Short Chain Fatty Acids as a Predictor of Acute Graft Versus Host Disease Outcomes

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Acute Graft Versus Host Disease is a Severe Complication of Hematopoietic Cell Transplant

- Patients suffering from cancers affecting the hematopoietic and lymphoid systems (commonly AML or ALL) commonly undergo hematopoietic cell transplants (HCT)
- Acute Graft Versus Host Disease (aGVHD) is a common complication of HCT, affecting 30-50%
- aGVHD is characterized by cases in which the transplanted stem cells attack the host organs in the skin and lower gastrointestinal tract (LGI)
- Around 50% of patients diagnosed with severe aGVHD and do not respond to treatment do not survive

Damage to the Gut Microbiome Can Affect aGVHD Prognosis

- Before HCT, AML and ALL patients undergo chemotherapy and antibiotic treatment
- These treatments have the potential to disrupt the gut microbiome, which plays numerous roles in maintaining bodily function
- One role is the production of Short Chain Fatty Acids (SCFAs)
- LGI lining cells (enterocytes) use SCFAs as fuel sources in protecting inner components of the LGI
- Damage to the LGI could result in the gut microbiome not being able to produce sufficient levels of SCFAs to protect itself
- We hypothesis that in aGVHD patients, relative amounts of SCFAs indicate the ability of the LGI to withstand attack, making them an indicator of treatment response and survival

Hypothesized Progression

1. An AML/ALL patient has a full functional, healthy LGI
2. The patient undergoes chemotherapy and antibiotic treatment, disrupting the gut microbiome
3. Damage to the gut microbiome hinders its ability to produce SCFAs
4. Insufficient SCFA levels weaken the LGI lining, making it susceptible to aGVHD attack
5. The LGI cannot protect itself from further attack, preventing the patient from recovering from aGVHD

Results

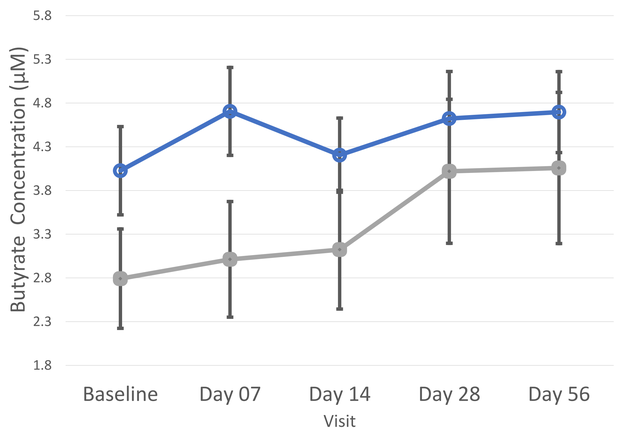

Figure 1: Butyrate levels over time

Butyrate levels on Day 7 after treatment were significantly ($p = 0.018$) lower for patients that did not respond to treatment

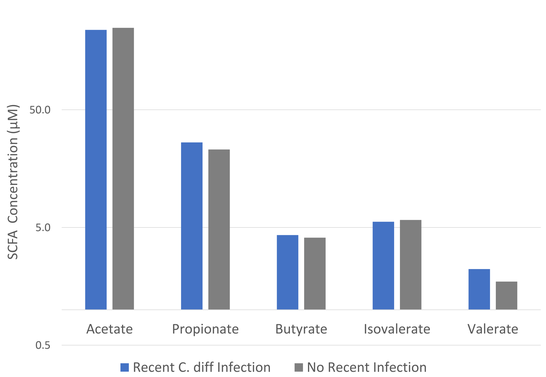

Figure 2: Comparison of SCFA levels to Recent *C. diff* Infection

Patients with recent C. *diff* infection did not have significantly different SCFA levels than patients who did not.

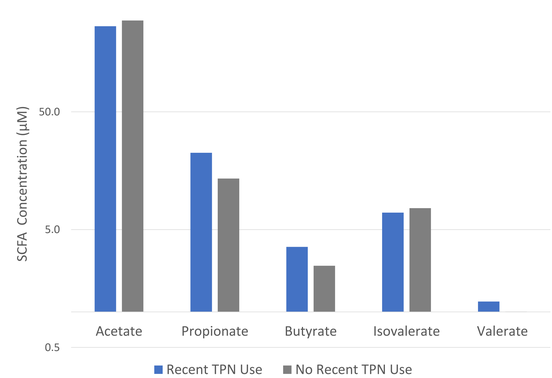

Figure 3: Comparison of SCFA levels to Recent TPN use

Patients that recently used TPN did not have significantly different SCFA levels than patients who did not.

Methods

- We collected and analyzed plasma samples from 43 patients diagnosed with severe aGVHD
- SCFA levels were quantified using liquid chromatography
- We compared SCFA levels at baseline and day 7, 14, 28, and 56
- Response was characterized based on symptoms on day 28 compared to baseline
  - Complete Responder (CR): Symptoms improve after treatment
  - Partial Responder (PR): No change in symptoms after treatment
  - Non-Responder (NR): Symptoms worsen after treatment

SCFAs and other Biomarkers Could be Used to Predict aGVHD Treatment Response

- Significant differences in SCFA levels between CR/PR and NR indicate these metabolites are important for maintaining LGI integrity and function
- SCFA levels could be measure prior to HCT to determine the likelihood that a patient will respond to treatment
- Low levels from these initial tests could suggest using a less intensive chemotherapy and/or antibiotic treatment such that minimal damage to the gut microbiome occurs.
- Further research on a greater sample size must be conducted to confirm our results and to also determine if there are additional metabolites that can be used to predict aGVHD treatment response and outcomes

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