[원저]

위장운동조절제의 유효성에 영향을 미치는 식습관에 관한 연구

김영식[1], 박혜순[1], 박지영[1], 조비룡[2], 허봉렬[2], 김대현[3], 서영성[3], 김병성[4], 원장원[4], 오상우[5], 약물시판후조사 연구회[6]

울산의대 서울아산병원[1], 서울대학교병원[2], 계명의대 동산병원[3], 경희의대[4], 인제의대 일산백병원[5], 약물시판후조사 연구회[6]

- 요 약 -

연구배경 소화불량 환자에서 위장운동조절제가 광범위하게 사용되고 있다. 소화불량 환자에서 어떠한 식습관이 위장운동조절제의 유효성에 영향을 미치는지 알아보고자 본 연구를 수행하였다.

방 법 2000년 12월부터 2001년 6월까지 24명의 가정의를 방문한 688명의 소화불량 환자들을 대상으로 itopride를 4주간 투여하고 추적조사 하였다. Itopride 유효성은 투여 2주와 4주에 임상증상, 흡연, 음주, 스트레스 및 식습관에 대한 항목이 포함된 구조화된 설문지를 이용하여 평가하였다.

결 과 4주 치료 후 증상이 중등도 이상 개선된 396명(57.6%)의 환자는 유효군으로, 증상개선이 미약하거나 없는 292명(42.4%)의 환자는 비유효군으로 분류하였다. 다변량분석 결과 하루 중 불규칙한 식사횟수(OR 1.81, 95% CI: 1.07, 3.06)와 주당 불규칙한 식사를 하는 일수(OR 2.07, 95%CI: 1.24, 3.45)가 많을수록 itopride의 유효성이 적은 것으로 나타났다. 반면에 음주, 흡연, 스트레스, 과식의 빈도, 자극적인 음식섭취, 식사속도 및 아침결식은 itopride의 유효성과 관련이 없었다

결 론 본 연구결과에 의하면 불규칙한 식사 습관이 위장운동조절제의 유효성을 낮추는 것으로 나타났다. 따라서 소화불량환자에서 위장운동조절제의 유효성을 높이기 위해서는 규칙적인 식습관이 권장된다.

(대한임상건강증진학회지 2006;6(2):129~135)

중심단어 소화불량, 식습관, 위장운동조절제

INTRODUCTION

Although dyspepsia is a common problem among the general population[1,2], etiology and pathophysiology has not been well established because of its heterogeneous character.[3] Several studies[4-6] have indicated that lifestyle and eating patterns are associated with dyspepsia, and our previous study suggested that irregular eating patterns and overeating are associated with dyspepsia.[7] Well designed studies of the relationship between symptom occurrence and eating patterns are lacking, and there have been few studies investigating the effects of dietary modifications on symptoms. Prokinetic drugs, including itopride, are widely used for symptomatic improvement of patients with dyspepsia[8,9], but little is known regarding the factors associated with the efficacy of these drugs. We therefore sought to determine whether dietary behaviors are associated with the efficacy of prokinetic drug in dyspeptic patients.

*본 논문은 중외제약 연구비 지원으로 이루어진 것임.
• 교신저자 : **김 영 식** 울산대학교 가정의학과
• 주 소 : 서울 송파구 풍납동 388-1
• 전 화 : 02-3010-3811
• E-mail :youngkim@amc.seoul.kr
• 접 수 일 : 2006년 2월 15일 • 채 택 일 : 2006년 5월 10일

METHODS

1. Subjects and study design

From December 2000 to June 2001, a total of 688 patients over 20 years old with dyspepsia were observed by 24 family physicians in Korea. We enrolled the consecutive patients with dyspeptic symptoms for at least 4 weeks during the last 4 months, a modification of the Rome II criteria.[10] All patients were newly prescribed 50mg of itopride three times a day; any patients who had been previously treated with itopride and whose compliance had been less than 80% were excluded. This was a prospective observational study. The enrolled patients were evaluated for treatment efficacy during the second and fourth weeks after the beginning of treatment. This study was approved by the Institutional Review Board of the Asan Medical Center, where the coordinating office is located.

