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Original Research Article

Effects of a combination of moxapride and fluoxetine on gastrointestinal function in patients with functional dyspepsia-associated anxiety

Yan Wang*, Mengchun Wang, Yan Li
Department of Gastroenterology, Shengjing Hospital, China Medical University, Shenyang 110004, Liaoning, China

For correspondence:* ***Email:* *jiaoleweicuzw@163.com;* ***Tel:*** *+86-18940259626*

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Abstract

Purpose: *To study the effects of a combination of mosapride and fluoxetine in patients with functional dyspepsia-associated anxiety, and its impact on gastrointestinal function.*
Methods: *One hundred (100) cases of patients with anxiety linked to functional dyspepsia, who were admitted to the Department of Gastroenterology of Shengjing Hospital, China Medical University from January 2019 to May 2020, were retrospectively selected and randomly divided into control and study groups (n = 50). The control group patients received moxapride monotherapy, while those in the study group were given moxapride in combination with fluoxetine. The two groups of patients were compared daily for 4 days with respect to treatment effectiveness, Mental Status Scale in Non-psychiatric Settings (MSSNS), Barthel Index (BI), Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale (SDS), time intervals for flatulence and defecation, as well as bowel sounds, and levels of gastric juice and cholecystokinin.*
Results: *Treatment effectiveness, BI index, number of intestinal rumblings, and level of gastrin in the study group were significantly higher than those in control group after 1, 2, 3 and 4 days of treatment ($p < 0.05$). Moreover, scores for SAS, SDS and MSSNS, as well as time intervals for flatulence and defecation, and level cholecystokinin in the study group were significantly lower than those in control group ($p < 0.05$).*
Conclusion: *The combination of mosapride and fluoxetine has high application benefit for patients with anxiety associated with functional dyspepsia when compared with the control.*

Keywords: *Mosapride, Fluoxetine, Functional dyspepsia, Anxiety; Gastrointestinal function, Gastrin, Cholecystokinin*

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INTRODUCTION

Functional dyspepsia, which refers to indigestion due to deterioration of gastrointestinal function and insufficient gastric acid secretion, increases the burden on the gastrointestinal tract. Long-term dyspepsia also increases the likelihood of gastric and intestinal cancer and other malignant diseases. Therefore, patients with functional dyspepsia require urgent medical attention [1]. The primary effect of mosapride, an anti-

dyspepsia drug, is to promote the secretion of gastric juice and accelerate gastric emptying [2].

Dyspepsia adversely affects the daily lives of the affected patients, since they experience bloating after meals. In consequence thereof, dyspepsia patients often suffer psychological disorders due to unhealthy emotions such as anxiety and depression [3]. In this regard, due importance should be given to psychological care and guidance during treatment of patients to avoid severe negative psychological responses.

Fluoxetine, a drug used for preventing depression and anxiety, acts by inhibiting neuronal uptake of hydroxy-tryptamine, and it also exerts anti-dyspepsia effects [4,5]. The objective of this study was to investigate the efficacy of combination of mosapride and fluoxetine in the treatment of patients suffering from functional dyspepsia-associated anxiety. Two groups of dyspepsia patients were used as research subjects. This study compared the two groups, one of which received mosapride alone, while the other was treated with combination of mosapride and fluoxetine, with respect to treatment effectiveness, scores in Mental Status Scale in Non-psychiatric Settings (MSSNS), Barthel Index (BI), Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale (SDS), time intervals for flatulence and defecation, number of intestinal sounds/rumblings, as well as levels of gastrin and cholecystokinin at post-treatment days 1, 2, 3 and 4.

METHODS

General patient profile

A total of 100 patients with functional dyspepsia-associated anxiety admitted to our hospital from January 2019 to May 2020 were retrospectively studied, and were randomly assigned to control group and study group, with 50 patients in each group. Patients in the study group were aged between 42 and 63 years, while those in the control group were aged from 44 to 65 years. Table 1 shows that general data on gender, age, history and other parameters, were comparable between the two groups ($p > 0.05$).

Inclusion/exclusion criteria

Inclusion criteria

Patients in the following categories were included: those aged ≥ 18 years, with clinical manifestations of functional dyspepsia and anxiety; patients with no other organic diseases, as well as patients who had no history of drug allergy, drug abuse and other bad habits.

