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Original Article

Domperidone plus pinaverium bromide and itopride for functional dyspepsia in the elderly: efficacy, symptom improvement, and gastric function panel

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Abstract: Objective: Focusing on functional dyspepsia (FD) in the elderly, this study analyzes how the triple therapy consisting of domperidone (DPD), pinaverium bromide (PB), and itopride (ITP) impacts curative efficacy, symptom amelioration, and the gastric function (GF) panel. Methods: A total of 96 elderly FD adults were selected and allocated to a control group treated with PB+ITP or a research group which additionally received DPD in addition to PB+ITP. Outcome measures included curative efficacy, symptom amelioration, gastric accommodation, electrogastrographic parameters (dominant frequency, dominant power), brain-gut axis (BGA)-related factors (vasoactive intestinal peptide [VIP], somatostatin [SS], calcitonin gene-related peptide [CGRP], serum neuropeptide S receptor 1 [NPSR1]), GF panel (pepsinogen [PG] I, PG II, gastrin [G]-17), other serum indices (motilin [MTL], 5-hydroxytryptamine [5-HT], nitric oxide [NO]), and adverse events. Results: According to statistics, the total effective rate was higher in the research group compared to controls, and the time to symptom improvement was shorter ($P<0.05$); The post-treatment gastric accommodation, dominant frequency, dominant power, NPSR1, GF panel, and MTL were higher in the research group, while VIP, SS, CGRP, 5-HT, and NO were lower ($P<0.05$); the total incidence of adverse reactions was equivalent across groups. Conclusion: The triple therapy (DPD+PB+ITP) demonstrates high therapeutic efficacy on elderly FD patients, helps improve symptoms, and actively up-regulates GF panel levels.

Keywords: Domperidone, pinaverium bromide, itopride, functional dyspepsia in the elderly, curative efficacy, symptom amelioration, gastric function panel

Introduction

Functional dyspepsia (FD) among the elderly, a common functional gastrointestinal (GI) disease, can be classified as postprandial distress syndrome (PDS), epigastric pain syndrome (EPS), or their overlapping subtypes [1]. Diagnosing and treating FD in elderly patients is challenging. The condition has an average prevalence of 23.5%; female gender, smoking, poor sleep quality, and Helicobacter pylori infection can increase the risk of the disease [2]. FD patients mainly present with belching, postprandial fullness, epigastric pain, early satiety, and other clinical symptoms, which can lead to a heavy socio-economic burden [3]. FD is also a gut-brain interaction disorder, which pathophysiologically involves impaired gastric regulation, mucosal barrier dysfunction, and inflammation, threatening patients' gastric function (GF) to varying degrees [4]. Despite the presence of multiple management methods, including prokinetics, diet adjustment, probiotics, antibiotics, neuromodulators, psychobehavioral therapy, and other alternative therapies like acupuncture, the therapeutic outcomes have room for improvement [5, 6]. It is thus pressing to further optimize related therapies for such patients.

As a common GI spasmolytic agent, pinaverium bromide (PB) helps alleviate intestinal dysfunction, biliary dyskinesia, and enterospasm [7]. It plays an antispasmodic role mainly by acting on muscarinic receptors, with high clinical safety, and is indicated for FD patients who respond poorly to proton pump inhibitors [8]. Being a benzamide derivative and a prokinetic agent, itopride (ITP) can restore gastric motility by antagonizing dopamine D2 receptors and inhibit-

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ing acetylcholinesterase [9]. Its application in FD has been proven to be clinically safe, contributing to one-year symptom amelioration in 66.7% of users [10]. Domperidone, functioning as a prokinetic agent and an antiemetic drug, has the effect of D2 receptor antagonists [11]. An experiment on FD in rats indicated that domperidone (DPD), by targeting the 5-hydroxytryptamine receptor 2B (5-HT2B), phospholipase C-β2 (PLC-β2), and inositol triphosphate (IP3) signal pathways, could improve gastrointestinal motility (GIM) and regulate intestinal flora, thus alleviating FD symptoms [12]. In another randomized controlled phase III clinical trial, DPD intervention in FD patients is shown to achieve a 31.9% disappearance rate of symptoms such as postprandial fullness, early satiety, epigastric pain, and upper abdominal burning sensation after 4 weeks of medication, while also effectively increasing the 2-hour postprandial gastric emptying (GE) rate [13].

