ORIGINAL ARTICLE

Functional dyspepsia treatment in Persian Medicine A mini-review and case series of 12 adults

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ABSTRACT

Background: Gastrointestinal diseases are very common in different populations in the world**.** Dyspepsia can be defined as various groups of symptoms localized in the epigastric region**.** Functional dyspepsia is a relapsing and remitting disorder. There are different unpromising and unsatisfactory interventions for functional dyspepsia in conventional medicine with no complete cure. In addition, the patients should always use the drugs to control the annoying symptoms, imposing additional costs on them.

Aim: To evaluate the patients treated by Persian Medicine as a complementary therapy**.**

Method: The cases were 12 patients referred to Persian Medicine physicians in the Motahari clinic affiliated to SUMS (Shiraz University of Medical Sciences) in 2015-2016. All patients had received conventional treatments with undesirable response, so they were referred to Persian Medicine physicians. Those patients diagnosed with cold/wet dystemperament of GI - according to Persian Medicine principles - were included in our study. The average follow up for the patients was 45 days**.**

Results: In this study, 83% (10 of 12) of the patients were female and 17% (2 of 12) male. The mean age of the patients in our study was 29.2 years. The patients' chief complaints were different: anorexia, heartburn, abdominal pain, and flatulence. Other complaints included overweight, increased appetite, headache, and sinusitis. Of 5 patients who complained of heartburn, 3 showed improvement in heartburn symptoms. Of 5 patients with flatulence, 3 showed improvement. 4 patients had increased appetite. Of the 6 patients with complaint of abdominal pain,4 improved. Of the 2 patients who didn't show any improvement, one was due to doxycycline consumption and the other patient improved by the second follow up (Table 1).

Conclusion: According to our study, Persian medicine treatments in functional dyspepsia can be considered as a safe complementary therapy in patients with poor response to conventional treatments. This preliminary study is an introduction to well-designed clinical trials in TPM department to evaluate the aforementioned claims in near future.

Keywords: dyspepsia, functional dyspepsia, Persian medicine

INTRODUCTION

Gastrointestinal diseases are very common in different populations in the world[1]. Dyspepsia can be defined as various groups of symptoms in the epigastric region. Also, it can be defined as pain or discomfort centered in the upper abdomen (especially the epigastrium)[2]. Functional dyspepsia is a relapsing and remitting disorder considered the most common cause of symptoms pertaining to the epigastric region[3]. Prevalence of functional dyspepsia globally is between 5% and 11%[3]. The annual global incidence rate of dyspepsia is estimated between 1% and 6%[2]. In Asia, 8%-30% of people suffer from uninvestigated dyspepsia and 8%-23% of them suffer from functional dyspepsia[4]. In Iran, the prevalence of dyspepsia ranges from 2.2% to 29.9%[5]. Dyspepsia is generally categorized into two groups: functional (dysmotility like) and structural (ulcer like). In endoscopic studies, it has been shown that the majority of the cases of dyspepsia are functional[5]. The Rome III criteria for definition of functional dyspepsia is the presence of chronic dyspeptic symptoms and the absence of simultaneous underlying structural or metabolic disease that readily explains the symptoms[2].Rome III criteria define functional dyspepsia as early satiety (inability to finish a normal-sized meal) or fullness during or after a meal, sensation of pain or burning in the epigastrium, or a combination of these symptoms. These symptoms must occur at least weekly and be chronic; also, an organic explanation should be absent and these symptoms must be over a period of at least 6 months[3]. Currently, the first-line treatments recommended for functional dyspepsia is antisecretory or prokinetic agents. Antisecretory and prokinetic agents are used for functional dyspepsia in patients with ulcer-like dyspepsia and dysmotility-like dyspepsia, respectively. Treatment of functional dyspepsia with antianxiety or antidepression agents may also be helpful; however, it should be investigated in future clinical trials. Serotonin type-3 receptor antagonists or opioid agonists are the agents considered to reduce visceral hypersensitivity. Eradication therapy for *Helicobacter pylori* infection can be helpful; however, its efficacy has not been confirmed yet[6]. Functional dyspepsia Treatment with conventional medicine is unsatisfactory. Primary treatment tfor those patients who have mild symptoms of functional dyspepsia is life style changes and reassurance. Proton pump inhibitors (PPIs) and Prokinetics are good choices for empirical pharmacotherapy in patients who have severe symptoms of functional dyspepsia or are unresponsive to the latter treatment. Special cases who were diagnosed with functional dyspepsia can benefit from psychiatric or

