

Research Article

The Effect of Injection of Erythromycin on Gastroparesis in Diabetic Patients after Laparotomy Surgery

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ABSTRACT

Introduction: Gastroparesis is a gastrointestinal motility disorder described by delayed gastric emptying in the absence of mechanical obstruction and occurs more frequently in patients with diabetes. Erythromycin has been reported to significantly increase gastric emptying by stimulation of gastric motilin receptor. Therefore the aim of our study was to determine the efficacy of administrating of erythromycin on recovery of symptoms and duration of hospitalization in patient with diabetic gastroparesis.

Methods: This interventional study was conducted on diabetic patients at Imam Hossein Hospital, Tehran, Iran, who were undergoing elective or emergency laparotomy. Forty diabetic patients with gastroparesis after laparotomy surgery (15 men and 25 women, age range 20 to 88 years, mean 50.97 ± 18.01 years) were randomized to receive either injectable erythromycin (n = 20) or control with conservative management (n = 20).

Results: The results of the study showed that 57.5% of patients had high blood pressure, 20% had heart disease, 10% had HLP, 2.5% had Alzheimer's, and 7.5% had hypothyroidism. Therefore, in this study, the blood pressure had highest frequency in the study population and Alzheimer's had lowest frequency among patients. Duration of symptom recovery significantly ($p < 0.001$) decreased in patients in the erythromycin group (3.2 days) compared with the control group (5.3 days). In addition, duration of hospitalization significantly ($p < 0.0002$) decreased in patients in the erythromycin group (9.55 days) compared with the control group (12.25 days). **Conclusion:** Administration of erythromycin in diabetic patients with gastroparesis after laparotomy surgery recovers gastric emptying and could decrease the duration of symptom recovery as well as duration of hospitalization.

Keywords: Diabetes, Erythromycin, Gastroparesis, Laparotomy surgery

INTRODUCTION

Gastroparesis is a gastrointestinal motility disorder described by delayed gastric emptying in the absence of mechanical obstruction [1]. It is not clear what leads to gastroparesis but damaging of vagus nerve and the dysfunction in muscles of the stomach are major reason of inducing

gastroparesis [2]. The most frequent symptoms of gastroparesis are bloating, abdominal pain, early satiety, nausea and vomiting [3] and occur more frequently in patients with diabetes compared with the general population but the precise prevalence of diabetic gastroparesis is not

well described [4]. In diabetic subjects which most general known cause of gastroparesis, high blood glucose levels damages the vagus nerve [5]. Other special causes of gastroparesis include idiopathic, post-surgical medication, post-viral infection and nervous system diseases such as Parkinson's disease [6].

Patients with gastroparesis had higher risk for malnutrition leading to increases the duration of hospitalizations, emergency room, and clinician visits for symptom management [5; 7; 8]. Then gastroparesis decreases the quality of life that accompanied with increases direct health-care costs and is associated with morbidity and mortality [5; 7; 8]. Moreover compared with other upper gastrointestinal disorders, patients with gastroparesis usually have an increased rate of inpatient death [6]. Given these trends, effective treatments for gastroparesis are increasingly essential [6].

Currently, erythromycin is a macrolide antibiotic and the potent treatment for subjects with gastroparesis symptoms such as nausea, vomiting and abdominal pain. Erythromycin accelerates gastric emptying to support the removal of food from the stomach into the intestine [6] and is more effective in gastric emptying than other prokinetic agents [6]. Therefore the aim of the present study was to assess the efficacy of administering of erythromycin on recovery of symptoms such as nausea, vomiting and abdominal pain and as well as duration of hospitalization in patient with gastroparesis.

MATERIALS AND METHODS

This interventional study was conducted on diabetic patients in all age groups at Imam Hossein Hospital, Tehran, Iran, who were undergoing elective or emergency laparotomy and all patient had gastroparesis. Before beginning of the study, all study steps were clarified to the patients and consent form was acquired. The study was approved by Shahid Beheshti University of Medical Sciences.

