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Research article

Altered heme metabolism and hemoglobin concentration due to empirical antibiotics-induced gut dysbiosis in preterm infants

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ABSTRACT

Background: High-risk infants are usually treated with empirical antibiotics after birth, regardless of the evidence of infection; however, their gut microbiome and metabolome have seldom been studied. This study investigated the influence of antibiotic exposure on the gut microbiome and associated metabolic pathways in term and preterm infants.

Methods: Thirty-six infants within 10 days of birth who were admitted to a neonatal intensive care unit/newborn nursery unit were divided into four groups based on maturity (gestational age) and use of empirical antibiotics. Genomic DNA was extracted from the fecal samples and underwent high-throughput 16S rRNA amplicon sequencing using the Illumina platforms. Taxonomic classification, diversity analysis, and metagenomic function prediction were performed.

Results: Preterm infants with empirical antibiotics showed a significantly decreased population of *Firmicutes* ($p = 0.003$) and an increased population of *Proteobacteria* ($p < 0.001$) compared to other groups. At the genus level, the populations of *Raoultella* ($p = 0.065$) and *Escherichia* ($p = 0.052$) showed an increased trend. The change in microbial composition was correlated with increased heme biosynthesis and decreased hemoglobin levels.

Conclusion: Collectively, our finding suggested that empirical antibiotic exposure in preterm infants alters the gut microbiome, potentially leading to adverse health outcomes. This dysbiosis may affect heme metabolism, increasing the risk of anemia in these vulnerable infants. Therefore, antibiotic use should be carefully tailored to minimize potential harm.

1. Introduction

Recently, the neonatal gut microbiome has attracted considerable attention. At birth, neonates have a low diversity and abundance of gut microbiome that can be easily disturbed depending on their maturity and type of care received, including antibiotic use [1–3]. The difficulty in distinguishing symptoms in preterm infants from actual infection risk has resulted in exposure to empirical antibiotics early in life. Consequently, perturbation of the gut microbiome in early life may affect both short- and long-term health outcome [4–6]. The effects of antibiotic therapy on the gut microbiome of term and preterm infants and on gut microbial metabolism are of emerging interest.

Microbial colonization is influenced at birth by the uterine environment, mode of delivery, type of feeding, and antibiotic administration [7–9]. The overuse of antibiotics early in life can disrupt the gut–brain axis, which could have lifelong consequences on health.

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