



Effects of ranitidine for exercise induced gastric mucosal changes and bleeding

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Abstract

AIM: To evaluate the effect of ranitidine on gastric mucosal changes and on GI bleeding in long distance runners.

METHODS: Twenty-four long distance runners (M: 16, F: 8, age: 18.2 ± 1.5 years) participated in this study. A symptom questionnaire, stool hemoccult test, and upper gastrointestinal (GI) endoscopy were performed on the subjects prior to the study. The subjects took oral ranitidine (150 mg, b.i.d.) for two weeks. The upper GI endoscopy and stool Hemoccult tests were repeated after the treatment.

RESULTS: Twenty-two of the 24 runners had at least one upper GI mucosal lesion before the medication. The Endoscopic improvements were seen in eleven of the 14 cases of erosive gastritis and four of the 5 cases of esophagitis. Six subjects were Heme occult positive prior to the study, but only one was positive after the medication.

CONCLUSION: Gastric mucosal lesions and GI bleeding in long distance runners seem to be associated to acid-related factors mediated by the high level of regular run-

ning. Ranitidine seems to be an effective prophylaxis to prevent gastric mucosal lesions and GI bleeding.

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Key words: Endoscopy; Exercise; Gastrointestinal bleeding; Ranitidine

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INTRODUCTION

Long-distance running has become a popular exercise during the past decade, and the number of people participating in endurance racing has increased. It has been reported that troublesome gastrointestinal (GI) symptoms associated with endurance running events has been occurring more frequently^[1,2]. Although the magnitudes of these symptoms are unknown, incidence rate varies from 10 to 81%, depending on factors such as the type, duration, and intensity of the exercise studied^[3].

GI bleeding is not an uncommon finding after long distance races. Some of runners^[3,4] who experienced macroscopic fecal blood and microscopic bleeding has been found in 8 to 87% of the runners^[5,6]. Running-related GI mucosal changes such as gastric ulcer^[7], hemorrhagic gastritis^[8], erosive gastritis^[9], ischemic colitis^[10] were observed by endoscopy. These changes may contribute to runner's anemia and, if sustained, may possibly result in an iron deficiency that may potentially affect the recovery and performance of competitive runners. The mechanism by which hemorrhagic gastritis and ischemic colitis develop in runners is unknown, but it is usually attributed, in part, to ischemia. One report showed that running reduced visceral blood flow by up to 80% of pre-exercise level^[11]. Another possible mechanism for the hemorrhagic gastritis is acid secretion^[12]. Moderate-intensity running is not generally thought to alter gastric acidity^[13] whereas heavier exertion paradoxically reduces acid secretion^[14]. But some reports have suggested that acid reducing agents, i.e. cimetidine or ranitidine, might be useful in preventing running-associated

gastrointestinal bleeding and symptoms^[6,15]. However, there has been only one case study regarding running related GI mucosal changes before and after treatment^[15]. We, therefore, performed an observational trial to evaluate the effect of ranitidine on gastric mucosal changes and GI bleeding in long distance runners by endoscopy.

MATERIALS AND METHODS

Study subjects

Twenty-four professional long distance runners (16 male, 8 female, age range: 16-19 years) participated in this study. The Human Investigations Committee of Wonkwang University Hospital approved the protocol and each subject signed an informed consent prior to the study.

The subjects were well trained and had several years of experience in competitive running. They underwent a strict training program of 200 km of running per week and participated in three long-distance running competitions per year. All subjects were instructed to avoid nonsteroidal anti-inflammatory drugs, red meat, alcohol, iron and vitamin supplementation for at least 2 wk prior to the study.

Symptom questionnaire

The questionnaire was designed with yes/no questions and a graded value scale (0: none = no symptom, 1: mild = intermittent symptoms but not interfere with the running, 2: moderate = want treatment for symptoms but rarely interfere with the running, 3: severe = want treatment for symptoms and interfere with the running) for the following symptoms: diarrhea, abdominal cramps, epigastric discomfort, epigastric pain, nausea, vomiting, and regurgitation related to running.

GI bleeding test

The presence of GI bleeding was tested before and after the study with hemeoccult test (LA Hemochaser, MIZUHO, Japan) by looking for the presence of agglutination after mixing the feces with a latex reagent within a 3 min.

Study protocols

Gastroscopy was performed on all subjects prior to the study. No pre-medication was used except for lidocaine (2 mL of viscous Xylocaine) as a local anesthetic. Two endoscopists performed the upper GI endoscopy with a flexible gastroscope (Pentax EG-2730, 9.0 mm diameter, Japan). Macroscopic observations of gastric mucosal damage were noted but not graded. *Helicobacter pylori* (*H. pylori*) infection was evaluated by a rapid urease test of the one biopsy specimen obtained during endoscopy. The subjects with abnormal endoscopic findings took 150 mg of oral ranitidine (30 min postprandial, b.i.d.). The subjects commenced regular training for 2 wk while taking the medication. A second endoscopy was given to the subjects who had abnormal upper GI mucosal findings before the treatment.

