Original Article

Treatment of NERD (Non-erosive Reflux Disease) with Red Chili Powder (Capsicum)

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ABSTRACT

Background: Capsaicin receptors are abundant in the esophagus of NERD (non-erosive reflux disease) patients. Heartburn may develop by acid stimulation of these receptors during gastroesophageal refluxes (GER) and may be improved by desensitization with capsaicin-containing chili.

Objective: To determine the therapeutic effects of chronic chili ingestion on GER symptoms in NERD patients.

Methods: Eight NERD patients with a positive 24 hr pH test were included. Patients were randomized to receive either chili powder in 2 gelatin capsules orally or identical-looking placebo capsules three times per day before meals (total capsaicin 2.7 mg/day in the capsaicin group) for 6 weeks, in a randomized double-blinded crossover fashion with a 6-week washout period. Heartburn, food regurgitation, epigastrium burning, epigastrium pain, abdominal fullness, nausea, chest discomfort, and early satiety symptom scores were assessed by 10-cm long visual analog scales (VAS) at week 0, 1, 2, 4, and week 6. Total symptom scores (the sum of all scores), GERD symptom scores (the sum of heartburn, acid regurgitation and food regurgitation scores), and each individual symptom score were compared between the chili treatment group and the placebo group. Two-hour postprandial acid and non-acid refluxes were evaluated in all patients at baseline and the end of treatment, using the MII-pH (Multichannel Intraluminal Impedance-pH) monitoring after ingestion of a cup of noodle soup with 2 grams of red chili powder.

Results: All patients completed the study without serious adverse events. At baseline, the total symptom scores (26 ± 14 vs 22 ± 16), GERD scores (7.6 ± 3.7 vs 4.7 ± 2.8), and individual symptom score were not statistically different in the chili and the placebo groups ($p > 0.05$). Ingestion of chili could significantly lower total symptom scores (10 ± 9 vs 20 ± 14), GERD symptom scores (0.9 ± 1.2 vs 4.9 ± 2.4), heartburn symptom scores (0.4 ± 0.6 vs 3.7 ± 1.6), and food regurgitation symptom scores (0.5 ± 0.8 vs 1.3 ± 1.6) in NERD patients compared to placebo at the end of treatment ($p < 0.05$). Other symptoms were not significantly improved by red chili ($p > 0.05$). The significant improvement of heartburn and food regurgitation was observed by the end of week-2, and persisted up to the end of treatment. Although the number of gastroesophageal refluxes was decreased, the numbers and the durations of the 2 hours postprandial acid and non-acid refluxes were not significantly different in the chili and the placebo groups, whether before or at the end of treatment ($p > 0.05$).

Conclusions: Chronic chili ingestion was shown in this study to improve heartburn and food regurgitation symptom in NERD patients compared to placebo, without significant effects on postprandial gastroesophageal acid/non-acid refluxes. The results suggested that capsaicin-containing red chili improved GERD symptoms mainly by its effect on esophageal sensation, rather than on the lower esophageal sphincter functions.

Key words : treatment, red chili, capsaicin, NERD (Non-erosive Reflux disease)

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INTRODUCTION

There are several known pathogenic mechanisms in GERD, including genetic and environmental factors. Acid regurgitation and visceral hypersensitivity[1] are considered responsible for GERD symptoms in most patients. The mainstay of treatment is based on life style modifications in conjunction with acid suppression medications, of which proton pump inhibitors (PPIs) are most frequently and effectively used. Proton pump inhibitor, however, are associated with less favorable outcomes for patients with NERD (20-30% reported response rates)[2], than in patients with erosive esophagitis. The role of visceral hypersensitivity in NERD may account for such discrepancy[3]. The aim of treatment in these patients, therefore, is to modify the hypersensitivity of the esophagus.

