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# Effect of triple viable bifidobacterium combined with mosapride on hemorheology and serum gastrointestinal hormone levels in patients with functional dyspepsia

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ABSTRACT

**Objective:** To observe the effect of triple viable bifidobacterium combined with mosapride on hemorheology and serum gastrointestinal hormone levels in patients with functional dyspepsia (FD). **Methods:** A total of 127 patients with FD were randomly divided into the observation group (67cases) and the control group (62 cases). The control group was given mosapride, the observation group was given triple viable bifidobacterium on the base of the control group. For 2 months, to observe the efficacy and changes of hemorheology [the whole blood viscosity (high and low shear), plasma viscosity] and serum gastrointestinal hormone levels (MTL, NPY, VIP). **Results:** After treatment, the observation group of the whole blood viscosity (high and low shear), plasma viscosity were decreased significantly ($P$<0.05), but those of the control group showed no significantly difference compared with before ($P$>0.05). There was significantly difference between the two groups ($P$<0.05); After treatment, serum MTL, NPY were increased and VIP was increased in both groups ($P$<0.05), and all indexes of the observation group were improved more significant than those of the control group ($P$<0.05). **Conclusions:** Efficacy of triple viable bifidobacterium combined with mosapride is more better than single mosapride in the treatment of FD. It may be related to its effects on hemorheology and gastrointestinal hormone.

## 1. Introduction

The pathogenesis of functional dyspepsia (FD) is full of complexity. So far, it has not been clarified yet. However, the affinity among abnormal gastrointestinal motility, alteration of intestinal flora and blood flow abnormality has been recognized[1]. Triple viable bifidobacteriun for intestinal flora regulation and mosapride for gastric motility stimulant promotion were commonly used FD therapeutic medicines, their combination could enhance the clinical efficacy of FD [2], but advantages of the combined mechanism were not clarified. In our study, influences of these two medicines on blood flow variation, motinlin (MTL), neuropeptide Y (NPY) and vasoactive peptide (VIP) of FD patients were observed to discover the possible mechanism.

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## 2. Materials and methods

### 2.1. General materials

All FD patients came to our outpatient department from Jan 2015 to Apr 2016. They all met the Roma III system standards[3]. Standards of exclusion were as follows: ① Juveniles under 18 years old were out of the above standards; ② Patients who had serious cardiovascular, renal, hepatic and endocrine comorbidities, who had autoimmune disease and neoplasms. ③ Patients found to have pathological changes of gastrointestinal, the liver and gallbladder by

ultrasound, endoscopy and imageological examination. ④ Patients received FD therapy during the nearly one-month time. ⑤ Patients who had incomplete clinical datas and dropouts during the research. ⑥ Patients who did not sign on the informed consent form. Then 127 cases were obtained, and they were randomly divided into the observation group and the control group. There were 65 patients in the observation group, 35 males and 30 females, their ages were between 19 and 73 years [(43.91±16.43) years old], their courses of disease were between 1 and 11 years [(3.45±1.70) years]. There were 62 patients in the control group, 32 males and 30 females, their ages were between 21 and 71 years [(42.14±18.14) years old], and their courses of disease were between 1.5 and 13 years [(3.21±1.75) years]. No significant differences ($P>0.05$) existed in genders or ages between the two groups, and they were comparable.

### 2.2. Therapeutic methods

The two groups of patients were received health education after enrollment, they were told to have a healthy diet, do proper exercises, quit smoking, avoid drinking, and get regular rest. Patients in the control group were given mosapride (Manufacturer: Shanghai Xinyi Pharmaceutical Co., Ltd. National License Medical Number: H20051719), dosage: 5 mg/each, 3 times/day, administered orally in 30 min before three meals. Patients in the observation group were added Triple viable bifidobacterium capsules (Manufacturer: Jincheng Hayes Pharmaceutical Co. Ltd. National License Medical Number: S19993065), dosage 630 mg/each, 3 times/day, administered orally in 30 min after three meals beside the treatment of control group. Two groups of patients were treated continuously for two months, without other FD therapeutic medicines involved.

### 2.3. Observation indexes

#### 2.3.1. Indexes of hemorheology

The indexes of hemorheology included whole blood viscosity (high and low shear viscosity) and plasma viscosity. HT-100 full automatic hemorrheology analyzer was used for detecting. Vein blood samples were collected one a time separately before and after treatment.