Table 1 Gastrointestinal symptoms in runners ($n = 24$)

	None	Mild	Moderate	Severe	Percentage of symptomatic subjects (%)
Diarrhea	9	13	1	1	63
Abdominal pain	10	12	2		58
Epigastric discomfort	10	12	2		58
Epigastric pain	12	10	2		50
Nausea	14	8	2		42
Regurgitation	16	8			33
Vomiting	19	4	1		21

RESULTS

Symptom questionnaire

The results of the symptom questionnaire are summarized in Table 1. Only two subjects had no GI symptoms related to running. The most frequently experienced GI symptom was diarrhea ($n = 15$), followed by abdominal pain ($n = 14$), epigastric discomfort ($n = 14$), and epigastric pain ($n = 12$).

Gastroscopy findings

The results of the endoscopic examination before and after the treatment are listed in Table 2. Twenty-two of the 24 runners had at least one upper GI mucosal lesion, including erosive gastritis ($n = 17$), esophagitis ($n = 8$), alkaline reflux gastritis ($n = 8$), and gastric ulcer ($n = 1$). Of the seventeen subjects with mucosal erosions, four subjects had stigmata of bleeding. Mucosal erosions were localized to the antrum ($n = 11$), gastric body ($n = 8$), fundus ($n = 6$), and gastric angle ($n = 2$). Sixteen out of 22 runners who had abnormal upper GI mucosal findings consented to have a second endoscopy after medication. Gastroscopic improvements were seen in eleven of the 14 cases of erosive gastritis, four of the 5 cases of esophagitis, but only one of the 5 cases of alkaline reflux gastritis.

GI bleeding

Six of the 24 participants were heme occult positive before the medication. Only one was positive after the medication (Table 2).

Helicobacter pylori status

Nine of the 24 participants were rapid urease test positive (Table 2). But there was no relation between *H. pylori* status and endoscopic findings.

DISCUSSION

This study reported a high incidence of running related GI symptoms and the results confirmed the previous studies^[2]. Moses reported that symptoms of the lower GI tract were more prevalent than those from the upper GI tract in most endurance events^[16] and others found that frequency of GI symptoms were much higher during marathon running and/or triathlons than during other endurance sports,

Table 2 Endoscopic findings and hemoccult test before and after treatment with ranitidine

Subject/Sex	Before treatment (n = 24)		After treatment (n = 16)		
	Endoscopic findings	Hp status	OB	Endoscopic findings	OB
1/M	Alkaline reflux gastritis	—	+	Procedure refused	—
	Erosive gastritis (upper body)				
2/M	Esophagitis, LA class A	—	—	Erosive gastritis	—
	Alkaline reflux gastritis				
	Erosive gastritis (fundus)				
3/M	Esophagitis LA class A	—	+	Normal finding	—
	Erosion with blood clot (antrum)				
4/M	Esophagitis, LA class A	+	+	Alkaline reflux gastritis	+
	Alkaline reflux gastritis				
5/M	Erosive gastritis	+	+	Normal finding	—
	(fundus, body, antrum)				
6/M	Esophagitis, LA class A	—	—	Procedure refused	
	Alkaline reflux gastritis				
7/M	Erosive gastritis	+	—	Procedure refused	
	(fundus, body)				
8/M	Gastric ulcer, Erosion with blood clot (midbody)	—	+	Normal finding	—
9/M	Erosive gastritis (fundus)	+	—	Normal finding	—
10/M	Erosive gastritis (fundus)	+	—	Erosive gastritis (body)	—
11/M	Esophagitis, LA class A	+	—	Procedure refused	
	Alkaline reflux gastritis				
12/M	Erosive gastritis (body, antrum)	—	—	Procedure refused	
	Duodenitis				
13/M	Normal finding	—	—	Procedure not performed	
14/M	Esophagitis, LA class A	+	—	Procedure refused	
15/M	Erosive gastritis (antrum)	—	—	Normal finding	—
16/M	Erosive gastritis (body, antrum)	—	—	Erosive gastritis (antrum)	—
17/M	Alkaline reflux gastritis, Erosive gastritis with blood clot (angle)	—	—	Alkaline reflux gastritis	—
18/F	Duodenitis	—	—	Normal finding	—
19/F	Esophagitis, LA class A	—	—	Alkaline reflux gastritis	—
	Alkaline reflux gastritis				
	Erosive gastritis (antrum)				
20/F	Erosion with blood clot (midbody)	—	+	Normal finding	—
21/F	Esophagitis, LA class A	—	—	Esophagitis, LA class A	—
	Erosive gastritis (fundus)				
22/F	Alkaline reflux gastritis	—	+	Alkaline reflux gastritis	—
	Erosive gastritis (antrum)				
23/F	Normal finding	+	—	Procedure not performed	
24/F	Erosive gastritis (antrum)	+	—	Normal finding	—

M, male; F, female; Hp, *Helicobacter pylori*; OB, occult blood; +, positive; -, negative; LA, Los Angeles.

i.e. cycling, rowing, and swimming^[3,17].