Red chili (Capsicum) is a common spicy ingredient worldwide. Chili ingestion produces a variety of gastrointestinal symptoms in up to 25% of patients with chronic symptoms such as upper abdominal pain, heartburn, nonburning chest discomfort, abdominal discomfort, nausea, belching, distension, burning sensation in the mouth and facial sweating[4,5]. Capsaicin (8-methyl-N-vanillyl-6-nonenamide) is the main component of chili that is responsible for its characteristic hot taste (pungency).

Vanilloid receptor type I[6] (VR1) is the capsaicin receptor. This receptor is also stimulated by acid, heat and ethanol. Activation of VR1 receptors by capsaicin- containing red pepper injection into the esophageal wall triggered significant chest pain and heartburn in healthy volunteers[7]. Yasser M. Bat, *et al*.[8] demonstrated that capsaicin receptors are found in abundance in the esophageal mucosa of NERD patients. Previous studies have demonstrated that repeated exposure to capsaicin can desensitize these receptors[9-12].

The main objective of this study was to evaluate the effect of repeated ingestion of red chili powder on gastroesophageal reflux symptoms in NERD patients.

MATERIALS AND METHODS

Subjects

Eight NERD patients (4 men and 4 women; mean age 52 ± 6.4 years) with at least a 3-month history of heartburn or acid regurgitation were included in this study. All patients had a negative oesophagogastroduodenoscopy (EGD) and a positive standard 24 hour esophageal pH monitoring performed within the preceding 3 months before entering the study. A positve 24 hour esophageal pH test result was defined as the distal esophageal pH 5 cm above the lower esophageal sphincter (LES) less than 4 for greater than 4.5% of the total time. All subjects were interviewed about their general health and gastrointestinal symptoms prior to the study enrollment.

Study protocol

All subjects were asked to avoid ingesting chili, spicy food, and acid suppression medications or other medications known to influence esophageal and/or gastric motility, for at least 7 days prior to entry.

Each subject underwent a 2-hour postprandial acid and non-acid reflux monitoring at the study baseline and at the end of treatment using the MII-pH (Multichannel Intraesophageal Impedance-pH) monitoring after ingestion of a standard meal admixed with chili powder [a cup of noodle soup with 2 grams of red chili powder (*Capsicum frutescens* Linn, 0.9 mg of capsaicin / 1 g dry weight, Hand Brand No. 1, Nguan Soon Co., Ltd., Bangkok, Thailand)]. All patients were randomized to receive either 1 gram chili powder in 2 gelatin capsules or identical placebo capsules orally before meals 3 times per day (equivalent to capsaicin 2.7 mg/day) for 6 weeks, in a randomized double-blinded crossover fashion with a 6-week washout period.

Multichannel Intraluminal Impedance-pH monitoring

Subjects were asked to fast overnight and in the morning of day 0 and at week 6 underwent a multichannel intraesophageal pH (MII-pH) monitoring for 2 hours postprandially, using the MII-pH catheter (OhmegaTM MII-pH, Medical Measurement Systems B.V.). The pH electrode was placed at 5 cm above the upper border of the lower esophageal sphincter. The impedance measuring segments consisted of 6 pairs of metal rings placed 2 cm apart, and centered at 3, 5, 7, 9, 15 and 17 cm from the tip.

Symptom assessment

Heartburn, food regurgitation, acid regurgitation, epigastrium burning, epigastrium pain, abdominal fullness, nausea, chest discomfort, and early satiety symptom scores were assessed by 10-cm long visual analog scales (VAS) at week 0, 1, 2, 4, and 6 of the treatment protocol. Total symptom scores (sum of all scores),

