IJMS
Vol 30, No 3, September 2005

Original Article

Effects of *Ocimum Basilicum* on Functional Dyspepsia: a Double-Blind Placebo-Controlled Study

M. Rafieian-kopaei,[1] K. Hosseini-asl[2]

Abstract

Background: Traditionally some people employ *Ocimum basilicum* (Shaspram) to relieve the symptoms of dyspepsia. We therefore studied the effects of oral extract of this medicinal plant on functional dyspepsia.

Methods: In a double-blind placebo-controlled clinical trial, the effect of a four-week treatment of Shaspram was evaluated on functional dyspepsia. Two hundred cases from all patients referred for dyspepsia without having any obvious pathologic signs were randomly divided into case and control groups (100 each). The hydroalcoholic extract of leaves of Shaspram was prepared and used. Patients were asked to have 30 drops of prescribed medications (placebo or the extract, equal to 1.5 gram leaves powder) daily at 30 min before lunch and dinner for four-weeks. Severity was scored for each symptom on a numbered scale and the results compared with the results of placebo group or pretreatment period.

Results: Patients in drug group responded to treatment better than patients in placebo group ($P<0.001$). Shaspram was more effective in female and young patients. Patients with functional dyspepsia that had dysmotility problems also responded to Shaspram better than others.

Conclusion: *Ocimum basilicum* seems to relieve the symptoms of functional dyspepsia especially in female and young patients with dysmotility.

Iran J Med Sci 2005; 30(3): 134-137.

Keywords ● *Ocimum basilicum* ● functional dyspepsia ● dysmotility

Introduction

Dyspepsia refers to an intermittent or recurrent pain or discomfort centered in the upper abdomen.[1] It is a common problem affecting up to one forth of adults in western countries.[2] Most patients with dyspepsia do not show a structural or biochemical abnormality identified on routine diagnostic procedures to explain the problem.[2] These patients are considered to have functional or non-ulcer dyspepsia (NUD).[3]

The pathophysiological mechanisms of non-ulcer dyspepsia are poorly understood.[4] It has been related to a variety of abnormalities including delayed gastric emptying of solid food,[4] failure of gastric fundus relaxation postprandially,[5] visceral

Cellular and Molecular Research Center,[1] and Department of Gastroenterology,[2] Shahrekord University of Medical Sciences, Sharekord, Iran.

Correspondence:
M Rafieian-kopaei PhD,
Cellular and Molecular Research Centre,
Shahrekord University of Medical Sciences,
Shahrekord, Iran.
Tel: +98 381 3330052
Fax: +98 381 3334911
E-mail: Rafieian@yahoo.com

hypersensitivity to mechanical distension,[3,4] and *H pylori* infection.[2] Non-ulcer dyspepsia affects a heterogeneous group of patients.[6] Therefore, attempts have been made to categorize them based on symptom clusters.[6]

Talley and his colleagues have divided NUD into three symptom subgroups.[6] 1) Ulcer-like dyspepsia in which pain is centered in the upper abdomen as the predominant symptom. 2) Dysmotility-like dyspepsia, in which unpleasant or troublesome non painful sensation is centered in the upper abdomen as the predominant symptom, and other symptoms including upper abdominal fullness, early satiety, bloating, or nausea. 3) Unclassified or nonspecific dyspepsia in which symptoms do not fulfill the criteria for ulcer-like or dysmotility-like dyspepsia.

The categorization of dyspepsia was introduced for the sake of better treatment. For example, patients with dysmotility-like symptoms should respond best to prokinetics, whereas patients with ulcer-like dyspepsia should respond best to antisecretory therapy.[4,6] Other groups of medications for NUD include antacids, cytoprotectors, *H pylori* eradicators, visceral hypersensitivity reducers, antispasmodics, antidepressants, and antiemetics have been employed for treatment of NUD, however, none of them are satisfactory.[6]

Ocimum basilicum (Shaspram4) is a medicinal plant, which is used to reduce inflammation and itching,[7] cough and bronchitis, chills and common colds, nervous exhaustion, mental fatigue, melancholy or fear.[7] It is also used to treat hyperlipidemia, and infections. It has been recommended to relieve symptoms of dyspepsia. In this study we have investigated the effects of hydroalcoholic extract of Shaspram on functional dyspepsia.

Patients and Methods

A double-blind placebo controlled clinical trial was conducted to compare the effects of a four-week treatment of Shaspram with control group on functional dyspepsia. Participants were selected from those referring to the Edoscopy division in Haajar Hospital of Shahrekord University, Shahrekord, Iran, for dyspepsia. The patients had functional dyspepsia for at least three months. A total of 200 patients with functional dyspepsia, who were more than 15 years old, and had non ulcer dyspepsia in endoscopic examinations, were invited to participate in the trial. Patients were designated into drug and control groups. Patients with a history of previous peptic ulcer disease, having symptoms related to irritable bowel syndrome, biliary disease, pregnancy, daily intake of non-steroidal anti-inflammatory drugs (NSAIDs), bismuth, and antibiotic, intake of H_2-blockers or proton pump inhibitors were excluded. Patients with organic causes of gastroparesis (*e.g.* diabetes mellitus) and other serious diseases (including drug dependencies, any bowel surgery or malignancy) and patients having mild dyspepsia were also excluded.

