Effect of antimicrobial drug on lung microbiota in healthy dogs.

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In human and dogs, baseline differences in lung microbiota (LM) have been associated with important clinical features in chronic lung diseases (CLD) and there is growing evidence that an altered LM contributes to disease pathogenesis. The common use of antibiotic drugs throughout the management of CLD likely represents a major confounding factor in the study of the LM. However, the effect of antibiotic treatment on the LM in healthy individuals has not been specifically investigated yet.
The aim of the present study was to assess the short and medium-term effect of an oral treatment with a large spectrum antimicrobial drug on the LM in healthy dogs.
Six healthy experimental beagle dogs were included. Amoxicillin/clavulanic acid (AC) was administered at a dose of 20 mg/kg twice daily for 10 days. In each dog, bronchoalveolar lavage fluid (BALF) was collected at 3 different timepoints: before administration of AC (J0) and immediately (J10) as well as 16 days (J26) after interruption of AC.
In each BALF, total and differentiated cell counts were obtained and metagenetic analyses were performed on the V1-V3 hypervariable region of 16S rDNA after total bacterial DNA extraction and sequencing on a MiSeq Illumina sequencer. Taxonomical assignation and microbiota community analysis were done with MOTHUR V1.35 with an OTU clustering distance of 0.03. Statistical comparisons between events for microbiota community and BALF cell counts were made using Friedman test and post-hoc t-tests with Bonferroni correction. Statistical differences in bacterial population relative abundance between timepoints were assessed using a mixed linear model with FDR correction for multiple comparisons.
Administration of AC did not induce significant changes in BALF cellular counts and had no effect on the richness, evenness and alpha diversity. Bacteroidetes and Proteobacteria abundance increased from J0 to J10 (mean 12.0 to 24.1, and 12.3 to 26.2%, respectively; $p<0.001$) and decreased at J26 (13.1 and 9.3%; $p<0.001$).

Firmicutes abundance decreased from J0 to J10 (45.6 to 18.3%; $p<0.001$) and increased at J26 (28.8%; $p<0.001$). Actinobacteria abundance increased at J26, compared with J0 and J10 (43.7 compared with 23.2 and 23.5% respectively; $p<0.001$). We failed to show significant differences between timepoints at the level of genera and species.

In conclusion, in healthy dog, oral administration of a commonly used large spectrum antimicrobial drug induces significant changes in microbial population abundance at the phyla level. Most but not all of these changes normalize within 2 weeks after discontinuation of the drug.