

The Evaluation of Potential Interventions for Early Preterm Infants with Pulmonary Dysfunction Disorder

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Abstract

Urinary metabolomics is of increasing importance as a means of identifying metabolic signatures associated with health and disease states. Thirty-one late preterm infants (LPs) admitted to the neonatal intensive care unit (NICU) and 23 age-matched healthy LPs admitted to the maternity ward of a tertiary hospital were enrolled in the study. Urinary metabolism was analyzed using proton nuclear magnetic resonance spectroscopy (¹H-NMR) on the first postnatal day of the neonate and on her third day. Data were analyzed using univariate and multivariate statistical analyses. A unique metabolic pattern of increased metabolites was found in her LP admitted to her NICU from the first day of life. LPs with pulmonary insufficiency had different metabolic profiles. This discrepancy may reflect variations in nutrient intake or differences in gut microbiota due to medical interventions such as administration of antibiotics and other drugs. Altered metabolites may serve as biomarkers to identify LP neonates with severe disease or at increased risk of adverse outcomes later in life, including metabolic risk. Novel biomarker discovery reveals potential drug development targets and optimal time periods for effective intervention, providing a personalized approach.

Keywords: Late preterm neonates; Neonatal intensive care unit/ NICU; Urine metabolomics

Introduction

Late prematurity (LP) is a newborn born between 34 and 36 weeks of gestation. In the United States, it accounts for 9.1% of all newborns and nearly three-quarters of preterm infants. Preterm infants are characterized by increased risk of morbidity and mortality compared with term newborns. Associated diseases include neurodevelopmental disorders, eating disorders, hypoglycemia, impaired immune response, sepsis, intraventricular hemorrhage, periventricular leukomalacia, pulmonary insufficiency, transient tachypnea of the newborn, pneumonia, apnea, Includes respiratory disorders such as pulmonary hypertension [1].

The term “metabolomics” refers to the systematic study of a wide range of endogenous small-molecule metabolites (<1500 Da) in biological samples and is a rapidly growing field of systems biology. Quantification of small molecules such as peptides, lipids, organic acids, vitamins, amino acids, drugs and other chemicals can identify metabolic signatures and changes associated with health and disease states [2]. Metabolomics is important for precision medicine approaches because changes in an individual’s metabolic profile occur much earlier than clinically identifiable signs and symptoms. The metabolome is most closely related to clinical phenotypes, as it is the result of biochemical processes regulated by proteins derived from gene expression [3]. As a result, there is a steady increase in the use of metabolomics as a tool to validate new biomarkers for early diagnosis or prognosis of pathophysiological diseases [4].

Extensive metabolic blood analysis was performed. However, other approaches using non-invasive matrices for metabolite profiling are also gaining popularity. Such approaches include the use of fecal metabolome profiles to predict disease outcome, as fecal metabolites reflect the microbial composition of the gut. Early intestinal colonization in infants is known to have long-term health consequences, including immune system development, growth, cognitive development, and the development of childhood diseases such as asthma, allergies, and obesity. Several studies have also reported the effects of delivery methods, antibiotic use, and early feeding habits on the fecal metabolome of infants. Different fecal metabolomes have also been identified between

formula-fed and breast-fed infants [5].

Furthermore, urinary metabolomics is of particular interest due to its ease of urine collection and its non-invasive nature. Additionally, a simple removal allows for serial sampling. This is especially important for neonates, especially premature infants, who also have low circulating levels. Another important advantage of urinary metabolites is that they are a rich source of cellular metabolites produced during hemofiltration in the kidney and represent the final step of metabolism, whereas metabolites in the blood is still able to participate in metabolism.

To date, over 600 diseases have been associated with identified urinary metabolites, including obesity, cancer, infectious diseases, and neurological disorders [6].

In addition, physiological conditions such as ovulation, pregnancy, diet, and exercise cause metabolic changes in urine. Nuclear magnetic resonance spectroscopy (NMR) and mass spectrometry (MS) are two major analytical techniques in the metabolomics analysis of biological fluids. NMR-based analysis followed by multivariate analysis of the obtained NMR spectra has many advantages, such as easy quantification and high reproducibility of the data.