There is limited evidence on the effects of the triple drug regimen (DPD+PB+ITP) on curative efficacy, symptom improvement, and GF panel levels in elderly FD patients. This study attempts to evaluate the effectiveness and clinical safety of the three-drug combination regimen to provide better treatments for such patients.

Information and methods

Patient selection

Inclusion requirements: All patients meet the relevant diagnostic criteria for FD [14]; clinical symptoms such as belching, postprandial fullness, epigastric pain, and early satiety; age of 60 years old or above, with no recent (one month) administration of antacids or prokinetic agents, good mental condition, normal communication and cognitive abilities, and clinical data completeness were also mandatory. Exclusion grounds: Concurrent gastroesophageal reflux disease, irritable bowel syndrome, benign or malignant tumor, biliary system diseases, atrophic gastritis, enteral infections, or other digestive tract diseases (e.g., gastric ulcer, esophagitis, erosive gastroenteritis, duodenal ulcer) indicate ineligibility; allergy to the drugs studied, individuals with an abdominal surgery history, patients with severe insufficiency of heart, lung, or kidney functions, mental illness-afflicted cases, as well as pregnant or lactating women, were also excluded.

This retrospective study included 96 elderly patients with FD who received treatment at our center between June 2023 and September 2025. Among them, 45 patients who received PB and ITP were assigned to the control group, whereas 51 patients who additionally received DPD were assigned to the research group. This study was approved by the Ethics Committee of Guannan County First People's Hospital.

Intervening methods

The control patients were treated with PB (50 mg/tablet) and ITP (50 mg/tablet), which was administered 15-30 min before meals, one capsule per time, three times a day. Based on the above treatment, the research group was further given DPD (10 mg/tablet), which was also taken 15-30 min before meals at 1 capsule/time, 3 times/d. A 4-week treatment cycle was implemented for both cohorts [15].

Data collection and outcome measures

Therapeutic effectiveness. Efficacy assessment was conducted 4 weeks following medication, applying the criteria described below: A cure was indicated by complete clinical symptom resolution and a normal food intake; obviously improved clinical symptoms and ≥3/4 recovery of the food intake vs. pre-treatment was considered marked effectiveness; effectiveness meant certain clinical symptom relief, plus a <3/4 restoration of the pre-treatment food intake; cases that met none of the above criteria were classified as treatment failures. Total effective rate = (cured cases + markedly effective cases + effective cases)/total case number.

Symptoms amelioration. We recorded the improvement time of symptoms such as belching, postprandial fullness, epigastric pain, and early satiety for both patient groups.

Gastric accommodation [16]. A comparative assessment of the gastric accommodation of the study cohorts before and after treatment was performed. The measurement was made by electronic air pump manometry. Under computer control, an appropriate fixed pressure or volume was set, and an intragastric balloon was automatically pumped or injected according to the proximal gastric pressure or volume. The variation of balloon pressure and volume

was observed and recorded to detect the gastric accommodation.

Electrogastrographic parameters [17]. An electrogastrogram was used to record pre- and post-prandial gastric myoelectric signals. The original data were converted into spectrograms by fast Fourier transform for analysis. The recorded parameters included dominant frequency and power, where the former is the frequency corresponding to the wave peak in the spectrogram and the latter is the power intensity corresponding to the peak frequency.

