by the MEDICAL COLLEGE OF GEORGIA

Season 2, Episode #3
Congenital Hypothyroidism

May 15, 2021

Hosts:
Dr. Jacqueline Chan, Pediatric Endocrinology
Dr. Zac Hodges, Pediatric Hospitalists
John Baek, Medical Student

Peer Reviewers and Contributors:
Dr. Christopher Houk, Pediatric Endocrinology

LEARNING OBJECTIVES AND KEY POINTS

1. Recall the incidence of and risk factors associated with congenital hypothyroidism.
    a. Most infants diagnosed with congenital hypothyroidism do not have identifiable risk factors.
    b. Overall incidence of congenital hypothyroidism is about 1 in 2000 to 1 in 4000 newborns in population where that iodine nutrition is sufficient.
    c. Children with Down syndrome are at higher risk.
    d. Maternal history such as exposure to radiation during pregnancy, presence of antibodies or intake of anti-thyroid medication, and poor iodine intake.
    e. Iodine deficiency is more common in countries with limited resources and access to health care. Iodine deficiency can be detected through a urine sample.
2. Understand the importance of early diagnosis and the harms of delayed treatment.
    a. Congenital hypothyroidism is one of the most preventable causes of severe intellectual disability and developmental delay.
    b. An inverse relationship between intelligence quotient and age at diagnosis and treatment indicating that the longer treatment is delayed the higher the risk of low IQ scores.
    c. Treatment within 2 weeks of age is ideal.
3. Understand the normal hypothalamic-pituitary-thyroid axis.
    a. Hypothalamus produces the thyroid releasing hormone (TRH).
    b. TRH then stimulates the anterior pituitary gland to produce the thyroid stimulating hormone (TSH); also known as Thyrotropin.
    c. TSH then signals the thyroid gland to produce Thyroxine (T4)
    d. T4 gets converted to the T3 which is the active form.
    e. The thyroid hormone produced then inhibits TSH and TRH production via negative feedback once a stable level is achieved.
4. Understand the methods of newborn screening for congenital hypothyroidism and interpret abnormal results.
    a. The newborn screen checks either the TSH, T4 or both. There are two screening strategies.
        i. TSH first followed by T4 if elevated.
            1. Can miss central hypothyroidism.
            2. Can produce false positive due to normal surge of TSH at birth. Surge occurs because of sudden change in the environment of the infant from in utero and this normalizes after 24 hours of life.

   ii. T4 first and if low, followed by TSH.
      1. Can detect infants with primary hypothyroidism if T4 is low.
      2. Can also detect Thyroxine binding globulin deficiency.
      3. Can miss infants that initially has normal T4 with delayed elevation in TSH.
   iii. The most ideal is the one that measures both TSH and T4.
 b. TSH > 40 milliunits/Liter, congenital hypothyroidism is suspected, and serum levels should be drawn as soon as possible.

5. Create a differential diagnosis for the potential causes of congenital hypothyroidism.
 a. The most common cause is thyroid dysgenesis or abnormal thyroid development.
   i. Ectopic thyroid, thyroid hypoplasia, or complete aplasia.
   ii. The most common location of ectopic thyroid is the lingual thyroid.
 b. Dyshormogenesis or an error in the thyroxine synthesis itself.
 c. Central hypothyroidism and iodine related hypothyroidism whether deficiency or excess.
   i. TSH will be low in central hypothyroidisms.
   ii. For central hypothyroidism, the signal to the thyroid gland via TSH is insufficient and lab result will show low TSH and FT4 or a low FT4 and inappropriately normal TSH.
   iii. It is important to check other hormone secreted by the pituitary for the possibility of panhypopituitarism most importantly adrenal insufficiency which is life threatening.
6. Recognize findings on physical exam that would support the diagnosis of congenital hypothyroidism.
 a. Most infant with congenital hypothyroidism will have normal vital signs and physical exam.
 b. Wide fontanel, poor suck, hoarse cry, umbilical hernia, hypotonia, hypothermia, dry skin and jaundice.
 c. Excess sleeping, poor feeding, and constipation
7. Interpret confirmatory testing required to diagnose congenital hypothyroidism.
 a. If the newborn screen comes back abnormal, serum TSH and free T4 should be drawn.
 b. Use age specific cut off.
 c. If you get a NBS with a TSH of > 100, it is almost always an indication to start therapy.
 d. If in doubt, treat.
 e. A lot of controversy regarding role in imaging.
8. Recognize that interpreting thyroid function tests should be considered in the context of special circumstances (i.e., premature infants).
 a. Premature babies are more likely to be diagnosed with hypothyroidism.
 b. There are various reasons why an infant that are critically ill and requires NICU admission have abnormal thyroid function test.
   i. Immaturity of the hypothalamic pituitary axis resulting to a low T4 and normal TSH levels.
   ii. These infants may be sick enough and require steroids, dopamine or dobutamine all of which can decrease TSH levels.
   iii. Critical illness can cause nonthyroidal illness or euthyroid sick syndrome where in total T4 will be low and TSH will be low during the illness then rises up during recovery.

9. Initiate appropriate treatment for suspected congenital hypothyroidism.
    a. LT4 (levothyroxine) is the treatment of choice with initial recommended dose of 10-15 mcg/kg/day.
    b. Tablet is the ideal form levothyroxine. There are no liquid formulations licensed by US FDA.
    c. In newborns, crush the tablet and mix with small amount of milk or formula.
    d. Around the same time every day
    e. For central hypothyroidism, it is very important to evaluate adrenal function. Starting levothyroxine on someone who has undiagnosed adrenal insufficiency can cause adrenal crisis since levothyroxine increases cortisol clearance.
10. Understand the prognosis, need for continued close follow-up and common methods of weaning thyroid replacement therapy.
    a. AAP recommend a follow up at 2-4 weeks after initiation of levothyroxine. Then every 1-2 months first 6 months of life, every 3-4 months at 6 months to 3 years of age, then every 6 to 12 months
    b. Follow up sooner if symptomatic or adjusting dose.
    c. During the course of therapy, the goal of therapy is to normalize T4 in 2 weeks and TSH in 1 month and FT4 on upper half of reference range and TSH to be low normal