#### 2.3.2. Laboratory indexes

Laboratory indexes included NTL, NPY and VIP. Radioimmunoassay was used to detect MTL, the kits were from Beijing Le Bo Biological Technology Co., Ltd. ELISA method was used to detect NPY and VIP, the kits were made by Shanghai enzyme linked Biological Technology Co., Ltd. All the operations were conducted following the requirements of instruction. Vein blood samples were collected one a time separately before and after treatment.

### 2.4. Therapeutic effect criterion

Standards of reference[4] were as follows: Effectual FD relevant symptoms disappeared absolutely or basically after therapy; Effective FD relevant symptoms were obviously alleviated after therapy; Invalid FD relevant symptoms had no obvious variation, or they were even aggravated.

### 2.5. Statistical analysis

All the data were processed by SPSS 17.0 software. Measurement data were analyzed by t-test, rank data were analyzed by Ridit. $P<0.05$ indicated that the differences were statistical significant.

## 3. Results

### 3.1. Comparison of clinical effects between two groups

In the observation group, 34 cases showed effectual results (52.3%), 28 cases showed effective results (43.08%), and 3 cases showed invalid results (4.62%). In the control group, 27 cases showed effectual results (43.55%), 23 cases showed effective results (37.10%), and 12 cases showed invalid results (19.35%). Ridit analysis showed significant differences in clinical efficacy between these two groups ($P<0.05$).

### 3.2. Comparison of hemorheological indexes before and after treatment between two groups

The differences in whole blood viscosity (high and low shear viscosity) and plasma viscosity before and after treatment of two groups were not statistical significant ($P>0.05$). After treatment, the above indexes of control group showed no significant variation ($P>0.05$), the whole blood viscosity (high and low shear viscosity) and plasma viscosity of observation group were significantly declined comparing with before ($P<0.05$). The differences between the two groups were statistical significant ($P<0.05$), as shown in Table 1.

### 3.3. Comparison of NPY, MTL and VIP levels between two groups before and after treatment

No significant difference existed in NPY, MTL and VIP levels between the two groups before treatment ($P>0.05$). After treatment, two groups of NPY and MTL levels significantly increased comparing with pre-treatment of the same group, and VIP level decreased significantly ($P<0.05$), as shown in Table 2.

## 4. Discussion

FD was comprised 20%-40%[5] of the total amount of

**Table 1**

Comparison of hemorheological indexes before and after treatment between two groups (mPa•s).

| Groups | Time | whole blood viscosity | | Plasma viscosity |
|---|---|---|---|---|
| | | High shear viscosity | Low shear viscosity | |
| Observation group (65 cases) | Pre-treatment | 5.86±1.04 | 17.73±4.38 | 1.63±0.21 |
| | Post-treatment | 4.64±0.86▲△ | 13.90±2.06▲△ | 1.24±0.16▲△ |
| Control group (62 cases) | Pre-treatment | 5.74±1.12 | 17.50±3.25 | 1.64±0.25 |
| | Post-treatment | 5.53±1.03 | 17.32±2.89 | 1.61±0.23 |

Compared with pre-treatment data in the same group, △$P$<0.05; Compared with data of the control group in the corresponding period, ▲$P$<0.05.

**Table 2**

Comparison of NPY, MTL and 5-HT levels between two groups before and after treatment (pg/mL).

| Groups | Time | MTL | NPY | VIP |
|---|---|---|---|---|
| Observation group (65 cases) | Pre-treatment | 217.46±45.36 | 1.52±0.34 | 22.46±3.31 |
| | Post-treatment | 335.68±53.41△▲ | 2.25±0.72△▲ | 11.43±2.96△▲ |
| Control group (62 cases) | Pre-treatment | 220.73±50.72 | 1.56±0.39 | 21.93±3.72 |
| | Post-treatment | 278.45±59.04△ | 1.85±0.67△ | 15.02±2.86△ |

Compared with pre-treatment data in the same group, △$P$<0.05; Compared with data of the control group in the corresponding period, $P$<0.05.

