The Role of Tandem Mass Spectrometry in Newborn Screening Programs

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Newborn screening (NBS) is the largest genetic testing effort in the United States and is primarily performed by state public health laboratories. The detection of treatable, inherited metabolic disorders is a major public health responsibility.[1] Screening tests are designed to identify asymptomatic newborns that likely have a disease from those who do not. Effective screening of newborns, with the use of dried blood spot (DBS) specimens collected at birth, helps prevent deleterious health outcomes. Newborn screening laboratories routinely screen DBS specimens for inborn errors of metabolism and other disorders that require immediate medical intervention.

The introduction of tandem mass spectrometry (MS/MS)-based methods for the detection of phenylalanine in DBS[2] revolutionized the practice of newborn screening for amino acid, fatty acid oxidation, and organic acid metabolic disorders. The initial acquisitions of MS/MS technologies by NBS laboratories presented a unique opportunity to expand the role of MS/MS in screening.[1] Its multianalyte detection capabilities allow the identification of several disease biomarkers in one specimen aliquot, making it an ideal platform for the modern NBS laboratory. The original sample preparation techniques use butyl esterification of amino acids and acylcarnitines from DBS extracts.[3] However, the use of electrospray ionization makes it possible to detect both acylcarnitines and amino acids as their native free acids (ie, nonderivatized). While the majority of NBS laboratories prepare and analyze butyl esters of amino acids and acylcarnitines, an increasing number of laboratories now use nonderivatized sample preparation methods in an attempt to simplify analytical operations, and to minimize the use of corrosive chemicals.

MS/MS offers many additional advantages, such as enabling the successful development of second-tier tests for disorders that could benefit from enhanced specificity of detection. Today, MS/MS-based NBS methods can detect more than 50 diagnostic metabolites used to identify more than 30 metabolic disorders. Many of these disorders are included in the US Department of Health and Human Services Recommended Uniform Screening Panel.

References

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