Title of Abstract:

Newborn screening (NBS) for Prader Willi Syndrome (PWS) - Earliest Diagnosis and Better Outcomes.

Name of Abstract Submitter:

Preeti Singh, MD - Neonatology Fellow

Organization:

UC Irvine

Co-Author / Co-Investigators:

R. Mahmoud2, A. Nalbandian1, 2, L. Weiss2, M. Oakes3, W. Hossain4, M. Butler4, V. Kimonis2

INSTITUTIONS (ALL):

1. Neonatology, UC Irvine, Orange, CA, United States.

2. Genetics, UC Irvine, Irvine, CA, United States.

3. Biological Chemistry & UCI Genomics High Throughput Facility, UC Irvine, Irvine, CA, United States.

4. Psychiatry and Behavioral Sciences and Pediatrics, Kansas University Medical Center, Kansas City, KS, United States.

Abstract Description:

Purpose of Study: Prader-Willi syndrome (PWS), affecting 1/15,000 individuals, is a genetic disease characterized by lack of expression of genes on the paternal chromosome 15q11-q13 region. Clinical presentation range from hypotonia and feeding problems in neonatal period; short stature in childhood to hyperphagia, obesity and behavioral problems in adolescents. Growth hormone replacement has revolutionized the stature/body composition and behavioral outcomes in PWS individuals who have started treatment early. Despite significant diagnostic advances, the mean age for diagnosis of PWS continues to lag behind. California Newborn Screening (NBS) program tests for many metabolic and genetic disorders allowing for early diagnosis and management. Disorders are being added to the NBS program, PWS meets all the criteria except for the economical method of testing. We propose Methylation specific Multiplex Ligation-dependent Probe Amplification (MS-MLPA) will be a time and cost effective test for PWS allowing for early diagnosis and treatment leading to lower morbidity and mortality and improved prognosis of PWS patients.

Objectives:1) Isolate DNA from newborn screening filter paper cards from 100 individuals (50 PWS; 50 controls) and test for PWS using MS-MLPA.

2) Evaluate time and cost effectiveness of MS-MLPA to test for PWS.

3) Share results with CA NBS program and advocate for addition of PWS to existing NBS panel.

Methods Used: DNA was isolated from newborn screening filter paper card using a modified combination of GenSolve and Qiagen DNA MicroKit. PWS testing was performed using MS-MLPA probe mix followed by fragment analysis using a 3730xl DNA analyzer.

Results: We were able to extract sufficient amount of DNA from dried blood spot on newborn screening filter paper. PWS testing done on 26 patients and 14 controls. 5 samples did not work. MS-MLPA was able to correctly identify 100% of PWS patients, able to differentiate between deletion and non-deletion in 100% and correctly identify the type of deletion in 80% of the patients.

Conclusions: Initial data is promising that MS-MLPA testing can be used to diagnose PWS patients and identify the type of deletion from the DNA extracted from newborn screen filter paper. Next step would be to use new digital newborn screening MLPA probe mix from MRC Holland with Next generation Sequencing, which may prove to be time and cost effective in testing PWS in newborns.

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Department of Neonatology, UC Irvine