gastroenterology clinical treatment, although it had no extremely serious complications, the repeated syndromes, such as upper abdominal swelling, nausea, vomiting, acid reflux, were one of the major diseases seriously impacted on life quality of patients[5]. So far, its pathogenesis is not fully understood as yet, however, it was realized that multi-factor symptoms, such as gastrointestinal motility disorder, intestinal dysbacteriosis, helicobacter pylori infection, visceral sensitivity, hemorheology abnormality and so forth, were concerned with the onset of FD. The relation between abnormal gastrointestinal motility and onset of FD exists with no doubt[6], and factor of intestinal dysbacteriosis has been received attention with an increasing tendency[7], this factor is also a theoretical basis for clinical combined application of prokinetic agents and supplemental probiotics. Gastrointestinal motility disorder is related to gastric electrical dysrhythmia and abnormal gastrointestinal hormone secretion[8]. In the observation of our study, gastrointestinal hormones, MT, NPY and VIP had function of gastrointestinal motility regulation. The former two hormones had low expression level in FD patients, which impacted on the lack of gastrointestinal motility[9]; and the later one could regulate gastrointestinal motility as a neurotransmitter in gastrointestinal nervous system. As a signaling molecule, it can regulate excretion of more than 40 kinds of gastrointestinal hormones, including MTL and NPY, and it has highly expression in FD patients, which can directly cause the abnormal gastrointestinal and make the abnormality worse by suppressing the excretion of MTL and NPY[10]. The hemorheology abnormality is also related with FD[11]. After increasing of whole blood viscosity and plasma viscosity, microcirculation disturbance would lead to gastrointestinal mucosal hypoxia-ischemia, which could cause the damage of gastrointestinal tissue, and in the meantime, could induce injury of the local nerve-endocrine system, then result in abnormal excretion of gastrointestinal hormones. It is clear that improvement of hemorheology could contribute to FD recovery. Therefore, the blood activating Chinese herbal medicines (The modern pharmacology research thought that this class of Chinese herbal medicine had function of improving hemorheology) were given by the doctors of traditional Chinese medicine to treat FD, and they had remarkable effects[12], but in modern medicine, few research was focus on this area.

Mosapride is a commonly used clinical gastric motility-promoting medicine. A lot of studies[13,14] indicated that it could lead to increasing of serum MTL and NPY levels, and decreasing of VIP level, our study was consistent with the indication. Besides of the accumulating of acetylcholine release by high selective excited 5-hydroxytryptamine (serontonin) and 4-receptor, which could accelerate gastrointestinal mobility, the function for regulating gastrointestinal hormone levels could also promote FD recovery, but the specific mechanism for regulation remains unclear. The effection of mosapride on hemorheology was poorly understood. Several researches[15] suggested it could bring down the whole blood viscosity and plasma viscosity, but they could not indicate possible mechanism. In our study, hemorheology showed no obvious changes before and after treatment. Triple viable bifidobacterium is a commonly used probiotic, the contained bifidobacterium, Lactobacillus bulgaricus and Streptococcus thermophilus are intestinal beneficial bacterias. Research[16] showed it could also raise serum MTL, NPY levels and bring down VIP level of FD patients. The effection on regulating gastrointestinal hormones might be related to the below mechanism: ① The effection on this class of hormones could be alleviated by intestinal barrier function[17]; ② The effection on recovery of normal intestinal flora and decreasing harmful substances (eg. endotoxin)[18]. ③ The function of digestion accelerating and appetite improvement could stimulate nerve-endocrine system for regulating this hormones[19]. There are the following several ways for triple viable bifidobacterium to improve hemorheology: ① Blood viscosity could be lightened by lipid

lowering function[20]; ② Endotoxin could activate platelet, spur erythrocyte aggregation, alter the electric charge of erythrocyte, and bring down the deformability of it [21]. Nevertheless, the absorption of endotoxin in intestine could be suppressed by triple viable bifidobacterium.

The results of our study indicated a better efficacy for FD treatment by triple viable bifidobacterium combined with mosapride than simply relying on mosapride, which was consistent with results in the literatures[13]. And effect on serum gastrointestinal hormones, namely, MTL, NPY, VIP, and hemorheology with combination of the medicines was the key point of our study, the results showed: after treatment of medicines combination for observation group, the MTL, NPY and VIP levels were better than which in control group . It indicated that combination of the medicines had a greater influence on serum gastrointestinal hormones than simply using mosapride. After treatment, whole blood viscosity and plasma viscosity of the observation group decreased significantly, and their hemorheology was remarkably better than the control group, which showed no obvious variation. Above all, it is considered that the two medicines combination for FD treatment had a better curative effect, which was related with the regulation of gastrointestinal hormone levels and hemorheology.

## References


[1] Talley NJ, Ford AC. Functional dyspepsia. *New Engl J Med* 2015; **373**(19): 1853-1863.