Methods

Proper information regarding the use of medications was provided to patients and informed consent was obtained before entry. Severity was scored for each symptom on a numbered scale (1 to 4 for each symptom) which is accepted as a tool for evaluating symptoms.[8,9] Patients were designated as mild (1-13), moderate (14-26), severe (27-39), and very severe (39-52), based on the total dyspepsia score (52).[9]

Hydroalcoholic extract of Shaspram, obtained from Gol-daru, Isfahan, Iran) was prepared by percolation method by keeping 1.5 kg of leaves powder in 2.2 liters of 80^o ethyl alcohol for 48 hrs and then filtered.[10] The resultant extract was evaporated in 80°C, to have a solution with final volume of about 160 ml. Then, 100 ml ethyl alcohol was added to this solution, to increase the solubility and final volume of the solution was reached to two litters by adding distilled water. The placebo was the base of the extract containing 5^o ethyl alcohol solution. The resultant solution and the placebo were placed in similar and separate drop containers and coded 1 and 2 by a pharmacist.

The gastroenterologist prescribed the drugs with codes of 1 or 2, without of being aware of the contents until the end of the study. Patients were asked to have 30 drops of prescribed medications (placebo or the extract, equal to 1.5 g leaves powder) daily at 30 min before lunch and dinner. The patients were visited by the gastroenterologist every 8-10 days for four weeks to a checkup and get the assurance of taking their daily medications. After a four-week treatment period, the obtained results were compared with those of pretreated period and placebo treated group.

Statistical analyses

Symptoms obtained from patients were designated as mild (1-13), moderate (14-26), severe (27-39), and very severe (39-52), based on the total dyspepsia score of 52.[9] Results of Shaspram treated and placebo groups before and after treatment are compared using χ^2 test. Student's t-test was also used to compare the severity of scores between the two groups and $p<0.05$ was considered as statistically different.

Table 1: Number of patients in relation to functional dyspepsia subtypes (FDS) at the beginning of the study in Shaspram treated and placebo groups

FDS	Age (yrs)	Ulcer-like		Dysmotility-like		Nonspecific		Total
		Gender #		Gender #		Gender #		
		Male	Female	Male	Female	Male	Female	
Treated	42±11	15	21	22	35	3	4	100
Placebo	39±11	11	32	15	32	4	6	100

Results

The mean±SD ages of drug and placebo treated groups were 42±11 and 39±10.6 yrs respectively. Sixty percent of patients of Shaspram treated group and 70% of placebo group were female. There were no statistical differences for age, or sex in two groups before treatment. The number of patients in relation to functional dyspepsia subtypes (Table 1), or severity of functional dyspepsia (Table 2), were statistically the same.

Table 2: Number of patients before and after treatment based on the severity of functional dyspepsia

group	treatment	MI #	MO #	S #	VS #
Treated	*before	0	52	43	5
	**after	79	5	13	3
Placebo	before	0	46	48	6
	after	26	32	36	6

Mild (MI; 1-13), Moderate (MO; 14-26), Severe (S; 27-39), and very severe (VS; 39-52), based on the total dyspepsia score (52).[9]
*p<0.05 between treated and placebo groups before treatment.
**P<0.001 between treated and control groups following treatment

Only five patients from placebo group and two patients from Shaspram treated group did not follow the four-week study procedures and dropped out. These patients were substituted with new participants.

Patients in drug group responded to treatment better than patients in placebo group (Table 2; p<0.001). Patients of drug treated group with dysmotility-like dyspepsia showed 80.25% and patients with other subtypes of functional dyspepsia demonstrated 43.75% reductions in the severity score (p<0.05).

