Automated nuclear magnetic resonance spectroscopy (NMR) urinary and plasma/serum analysis: A new approach for pediatric health management and selective screening of inborn errors of metabolism (IEM)

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Background & Aim: Analysis of body fluids and especially selective screening of IEM is mainly performed by GC/MS, HPLC/MS, IEC and other methods. Work up of samples and analyses are time consuming and not all methods are applied in a sample with unspecific symptoms like autism or mental disability. As technology and automation in NMR analysis have greatly improved, we applied NMR as first line method pediatric health management in general and for selective screening of IEM using ERNDIM proficiency testing for proof of principle.

Methods: Urine: To 900 ul urine 10 0ul buffer was added and analyzed with a Bruker IVDr System at 600 MHz. Spot urine samples of 2200 newborns, healthy children and adolescents were used as a reference. 16 urine samples of the ERNDIM proficiency testing program were analyzed using a panel of 150 metabolites tested in the reference group. Plasma/Serum: To 300 ul plasma or serum, 300 ul of buffer was added and analyzed with the same instrumentation as for urine. Lipoprotein subclass analysis (115 parameters) and small molecule quantification (20 parameters) was performed. Validation was done against conventional analysis of the main fraction results for lipoproteins.

Results: In 15 out of 16 samples the correct diagnosis could be made: 2 normal findings, 6 organic acidurias, 3 aminoacidopathies, one MCAD- and one dihydropyrimidinase-deficiency, one sialidosis I and one odontohypophosphatasia. A patient with glutaric aciduria type I (low excretor) could also correctly be diagnosed. A patient with aromatic acid decarboxylase deficiency could not be diagnosed (as it was the case in 17 out of 20 laboratories using other methods). As decided by ERNDIM this became an educational sample.

Discussion: The advantage of NMR is the broad spectrum of analytes which can be measured in a single run without time consuming work up of samples and without running additional methods, be it in urine or plasma/serum. The reproducibility of results enables not only targeted but also untargeted analysis showing statistical deviations from reference profiles. Lipoprotein subclass analysis supports risk management and treatment optimization e.g., in obese children.

Biography
Manfred Spraul is from Bruker BioSpin GmbH, Germany.

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