Little is known about the association between neonatal metabolic maturation and neonatal morbidity and short- and long-term health outcomes. Much less is known about the metabolic characteristics of preterm infants and the impact of conditions such as diet, pharmacological interventions, ICU admission and IBS on the neonatal metabolic profile. Data on normal urinary levels of many metabolites in neonates are also lacking [7].

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The aim of this study was to use NMR metabolomics to identify urinary metabolites that may have different concentrations between LP neonates admitted to the NICU and healthy LP neonates. In addition, this study compares the urinary metabolic profiles of LP neonates admitted to the NICU with IBS and those admitted to the NICU without IBS to identify neonates with this condition and to identify relevant metabolic Aiming at defining patterns [8].

Materials and Methods

Study population

The aim of this study was to use NMR metabolomics to identify urinary metabolites that may have different concentrations between LP neonates admitted to the NICU and healthy LP neonates. In addition, this study compares the urinary metabolic profiles of LP neonates admitted to the NICU with IBS and those admitted to the NICU without IBS to identify neonates with this condition and to identify relevant metabolic Aiming at defining patterns [9].

Statistical analysis

Statistical analysis of all NMR metabolome data performed in this study follows the previously described methodology. Multivariate and univariate analyzes of urine NMR data were performed using SIMCA was applied to the urine NMR data and automatically scaled before analysis. Cumulative values of R² and Q² were calculated by 7-fold cross-validation, and the statistical significance of the PLS-DA model was assessed by γ -variable permutation tests of 200 random sequences. Autoscaling was chosen as the most appropriate scaling method for the current dataset. A univariate analysis of successfully assigned metabolites was performed. Analyzes were completed via the nonparametric Kruskal test and paired t-tests were used for IBS day group comparisons (significance level $\alpha = 0.01$). Statistical significance, expressed as p-value, was estimated after applying FDR (false discovery rate) correction [10].

Results

The gestational age of neonates admitted to the NICU was 34.93 \pm 0.929 weeks (mean \pm standard deviation) (min). Neonates, 5 neonates developed hypercalcemia, and 96.20% of neonates had no metabolic disease. No neonatal deaths occurred. At 5 days of age, 94.45% of newborns were treated with antibiotics. In addition, the majority of newborns on the fifth day of life were exclusively formula-fed (55.60%), 31.50% were fed both formula and breast milk, and 11% were fortified and exclusively breast-fed. was only 1.90%. On the day of discharge from the NICU, 51% of newborns were fed exclusively formula, 43% received formula and breast milk, 2% received antidepressants, and 2% were exclusively breastfed.

Discussion

The aim of the current study is to determine whether LP neonates admitted to the NICU, especially LP neonates with IBS, have different urinary metabolism fingers from healthy LP neonates or LP neonates admitted to the NICU without IBS. It was to decide whether to have a print or not. Metabolic analysis, based on information extracted from

urine NMR spectra at two time points, supports the presence of distinct metabolic profiles among the categories investigated from the first day of life. According to our findings, multiple metabolite levels were disrupted in multiple metabolic pathways and identified as potential biomarkers for neonatal hospitalization in the NICU or IBS. Given that metabolic immaturity early in life is associated with poor growth and metabolic disease later in life, the metabolic differences demonstrated in this study may be of clinical importance.

Healthy neonates have smaller and simpler measurable metabolome size and chemical diversity compared to children and adults, reporting differences in diet, metabolism and gut microbiota composition. It has been. The high concentrations of essential amino acids, collagen-related amino acids, and acylcarnitines in the urine of neonates are likely due to their increased requirements due to rapid cell growth and cell division. It is also known that neonatal metabolic fingerprints and biochemical pathways change over time.

Diet is thought to be an important environmental factor regulating the metabolic function of the gut microbiota. The composition of milk, the first food to enter the gastrointestinal tract, directly influences the infant's gut microbiota and neurodevelopment.

This is due to the provision of essential nutrients for bacterial growth (carbohydrates, proteins, iron, human milk oligosaccharides (HMOs), etc.). Human bacterial colonization begins during the fetal period, and maternally derived microbial metabolites passed to the infant via breast milk can affect the neonatal microbiome and affect infant health. There appears to be a period in early infancy that is highly diet-dependent and associated with a healthy microbiota profile.

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