2. Questionnaire

Prior to treatment, participants were asked to fill out the standardized questionnaire, which consisted of questions regarding demographic and socioeconomic factors, medication, lifestyle factors, and eating patterns. Items addressing dietary behaviors consisted of questions regarding meal frequency per day, regularity of mealtimes per week, frequency of overeating per week, pace of eating, frequency of spicy food consumption and skipping breakfast. Five items from the Korean version of the Brief Encounter Psychosocial Instrument(BEPSI) were also included for stress assessment.[11,12]

3. Evaluation of efficacy and symptoms

The case record form(CRF) included information on symptoms of bloating, nausea, upper abdominal pain, pyrosis, regurgitation and lack of appetite, all of which were evaluated at baseline and during the second and fourth weeks of treatment. Each symptom was assessed on a 4-point Likert scale, with 0=none, 1=mild, 2=moderate, and 3=severe. A dyspeptic symptom score was calculated as the sum of the symptom score, with a maximum symptom score of 18 points. Improvement of symptoms was defined as the disappearance of at least one of the above symptoms or a decrease in score of 2 or more points. Based on the results, the participants were divided into two groups, those who showed improvement(affected group) and those who did not(unaffected group).

4. Data collection and analysis

Standardized CRFs were completed by participating physicians, and the completed forms were sent to a coordinating center of the Korea Post-Marketing Surveillance Research Group. The patient-completed questionnaires were also collected and recorded for analysis. All patients underwent routine medical examination, including measurement of body mass index (weight/height^2). The level of stress was estimated using the 5 items from the BEPSI, with each assessed on a 5-point Likert scale from 1 to 5, and the mean score of reported items was calculated. A high level of stress was defined as a BEPSI amount of 2 or more, and a low level of stress was defined as a BEPSI amount of less than 2. Univariate analysis of categorical variables was done by Chi-square test and multivariable analysis by logistic regression. All analyses were carried out on a personal computer using SAS PC software.

RESULTS

1. Patient characteristics

Baseline characteristics of the patients are shown in Table 1. The mean age of the male patients was 49.4 years, whereas that of the women was 51.1 years. The proportions of smokers and drinkers were lower than those in the general population, and fewer than 20% were overweight. About 45% of the patients had a history of taking gastrointestinal medications, less than 40% had a high level of stress, and 27% of the patients reported that they exercised regularly.

1) Factors associated with prokinetic drug efficacy

According to the univariate analysis, BMI and a history of taking gastrointestinal medication were associated with the efficacy of prokinetic drug($P<0.05$)(Table 2). Possible risk factors, such as stress, smoking, alcohol consumption,

Table 1. Baseline characteristics of 688 dyspeptic patients.

Variables	Number	(%)
Gender		
Male	265	38.5
Female	423	61.5
Age(years)		
40~49	306	44.5
50~59	191	27.8
≧60	191	27.8
Body mass index(kg/m^2)		
<22	405	58.9
22~24.9	156	22.7
≧25	127	18.5
Previous GI* medication		
Yes	225	45.4
No	271	54.6
Exercise		
No	358	72.6
Yes	135	27.4
Daily activity		
Low	238	60.0
Medium	123	31.0
High	36	9.1
Stress amount		
Low	271	59.0
High	188	41.0
Income(US$/month)		
<2,000	156	38.1
2,000~3,999	176	42.9
≧4,000	78	19.0
Education(years)		
<12	161	36.6
12	161	36.6
>12	118	26.8
Marital status		
Married	356	77.9
Unmarried/divorced/widowed	101	22.1
Smoking		
Non-smoker	259	67.3
Ex-smoker	44	11.4
Current smoker	82	21.3
Alcohol		
Non-drinker	211	58.1
Drinker	152	41.9

Missing values are excluded. * GI, gastrointestinal.

physical activity and exercise, however, were not associated with the efficacy of this medication(P>0.05).

