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The Effect Of Fecal Material Transplantation On Hepatic And Brain Diseases In A Non-human Primate Model: Several Considerations For Future Application To Liver Disease Patients

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Background : Recently, fecal microbiome transplantation (FMT) has been used to show effective treatment for human diseases. A preclinical animal model, a primate animal model most similar to humans, to study the overall physical effects of intestinal microflora and probiotics, and the direct effects on the liver and brain, is a very challenging and innovative task that is attempted for the first time in the world.

Methods : Acquisition of primates (9 animals) (Cynomolgus monkeys). Feces obtained from chronic diarrheal disease monkeys were transplanted into primates' transverse colons using FMT. Oral administration of human-derived probiotic strains to primates for six weeks (3 times). A sampling of liver tissue and portal vein blood through surgical treatment of primates. Microbiome analysis by performing 16S rRNA sequencing on fecal samples 2 and 6 weeks after fecal microbial transplantation and probiotics administration. Performing blood sampling from primates' femoral vein and hepatic portal vein. Hematological/blood biochemical analysis on obtained blood samples. Confirmation of inflammation induction through radiological analysis (18FDG PET-CT) analysis of primates. Metabolome analysis, such as fatty acids in the blood and hormones in the CSF.

Results : In blood samples from the portal vein, severe neutropenia was consistently observed in the subjects of fecal microbial transplant. The probiotics administration group observed no significant change in neutrophils. However, in the case of lymphocytes, a decrease or increase was observed for each individual. As a result of analysis before/after primate fecal microbial transplantation, a statistically significant increase in insulin, C-peptide, MCP-1, ACTH, and GH levels was observed. No changes in hormone levels were observed according to the fecal condition (diarrhea, normal stool) of fecal microbial transplantation. As a result of analysis before/after the administration of primate probiotics per oral, no significant changes in hormone levels were observed.

Conclusions : A significant change in the neutrophil/lymphocyte ratio in the portal vein is one of the considerations for the effect of FMT on the treatment of hepatocellular carcinoma. Hormonal changes in CSF may help control metabolic diseases (diabetes, hyperlipidemia) following immunosuppressive drugs in liver transplant patients. Considering that oral probiotics intake and the effect of FMT on primates are different, it will be necessary to view the route of administration when developing microbiome therapeutics in the future.

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