Exclusion criteria

Patients with a history of digestive system disease; those with complete intestinal obstruction or mental disorder, as well as patients who were unable or unwilling to cooperate in the study, were excluded.

This study was approved by our hospital ethics committee. All patients participated voluntarily, and each one submitted written and signed informed consent.

Treatments

Patients in the control group were treated orally with moxapride tablets (Lunanbeite Co. Ltd; SFDA approval number: H19990317; specification: 5 mg) alone, at the dose of 1 tablet 3 times/day. The study group was given mosapride combined with fluoxetine. To be specific, 1 tablet of mosapride was administered orally 3 times a day. In addition, 1 tablet of fluoxetine (Eli Lilly and Company; SFDA approval number: J20170022; specification: 20 mg) was given orally once a day. The patients were asked to do exercise and rub the abdomen properly during the treatment.

Table 1: General profile of dyspepsia patients

Group	Study group	Control group	t/χ2	*P*-value
Gender (Male/Female)	25/25	27/23	0.16	0.69
Age (years)	51.61±4.45	52.08±4.77	0.51	0.61
Height (cm)	166.37±7.50	166.67±7.53	0.20	0.84
Weight (kg)	68.89±8.41	69.22±8.55	0.19	0.85
Medical history (months)	2.20±1.09	2.28±1.12	0.36	0.72
History of Smoking (years)	7.73±1.28	7.60±1.54	0.46	0.65
History of drinking (years)	10.44±2.21	10.30±2.38	0.30	0.76
Hypertension (n)	10	12	0.23	0.63
Diabetes (n)	10	7	0.64	0.42
Hypertension (cn)	6	8	0.33	0.56

Enteral nutrition support was also offered to ensure adequate intake of nutrients and reduction of the burden on the gastrointestinal tract, when necessary. Patient's emotional swings were observed too, and psychological counseling was conducted timely when negative emotions were identified.

Evaluation of treatment indices

Treatment effectiveness

Treatment effectiveness was considered *significantly effective* if dyspepsia completely disappeared, negative emotions were non-existent, and time intervals for flatulence and defecation became normal. The treatment was considered *effective* if dyspepsia and negative emotions were mitigated to a certain degree. However, the treatment was deemed *ineffective* if the patient suffered from serious adverse reactions, and the clinical symptoms were largely present.

The cutoff SAS score was fixed at 50. A score below 50 indicated *normal status*; a score within the range of 50 - 59 indicated *mild anxiety*. On the other hand, a score within the range of 60 - 69 suggested *moderate anxiety*, while a score above 70 points implied *severe anxiety*. Given that the score of 53 is usually the reference value when interpreting SDS scores, a score under 53 was deemed *normal*; a score between 53 and 62 indicated *mild depression*; a score between 63 and 72 points showed *moderate depression*, while a score more than 72 represented *severe depression*.

MSSNS score and BI score

For MSSNS, a score lower than 60 indicated *normal mental state*; a score between 60 and 70 suggested a *mildly abnormal mental state*, while a score above 70 indicated *abnormal mental state*. The BI scale ranged from 0 to 100 points, with a score of 100 indicating *good self-care ability*, that is, no extra care from others was needed. Scores between 61 and 99 indicated *basic self-care skills* and *occasional need for support*; scores between 41 and 60 suggested *low capability for self-care*, while scores below 40 showed *complete inability to look after oneself,* thereby requiring careful nursing from other people.

Miscellaneous indices

Time interval for flatulence and defecation, number of bowel sounds, as well as secretion levels of gastrin and cholecystokinin on post-treatment days 1, 2, 3 and 4 were collected and compared. The effect of gastrin is opposite to that of cholecystokinin. Gastrin is a hormone that accelerates gastric emptying and promotes digestion. However, cholecystokinin inhibits gastric secretion and gastric motility [10].

Ethical issues

This study was approved by Medical Science Research Ethics Committee of *China Medical University* (approval no. 2018 (NSTS)-8376) and international guidelines for human studies were followed [6].

Statistical analysis

All information and data in this paper were processed and analyzed using the statistical software SPSS21.0, and also put into graphs with GraphPad Prism 7 (GraphPad Software, San Diego, USA). Measurement data are expressed as mean ± SD, and were analyzed using *t*-test. Counting data are expressed as numbers and percentage [n (%)] and were analyzed with χ^2 test. Statistical significance of difference was assumed at $p < 0.05$.