Exclusion criteria in selected subject in this study included:

- 1) Symptoms of gastroparesis before surgery.
- 2) Similar gastroparesis symptoms such as abdominal pain, nausea, vomiting after surgery due to complications of surgery such as blockage or ileus after surgery.
- 3) Post-operative comorbidities (pulmonary edema and myocardial infarction).
- 4) Evidence of tenderness.
- 5) Evidence of cholecystitis or pancreatitis after ultrasound or based on tests
- 6) History of abdominal surgery and abdominal radiotherapy.
- 7) History of influenza that causes temporary gastroparesis.
- 8) Use of drugs affecting gastric emptying
- 9) Eating disorders like anorexia nervosa
- 10) History of severe gastroesophageal reflux.

According to mentioned criteria, 1784 patients underwent laparotomy during the study period (about 18 months). Of these 1784 patients, 174 people had diabetes, and of these 174 people with diabetes, 40 had gastroparesis (23% of patients with diabetes). Of these, 40 patients elected to continue treatment. 13 subjects (32.5%) were operated emergency and 27 subjects (67.5%) were operated elective.

Protocol of study

A diabetic patient with gastroparesis under laparotomy was enrolled in this study. Patients were selected according to the inclusion and exclusion criteria mentioned in the relevant section. To begin the study in patients do not tolerate eating to P.O. after surgery, the symptoms of gastroparesis including nausea, vomiting, abdominal bloating, irregular blood glucose levels, appetite loss, GERD, wall spasm of stomach, night sweats and muscle weakness in all patients was registries in the relevant forms and patients with the mentioned symptoms were considered as suspected to have gastroparesis. Among these subjects, those who have a tenderness examination, as well as evidence of cholecystitis or pancreatitis after ultrasound carried by expert radiologist were also excluded.

After selected these subjects further studies are needed to confirm their disease by upper GI techniques. In summary, this method was performed after 8 hours of fasting to determine the residual food in the stomach and then repeated with a delay of 4 hours to determine the amount of contrast agent consumed by patients and covered the stomach surface. Patients who have residual food in their stomach after 8 hours in the first x-ray and as well as more than 10% of the contrast agent in the stomach after 4 hours in second x-ray considered as patients with gastroparesis. Then, 40 diabetic patients with gastroparesis after laparotomy surgery were randomized to receive either injectable erythromycin (n=20) or control with conservative management (n=20). At the end of study, the gastroparesis symptoms mentioned above were reconsidered in both groups until symptoms were resolved. At the end of the study, patients were discharged from the hospital, whose symptoms resolved and could be eaten.

STATISTICAL ANALYSIS

For statistical analysis, SPSS Statistics V22 (Inc., Chicago, Illinois) was used. Data are presented as mean \pm standard deviation. Frequency data were analyzed by χ^2 analysis, means by unpaired t test. Significance was defined as $p < 0.05$.

RESULTS

Patient characteristics

As shown in Table 1, 40 subjects were listed in this study [15 male: (15.5%), 25 female (62.5%), mean age of total subject 50.97 ± 18.01 yr (range 20–88 yr), mean age of males 49.06 ± 17.35 yr and mean age of females 52.1 ± 18.6 yr]. The minimum and maximum ages for entry into the study were 20 and 88 years respectively. 20 (12 female (60%), 8 male (40%)) subjects were randomized to receive erythromycin (treatment group, mean age 47.05 ± 21.03 yr) and 20 subjects (13 female (65%), 7 male (35%)) received control with conservative management (mean age 54.9 ± 13.82 yr).

Associated diseases in patient with gastroparesis

In this study, people who were included in the study also had other associated diseases that were studied. The results of the study according to Table 2 showed that 57.5% of patients had high blood pressure, 20% had heart disease, 10% had HLP, 2.5% had Alzheimer's, and 7.5% had hypothyroidism. Therefore, in this study, the blood pressure was 23 with the highest frequency in the study population and Alzheimer's with one case had the lowest incidence among patients (Table 2).

Duration of symptom recovery

Duration of symptom recovery significantly ($p < 0.0001$) decreased in patients in the erythromycin group (3.2 days) compared with the control group (5.3 days) (Table 3 and figure 1).

Duration of hospitalization

Duration of hospitalization significantly ($p < 0.00002$) decreased in patients in the erythromycin group (9.55 days) compared with the control with conservative management group (12.25 days) (Table 3 and Figure 2).