Brain-gut axis (BGA)-related factors. Fasting venous blood (4 mL) was sampled from each patient before and after treatment, and centrifuged to separate the serum for enzyme-linked immunosorbent assay (ELISA)-based quantification of vasoactive intestinal peptide (VIP), somatostatin (SS), calcitonin gene-related peptide (CGRP), and neuropeptide S receptor 1 (NPSR1). Among them, the human VIP ELISA kit was ordered from Wuhan Yansheng Biotechnology Co., Ltd. (CSB-E08354h), the human SS and CGRP ELISA kits from Shanghai Fusheng Industrial Co., Ltd. (A127441, A127159), and the human NPSR1 ELISA kit from Shanghai Sig Biotechnology Co., Ltd. (XG-E104076).

GF panel. Pre- and post-treatment measurements of pepsinogen (PG) I, PG II, and gastrin (G)-17 were conducted by employing the ELISA technique. Among them, the human PGI ELISA kit was purchased from Wuhan Elabscience Biotechnology Co., Ltd. (E-UNEL-H0229), and the human PGII and G-17 ELISA kits were ordered from Wuhan Yansheng Biotechnology Co., Ltd. (CSB-E17539h, ELK0740).

Other serum indices. This study examined serum motilin (MTL) and 5-hydroxytryptamine (5-HT) by ELISA, and nitric oxide (NO) by the nitrate reductase method. Among them, the human MTL ELISA kit, human 5-HT ELISA kit, and human NO Assay Kit (Nitrate Reductase Method) were purchased from Shanghai Boke Biotechnology Co., Ltd. (BKE7524), Wuxi Tiancui Biotechnology Co., Ltd. (YPH103627), and Shanghai Jingke Chemical Technology Co., Ltd. (JK4024), respectively.

Adverse events (AEs). Patients were observed for the occurrences of dry mouth, constipation, diarrhea, dizziness, and nausea after treatment, with the total incidence calculated.

Statistical methods

In this research, we statistically described measurement data as the mean ± standard deviation (SD), adopted the independent sample t-test to identify between-group differences, and employed the paired t-test to examine pre- vs. post-treatment differences. Counting data, expressed by ratios (percentages), were tested by the χ^2 test for between-group differences. All analyses were performed in SPSS 22.0, with statistical significance set at $P<0.05$.

Results

General data of the two groups of FD patients

When comparing baseline information between groups, we found no significant differences in sex, age, disease duration, body mass index (BMI), educational attainment, FD classification, and smoking/alcoholism history ($P>0.05$; **Table 1**).

Therapeutic effects of FD patients in the two groups

The control group reported 31 effective cases (12 cured, 14 markedly effective, and 5 effective). In the research group, 20 cured, 18 markedly effective, and 8 effective cases were identified, with the total effective case number being 46. The data translated into a total effective rate of 90.20% for the research group and 68.89% for the control group, with statistical significance ($P=0.009$; **Table 2**).

Comparative assessment of symptom amelioration

Patients in the research group experienced accelerated alleviation of belching, postprandial fullness, epigastric pain, and early satiety compared to controls ($P<0.05$; **Table 3**).

Gastric accommodation across groups

There was non-significant inter-group difference in pre-treatment gastric accommodation ($P>0.05$). Post-medication, both cohorts showed gastric accommodation enhancement, with the research group outperforming the control group ($P<0.001$; **Table 4**).

Table 1. General data of the two groups of functional dyspepsia (FD) patients

Category	Control group (n=45)	Research group (n=51)	χ^2/t	P
Sex			1.384	0.240
Male	30 (66.67)	28 (54.90)		
Female	15 (33.33)	23 (45.10)		
Age (years)	69.60±4.53	70.71±4.93	1.143	0.256
Disease duration (months)	16.84±8.04	17.10±8.55	0.153	0.879
Body mass index (kg/m^2)	22.53±2.51	22.78±2.28	0.511	0.610
Educational attainment			0.642	0.423
Below senior high school	35 (77.78)	36 (70.59)		
Senior high school or above	10 (22.22)	15 (29.41)		
FD classification			0.319	0.572
Postprandial distress syndrome	29 (64.44)	30 (58.82)		
Epigastric pain syndrome	16 (35.56)	21 (41.18)		
Smoking history			0.256	0.613
No	33 (73.33)	35 (68.63)		
Yes	12 (26.67)	16 (31.37)		
Alcoholism history			0.480	0.489
No	37 (82.22)	39 (76.47)		
Yes	8 (17.78)	12 (23.53)		

