Efficacy of vonoprazan triple therapy combined with encapsulated fecal microbiota transplantation (FMT) as adjuvant for *Helicobacter pylori* eradication: A Double-blind, Randomized, Placebo-controlled study (FMT-HP Trial)

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BACKGROUND: *H. pylori* causes chronic gastritis which can progress to peptic ulcer diseases and gastric cancer. Vonoprazan is a potent acid inhibitor which has been recently proposed in *H. pylori* treatment regimen. Both *H. pylori* infection and eradication therapy can exert effects on gut microbiota. FMT has been demonstrated to effectively restore gut microbiota and improve dysbiosis. This study aimed to evaluate the efficacy of vonoprazan triple therapy combined with oral FMT for *H. pylori* eradication.

METHODS: This randomized, double-blind, placebo-controlled study was conducted between August 2023 and November 2023. Eligible dyspeptic patients with *H. pylori* gastritis were randomized to receive 14-day vonoprazan triple therapy with encapsulated FMT or placebo. Treatment regimen was composed of 20 mg vonoprazan twice daily, 1000 mg amoxicillin twice daily, and 1-gram clarithromycin modified-release formulation once daily. Stool material (50 grams) were used for encapsulation. Six capsules (FMT or identical-looking placebo capsules) were administered twice daily for 2 consecutive days at 1 week prior to vonoprazan triple therapy. CYP3A4/5 polymorphisms (1*/1*, 1*/3*, 3*/3*) and antimicrobial susceptibility testing (Epsilometer test or GenoType® HelicoDR) were performed. Successful *H. pylori* eradication was defined as negative ^{13}C-urea breath test at least 4 weeks after complete eradication.

RESULTS: Twenty *H. pylori*-positive patients were randomized to receive 14-day vonoprazan triple therapy with FMT (N=10) or placebo (N=10). The mean age of patients was 55.2±16.3 years and 40% were men. Eradication rates of both 14-day regimen with FMT or placebo were 90% (p=1.00). CYP3A4/5 genotyping was performed in both groups and revealed 37.5%, 50%, and 12.5% for CYP3A5 poor, intermediate and extensive metabolizers, respectively, whereas all patients were CYP3A4 extensive metabolizers. Antibiotic resistance rates were 50% for metronidazole. Moreover,

FMT group significantly had improvement of Gastrointestinal Symptom Rating Scale (GSRS) score (20.1±4.0 vs. 26.2±6.7, p=0.034) and higher SF-36 quality-of-life score (127.2±8.5 vs. 117.1±11.6, p=0.023) at 6 weeks after treatment. Furthermore, FMT group tended to have lower side effects including bitter taste (20% vs. 60%, p=0.17) and nausea (10% vs. 20%, p=1.00). No serious adverse event was observed in both groups.

CONCLUSIONS: Vonoprazan triple therapy with encapsulated FMT could provide an excellent *H. pylori* eradication rate. Adding FMT as adjuvant for *H. pylori* treatment could improve gastrointestinal symptoms and increase patient's general health-related quality of life with good safety profile.

Table 1. Baseline characteristics, eradication rates, GSRS, and SF-36 scores of vonoprazan triple therapy with FMT or placebo

Characteristics	Vonoprazan triple therapy plus placebo (N = 10)	Vonoprazan triple therapy plus FMT (N = 10)	P-value
Gender, male	4 (40%)	4 (40%)	1.000
Age, years (mean ± SD)	58.7 ± 10.9	51.6 ± 20.3	0.342
Comorbidities			
None	2 (20%)	4 (40%)	0.628
Hypertension	5 (50%)	4 (40%)	1.000
Dyslipidemia	4 (40%)	3 (30%)	1.000
Diabetes mellitus	2 (20%)	2 (20%)	1.000
Eradication rate	9 (90%)	9 (90%)	1.000
GSRS score			
Pretreatment	39.4 ± 10.1	40.1 ± 12.6	0.903
During treatment	28.9 ± 8.3	25.6 ± 6.9	0.358
Posttreatment	26.2 ± 6.7	20.1 ± 4.0	0.034
SF36 score			
Pretreatment	108.9 ± 18.8	102.5 ± 11.3	0.376
During treatment	113.2 ± 15.1	121.6 ± 11.4	0.186
Posttreatment	117.1 ± 11.6	127.2 ± 8.5	0.023

Figure 1. Gastrointestinal symptom rating scale and quality of life scores of vonoprazan triple therapy with FMT or placebo