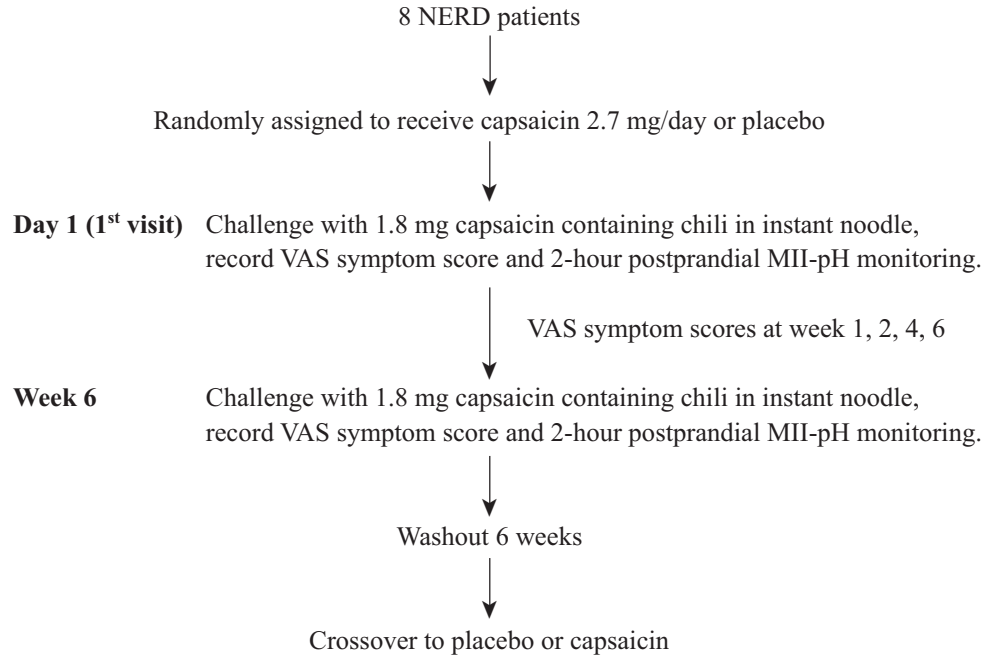


Figure 1. Diagram of study protocol

GERD symptom scores (sum of heartburn, acid regurgitation and food regurgitation scores), and each individual symptom score were compared between the chili and the placebo treatment groups.

Statistics

Data are expressed as mean ± SEM and percentages. Symptom scores at baseline and at weeks 1, 2, 4, 6 and reflux parameters after chili-containing meal at baseline and at the end of treatment were compared between the two groups, using pair T test. Differences were considered statistically significant with $p < 0.05$.

Table 1. Patients' characteristics.

Patients' characteristics	n = 8
Age (yrs)	
Mean ± SEM	52 ± 6.4
Range	42-61
Sex	
M: F	4:4
Predominate symptom, n (%)	
Heartburn	5 (62.5%)
Acid regurgitation	3 (37.5%)