2) Dietary behaviors associated with prokinetic drug efficacy

Table 3 shows a univariate analysis of the association between dietary behaviors and prokinetic drug efficacy.

Table 2. Characteristics of subjects affected and unaffected by prokinetic drug treatment.

Variables	Affected group (n=396)		Unaffected group (n=292)	
	No.	(%)	No.	(%)
Gender				
Male(n=265)	156	(39.4)	109	(37.3)
Female(n=423)	240	(60.6)	183	(62.7)
Age(years)				
40~49(n=306)	166	(41.9)	140	(48.0)
50~59(n=191)	116	(29.3)	75	(25.7)
≧60(n=191)	114	(28.8)	77	(26.4)
Body mass index(kg/m^2)*				
<22(n=405)	245	(61.9)	160	(54.8)
22~24.9(n=156)	86	(21.7)	70	(24.0)
≧25(n=127)	65	(16.4)	62	(21.2)
Education(years)				
<12(n=161)	79	(34.4)	82	(39.1)
12(n=161)	82	(35.7)	79	(37.6)
>12(n=118)	69	(30.0)	49	(23.3)
Marital status				
Married(n=356)	188	(77.7)	168	(78.1)
Unmarried/divorced/widowed (n=101)	54	(22.3)	47	(21.9)
Income(US$/month)				
<2,000	80	(36.7)	76	(39.6)
2,000~3,999	99	(45.4)	77	(40.1)
≧4,000	39	(17.9)	39	(20.3)
Stress amount				
Low(n=271)	140	(57.4)	131	(60.9)
High(n=188)	104	(42.6)	84	(39.1)
Smoking				
Non-smoker(n=259)	146	(67.0)	113	(67.7)
Ex-smoker(n=44)	28	(12.8)	16	(9.6)
Current smoker(n=82)	44	(20.2)	38	(22.8)
Alcohol				
Non-drinker(n=211)	114	(75.0)	97	(60.2)
Drinker(n=102)	38	(25.0)	64	(39.8)
Previous GI† medication*				
No(n=271)	132	(50.0)	139	(59.9)
Yes(n=225)	132	(50.0)	93	(40.1)
Exercise				
Yes(n=135)	74	(27.9)	61	(26.8)
No (n=358)	191	(72.1)	167	(73.3)
Daily activity				
Low(n=238)	133	(61.9)	105	(57.7)
Medium(n=123)	64	(30.0)	59	(32.4)
High(n=36)	18	(8.4)	18	(9.9)

* p<0.05 by chi-square test.
† GI, gastrointestinal.

Frequency of meals per day, regularity of mealtimes per week, and pace of eating were each significantly associated with the prokinetic drug efficacy(P<0.05). However, frequency of overeating per week, frequency of spicy food consumption and skipping breakfast were not associated with the efficacy of this medication(P>0.05).

We also performed multivariable analysis of the association between dietary behaviors and prokinetic drug efficacy(Table 3). After adjustment for sex, age, BMI and history of taking gastrointestinal medications, we found that prokinetic drug efficacy was notably lower among patients with irregular meal intake per day(odds ratio [OR], 1.81; 95% confidence interval [CI],1.07-3.06) compared with patients with more regular mealtime habits. In addition, irregularity of weekly mealtimes showed a significant association with a lack of efficacy of prokinetic drug. That is, patients who had meals at regular times on only one or two days during the week(OR, 2.07; 95% CI, 1.24-3.45) were at a higher risk for poor prokinetic drug efficacy compared with patients who ate at regular times six to seven days per week. In this multivariable model, pace of eating was not related to prokinetic drug efficacy(P>0.05).

DISCUSSION

We have shown here that irregular meal frequency during the day and irregularity of mealtimes during the week are significantly associated with the poor efficacy of prokinetic drug in dyspeptic patients. In contrast, we also found that frequency of overeating, consumption of spicy foods, pace of eating and skipping breakfast are not associated with the prokinetic drug efficacy.