RESULTS

Treatment effectiveness

In the study group, there were 33 cases of significant effectiveness, 12 cases of moderate effectiveness, and 5 cases of ineffectiveness, with the total effectiveness was 90%. In the control group, there were 16 cases of significant effectiveness, 18 cases of moderate effectiveness, and 16 cases of ineffectiveness, with the total effectiveness of 68%. Treatment effectiveness in the study group was significantly higher than that in the control group ($p < 0.05$). These results are shown in Table 2.

Table 2: Treatment effectiveness in the two groups

Variable	Significantly effective	Effective	Ineffective	Total effective
Study group (n=50)	33	12	4	45 (90%)
Control group (n=50)	16	18	16	34 (68%)
$\chi 2$				7.294
P-value				0.007

SAS and SDS scores

Figure 1 indicated that SAS and SDS scores in the study group were significantly lower than those in the control group ($p < 0.05$).

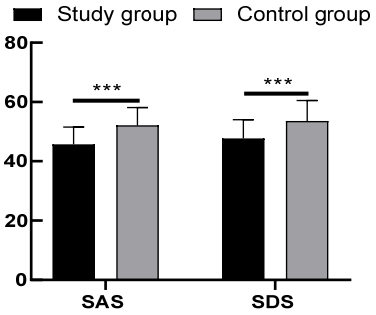

Figure 1: Comparison of SAS and SDS scores between the two groups. *** indicated $p < 0.001$

MSSNS and BI scores

Figure 2 shows that the MSSNS score of participants in the study group was significantly lower than the corresponding score of the control group ($p < 0.05$), while the rating of BI in the study group was markedly higher ($p < 0.05$).

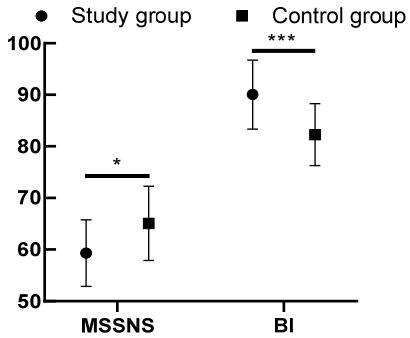

Figure 2: MSSNS and BI scores in both groups. *$P < 0.05$, ***$p < 0.001$

Time intervals for flatulence and defecation

There were statistically significant differences between the two groups of patients with regard to time intervals for flatulence and defecation. As shown in Table 3, the duration of interval measured in the study group was noticeably shorter than that in the control group ($p < 0.05$).

Number of intestinal rumblings after at post-treatment days 1, 2, 3 and 4

It was discovered from comparison of incidence of intestinal rumblings at post-treatment days 1, 2, 3 and 4 that the number of occurrences in the study group at each time point was much higher than that in the control group. ($p < 0.05$). These results are shown in Figure 3.

Table 3: Comparison of time intervals for flatulence and defecation (h)

Group	Flatulence	Defecation
Study group	14.32±2.08	39.51±6.17
Control group	18.87±2.55	47.06±7.00
T	9.78	5.72
P-value	<0.001	<0.001

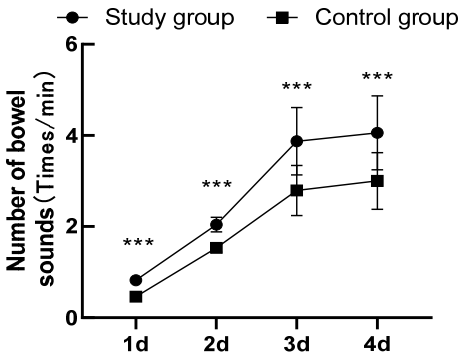

Figure 3: Comparison of number of intestinal sounds at post-treatment days 1, 2, 3 and 4. ***$P < 0.001$

Secretion levels of gastrin and cholecystokinin

The gastric and cholecystokinin levels of the study group were (86.31 ± 10.14) ng/L and (432.09 ± 33.15) ng/L; those of the control group were (73.20 ± 9.55) ng/L and (500.61 ± 38.74) ng/L. It can be seen from Figure 4 that the study group generated a much higher level of gastrin and a significantly lower level of cholecystokinin than the control group ($p < 0.001$).