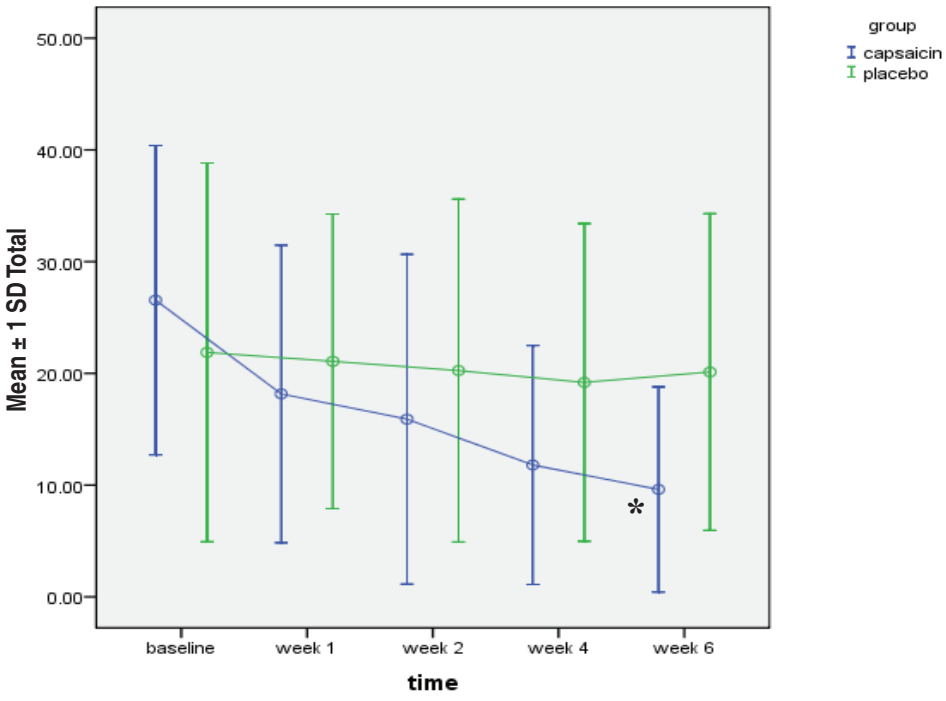
Results

Patients' characteristics

There were 8 patients, 4 males and 4 females, with a mean age of 52 ± 6.4 years (range 42-61 years). Five patients presented predominantly with heartburn and 3 patients presented with acid regurgitation. All subjects avoided spicy foods and chili during the study period. All subjects completed the study without serious adverse events.

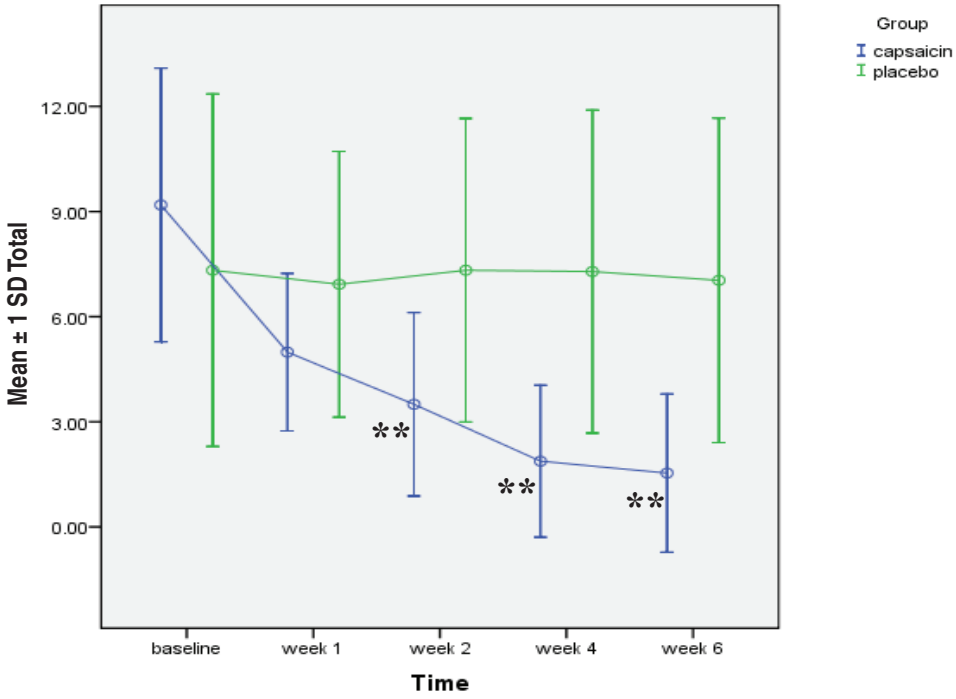
Symptoms

The baseline gastrointestinal symptoms were not statistically different in the two groups; total symptom scores (26 ± 14 vs 22 ± 16), GERD scores (7.6 ± 3.7 vs 4.7 ± 2.8), and each symptom score were similar (chili vs placebo, $p > 0.05$). The total symptom scores (10 ± 9 vs 20 ± 14), GERD symptom scores (0.9 ± 1.2 vs 4.9 ± 2.4), heartburn symptom scores (0.4 ± 0.6 vs 3.7 ± 1.6), and food regurgitation symptom scores (0.5 ± 0.8 vs 1.3 ± 1.6) decreased significantly at end of treatment after 6 weeks of either capsaicin or placebo ingestion ($p < 0.05$). The differing degrees of symptoms, including GERD symptom, heartburn and food regurgitation were detected early at week 2, and continue to improve up to the end of treatment. Total symptoms were significantly improved at week 6 ($p < 0.05$). There was no difference of acid regurgitation, epigastrium



