AMOXICILLIN / CEFTAZIDIME PROPHYLAXIS DURING THE FIRST POSTNATAL WEEK AFFECTS DEVELOPMENT OF THE INTESTINAL MICROBIOTA IN PRETERM INFANTS

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Introduction and Objectives: Broad spectrum antibiotics are commonly prescribed in the neonatal ward for the prevention and treatment of bacterial infections. Applied antibiotic strategies decrease mortality and morbidity rates among preterm infants, however, it might interfere with development of their intestinal microbiota. It is important to understand the consequences of antibiotic treatment, as disturbances in microbiota development during this key developmental time frame might affect early and later life health outcomes. Our aim was to study the effect of intravenous amoxicillin/ceftazidime administration during the first postnatal week on microbiota development in preterm infants.

Material and Methods: Faecal samples from 63 infants born at 35.1 ± 2.4 weeks gestation (mean±SD) were collected at postnatal weeks one, two, three, four and six and stored at -80°C. Infants received either no (control, n=28), short term (<3 days, ST, n=22) or long term (>5 days, LT, n=13) treatment with a combination of amoxicillin and ceftazidime during the first postnatal week. Microbiota composition was determined by sequencing of the V3-V4 region of the 16S rRNA gene.

Results and Discussion: The intestinal microbiota of control infants was characterised by high abundance of *Bifidobacterium, Streptococcus, Enterococcus, Staphylococcus, Escherichia-Shigella* and members of the *Enterobacteriaceae* family. Relative abundance of *Bifidobacterium* and *Staphylococcus* respectively increased (18.9% to 41.1%; p=0.007) and decreased (15.5% to 7.0%; p=0.0002) during the first six postnatal weeks. In addition, community richness and diversity gradually increased over time, being significantly higher at later time points compared to early time points ($p<0.05$). Compared to control infants, ST and LT infants' microbiota contained a significantly higher abundance of *Enterococcus* during the first two postnatal weeks ($p<0.05$). In addition, microbiota composition was more stable over time within control infants compared to ST and LT infants as indicated by lower unifrac distances ($p<0.05$). Community richness and diversity were not consistently affected by antibiotic treatment. Instead, richness and diversity increased over time, and were related to which bacterial taxa was dominant. Overall, our findings show that intravenous administration of amoxicillin and ceftazidime affects intestinal microbiota composition, particularly by increasing the relative abundance of *Enterococcus* species.

Theme: The gut and beyond