Modification of gut microbiota in response to the toxin of equine atypical myopathy: a preliminary study using a dynamic human intestinal simulator

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Background: Hypoglycin A (HGA) is a toxin found in the botanical family of the *Sapindaceae* which contains *Acer* species, *Blighia sapida* or *Litchi chinensis*. In equids, this naturally occurring toxin can cause atypical myopathy (AM) following ingestion of seeds and/or seedlings of some *Acer* species such as *Acer pseudoplatanus* in Europe and *Acer negundo* in North America. In human, HGA intoxication following ingestion of ackee or litchi fruits can cause Jamaican vomiting sickness or acute toxic encephalopathy respectively, both affecting more often young kids.

Equine AM has a high fatality rate but some co-grazers of cases remain healthy despite exposure to HGA. In a preliminary study about fecal microbiota in horses grazing on pastures containing HGA, a significantly lower relative abundance of the *Lachnospiraceae* family was detected in AM affected horses when compared to healthy co-grazers.

Hypothesis/Objective: We hypothesized that HGA may alter the gut microbiota.

Methods: The Simulator of Human Intestinal Microbial Ecosystem (SHIME®) was used to mimic the gastrointestinal system of a child whose diet is predominantly solid. The SHIME was separated into different compartments: stomach/duodenum (SD), jejunum/ileum (JI), ascending colon (AC), transverse colon (TC) and descending colon (DC). Following inoculation with fecal microbiota from a child aged around 3 years and after reaching stabilization, purified HGA (6000 µg) was added to the daily diet of the SHIME for one week. Samples from AC, TC and DC for microbiota analysis were obtained before and after one week of HGA intoxication. Bacterial taxonomy profiling was obtained by V1V3 16S amplicon sequencing from feces. Being an observational pilot study made on a single SHIME run, no statistical analysis was performed.

Results: Major changes in dominant bacterial populations were observed following HGA administration. After HGA's administration, the relative abundance (1) of *Enterobacteriaceae* family is more important in TC and DC, (2) of *Clostridiaceae* family is lower in AC, (3) of *Veillonellaceae* family is more important in AC and TC, and (4) of *Lachnospiraceae* family is lower in TC and DC. This last family seems to be influenced by HGA in humans as in horses.

Conclusions: Major alterations in fecal microbiota were observed in response to HGA administration when using a human gastrointestinal system simulator. This model is validated for humans but not for horses, thus these results may not be extrapolated to horses. However, this preliminary study strengthens the hypothesis that HGA may affect the microbial population.