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Development of tandem mass spectrometry-based creatinine measurement using dried blood spot for newborn mass screening.

【Background】

Congenital anomalies of the kidney and urinary tract (CAKUT) are the most prevalent etiologies of pediatric chronic kidney disease (CKD). It has been reported that early intervention for CAKUT can prevent disease progression. Therefore, early identification of patients with CAKUT is crucial to protect the remaining renal function and to prevent complications in other organs due to CKD. However, no robust mass screening methods have been developed to detect patients with CAKUT, making early intervention to prevent progressive renal failure challenging. In Japan, newborn mass screening using tandem mass spectrometry (MS/MS) and dried blood spot (DBS) analysis for 19 inherited metabolic disorders has been in effect since 2013. Therefore, renal function-based mass screening for CAKUT using the same DBS analysis is reasonable and applicable for all Japanese children. In the present study, we sought to establish a new method for mass screening of renal function using DBS analysis and MS/MS.

【Methods】

We applied tandem mass spectrometry to measure the creatinine (Cr) value from dried blood spot analysis, which has been used for newborn mass screening. Subsequently, we evaluated the correlation between DBS Cr measured by MS/MS and serum Cr measured by the conventional method in pediatric patients with CKD. Finally, DBS Cr was measured in 190 full-term, healthy newborns on days 4-6 after birth.

【Results】

We established a system of MS/MS-based measurement of Cr from DBS. A high correlation ($R = 0.863$) of the serum Cr level with the DBS Cr level (0.5693 times lower than the serum Cr level) was observed in the full range. The median DBS Cr value in newborns was 0.222 (interquartile range: 0.189, 0.269) mg/dl. No significant correlations were found between DBS Cr values and body weight, Apgar score, gestational age, and sex in newborns.

【Conclusion】

We have developed a new method of MS/MS-based measurement of DBS Cr, and we demonstrated that it is practical, cost-effective, and could be used as a screening method to detect CAKUT in the neonatal period. This method can be a realistic screening method with respect to the fact that nationwide screening is possible owing to the tandem mass screening method that is already in use. Further studies involving more neonates including CAKUT patients should be carried out.