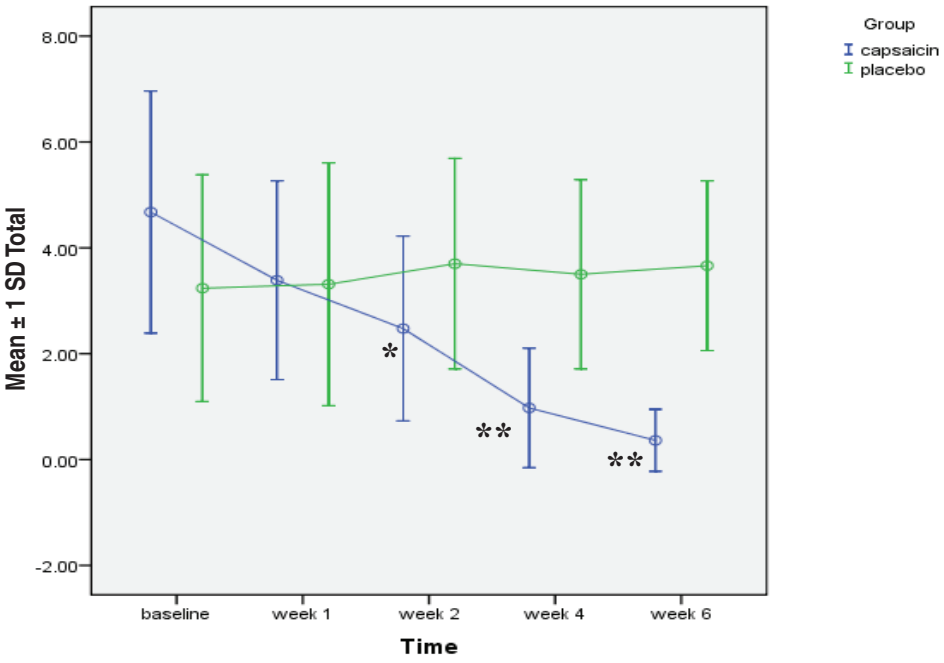
*$p \leq 0.05$

Figure 2. Histogram of total symptom scores (mean ± SD)



