DYNAMICS OF THE INTESTINAL MICROBIOTA DURING SELECTIVE AND TOTAL GUT DECONTAMINATION AS GRAFT-VERSUS-HOST PROPHYLAXIS IN THE COURSE OF STEM CELL TRANSPLANTATION

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Introduction and objectives: Graft-versus-host disease (GvHD) is a frequent complication in patients undergoing haematopoietic stem cell transplantation (HSCT). Total gut decontamination (TGD, piperacillin/tazobactam) is routinely applied at our centre as part of GvHD prophylaxis. In patients with lower risk for GvHD, selective gut decontamination (SGD, polymyxin/neomycin) is applied instead. We aim to elucidate the effect of TGD and SGD on the intestinal microbiota and to understand the relation between the patients and stem cell donor microbiota and between the microbiota and GvHD.

Materials and methods: Nineteen children (<18y) eligible for HSCT were recruited (TGD n=12, SGD n=7). Faecal samples were collected weekly during admission and monthly thereafter, up till six months after transplantation. In addition, faecal samples from three stem cell donors were collected. Microbiota composition was determined by sequencing of the 16S rRNA gene (V4 region, HiSeq2500, PE250), and data was analysed using Qiime 1.9.1.

Results and discussion: The intestinal microbiota of patients receiving SGD was characterised by a high relative abundance of *Bacteroides* (60±22% [mean±SD]), which remained after SGD cessation. Apart from *Bacteroides*, an individual specific microbiota composition remained during and after SGD. Microbiota composition during and after TGD was not characterised by a particular profile, but showed high variability between and within patients. Microbiota diversity markedly decreased during SGD and TGD, reaching the nadir around 30 days of treatment. After cessation of the decontamination treatment, microbiota diversity recovered within two months. Spearman correlations between microbiota composition of donor-donor, patient-patient and patient-donor were 0.78, 0.66 and 0.59 respectively. Thus, receiving a stem cell transplant does not alter the patient's microbiota to become more similar to that of its donor. Four patients (21%) developed GvHD, without consistent differences in microbiota composition and diversity compared to other patients. Our findings indicate that both, SGD and TGD, affect the intestinal microbiota. SGD, however, allows for enduring individual profiles and has less impact on microbiota diversity than TGD. This dataset did not allow linking the microbiota to GvHD.

Theme: The gut and beyond