Although several studies[3,7,13] have indicated that dyspeptic patients are less likely to eat three meals per day on a regular basis than non-dyspeptic controls, controlled studies on the

Table 3. Relationship between dietary behavior and efficacy of prokinetic drug.

Risk factors	Affected group		Unaffected group		Odds ratio(95% CI)			
	No.	(%)	No.	(%)	Crude		Adjusted†	
Meal frequency*								
3 times or more regularly	189	(73.3)	151	(66.5)	1.00		1.00	
1 or 2 times regularly	40	(15.5)	32	(14.1)	1.21	0.74-1.99	0.99	0.59-1.67
irregularly	28	(11.2)	44	(19.4)	2.30**	1.39-3.78	1.81*	1.07-3.06
Regularity of mealtime(days/wk.)**								
6~7 days	35	(15.2)	54	(26.3)	1.00		1.00	
3~5 days	99	(42.9)	83	(40.5)	1.42	1.00-2.02	1.17	0.78-1.77
1~2 days	97	(42.0)	68	(33.2)	2.61***	1.63-4.17	2.07**	1.24-3.45
Overeating (days/wk.)								
No	96	(45.1)	81	(42.9)	1.00		1.00	
1~2 days	84	(39.4)	76	(40.2)	1.29	0.91-1.85	0.99	0.68-1.46
3~7 days	33	(15.5)	32	(16.9)	0.36	0.04-3.23	0.26	0.03-2.40
Pace of eating								
Slow (≧25 min.)	20	(7.8)	27	(11.9)	1.00		1.00	
Moderate (11~24min.)	120	(46.7)	93	(41.0)	1.34	0.92-1.95	0.67	0.38-1.20
Fast (<10min.)	117	(45.5)	107	(47.1)	1.58*	1.10-2.29	0.80	0.45-1.42
Eating spicy food (days/wk.)								
No	60	(24.4)	60	(27.9)	1.00		1.00	
1~2 days	88	(35.8)	77	(35.8)	1.34	0.92-1.95	0.88	0.56-1.38
3~5 days	86	(35.0)	64	(30.0)	1.14	0.77-1.68	0.76	0.47-1.20
6~7 days	12	(4.9)	14	(6.5)	1.79	0.80-3.98	1.16	0.50-2.69
Skipping breakfast								
No	180	(71.2)	144	(66.7)	1.00		1.00	
Yes	73	(28.9)	72	(33.3)	1.23	0.83-1.83	1.26	0.83-1.89

* p<0.05, ** p<0.01, *** p<0.001, by chi-square test.
† After adjustment for age, sex, and previous gastrointestinal medication.

effects of dietary modifications on dyspeptic symptoms are lacking.[14,15] Our finding, that irregular meal frequency per day and irregularity of mealtimes per week were significantly associated with the poor efficacy of prokinetic drug, suggests that regularly eating three meals per day for six to seven days per week may improve symptoms in dyspeptic patients with irregular eating patterns. Further clinical trials are needed, however, to determine if there is any correlation between modification of irregular eating habits and symptom improvement among dyspeptic patients.

Although our previous study suggested that overeating behavior was associated with dyspepsia[7], in this study we found that frequency of overeating was not associated with prokinetic drug efficacy. In these studies, overeating occurred most commonly at dinner. Although rapid meal consumption (less than 10 minutes) was not associated with prokinetic drug efficacy by multivariate analysis, it did show significant association by univariate analysis. Further studies are necessary to determine whether there is any relationship between the pace of eating and the efficacy of a prokinetic drug. We also found that consumption of spicy foods and skipping breakfast were not associated with prokinetic drug efficacy. Lack of appetite was the most commonly cited reason for skipping breakfast, followed by habitual behavior and lack of time.

Psychological stress is widely believed to play a role in functional dyspepsia by precipitating the exacerbation of symptoms[14,16] In the present study, however, we found that the amount of stress was not associated with prokinetic drug efficacy. This finding was similar to that observed in a previous study, in which gastrointestinal medications improved symptoms of dyspepsia, regardless of their causes.[14] Other studies, however, have suggested that some anxiolytics improve dyspeptic symptoms.[17,18] Thus, further studies are necessary to explain the combined effects of anxiolytics and prokinetics in dyspepsia.

