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Impact on the gut microbiota of the prolonged antimicrobial therapy in patients with bone and joint infection (BJI): results from the OSIRIS prospective study in France

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Background

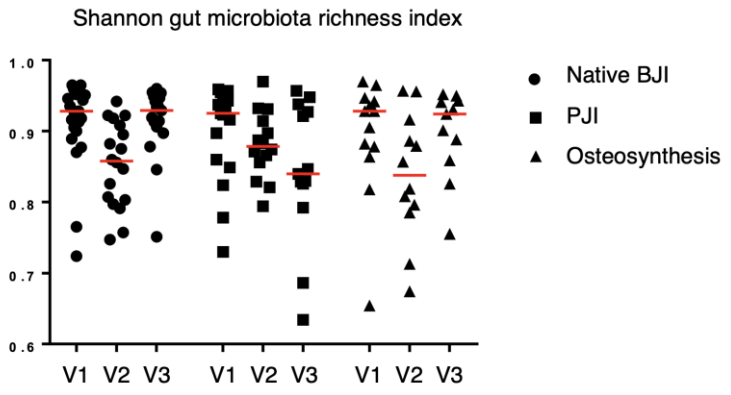
There is growing interest about the potential deleterious iatrogenic impact of antibiotics on loss of gut symbiosis (called dysbiosis). As patients with bone and Joint infection (BJI) require antibiotics usually during 6 to 12 weeks, it is of interest to determine if gut dysbiosis is frequent in this population, and if it could potentially immediately reversible or not.

Material and method

We performed a multicentric prospective cohort study in France (EudraCT 2016-003247-10) including patients with BJI. Among these patients, 3 sub-categories were investigated based on the BJI type: native BJI, osteosynthesis-related BJI and prosthetic joint infection. At time of suspicion (V1), at the end of antibiotherapy (V2) and then 2 weeks after stopping antibiotherapy (V3), blood and fecal samples of the patients were harvested and frozen for batch analysis, including fecal neopterin, a maker of gut inflammation. During 9 months, 62 patients were included and finally the stools from 42 of them were analyzed as per protocol. Extracted DNA from stool samples was sequenced using Shotgun metagenomic sequencing based on illumina library and Iseq instrumentation. Raw data generated were then transmitted to the MaaT Pharma GutPrint™ Platform and run through the Shotgun pipeline in order to produce microbiome indexes such as Sympson or Shannon diversities indexes. Gut microbiome and inflammation markers were respectively analyzed in feces and/or blood samples. .

Results

Concerning the 62 patients included, 40 were male (65%), 27 had native BJI, 14 had osteosynthesis-related BJI and 21 had PJI with a mean age of 60 years and a mean duration of antibiotics of 66 days. The most frequently prescribed drug was an oral fluoroquinolone, followed by an IV 3rd generation cephalosporin and IV vancomycin. Overall, the mean Shannon gut microbiota richness index was 0.904 at V1, and 0.845 at V2. The Bray-Curtis index underlines the difference in microbiome reconstitution at V3 compared to the original microbiomes at V1. In the 3 different subpopulations, we report significant microbiome loss of diversity at V2, that was reversible at V3 in patients with native BJI and osteosynthesis-related BJI, but not in patients with PJI (figure).



We also found that fecal neopterin presents a common feature between all patients (mean at V1, 221.6; V2, 698.1; and V3, 422.5 pmol/g of feces), and could be a potential surrogate marker of gut dysbiosis. Of note, patients with abnormal CRP at the end of antibiotics had high neopterin values, that raises the hypothesis that abnormal CRP at the end of antibiotics could be in relation with gut dysbiosis rather than uncured BJI.

Conclusions

The impact of antibiotics on the gut microbiota of patients with BJI seems to be significant, especially in patients with prosthetic-joint infections who could be candidate for fecal microbiota transplantation. Abnormal CRP at the end of antibiotics could be in relation with gut dysbiosis rather than uncured BJI.

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