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psychotherapist consultation and consumption of antidepressant drugs. Surgical interventions are also proposed by some researchers to relieve the symptoms, but some side effects may appear later after the surgery. The gold standard treatment for anatomic correction of cardia is Niessen fundoplication, especially in those patients who have typical symptoms of heartburn and regurgitation. Many patients complain of retching and bloating after antireflex surgery. On the other hand, this surgery controls the GE refluxes in afflicted patient[1].Persian Medicine, also called humoral medicine, is based on the four humors (bile, blood, phlegm, black bile). Imbalance in humoral equilibrium (dystemperament) including the GI system may result in organ disorder. Elites of Persian Medicine believe that gastrointestinal (GI) system has a major role in health maintenance. If the GI system works properly, the result is production of normal humors in a balanced quality and quantity (*mezaj-e-sehhi*)[7]. Digestion is the main task of the GI systemand any condition affecting the GI system function may result in dystemperament[8,9].The signs and symptoms of dyspepsia have been mentioned in Persian Medicine (PM) texts, but there is no definite terminology describing dyspepsia in PM texts[8,10,11]. In Persian Medicine, GI diseases are the result of the body organs' dissociation (*Tafarrogh-e-ettessa'l*), dystemperament (*Su'e-mezaj*), or both[8]. There are specific signs and symptoms for each dystemperament. Detection of the originalorgan temperament (*mezaj-e-khelqati*) and the acquired one (*mezaj-e-âdati*) necessitatesa comprehensive history and physical exam[12]. After the detection of the organ temperament, the therapeutic strategies which return the organ to its default condition includes: principles of preventive health measures (PM) (*ossul-e hefz-o-sehheh*), or/and simple medicines (*daru-ye mofradeh*) or/and compound medicines (*daru-ye-morakkabeh*) or/and physical interventions (*a'mal-e-yadavi*). There is no equivalent term for functional dyspepsia in Persian Medicine, however, similar signs and symptoms can be detected in terms like indigestion, digestion debility and simple cold dystemperament of the stomach in Persian Medicine references[1]. Dyspepsia has considerably reduced the quality of life in the afflicted patients, especially those having functional dyspepsia[2]. Functional dyspepsia imposes a notable burden on the society due to the use of healthcare resources, work absenteeism, and reduced productivity[4].

Functional dyspepsia treatment in conventional medicine is unpromising and unsatisfactory and there is no complete cure by conventional treatments. In addition, the patients should always use the drugs to control the disease and this will impose additional costs to the patient. Accordingly, we aimed to evaluate the patients treated by Persian Medicine as a complementary therapy and follow the treatments in a case series study.

METHOD

In this case series study, we used the data of 12 patients referring to Persian Medicine physicians in the Motahari clinic affiliated to SUMS (Shiraz University of Medical Sciences) in 2015-2016. These patients first received conventional treatments, but didn't respond to it, so they were referred to Persian Medicine physicians. Those patients who were diagnosed with cold/wet dystemperament of GI- according to Persian Medicine principles - were included in our study. At first, the patients were advised to use preventive health measures (PM) (*hefz-o-sehheh*), which includes air, eating-drinking, sleep-wake, activity-rest, retention-release and mental states in order to alleviate their annoying symptoms. The most important nutritional measures comprised chewing well, drinking water and other drinks out of meal time, using the simple kind of food in a meal and using dairies and meats in different meals and not in a single meal, considering at least 2 hours distance between meal and using fruits, avoiding junk foods and making proper distance (at least 2 hours) between eating and strenuous physical activity, intercourse as well as bathing[9]. The average follow up for the patients was 45 days. Two patients had second follow up.

RESULTS

The results are displayed in Table 1. In this study,83% (10) of the patients were female and 17% (2) were male. The mean age of the patients in our study was 29.2 years. The chief complaint of patients was different: Anorexia in 3 patients, heartburn in 4 patients, abdominal pain in 5 patients, and flatulence in 3 patients. Other complaints included overweight, increased appetite, headache, and sinusitis. As to the patients who developed a drug reaction in the form of urticaria after 10 days of treatment, we advised to use the drug once a day instead of twice a day. Of 5 patients who complained of heartburn, 3 had improvement in heartburn symptoms. Of 5 patients who had flatulence, 3 showed improvement. Of the 2 patients who didn't have improvement, one improved by the second follow up. 4 of the patients increased appetite. One of the patients with overweight decreased his weight by 2 kilograms. Of the 2 patients with increased weight, one used doxycycline in the course of treatment so had recurrence in gastric pain. Of the 6 patients with complaint of abdominal pain, 4 had improvement. Of the 2 patients who didn't have improvement, one was due to doxycycline consumption.