We found that prior intake of gastrointestinal medications was associated with good efficacy of prokinetic drug. This may be due to differences in compliance and motivation among patients who did or did not take previous medication.[19] Although smoking and alcohol have been reported to be associated with dyspepsia.[20,21] this finding is controversial.[22] We found that smoking and alcohol were not associated with prokinetic drug efficacy, whereas others have found that smoking had an additive deleterious effect on gastroduodenal pathology in dyspeptic patients.[23] Further detailed study is required to explore this issue.

One limitation of our study was the lack of endoscopic data from the subjects. This may have led to a misclassification of some study subjects, especially during the enrollment of patients with ulcers and gastrointestinal reflux. The general effect of misclassification, however, could weaken the association, leading to a bias towards the null. Despite these limitations, our findings provide valuable information on dietary behaviors that may be associated with the poor efficacy of prokinetic drug in dyspeptic patients.

In summary, we have shown that irregular eating patterns are significantly associated with the poor efficacy of prokinetic drug in dyspeptic patients. Factors not associated with prokinetic drug efficacy include alcohol consumption, smoking, stress, frequency of overeating, consumption of spicy foods, pace of eating, and skipping breakfast. To increase the efficacy of prokinetic drug, behavioral modifications, such as eating regularly, should be encouraged.

ACKNOWLEDGEMENTS

This study was an add-on study of post-marketing surveillance for itopride and was supported by a grant from Choongwae Pharma Corporation.

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[Abstract]

Dietary Behaviors Associated with the Efficacy of Prokinetic Drug in Dyspeptic Patients

Young Sik Kim[1], Hye Soon Park[1], Ji Young Park[1], Be Long Cho[2], Bong Yul Huh[2], Dae Hyun Kim[3], Young Sung Suh[3], Byung Sung Kim[4], Chang Won Won[4], Sang Woo Ou[5], Korea Post-Marketing Surveillance Research Group[6]

Department of Family Medicine, University of Ulsan College of Medicine[1], Department of Family Medicine, Seoul National University College of Medicine[2], Department of Family Medicine, College of Medicine Keimyung University[3], Department of Family Medicine,College of Medicine Kyunghee University[4], Department of Family Medicine, Inje University College of Medicine[5], Republic of Korea[6]

Background We sought to determine whether dietary behaviors are associated with the efficacy of prokinetic drug in dyspeptic patients.

Methods From December 2000 to June 2001, 688 patients with dyspepsia were treated with itopride for 4 weeks by 24 family physicians. Itopride efficacy was determined by follow-up during weeks 2 and 4 at which time, using a structured questionnaire, patients were assessed on symptoms, as well as smoking, alcohol, stress and dietary behaviors.

Results At the end of the 4 week treatment, moderate to complete relief of symptoms was reported by 396 patients (57.6%, affected group), whereas 292 (42.4%, unaffected group) reported slight or no improvement. Factors associated with poor efficacy of itopride included irregular meal frequency per day (OR 1.81, 95% CI: 1.07, 3.06) and irregularity of mealtime per week (OR 2.07, 95%CI: 1.24, 3.45). Factors not associated with efficacy included alcohol consumption, smoking, stress, frequency of overeating, consumption of spicy foods, pace of eating, and skipping breakfast.

Conclusions Irregular eating patterns were significantly associated with the poor efficacy of prokinetic drug in dyspeptic patients. To increase the efficacy of prokinetic drug, patients should be advised to eat regularly and at set times.

(Korean J Health Promot Dis Prev 2006 ; 6(2) : 129~135)

Key words dyspepsia: dietary behavior; prokinetic drug

• Address for correspondence : **Young Sik Kim**
Department of Family Medicine, University of Ulsan College of Medicine
• T e l : 02-3010-3811
• E-mail : youngkim@amc.seoul.kr