Discussion

The aim of this study was to assess the effect of Shaspram on functional dyspepsia. Patients in Shaspram treated group responded to treatment better than those of in placebo group. Since the pathophysiology of functional dyspepsia is imperfectly understood, it is difficult to evaluate the mechanisms involved in the effect of Shaspram on functional dyspepsia. Disturbed sensory function, disturbed motor function, duodenogastric reflux, increased gastric acid secretion, mucosal inflammation, *H pylori* infection, psychosocial factors and alterations of the central nervous system are factors which have been postulated to be involved in the pathogenesis of functional dyspepsia.[2,6] Therefore, more than one of these factors may interact with the effects of Shaspram on functional dyspepsia.[7]

Patients with dysmotility problems (pure dysmotility-like, reflux-dysmotility, ulcer dysmotility-like and ulcer-reflux dysmotility-like dyspepsia) benefited from Shaspram more than others. The relevance of gastrointestinal motor disturbances in functional dyspepsia has already been established.[3] Eugenol, the major chemical content of Shaspram, has been shown to reduce gastrointestinal motility.[7] However, other mechanisms might get involved in the effects of Shaspram on functional dyspepsia. It is so because prokinetic drugs, which increase GI motility, have shown to be useful in functional dyspepsia.[9] Eugenol has also demonstrated an anti-stress activity, a factor that may cause dyspepsia.[11] In this regard, Shaspram was found to possess a significant antiulcer activity against stress-induced ulceration in experimental animals,[11] and this may strengthen this conclusion.

Shaspram has been demonstrated to decrease acid and pepsin outputs.[12] These effects enhance gastric mucosal strength and possibly reduce the generation of peptic ulcer and thereby benefit patients with dyspepsia.[6] The extract of Shaspram has also yielded appreciable quantities of linoleic acid,[7] which has been shown to possess significant anti-inflammatory activity.[13] This effect was related to inhibition of arachidonate metabolism by linoleic acid.[13] It has been suggested that linoleic acid of Shaspram blocks both cyclo-oxygenase and lipo-oxigenase pathways of arachidonate metabolism which is responsible for the anti-inflammatory activity of this agent.[13] Therefore, it seems that Shaspram might have multiple mechanisms responsible for the improvement of functional dyspepsia.

Conclusion

A mutual anti-inflammatory and antidyspepsia (or antiulcer) effect of *Ocimum bacilicum* is notable. Most anti-inflammatory drugs, such as non-steroidal anti-inflammatory drugs or glucocorticosteroids, induce peptic ulcer or dys-

pepsia. Therefore, patients with inflammatory disorders along with gastrointestinal disease may tolerate *Ocimum bacilicum,* a natural product, better than non-steroidal anti-inflammatory or steroid drugs.

Acknowledgment

We would like to thank Dr. Hamid Khalilian and Dr. Majid Rohi for their research help, Dr. Hossein Kheiri for his statistical advice, and to vice-presidency in research, Shahrekord University of Medical Sciences, for financial support of the study.

References

1 Talley NJ. Drug treatment of functional dyspepsia. *Scand J Gastroenterol* 1991; 26: 47-60.
2 Talley NJ, Stanghellini V, Heading RC, et al. Functional gastrodoudenal disorders. *Gut* 1999; 45: 37-42.
3 Stanghellini V, Tosetti C, Paternico A, et al. Risk indicators of delayed gastric emptying of solids in patients with functional dyspepsia. *Gastroenterology* 1996; 110: 1036-42.
4 Stanghellini V, Corinaldesi R, Tosetti C. Relevance of gastrointestinal motor disturbances in functional dyspepsia. *Baillieres Clin Gastroenterol* 1998; 12: 533-44.
5 Holtmann G, Goebell H, Talley NJ. Functional dyspepsia and irritable bowel syndrome: is there a common pathophysiological basis? *Am J Gastroenterol* 1997; 92: 954-9.
6 Talley NJ, Holtman G, Approach T. The patients with dyspepsia and related functional gastrointestinal complains. In: Yamada the textbook of gastroenterology 3rd edition. Philadelphia. Lippincott. Williams and Willkins; 1999. p. 82-66.
7 Tina HI, Tany AL, Kate SA, et al. The herb society's complete medicinal herbal penelope. London. Dorling Kindersley; 1995. p. 82-3.
8 Talley NJ, Colin-Jones D, Koch KL, et al. Functional dyspepsia: a classification and guidelines for diagnosis and management. *Gastroenterol Int* 1991; 4: 145-60.
9 Talley NJ, Zinsmeister AR, Schleck CE, Melton LJ. Dyspepsia and dyspepsia subgroups: a population based study. *Gastroenterology* 1992; 102: 1259-68.
10 Ansel HC. Introduction to pharmaceutical dosage form. London: Lea and Febigerm; 1999. p. 212-8.
11 Singh S. Evaluation of gastric anti-ulcer activity of fixed oil of Ocimum basilicum and its possible mechanism of action. *Indian J Exp Biol* 1999; 37: 253-7.
12 Akhtar MS, Munir M. Evaluation of the gastric antiulcerogenic effects of Solanum nigrum, Brassico oleracea and Ocimum basilicum in rats. *J Ethnopharmacol* 1989; 27: 163-76.
13 Singh S. Comparative evaluation of anti-inflammatory potential of fixed oil of different species of Ocimum and its possible mechanism of action. *Indian J Exp Biol* 1998; 36: 1028-31.