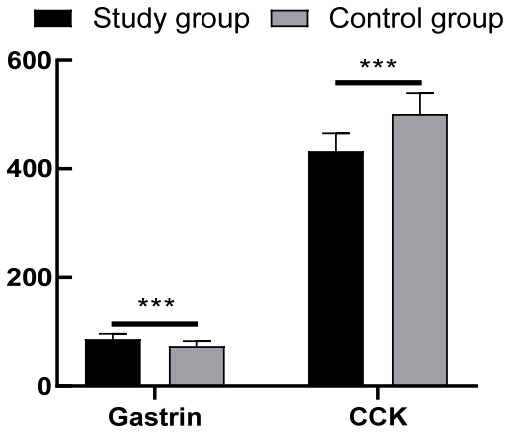

Figure 4: Comparison of the levels of gastrin and cholecystokinin. ***$P < 0.001$

DISCUSSION

The digestive system, in which the gastrointestinal tract serves as a primary part, plays a vital role in guaranteeing normal functioning of the human body [7]. Functional dyspepsia is characterized principally by defects in the digestive system, resulting in impairment of normal digestion after meals. This results in syndromes such as abdominal distension and constipation which adversely affect the daily life of patients [8]. In general, there is a decline in smooth functioning of the gastrointestinal tract among dyspepsia patients.

In addition, gastrointestinal hormonal secretion may also be affected, resulting in associated disorders [9]. Changes in mental state of humans are driven by mood, environment, external and factors within individuals, among which are variations in hormone secretions [10]. Consequently, patients with functional dyspepsia which is usually accompanied by depression, anxiety and other harmful emotions, may also experience severe mental illness when they are subjected to long-term negative mood [11].

Mosapride, a drug that acts on the digestive system and promotes gastric emptying, is effective for dyspepsia [12]. Fluoxetine not only prevents anxiety; it is also effective against dyspepsia. These two types of drugs are frequently used in clinical settings, and it has been reported that their combination produces better treatment outcomes [13-15]. In this study, patients with functional dyspepsia and anxiety were used retrospectively to compare the performances of treatment using mosapride alone, and treatment that used a combination of mosapride and fluoxetin. The parameters compared were between the two treatment groups were total effectiveness of treatment, scores of SAS, SDS and MSSNS; BI index, time intervals for flatulence and defecation, number of bowel sounds/rumblings, as well as levels of gastrin and cholecystokinin at post-treatment days 1, 2, 3 and 4.

The results demonstrated that the combination of mosapride and fluoxetine yielded significantly higher treatment effectiveness, BI index, and shorter time intervals for intestinal sounds, and higher gastric levels at post-treatment days 1, 2, 3, and 4 than the control group. These results suggest positive outcomes, improvement of therapeutic efficacy, as well as pain relief. Constipation leads to decreased intestinal motility and digestive dysfunction which may affect the elderly, resulting in decreased intestinal sounds [16].

The relief of functional dyspepsia was improved by providing mosapride and fluoxetine together. Gastrin, a hormone that promotes secretion of gastric juice, functions chiefly in enhancing digestion and gastric emptying [17]. Increased gastric secretion level is an indication of the improvement in digestion. In addition, the performance of the study group was considerably lower than that of the control group in terms of scores in SAS, SDS and MSSNS, as well as intervals for flatulence and defecation, and cholecystokinin levels.

In the study group, there was decrease in untoward manifestations such as constipation and abdominal distension, which were favored by improved psychological state, and reduced intervals for flatulence and defecation. The results of this study are in agreement with previous findings [18], in which it was reported that the use of combined treatment with fluoxetine and mosapride improved treatment effectiveness in patients with functional dyspepsia, and also reduced the clinical manifestations and possible negative emotions.

CONCLUSION

The findings of this study show that treatment of functional dyspepsia patients with anxiety using a combination of mosapride and fluoxetine produces significant improvement in effectiveness in clinical settings, with respect to therapeutic efficacy, mental health, gastrointestinal function and digestion.