Table 2. Therapeutic effects of the two groups of functional dyspepsia (FD) patients

Category	Control group (n=45)	Research group (n=51)	χ^2	P
Cure	12 (26.67)	20 (39.22)		
Marked effectiveness	14 (31.11)	18 (35.29)		
Effectiveness	5 (11.11)	8 (15.69)		
Ineffectiveness	14 (31.11)	5 (9.80)		
Overall effectiveness	31 (68.89)	46 (90.20)	6.837	0.009

Table 3. Symptom amelioration of functional dyspepsia (FD) patients in the two groups

Category	Control group (n=45)	Research group (n=51)	Z	P
Belching (d)	2.00 (2.00, 3.00)	2.00 (1.00, 3.00)	-2.185	0.029
Postprandial fullness (d)	2.00 (1.00, 3.00)	2.00 (1.00, 2.00)	-2.335	0.020
Epigastric pain (d)	2.00 (1.00, 3.00)	2.00 (1.00, 2.00)	-2.315	0.021
Early satiety (d)	2.00 (2.00, 2.00)	2.00 (1.00, 2.00)	-2.503	0.012

Table 4. Gastric accommodation of the two groups of functional dyspepsia (FD) patients

Category	Control group (n=45)	Research group (n=51)	t	P
Pre-treatment	326.60±63.53	327.33±69.15	0.054	0.957
Post-treatment	353.20±66.58	399.76±56.58	3.704	<0.001

Electrogastrographic parameters in the two groups of FD patients

The pre-treatment dominant frequency and dominant power of the two groups had no statistical significance (P>0.05). Both parameters of the two groups exhibited a rising trend post-medication, with higher dominant frequency and power in the research group (P<0.001; **Table 5**).

Table 5. Electrogastrographic parameters of functional dyspepsia (FD) patients in the two groups

Category	Control group (n=45)	Research group (n=51)	t	P
Dominant frequency (times/min)				
Pre-treatment	1.86±0.60	1.87±0.54	0.086	0.932
Post-treatment	2.43±0.70	3.54±0.77	7.353	<0.001
Dominant power (dB)				
Pre-treatment	40.34±6.06	39.64±4.89	0.626	0.533
Post-treatment	46.67±5.51	56.90±4.52	9.988	<0.001