DISCUSSION

In our study, the patients received treatments with herbal drugs according to their diagnosis in Persian medicine. Most of the patients were advised to avoid cold and wet foods, because all of the patients were diagnosed with cold and wet dystemperament of GI. In Persian medicine (PM), the first line of treatment is using preventive health measures(*hefz-o-sehheh*)[13]. The second line of treatment is avoidance of foods which have the same quality as the dystemperament of the organ[14]. *Lallemantiaroyleana* seed (*balangu*) was prescribed for six of the patients. *Balangu* seeds have antioxidant activity. It seems that phenolic constituents of *balangu*seeds in addition to unsaturated fatty acids (including linoleic and oleic acid) may account for its antioxidant property[15].Cumin was prescribed for 5 of the patients. In traditional medicine, cumin is used widely for treatment of digestive disorders, diarrhea, and flatulence and in the treatment of wounds. Also, cuminis

beneficial inhoarseness, dyspepsia and is used as a remedy for indigestion and colic. There is a high amount of dietary fiber in cumin and depending upon the varieties it is up to 59%. Two potential sources of natural antioxidants in foods are cumin and ginger[16]. Cumin was used in the form of half-comminuted (*nimkub*) with comminuted rock candy (*nabat*). Coriander with triphala (triphala=*etrifel*) was prescribed for two of the patients and coriander *sofoof* (powder)was prescribed for one patient.*Coriandrum sativum* (coriander)and Umbelliferae seeds have medical effects as a drug for rheumatism, joints pain, worms and indigestion. Also, studies have demonstrated effects on carbohydrate metabolism and the hypoglycemic action of coriander seeds. Both seeds and leaves have volatile components in essential oil that has been reported theinhibitor of lipid peroxidation and some micro-organisms' reproduction. Coriander has antioxidant activity and coriander leaves have shown stronger antioxidant activity than the seeds[17].Traditionalmedicine recommends coriander and caraway for fullness, flatulence, spastic conditions of the gastrointestinal tract, and loss of appetite due to their antispasmodic and antimicrobial actions. However, inconventional Medicine ,they are recommended only for dyspeptic problems. Use of coriander and caraway is sometimes restricted because allergic contact dermatitis may occur. In the study of Samojilik, in vitro and in vivo antioxidant effects of chemically characterized essential oils of caraway (*Carum Carvi*) (Apiaceae) and coriander (*Coriandrum sativum*) are reported[18]. In Persian medicine,coriander with triphala (triphala=*etrifel*), cumin and *balangu*seed are tonifying agents for the GI system[8,19]. There are some similarities to functional dyspepsia symptoms among the12 types of dystemperaments arising from the stomach. Simple cold/moist dystemperament without excess humor is the closest condition to functional dyspepsia in Persian medicine. The signs and symptoms of functional dyspepsia in Persian medicine are nearly the same asthose of Rome III criteria for functional dyspepsia. In physical exam, some signs are present which include symptoms like postprandial fullness and abdominal discomfort and weak digestion, but all the necessary criteria are not fulfilled. In Persian medicine, treatment of gastric temperaments is different from conventional medicine although there are some similarities including promoting mental health and changing dietary habits and lifestyle. For instance, a modality that can decrease the chance of GE reflux in infants with GERD is havingright decubitus position in the first postprandial hour and then changing to the left decubitus position. This is a frequent advice found in Persian medicine textbooks. Regulating the dietary habits (quality, amount, time, order and temperament of ingesting drink or food) is very important and it may be curative by itself. Using a proper herbal drug in different dosage forms is the next step in therapeutic protocols of Persian medicine for gastric dystemperament[1]. Scientists of Persian medicine believe that there is a basic role for the stomach in the body health. Stomach functions as a main system in supplying other organs' demands such as growth and development; if it works properly, balanced humors will be produced, which is crucial for health[20]. Stomach is the main route for food entrance and digestion, so in Persian medicine principlesis considered as one of the most important organs[9]. There is no definitive evidence for the correlation between H.Pylori and dyspepsia despite many studies that have been conducted on this issue[5]. In one study that was conducted in Ilam, the increase in prevalence of dyspepsia was claimed to be related to changes in lifestyle and dietary habits (including fast food consumption)[21] . A meta-analysis which was published in 2003 showed that antisecretory agents such as histamine-2 receptor antagonists were significantly superior to placebo (relative risk reduction, 22%). As to proton-pump inhibitors (PPIs), 38% of patients who used omeprazole 20mg showed complete symptom relief compared with 28% on placebo (P = 0.002). Also, prokinetic agents were reported to be significantly superior to placebo (relative risk reduction, 40%)[6]. Emami Alorizi et al. designed a study for assessment of effects of Persian medicine measures and recommendations for management of functional chronic constipation compared to classic medicine lactulose. The study showed that the effectiveness of lactulose-a gold standard in the management of constipation- was equal to the studied schemes. The study concluded that TPM schemes and recommendations, as lifestyle modification, for at least 3 months can be introduced as accessible, available and cheap approaches for the management of constipation[22]. A study carried out by Zohalinezhad et al. compared the pharmaceutical effects of *Myrtus communis* (myrtle) with omeprazole in reflux disease through a double blind randomized controlled clinical trial. It concluded that there was no significant difference between the groups of the study[23]. These studies showed that Persian medicine recommendations may be an effective complementary therapy beside conventional treatments, however more randomized controlled clinical trials are needed to prove it. Also in our study, we insisted on preventive health measures in the first and the most important strategy of treatment. According to our study, Persian medicine treatments in functional dyspepsia can be a safe complementary therapy in patients which do not respond to conventional treatments and seek alternative medical care. Also, we believe that Persian medicine treatments may be used as a complementary therapy beside conventional methods for treatment of functional dyspepsia. Furthermore, according to PM view, the probable mechanism of action of PM measures in relieving symptoms of dyspepsia is evacuation of GI tracts out of phlegm and moistures as well as tonifying effect of herbal remedies on stomach due to tannin compounds. Accordingly, lifestyle changes, especially correcting diet, could improve digestion and remove the annoying moisture in the GI tract and even play a role in the eradication of *H. pylori*, as we found in some cases in clinics. In sum, we hope to conduct well-designed clinical trials in the TPM department to evaluate the aforementioned claims in near future.