DISCUSSION

Gastroparesis is a heterogeneous, severe motility dysfunction and difficult-to-treat in upper gastrointestinal system and that characterized by delay in normal gastric emptying in the absence of mechanical obstruction [2; 9]. Many previous results showed that main causes of gastroparesis are diabetes, idiopathic, post-surgical medication, post-viral infection and nervous system diseases [6]. The 3 main causes of gastroparesis are idiopathic, diabetes and postsurgical [10]. Soykan et al presented that in 146 patients of gastroparesis, idiopathic, diabetic and postgastric surgery accounted for 36%, 29%, 13% of patients [11]. Result from another study showed that diabetes and postsurgical accounted 29% and 13% of patients with respectively [10]. Gastroparesis affected both type 1 and type 2 diabetes patients that have high blood glucose levels caused by lack of insulin secretion or the decrease of insulin sensitivity. Gastroparesis was more well-defined

in patients with type 1 in the NIH consortium cohort study which reported that incidence of gastroparesis are 5.2 % and 1% in type1 and type 2 diabetes, and 0.2 % in healthy subjects.[12; 13]. In addition, Pakman et al, reported that Gastroparesis affects about 40% and up to 30% of patients with type 1 and type 2 diabetes [14].

In this study, the prevalence of gastroparesis was higher in women subject compared with men subjects (62.5.6% in women and 37.5% in men). The higher prevalence of gastroparesis in women than in men was reported in previous studies [2; 10]. Jung et al reported that prevalence of gastroparesis has been estimated at 9.6 and 37.8 per 100 000 in men and women respectively [15], and data on gastroparesis related hospitalizations suggest that its prevalence is increasing [2; 16]. They showed that hospitalizations with gastroparesis increased 158% between 1995- 2004 (from 3,977 to 10,252) as a primary diagnosis and 136% increased (from 56,726 to 134,146) as the secondary diagnosis [2; 16]. In addition, Soykan et al reported that greater parts of those with gastroparesis are women [10; 11].

Similar with our results, pervious study have been reported that the symptoms related to gastroparesis include nausea, vomiting, early satiety, bloating, postprandial fullness, abdominal pain, and weight changes [17]. In a study by Soykan et al. nausea, vomiting, abdominal bloating, early satiety and abdominal pain was present in 92%, 84%, 75%, 60%, and 46% of 146 patients with gastroparesis respectively [11]. In sum up, nausea is found in over 90% of patients , bloating is found in 75% and early satiety are present to a lesser degree, being found in 60%,. Abdominal pain be present in 46–89% of patients but is unlikely to be the predominant symptom [2; 10; 18; 19]. It should be noted that the severity of this symptoms does not correlate with the rate of gastroparesis[20; 21]

Our result showed that in patients with gastroparesis, duration of symptom recovery as well as duration of hospitalization erythromycin administrating significantly decreased in patients in the erythromycin group compared with the

control with conservative management. however, to date there have been few studies addressing the effect of erythromycin administrating on duration of symptom recovery and hospitalization but Ardakani et al reported that, use of erythromycin in patients with acute upper gastrointestinal bleeding before endoscopy significantly decreases the time of hospitalization and improves the quality of EGD [22]. They reported that median duration of hospitalization tended to be shorter for patients in the erythromycin group compared with those in the control group days [22]. The efficacy of erythromycin in gastroparesis have been reported in most pervious published trials [2; 22; 23; 24; 25]. Although according to previous studies erythromycin clearly a potent drug for treatment of patients with gastroparesis, but Maganti reported that efficacy of erythromycin due to small sample sizes of most pervious report, short duration of studies, and inadequate symptom assessment limit available studies and well-designed trials designed to examine symptom relief in gastroparesis are needed [26]. Erythromycins had protective effect on smooth muscles and neurons in the gastrointestinal system and exert these effects via stimulating the motilin receptors [24].

