Editorial

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Joon Hee Lee, M.D.[1,2] and Junghan Song, M.D., Ph.D.[1,2]

[1]Department of Laboratory Medicine, Seoul National University Bundang Hospital, Seongnam, Korea; [2]Department of Laboratory Medicine, Seoul National University College of Medicine, Seoul, Korea

Non-derivatizing Tandem Mass Spectrometry Assay for Expanded Newborn Screening and Cutoffs for Preterm Neonates

Liquid chromatography-tandem mass spectrometry (LC-MS/MS) has been increasingly utilized in clinical laboratory testing through adequate method development and operation [1, 2]. Based on tandem mass spectrometry (MS/MS) analysis of amino acids and acylcarnitines in newborn dried blood spots, extended newborn screening for amino acid disorders, fatty acid oxidation defects, and some organic acidemias has been successfully implemented worldwide [3, 4]. In early newborn screening, dried blood spots were derivatized by butyl esterification and subsequently tested by MS/MS using the 102 neutral loss scan and 85 precursor ion scan methods. Due to drawbacks of the derivatization method, including the handling of hazardous reagents and a relatively complex and long sample preparation process, non-derivatization techniques for selected amino acid and acylcarnitine tests have been introduced. Initially, all laboratories that conducted MS/MS newborn screening tests used in-house developed tests, including derivatization as well as non-derivatization tests. However, since the introduction of specialized commercial kits, such as the NeoBase kit (PerkinElmer Finland, Turku, Finland), MassChrom (Chromsystems, Munich, Germany), and NeoMass AAAC (Labsystems Diagnostics, Vantaa, Finland), all of which are for non-derivatization tests, many laboratories use commercial kits for MS/MS newborn screening. Recently, PerkinElmer Finland launched the NeoBase 2 Non-derivatized MSMS kit, which can additionally analyze adenosine for adenosine deaminase deficiency, very-long-chain acylcarnitines and lysophosphatidylcholines (LPC) for X-linked adrenoleukodystrophy, and succinylacetone for second-tier differential diagnosis of tyrosinemia type 1 and transient tyrosinemia of the newborn.

It is crucial to use appropriate cutoffs for preterm babies for accurate result interpretation and to minimize false negatives without generating an excessive number of false positives. Zytkovicz, *et al.* [5] pointed out that different cutoffs need to be established for different subpopulations of newborns, including full-term, premature or low birth weight, very low birth weight, very low birth weight on total parenteral nutrition, and different specimen collection ages.

In this issue, Lee, *et al.* [6] comprehensively evaluated the analytical performance of the NeoBase 2 kit. The authors found that it showed adequate analytical performance in terms of precision, concordance with their in-house derivatization-based assay, limit of detection, lower limit of quantification, linearity, recoveries, and carryover. Tyrosinemia type 1 and transient tyrosinemia of the newborn were successfully differentiated by measuring succinylacetone. The authors also evaluated different cutoffs in preterm neonates in the Korean population. They identified 15 analytes (arginine, citrulline, tyrosine, adenosine, C0, C2, C4, C5, C6DC, C8:1, C12:1, C14:1, C16, C18:2, and C20:0-

LPCs) showing different cutoffs between preterm and term babies and proposed higher preterm cutoffs for three analytes (tyrosine, adenosine, and C20:0-LPC) for the first time in Korea.

This study will be of help to readers interested in MS/MS-based special chemistry tests, especially, those affiliated to laboratories that conduct extended newborn screening using MS/MS. The authors proposed different cutoffs for preterm neonates, which is helpful for the accurate interpretation of newborn screening tests to minimize false negatives without generating an excessive number of false positives.

AUTHOR CONTRIBUTIONS

Lee JH and Song J contributed to manuscript writing and approved the submission of the final manuscript.

CONFLICTS OF INTEREST

None declared.

ORCID

Joon Hee Lee https://orcid.org/0000-0002-9649-1371
Junghan Song https://orcid.org/0000-0003-0576-9938

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Corresponding author: Junghan Song, M.D., Ph.D.
Department of Laboratory Medicine, Seoul National University Bundang Hospital, 82 Gumi-ro 173 beon-gil, Bundang-du, Seongnam 13620, Korea
Tel: +82-31-787-7691, Fax: +82-31-787-4015, E-mail: songjhcp@snu.ac.kr

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