[2] Peng D, Gao L. Therapeutic evaluation of mosapride combined with vitamin B1 and bifid triple viable powder in treatment of functional constipation. *J Clin Med Pract* 2013; **13**(23): 37.

[3] Drossman DA. The functional gastrointestinal disorders and the RomeIII Rrocess. *Gastroenterology* 2006; **130**: 1377-1390.

[4] Xu KC, Jiang SH. *Modern treatment of digestive disease*. Shanghai: Shanghai Press of Technology and Education; 2001, p.50.

[5] Suzuki H, Moayyedi P. Helicobacter pylori infection in functional dyspepsia. *Nat Rev Gastroenterol Hepatol* 2013; **10**(3): 168-174.

[6] Ford AC, Luthra P, Tack J, et al. Efficacy of psychotropic drugs in functional dyspepsia: systematic review and meta-analysis. *Gut* 2015. gutjnl-2015-310721.

[7] Walker MM, Aggarwal KR, Shim LSE, et al. Duodenal eosinophilia and early satiety in functional dyspepsia: confirmation of a positive association in an Australian cohort. *J Gastroenterol Hepatol* 2014; **29**(3): 474-479.

[8] -Wang WJ. Research on variation of gastrointestinal hormone and Th1/Th2 indexes of perioperative gastric cancer patients. *J Hainan Med Coll* 2015; **21**(10): 1402-1404.

[9] Jiang SM, Jia L, Liu J, et al. Beneficial effects of antidepressant mirtazapine in functional dyspepsia patients with weight loss. *World J Gastroenterol* 2016; **22**(22): 5260-5266.

[10]Luttikhold J, Ruijter FM, Norren K, et al. Review article: the role of gastrointestinal hormones in the treatment of delayed gastric emptying in critically ill patients. *Alimentary Pharmacol & Ther* 2013; **38**(6): 573-583.

[11]Wang XH, Zhang WG, Wu QM, et al. Variation of hemorheology on functional dyspepsia patients. *Chinese J Clin Gastroenterol* 2003; **15**(3): 133-134.

[12]Liu YF, Yang H, Feng C, et al. Analysis of Chinese medicine on disease of gastrointestinal motility disorders. *Hainan Med J* 2015; **27**(22): 3356-3357.

[13]Bang CS, Kim JH, Baik GH, et al. Mosapride treatment for functional dyspepsia: A meta - analysis.*J Gastroenterol Hepatol* 2015; **30**(1): 28-42.

[14]Cho YK, Choi MG, Park EY, et al. Effect of mosapride combined with esomeprazole improves esophageal peristaltic function in patients with gastroesophageal reflux disease: a study using high resolution manometry. *Dig Dis Sci* 2013; **58**(4): 1035-1041.

[15]Li LJ. Therapeutic effect analysis of mosapride combined with gastritis misture for chronic atrophic gastritis. *Chin Continuing Med Ed* 2015; **7**(24): 209-210.

[16]Zhou W, Su J, Zhang H. Efficacy and safety of acupuncture for the treatment of functional dyspepsia: Meta-analysis. *J Altern Compl Med* 2016; **22**(5): 380-389.

[17]Dore M P, Goni E, Di Mario F. Is there a role for probiotics in Helicobacter pylori therapy? *Gastroenterol Clinics North America* 2015; **44**(3): 565-575.

[18]Ji XJ. Threaputic effects on functional dyspepsia treatment and recurrence prevention by triple viable bifidobacterium capsule combined with mosaprid. *Chin J Microecol* 2014; **26**(5): 555-557.

[19]Jiang H, Jiang LL, Zhang K, et al. Clinical Effects of early enteral nutrition combined with triple viable bifidobacterium capsule to treat severe acute pancreatitis and influence on inflammatory factor and protection of intestinal barrier function. *J Hainan Med Coll* 2015; **21**(11): 1496-1498.

[20]Zanotti I, Turroni F, Piemontese A, et al. Evidence for cholesterol-lowering activity by Bifidobacterium bifidum PRL2010 through gut microbiota modulation. *Appl Microbiol Biotechnol* 2015; **99**(16): 6813-6829.

[21]Nemeth N, Berhes M, Kiss F, et al. Early hemorheological changes in a porcine model of intravenously given E. coli induced fulminant sepsis. *Clin Hemorheol Microcirculation* 2016; **61**(3): 479-496.