CONCLUSION

The results of our study presented that the duration of hospitalization was lower (2.7 days) in the erythromycin group compared withuntreated group. In addition the time for recovery of symptoms after erythromycin injectionwas lower(2.1 days) in the erythromycin treatment group. Therefore, in general, we can conclude that erythromycin can be used as an appropriate drug for the treatment of gastroparesis after laparotomy in diabetic patients. However, supplementary studies are recommended with more samples.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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Table 1 Demographic characteristics of patient with gastroparesis

Group		Frequency	Percentage (%)	Age
Treatment	Male	8	40	
	Female	12	60	
	Total	20	100	47.05 ± 21.03
Control	Male	7	35	
	Female	13	65	
	Total	20	100	54.9 ± 13.82

Table 2 Associated diseases in patient with gastroparesis

Group	Disease type	Frequency	Percentage (%)
Treatment	Hypertension	11	55.0
	Hypothyroidisms	1	5.0
	Heart disease	5	25.0
	HLP	3	15.0
	Total	20	100.0
Control	Hypertension	12	60.0
	Hypothyroidisms	2	10.0
	Alzheimer	1	5.0
	Heart disease	3	15.0
	HLP	2	10.0
	Total	20	100.0

Table 3 Duration of symptom recovery both in patients in the erythromycin group and control group

Group		Number	Minimum	Maximum	Mean	Median	SD	P value
Treatment	Recovery of symptom	20	2	5	3.2	3	0.96	P < 0.0001
Control	Recovery of symptom	20	3	9	5.3	55	1.26	

Table 4 Duration of hospitalization both in patients in the erythromycin group and control group

Group		Number	Minimum	Maximum	Mean	Median	SD	P value
Treatment	hospitalization	20	7	13	9.55	10	1.6	P < 0.00002
Control	hospitalization	20	9	17	12.25	12	2.33	

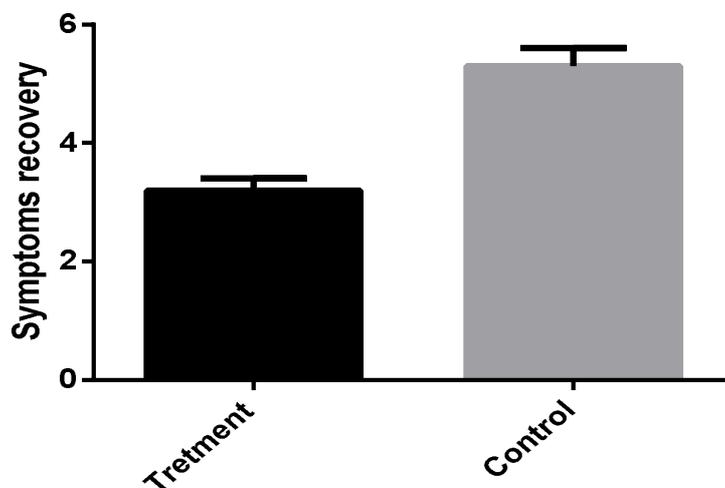


Figure 1 Duration of symptom recovery both in patients in the erythromycin group and control group.

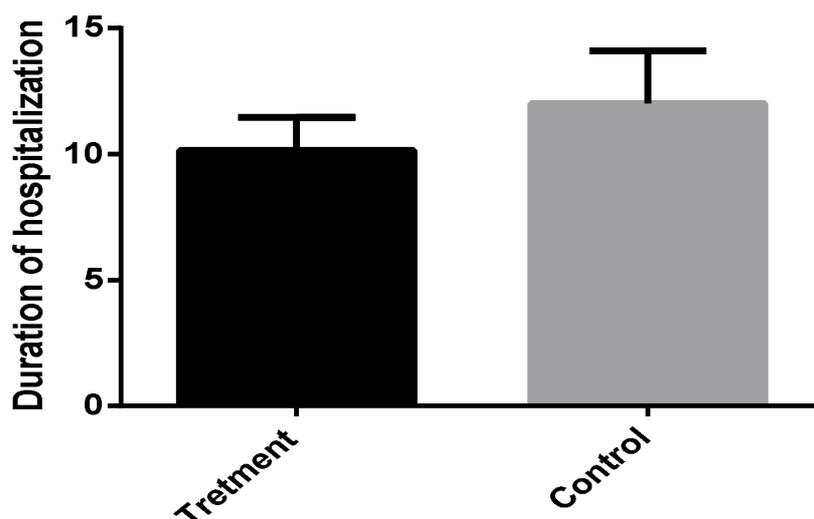


Figure 2 Duration of hospitalization both in patients in the erythromycin group and control group