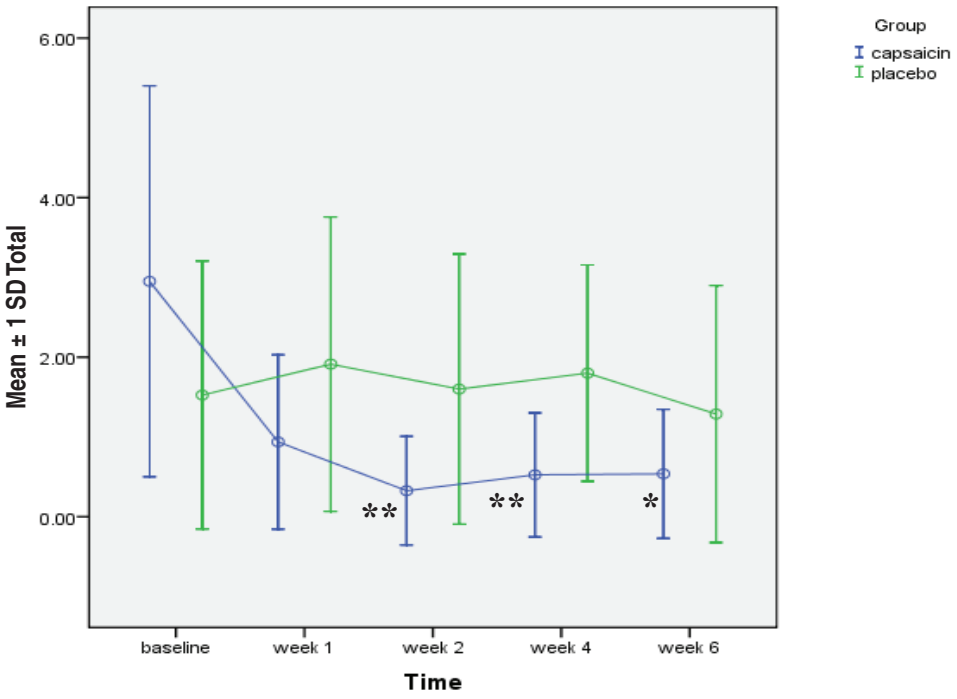
*$p \leq 0.05$, **$p \leq 0.01$

Figure 3. Histogram of GERD symptom scores (mean ± SD)



*$p \leq 0.05$, **$p \leq 0.01$

Figure 4. Histogram of heartburn symptom scores (mean ± SD)



*$p \leq 0.05$, **$p \leq 0.01$

Figure 5. Histogram of food regurgitation symptom scores (mean ± SD)

Table 2. Mean symptom scores (mean ± SD)

	Baseline		Week 1		Week 2		Week 4		Week 6	
	Capsicum	**Placebo**	**Capsicum**	**Placebo**	**Capsicum**	**Placebo**	**Capsicum**	**Placebo**	**Capsicum**	**Placebo**
Total symptoms	26.55 ± 13.84	21.87 ± 16.94	18.16 ± 13.31	21.07 ± 13.17	15.90 ± 14.75	20.25 ± 15.33	11.80 ± 10.69	19.18 ± 14.21	9.61 ± 9.18*	20.12 ± 14.17
GERD symptoms	9.18 ± 3.90	7.32 ± 5.03	4.98 ± 2.24	6.92 ± 3.79	3.50 ± 2.61**	7.32 ± 4.33	1.87 ± 2.17**	7.28 ± 4.61	1.53 ± 2.25**	7.03 ± 4.63
Heartburn	4.67 ± 2.29	3.24 ± 2.14	3.38 ± 1.88	3.31 ± 2.29	2.47 ± 1.74*	3.70 ± 1.98	0.97 ± 1.13**	3.50 ± 1.78	0.36 ± 0.58**	3.66 ± 1.60
Food regurgitation	2.95 ± 2.45	1.52 ± 1.67	0.93 ± 1.09	1.91 ± 1.84	0.32 ± 0.68**	1.60 ± 1.69	0.52 ± 0.77*	1.80 ± 1.35	0.53 ± 0.81*	1.28 ± 1.61
Acid regurgitaiton	1.56 ± 1.73	2.56 ± 2.64	0.66 ± 1.34	1.70 ± 2.41	0.70 ± 1.49	2.02 ± 2.61	0.37 ± 1.06	1.98 ± 2.67	0.63 ± 1.24	2.08 ± 2.54
Epigastrium burning	3.87 ± 2.54	3.43 ± 2.47	2.67 ± 2.19	3.07 ± 2.34	2.96 ± 2.64	2.82 ± 2.20	1.73 ± 1.79	2.73 ± 1.85	1.08 ± 1.40	2.20 ± 1.83
Epigastrium pain	2.76 ± 3.00	1.51 ± 2.38	1.37 ± 2.82	1.52 ± 2.13	1.92 ± 2.57	1.84 ± 2.19	1.71 ± 2.16	1.46 ± 2.05	1.00 ± 1.28	1.93 ± 2.73
Abdominal fullness	3.65 ± 2.95	2.88 ± 2.88	3.68 ± 2.90	3.47 ± 2.72	2.11 ± 3.04	2.68 ± 2.68	1.61 ± 1.29	2.95 ± 2.25	1.68 ± 1.02	2.98 ± 2.44
Nausea	1.62 ± 2.09	0.72 ± 1.56	1.15 ± 1.65	0.87 ± 1.62	0.73 ± 1.37	0.90 ± 1.70	0.68 ± 1.27	0.75 ± 1.41	0.52 ± 1.13	1.35 ± 1.89
Chest discomfort	2.46 ± 2.90	2.76 ± 2.59	2.27 ± 1.76	2.32 ± 2.44	1.37 ± 1.88	2.26 ± 1.86	1.22 ± 2.08	2.10 ± 1.81	0.87 ± 1.94	2.22 ± 1.94
Early satiety	2.05 ± 1.84	2.25 ± 3.18	1.97 ± 3.16	1.56 ± 2.96	2.38 ± 2.89	1.45 ± 2.83	1.60 ± 2.19	1.22 ± 2.37	1.57 ± 1.78	1.53 ± 2.74