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Table 1. Summary results of patients with GI problems treated with TPM's recommended modality

ID	AGE	SEX	Chief complaint	Diagnosis of Persian medicine	Diagnosis of modern medicine	Treatment	F/u after 45 days
1	54	F	Heartburn	Cold/wet dystemperament of GI	functional dyspepsia + reflux	First treatment: Preventive health measures. Avoidance of cold and wet foods. Coriander + triphala [1]. half grinded cumin + grinded rock candy (#).*Balangu* [2] seed. Second treatment: D/C [3] Coriander + triphala and #. Coriander powder (*sofoof*) after food. Continue *Balangu* seed.	Heartburn ↓ (50%)
2	30	F	Heartburn + Headache + sinusitis	Cold/wet dystemperament of GI	functional dyspepsia + reflux	First treatment: Preventive health measures. Avoidance of cold and wet foods. *Balangu* seed. half grinded cumin + grinded rock candy Second treatment: Thyme potion.	After 1 months: GI problems (no change) Loss to f/u Telephone f/u: Gastric pain and headache ↓ (50%) flatulence (no change)
3	38	F	Feeding fullness	Cold/wet dystemperament of GI	Functional dyspepsia + maldigestion	First treatment: Preventive health measures. Avoidance of cold and wet foods. Mood elevator syrup (*neshat* syrup)[4] and*Balangu* seed twice a day. Second treatment: The use of the above drug once a day due to drug reaction of urticaria, instead of twice a day. Lamb juice, compound of rose and honey (*golghand*) and half-boiledegg advised (for ↓weakness).	The first 10 days: GI problems ↓ (50%) but then developed urticaria, so we advised them to use the drugs once a day. + severe generalized weakness
4	28	M	Heartburn + flatulence	Cold/wet dystemperament of GI (and liver)	Functional dyspepsia + Acid peptic disease	First treatment: Preventive health measures. Avoidance of cold and wet and flatulent foods. Liver capsule [5]. *Balangu* seed Second treatment: D/C *Balangu* seed continue liver capsule .Stew regimen	Heartburn and flatulence ↓ (75%) Weight ↑ (satisfied) Appetite ↑ (50%)
5	32	F	Overweight +GI problems	Cold/wet dystemperament of GI	Functional dyspepsia + Ge reflux + overweight	First treatment: Preventive health measures. Avoidance of cold and wet foods. *Balangu* seed . Coriander powder (*sofoof*). Lemon balm [6] potion (for ↓ stress). Thyme potion. honey (for ↓ weakness) Second treatment :Decrease Thyme potion. Third treatment: *Javaresh khozi*[7]. steam of *Origanum majorana* or thyme.Thyme potion. Lemon balm potion.	First f/u : GI problems cured weight ↓ (satisfied) (2 kilograms) Second f/u : Due to doxycycline consumption, the pt experienced recurrence of gastric pain. Weakness (cured). + Many PND.
6	35	F	Heartburn + Severe flatulence + hair loss	Cold/wet dystemperament of GI	Functional dyspepsia	First treatment: Preventive health measures. Avoidance of phlegm and dense and wet-cold foods. *Balangu* seed. Half grinded cumin + grinded rock candy. Oxymel.Quince paste. Second treatment :continue the previous drugs	Heartburn ↓ (50%) Reflux ↓ (50%) Flatulence ↓ (50%)
7	48	F	Stomach pain + Anorexia + Generalized weakness	Cold/wet dystemperament of GI and dryness of CNS	Functional dyspepsia	First treatment: Preventive health measures. Coriander + triphala. Almond and violet oil.Zante currants .Apple sauce. Oxymel. white tea (*Camellia sinensis)* Second treatment : Whey powder. Grated apple. D/C Coriander + triphala and oxymel.	Gastric pain ↓ (25%)
8	4	M	Abdominal pain	Cold/wet dystemperament of GI	functional dyspepsia + reflux	First treatment: Preventive health measures. Avoidance of cold, wet, flatulent and dense foods. Quince paste. Coconut powder. Oxymel. {Half grinded cumin + grinded rock candy}. (#) Second treatment:D/C coconut powder. continue oxymel and #	Thirst ↓ (50%) Night Drooling ↓ (50%) Abdominal pain (no change) Appetite ↑ (50%) Weight ↑ (satisfied) Flatulence ↓ (50%)
9	4.5	F	Abdominal pain	Cold/wet dystemperament of GI	Functional dyspepsia	First treatment: Preventive health measures. Avoidance of thick foods. Oxymel.	Abdominal pain (cured) Appetite ↑ (75%)