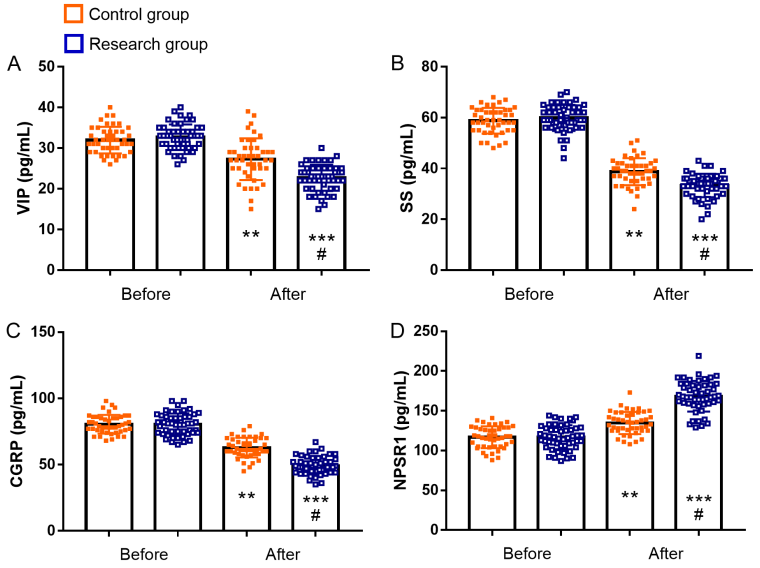

Figure 1. Brain-gut axis-related factors in the two groups of functional dyspepsia (FD) patients. A. Pre- and post-treatment changes in vasoactive intestinal peptide (VIP) levels. B. Pre- and post-treatment somatostatin (SS) levels. C. Calcitonin gene-related peptide (CGRP) levels before and after treatment. D. Neuropeptide S receptor 1 (NPSR1) levels pre- and post-treatment. Note: **P<0.01, ***P<0.001 *vs.* pre-treatment; #P<0.05 *vs.* Control.

BGA-related factors in the two FD patient groups

VIP, SS, CGRP, and NPSR1, all BGA-related factors, were evaluated. According to statistics, these indices showed comparable baseline levels across groups (P>0.05). A treatment-induced significant drop in VIP, SS, and CGRP, as well as a marked rise in NPSR1 (P<0.01), were noted in both groups upon treatment completion; the inter-group comparison of post-treatment levels indicated lower VIP, SS, and CGRP, alongside a higher NPSR1, in the research group compared to controls (P<0.05; **Figure 1**).

GF panel in the two groups of FD patients

Three GF items, namely PG I, PG II, and G-17, were evaluated. As indicated by the measurements, the groups did not differ in pre-treatment levels of the GF panel (P>0.05). All indexes of both groups were significantly increased post-treatment (P<0.01), with higher PG I, PG II, and G-17 in the research group versus controls (P<0.05; **Figure 2**).

Other serum indices of FD patients in the two groups

No significant differences were observed between groups in terms of pre-treatment MTL, 5-HT, and NO levels (P>0.05). After treatment, MTL levels significantly increased, while 5-HT and NO levels significantly decreased in both groups (P< 0.01). Compared with the control group, the research group exhibited greater changes in these serum markers (P<0.05; **Figure 3**).

AEs of FD patients in the two groups

Dry mouth, constipation, diarrhea, dizziness, and nausea were reported in 2, 1, 1, 1, and 1 control patients, and 3, 1, 2, 1, and 1 in the research group, respectively. As shown in **Table 6**, the groups were equivalent in the total AE rate (P>0.05).

Discussion

In this study, the clinical effects of a triple therapy (DPD+PB+ITP) were contrasted against a dual-drug regimen (PB+ITP) for elderly FD patients. It is confirmed that the triple drug combination has more clinical advantages. The detailed report is as follows.

The triple therapy demonstrated superior therapeutic efficacy in elderly FD patients, increas-

