The Effect of Gastric Acid Suppression on Probiotic Colonization

Study Protocol

NCT03327051

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BACKGROUND

A major role of gastric acidity is the digestion of food products and the elimination of potentially pathogenic bacteria that enter the gastrointestinal tract. The use of pharmacologic agents that reduce gastric acid secretion (i.e., H_2 receptor antagonists and proton pump inhibitors) has consequently been shown to influence the composition of the intestinal microflora.[1-3] Probiotics contain living microorganisms that are consumed for its putative benefits on the intestinal microbiota and intestinal health. However, despite widespread use of probiotics and acid suppressing effects, the effect of gastric acid suppression on the survival and colonization of probiotics organisms is currently unclear. We hypothesize that pharmacology-mediated gastric acid suppression will increase the colonization potential of probiotics. We propose to test this hypothesis in a randomized double-blinded placebo-controlled trial among healthy controls who initiate probiotics.

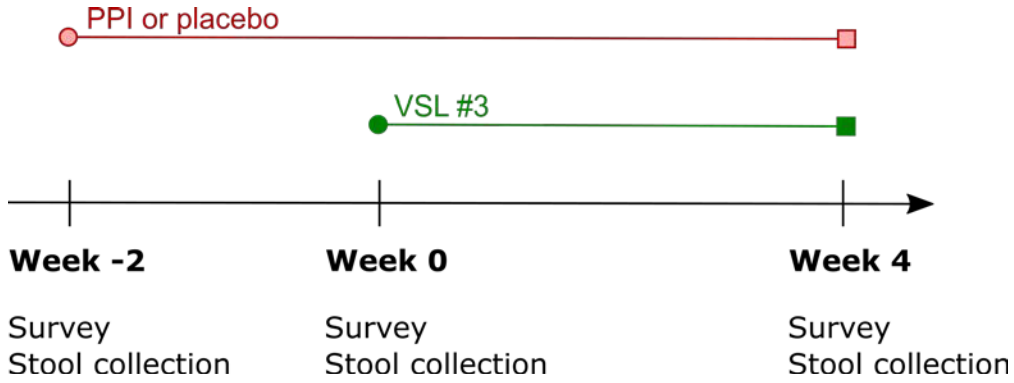
METHODS

- Study design: Randomized double-blind placebo-controlled trial
- Population: 15 + 15 healthy controls
- Exclusion criteria: any gastrointestinal condition, soy or gluten sensitivity, allergy to proton pump inhibitors, any chronic medical condition other than hypertension or hyperlipidemia, pregnancy, consuming herbs or probiotics
- Interventions
    - PPI (omeprazole 20 mg/day) + VSL #3 (900 billion bacteria)
    - VSL #3 (900 billion bacteria)
- Primary outcome
    - Quantitation of bacterial strains found in VSL #3 (*S. thermophiles, B. breve, B. longum, B. infantis, L. acidophilus, L. plantarum, L. paracasei, L. delbrueckii subsp. bulgaricus*)
- Secondary outcomes
    - Characterization of microbiota
    - Metabolome
    - Safety (reported symptoms)

Study Visits

- Timeline
    - Week -2: Run-in with either PPI or nothing x 2 weeks
    - Week 0: Initiation of VSL #3 x 4 weeks
    - Diet/symptom survey, blood, and stool collection at weeks -2, 0, and 4

Interested participants will be contacted on the phone and screened by the clinical research coordinator (CRC). If interested and eligible, the participant will be sent a stool collection kit by mail and scheduled for the initial study visit (Week -2).



Week -2

- Undergo formal informed consent process
- Complete baseline questionnaire
- Provide pre-collected stool
- Blood collection
- Receive and initiate blinded drug (PPI or placebo); no observation required
- Receive stool collection kit

Week 0

- Complete follow-up questionnaire
- Provide pre-collected stool
- Blood collection
- Receive and initiate VSL #3; no observation required
- Receive stool collection kit

Week 4

- Complete final questionnaire
- Provide pre-collected stool
- Blood collection

Drug Sourcing

- VSL #3, omeprazole, and placebo to be purchased from compounding pharmacy

Financial Considerations:

<u>Payment</u>
Research participants will be compensated [redacted] at completion of the study to cover travel expenses. A gift card may be used for human subject reimbursement.

Specimen Storage and Processing
Specimens will be collected, processed, and stored in the -80° freezer in the Habtezion Laboratory. Microbiome and metabolome analyses will be performed at a core facility.

Data Storage
Paper records will be stored in a secure, locked cabinet at the Stanford Center for Clinical Research. Electronic clinical data will be stored on a REDCap database hosted on Stanford IT-managed servers.

REFERENCES

1. Freedberg DE, Toussaint NC, Chen SP, et al. Proton Pump Inhibitors Alter Specific Taxa in the Human Gastrointestinal Microbiome: A Crossover Trial. *Gastroenterology.* 2015;149(4):883-885 e889.
2. Imhann F, Bonder MJ, Vich Vila A, et al. Proton pump inhibitors affect the gut microbiome. *Gut.* 2016;65(5):740-748.
3. Jackson MA, Goodrich JK, Maxan ME, et al. Proton pump inhibitors alter the composition of the gut microbiota. *Gut.* 2016;65(5):749-756.