						{Half grinded cumin + grinded rock candy + coconut powder}. (@) Second treatment: D/C oxymel. decrease @ consumption.	
10	45	F	Flatulence + stomach pain + increased appetite	Cold/wet dystemperament of GI	Functional dyspepsia	First treatment: Preventive health measures. Oxymel.*javaresh khozi*. lemon balm potion. Thyme potion. White tea (*Camellia sinensis*) + rose flower. Second treatment : Grated apple. Continue oxymel consumption. Half grinded cumin + grinded rock candy. Continue lemon balm potion. *Sphidbaj* porridge. *Mentha pulegium*. Thyme potion Third treatment: Celery seed. Fennel[8]. *Pimpinella anisum. Mentha pulegium* + rose and honey (*golghand*)	First f/u: GI problems ↓ (25%) + flatulence Second f/u : Flatulence ↓ (75%) GI problems ↓ (50%)
11	7	F	Abdominal pain + anorexia	Cold/wet dystemperament of GI	Functional dyspepsia + reflux	First treatment: Preventive health measures. Avoidance of dense and wet-cold foods. Honey. Triphala. Fruit juice .pickle. Onion and pomegranate paste. Recommend fried foods. Second treatment: Continue previous avoidances. Continue triphala. Almond nut. Pistachios. Pumpkin seeds.	Abdominal pain ↓(75%)(once in two months) Constipation (cured) + Anorexia.
12	26	F	Anorexia	Cold/wet dystemperament of GI (including liver) Dryness of CNS	Functional dyspepsia + reflux	Preventive health measures. Honeycomb. Grated apple and saffron. Almond nut. White tea (*Camellia sinensis*) + saffron +*Echium amoenum* + *Citrus aurantifulia*. Rub almond oil on fontanel	Appetite ↑ (50%)

1- Triphala (*etrifel*):*Emblica officinalis* + *Terminalia bellirica*+ *Terminalia chebula*
2- Balangu: *lallemantia royleana*
3- D/C: discontinue
4- Mood elevator syrup (*neshat* syrup):saffron + smelling *apple*
5- Liver capsule: coriander seed +*Fumaria officinalis* + lettuce seed+ *Ziziphus zizyphus* + *Cichorium intybus*seed + Thyme leaves + *Cassia angustifolia*+ *Rheum officinale*
6- Lemonbalm:*Melissa officinalis*
7-*Javaresh khozi*: *Terminalia chebula*+ *Trachyspermum ammi* + *Thymes vulgaris*
8- fennel:*Foeniculum vulgar*