MAYO CLINIC

THE INFLUENCE OF ALGORITHMS AND ANALYTES ON THE DETECTION OF CONGENITAL HYPOTHYROIDISM

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EN LA ERA DE LAS ÓMICAS

I have no conflicts of interest related to this material.

AREAS OF EMPHASIS

- Congenital hypothyroidism (CH) in newborn screening
- Harmonization in NBS (generally and CH specific)
- Common algorithms
- The role of case definitions

CONGENITAL HYPOTHYROIDISM IN NEWBORN SCREENING

- Newborn screening (NBS):
  - Public health program designed to identify infants with treatable conditions before symptoms are evident and before irreversible damage has occurred
  - Number of conditions included varies by region, as do algorithms for screening, follow-up protocols and access to specialists / treatment options
- Congenital hypothyroidism (CH):
  - Partial or complete loss of thyroid function from birth
    - 80 – 85 % caused by thyroid dysgenesis
    - Remainder caused by low or absent hormone production
  - Untreated can cause intellectual disability, slow growth
  - Treatment: replacement of thyroid hormone, usually lifelong
- Incidence: varies widely – seems to be increasing

HARMONIZATION EFFORTS IN NBS

- General agreement on “good” for NBS, but “perfect” might not exist
  - MCAD deficiency – low-cost intervention, high effectiveness, high impact, good test (expensive to start with MS/MS)
  - Sickle cell disease – high frequency, good test, treatment can reduce morbidity and mortality (can be access issues)
  - Congenital hypothyroidism – widely available intervention, high effectiveness (testing specificity an issue)
- Even when conditions are agreed upon – the “how” is often not standardized
  - Recommended Uniform Screening Panel (RUSP) in US harmonizes recommendations across the country, but final decisions and implementation are done at the state level

WHY IS HARMONIZATION DIFFICULT?

- Regionalization of testing
- Incidence of rare targeted conditions
- Methodology variations
- Contracting and budgets
- Local regulations and resources

LABORATORY TESTING FOR CH

- Screening:
  - Measurement of TSH and/or T4 from dried blood spot
- Confirmation:
  - Serum TSH
  - Additional studies may be required to uncover etiology – treatment can start based on initial abnormal test results
- Seems straightforward, how many variations could there be?
- Prime target for harmonization

KNOWN NBS ALGORITHMS

TSH only

Screen is abnormal if TSH is elevated, no T4 measurement

T4 reflex TSH

TSH is measured if T4 is low; screen is abnormal is TSH is elevated

T4 and TSH

Screen is abnormal if T4 is low or TSH is high (reported independently)

Small babies

In addition to lab algorithm – account for delayed TSH rise

Based on published literature

GEORGIA NBS ALGORITHM

- Georgia algorithm:
  - NBS is abnormal if TSH is elevated (8 age based cutoffs) **OR** T4 is decreased (3 age & weight based categories)
    - Reported independently of each other
    - For LBW (< 2500 g) babies – multiple screen protocol recommends 3 screens (one prior to transfusion, one @ ~ 48 hours, one @ 28 DOL or NICU discharge) – these can each be reported out independently
    - Follow-up protocols vary based on age, value of lab result, clinical status of baby
- Screen is closed as normal / abnormal / lost to follow up based on laboratory findings and provider report

THREE POTENTIAL CASES

IMPACT OF ALGORITHM ON INCIDENCE

GA NBS Laboratory	TSH only; LBW < 2000 g
• Isolated low T4	• Not detected by TSH only screen
• Elevated TSH on second screen (BW = 2250 g)	• No routine second screen
• Provider reports CH vs transient hypothyroidism of prematurity	• Provider reports transient hypothyroidism of prematurity; program does not count as CH

+3

WHAT IS THE REAL WORLD IMPACT?

OVERTREATMENT VS UNDERDIAGNOSIS

- Regions that screen using T4 and TSH independently of each other report higher incidence of CH
- Regions that use a reflex strategy or TSH are not reporting a high burden of untreated CH manifesting clinically
- How can these two situations be reconciled?
  - Overtreatment?
  - Underdiagnosis?
  - Both?
  - Neither?

AREAS FOR IMPROVEMENT

Challenges

- Variations in screening strategy make comparisons difficult
- Outcomes reported are short term only – the immediate outcome of screen + follow-up
- Is there a gold standard?

Opportunities

- Apple to apple comparisons only
- Investment in case definitions and long-term follow-up
- Active monitoring for missed cases or suboptimal outcomes

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QUESTIONS & ANSWERS