*$p \leq 0.05$, **$p \leq 0.01$

Table 3. Parameters of 2-hour postprandial reflux (mean ± SD or median)

Parameter	Placebo		Capsicum	
	Baseline	At 6 week	Baseline	At 6 week
Numbers of reflux	5.62 ± 3.06	5.62 ± 3.46	5.25 ± 3.19	3.75 ± 1.90
Numbers of meal related reflux	0.87 ± 1.35	1.00 ± 1.30	1.00 ± 1.51	0.87 ± 0.99
Numbers of non-meal related reflux	3.62 ± 3.06	3.37 ± 3.06	3.87 ± 3.72	2.75 ± 2.25
Median duration of reflux (sec)	86.50 (7-390)	91.50 (20-491)	71.50 (0-487)	43.50 (0-546)
Median duration of acid reflux (sec)	484.00 (0-1616)	485.50 (0-2937)	107.50 (0-2570)	150.50 (0-4495)
Median duration of non-acid reflux (sec)	12.00 (0-66)	24.00 (0-92)	0 (0-46)	16.50 (0-46)

$p > 0.05$

burning, epigastrium pain, abdominal fullness, nausea, chest discomfort and early satiety symptom scores.

Multichannel Intraluminal Impedance-pH monitoring

The number of gastroesophageal refluxes during the 2-hour postprandial period in the capsicum group was much lower at the end of treatment compared to at baseline, though not statistically significant (5.25 ± 3.19 to 3.75 ± 1.90, $p > 0.05$). The median durations of acid and non-acid refluxes were not significantly different between the chili and the placebo treatment groups, both before and at the end of treatment ($p > 0.05$).

DISCUSSION

Most patients with NERD do not usually respond adequately with proton pump inhibitors (PPIs) as the principal underlying pathophysiologic mechanism is related to visceral hypersensitivity[1]. Currently, there is no data concerning treatment efficacy of chronic capsicum ingestion in such patients. The present study demonstrated that six weeks of red chili powder ingestion was significantly more efficacious than placebo in reducing reflux symptoms in NERD patients. In particular, heartburn and food regurgitation improved significantly after red chili more than after placebo. Red chili powder became significantly more effective than placebo as from the second week of treatment, and persisting through the end of treatment period. This observation is also consistent with previous studies[10-14], in which repeated applications of capsicin reduced C-type fiber activity of afferent neurons by desensitization mechanism in the skin and various mucous membranes. No serious side-effects of capsicum were observed in the study.

The multichannel intraesophageal impedance monitoring was employed in our study to demonstrate the changes of reflux variables during the 2-hour postprandial period. It was noted that the number of reflux episodes appeared to decrease in the capsicum group, although not statistically significant ($p > 0.05$). In addition, the median numbers of both acid-and non-acid refluxes during the 2-hour the postprandial period were not statistically different between the capsicum and the placebo groups. A previous study[15] in healthy volunteers suggested that chronic ingestion of chili significantly increased the number of reflux episodes and time the percentage of acid reflux, but the duration of chili ingestion in that study was only one week. This suggests that capsaicin ingestion mainly affects esophageal visceral hypersensitivity and not by way of the reflux mechanism.

In conclusion, the present study suggested that chronic ingestion of capsaicin-containing red chili improves GERD symptoms mainly by its effect on the esophageal sensation, rather than on the lower esophageal sphincter functions.

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