The duration of the exercise can be an important factor. Peters *et al*^[18] showed that during a protocol of alternately cycling and running, the number of subjects with GI symptoms increased exponentially with time. They also reported that running induced more GI symptoms when compared to cycling^[18]. Another factor thought to influence the exercise induced GI symptoms is the intensity of the exercise. It has been reported that as intensity increases, gastric emptying is delayed^[13,19] and splanchnic blood flow decreased^[11]. Other factors such as mechanical trauma of the gut^[20], intestinal permeability^[21], and absorption^[22] may also be affected by the intensity of the exercise.

The existence of gastrointestinal bleeding associated with endurance running has previously been demonstrated^[2,23].

Sullivan^[2] reported bloody stools after endurance events, and another study demonstrated the high frequency of occult GI bleeding, in which 23% of runners converted from blood test negative to blood test positive using the Hemeoccult card^[23]. Stewart *et al*^[24] reported that 83% of runners had positive stool occult blood after competitive running and the presence of iron-deficiency anemia possibly caused by multiple etiologies including GI bleeding.

While GI blood loss can be clearly attributed to running, its etiology or pathophysiology is not readily apparent. McMahon *et al*^[25] suggested an ischemic etiology for the blood loss. They studied 32 runners after a marathon, and showed that six runners, who developed hemoccult-positive stools after a marathon race, were significantly younger and had faster race times when compared to those

with hemocult-negative stool.

Another possible mechanism for the development of GI bleedings may be mucosal damages caused by gastric acid secretion^[12]. Very little data exists regarding acid secretion during exercise and immediately following exercise due to the technical difficulties in such measurements during the exercise. Several reports have suggested that cimetidine or ranitidine might be useful in preventing running associated GI bleeding^[6,8,15]. Our study found that six out of 24 participants had positive heme occult positive before medication and each of these 6 subjects had abnormal endoscopic findings before medication. After 2 wk of medication, five out of these 6 subjects became heme occult negative and had improved endoscopic findings (3 normal, 2 partial improvement, 1 dropout). These findings strongly suggest that GI bleeding induced by long distance running is closely related to gastric acid secretion, and reducing acid output with ranitidine seems to be an effective treatment.

With the wide spread popularity of this kind of sport, these complications might be more frequently observed than one would expect, and physicians should be aware of them when evaluating runners with occult GI bleeding with anemia.

The actual site of GI bleeding associated with running is uncertain, but some reports have identified bleeding lesions in the stomach and colon by endoscopy^[7-10]. The most frequently reported endoscopic abnormalities in runners are erosive gastritis with bleeding stigmata in the stomach^[8,9] and erosion with hemorrhage in the colon^[10]. GI mucosal erosions have mainly been found in the corpus region of the stomach^[9,15] where stress or shock associated gastritis is normally seen^[26]. In contrast, one study has shown abnormal histological features in gastric antral mucosa with decreased mucosal secretion^[27]. To our knowledge, only one case report using endoscopy has demonstrated that exercise induced hemorrhagic lesions were improved after taking a therapeutic course of cimetidine^[15].

Our study shown that twenty-two of the 24 runners had at least one upper GI mucosal abnormality, of which seventeen subjects had mucosal erosions, and four had stigmata of bleeding. These mucosal erosions were found mainly in the antrum, but also in the gastric body, fundus, and angle. Sixteen of 24 runners had follow-up endoscopy after 2 wk medication of ranitidine. The endoscopic improvements were seen in eleven subjects with erosive gastritis.

Gastroesophageal reflux occurs more frequently with exercise than at rest^[28]. Some GI symptoms occurring with exercise can be of esophageal origin, including chest pain and heartburn. These phenomena might be caused by reduced salivary secretion, which results in poor acid clearance^[30]. In addition, esophageal ischemia, due to a decrease in visceral blood flow during exercise, may play an important role in development of esophagitis^[11]. Esophageal acid exposure may be reduced by a histamine H₂-receptor antagonist during running^[29]. However, there are no reports describing exercise-induced esophagitis assessed by endoscopy. Long-term implications of gastro-esophageal reflux in the habitual runner or exerciser are also unknown. Our study showed that eight of the 24 runners had esophagitis before treatment and four out of 5 who received a second

endoscopy had improvements after medication. This suggests that gastroesophageal reflux associated with running is also closely related to acid secretion.

In conclusion, this is the first study that was evaluated by endoscopy on running associated GI symptoms before and after acid reducing medication. Our results have shown that mucosal abnormalities, such as erosive gastritis and esophagitis in long distance runners are related to gastric acid. Therefore, acid suppressive agent is an effective treatment for running related GI symptoms.

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