DECLARATIONS

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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REFERENCES

1. *Tack J, Carbone F. Functional dyspepsia and gastroparesis. Curr Opin Gastroenterol 2017; 33(6): 446-454.*
2. *Madisch A, Andresen V, Enck P, Labenz J, Frieling T, Schemann M. The Diagnosis and Treatment of Functional Dyspepsia. Dtsch Arztebl Int 2018; 115(13): 222-232.*
3. *SE, Bolling-Sternevald E, Storskrubb T, Ronkainen J. Functional dyspepsia impairs quality of life in the adult population. Aliment Pharmacol Ther 2011; 33(11): 1215-24.*
4. *Alboni S, van Dijk RM, Poggini S, Milior G, Perrotta M, Drenth T, Brunello N, Wolfer DP, Limatola C, Amrein I, et al. Fluoxetine effects on molecular, cellular and behavioral endophenotypes of depression are driven by the living environment. Mol Psychiatry 2017; 22(4): 552-561.*
5. *Scott K, Lewis CC, Marti CN. Trajectories of Symptom Change in the Treatment for Adolescents With Depression Study. J Am Acad Child Adolesc Psychiatry 2019; 58(3): 319-328.*
6. *Department of Health, Education, and Welfare; National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report. Ethical principles and guidelines for the protection of human subjects of research. J Am Coll Dent 2014; 81(3): 4-13.*
7. *Clarke G, Stilling RM, Kennedy PJ, Stanton C, Cryan JF, Dinan TG. Minireview: Gut microbiota: the neglected endocrine organ. Mol Endocrinol 2014; 28(8): 1221-38.*
8. *Camilleri M, Stanghellini V. Current management strategies and emerging treatments for functional dyspepsia. Nat Rev Gastroenterol Hepatol 2013; 10(3): 187-94.*
9. *Ogiso K, Asakawa A, Amitani H, Inui A. Ghrelin: a gut hormonal basis of motility regulation and functional dyspepsia. J Gastroenterol Hepatol 2011; 26 Suppl 3: 67-72.*
10. *Lange-Asschenfeldt C, Kojda G, Cordes J, Hellen F, Gillmann A, Grohmann R, Supprian T. Epidemiology, symptoms, and treatment characteristics of hyponatremic psychiatric inpatients. J Clin Psychopharmacol 2013; 33(6): 799-805.*
11. *Van Oudenhove L, Vandenberghe J, Vos R, Holvoet L, Demyttenaere K, Tack J. Risk factors for impaired health-related quality of life in functional dyspepsia. Aliment Pharmacol Ther 2011; 33(2): 261-74.*
12. *Yang YJ, Bang CS, Baik GH, Park TY, Shin SP, Suk KT, Kim DJ. Prokinetics for the treatment of functional dyspepsia: Bayesian network meta-analysis. BMC Gastroenterol 2017; 17(1): 83.*
13. *Luo L, Du L, Shen J, Cen M, Dai N. Benefit of small dose antidepressants for functional dyspepsia: Experience from a tertiary center in eastern China. Medicine (Baltimore) 2019; 98(41): e17501.*
14. *Siroosbakht S, Rezakhaniha S, Rezakhaniha B. Which of available selective serotonin reuptake inhibitors (SSRIs) is more effective in treatment of premature ejaculation? A randomized clinical trial. Int Braz J Urol 2019; 45(6): 1209-1215.*
15. *Oliva V, Lippi M, Paci R, Del Fabro L, Delvecchio G, Brambilla P, De Ronchi D, Fanelli G, Serretti A. Gastrointestinal side effects associated with antidepressant treatments in patients with major depressive disorder: A systematic review and meta-analysis. Prog Neuropsychopharmacol Biol Psychiatry 2021; 109: 110266.*
16. *Najeeb-ur-Rehman, Mehmood MH, Al-Rehaily AJ, Mothana RA, Gilani AH. Species and tissue-specificity of prokinetic, laxative and spasmodic effects of Fumaria parviflora. BMC Complement Altern Med 2012; 12: 16.*
17. *Petersen KU. Pepsin and Its Importance for Functional Dyspepsia: Relic, Regulator or Remedy? Dig Dis 2018; 36(2): 98-105.*
18. *Azadbakht S, Azadbakht S, Esmaili A, Rahmani P. Comparison of clinical symptoms after Helicobacter pylori eradication in functional dyspepsia patients based on endoscopic view of antral gastropathy. New Microbes New Infect 2020; 38: 100806.*