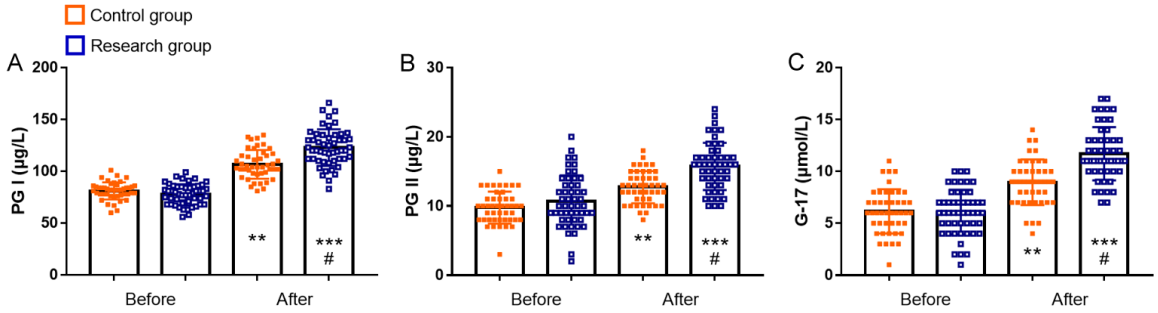

Figure 2. Gastric function panel in two groups of functional dyspepsia (FD) patients. A. Pepsinogen (PG) I levels before and after treatment. B. Pre- and post-treatment alterations in PG II levels. C. Pre- and post-treatment gastrin (G)-17 levels. Note: **P<0.01, ***P<0.001 *vs.* pre-treatment; #P<0.05 *vs.* Control.

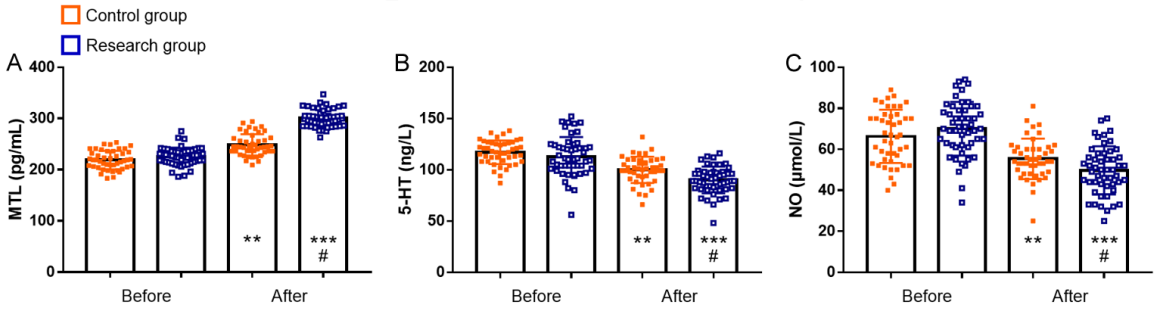

Figure 3. Other serum indices of functional dyspepsia (FD) patients in the two groups. A. Pre- and post-treatment motilin (MTL) levels. B. 5-Hydroxytryptamine (5-HT) levels pre- and post-treatment. C. Nitric oxide (NO) changes before and after medication. Note: **P<0.01, ***P<0.001 *vs.* pre-treatment; #P<0.05 *vs.* Control.

Table 6. Adverse events of functional dyspepsia (FD) patients in the two groups

Category	Control group (n=45)	Research group (n=51)	χ^2	P
Dry mouth	2 (4.44)	3 (5.88)		
Constipation	1 (2.22)	1 (1.96)		
Diarrhea	1 (2.22)	2 (3.92)		
Dizziness	1 (2.22)	1 (1.96)		
Nausea	1 (2.22)	1 (1.96)		
Total	6 (13.33)	8 (15.69)	0.106	0.745

ing the efficacy from 68.89% to 90.20%. This may be attributed to the fact that DPD, by selectively blocking GI tract dopamine receptors, enhances the lower esophageal sphincter tone and coordinated gastroduodenal contractions, and antagonizes dopamine-mediated gastric smooth muscle relaxation, thus promoting GE and preventing duodenal regurgitation [18]. In the report of Fang et al. [19], DPD intervention in Chinese adult FD patients achieves a higher overall treatment response rate than placebo after 2 weeks of treatment, without inducing serious AEs, supporting our observations.

Besides, the DPD+PB+ITP combination shortened the improvement time of symptoms such as belching, postprandial fullness, epigastric pain, and early satiety in elderly FD patients, accelerating symptom amelioration. This may be because DPD can affect the chemoreceptor trigger zone and motility of patients' stomach and small intestine, thus strengthening gastric peristalsis and improving antroduodenal coordination to promote GE. This, in turn, effectively alleviates GIM disorder-associated clinical symptoms [20]. Chen et al. [21] researched the application of DPD in FD patients, noting the drug's ability to effectively relieve

nocturnal dyspeptic symptoms through its effective inhibition of excessive nocturnal duodenal and gastric refluxes, which complements our results.

The triple drug regimen also effectively improved patients' gastric accommodation. This may be related to the fact that DPD can directly play a role in the gastric wall after oral administration, promoting gastric wall contractions and GI peristalsis, which is beneficial to regulating the GI immune system, balancing the flora, and speeding up GI function recovery [22, 23]. Also, the triple drug combination showed higher efficacy in restoring the electrogastrographic rhythm and contractile motility among elderly FD patients.

VIP, as a neurotransmitter widely distributed in the GI tract, can modulate GI mobility, secretion, blood flow, and other physiological functions to slow down GE [24]. SS, secreted by D cells in the stomach and intestinal tract, can inhibit GIM by affecting GI peristalsis, hormone release, enzyme secretion, gastric acid production, and intestinal barrier integrity [25]. CGRP, a neuropeptide composed of 37 amino acids, is related to visceral hypersensitivity, which may delay GE and inhibit GIM [26]. NPSR1 is a G protein-coupled receptor with seven transmembrane domains. It regulates the expression of various neuropeptides involved in intestinal function regulation, and its genetic polymorphism has been associated with FD-related GIM and sensory dysfunction [27]. In this study, DPD+PB+ITP significantly decreased VIP, SS, and CGRP while up-regulating NPSR1 in elderly FD patients, suggesting that this therapy can actively regulate the BGA, reduce visceral hypersensitivity, and alleviate nerve irritation.

Being secreted by gastric chief cells and mucosal cells, PG I reflects gastric mucosal secretory function. PG II, produced by the whole stomach and proximal duodenum, is indicative of the secretion ability of a wider area of the gastric mucosa [28]. G-17 secreted by G cells in the duodenal mucosa and gastric antrum can effectively stimulate GI smooth muscle contractions to promote GE and gastric acid secretion [29]. GF panel measurements revealed that the triple therapy effectively enhanced GF in elderly FD patients, manifested by significantly up-regulating PG I, PG II, and G-17 levels.

MTL is released by enteroendocrine Mo cells, which helps to stimulate the peristalsis of the stomach and small intestine, thus accelerating GE [30]. 5-HT shows a strong connection with FD-related visceral hypersensitivity, with its high levels significantly related to an increase in gastric sensitivity [26]. As a bioactive molecule, NO is linked to impaired GIM and delayed GE when expressed at an abnormally high level, further aggravating FD symptoms [31]. Other serum indices were also tested. The results showed that the triple therapy could effectively regulate the balance of GI hormones and neurotransmitters (up-regulating MTL and inhibiting 5-HT and NO) in elderly FD patients.

Finally, it was found that although DPD was added, it did not significantly increase the risk of total AEs such as dry mouth, constipation, diarrhea, dizziness, and nausea. It supports the certain tolerability of the triple drug regimen, echoing the findings of Yu et al. [32].

Several limitations of this study need to be addressed. First of all, the research results, due to the limitations of the single-center retrospective design, have limited generalizability and require further verification through prospective multi-center trials. Second, there is no subgroup analysis by Helicobacter pylori infection status, which should be included in future research to further clarify the population that could benefit from triple therapy. Finally, basic research is lacking. Subsequently, a mechanistic exploration should be supplemented to further clarify the underlying mechanism of triple therapy.

Through the above-mentioned series of statistics and evaluations, it is found that DPD combined with PB and ITP for elderly FD patients can effectively enhance curative efficacy, promote symptom amelioration, and improve gastric accommodation. Also, it demonstrated higher efficacy than the dual-drug regime in regulating patients' electrogastrographic parameters, GI hormones, and neurotransmitters, relieving BGA disorders, and improving GF, on the premise of not increasing the total AE rate.

Disclosure of conflict of interest

None.

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