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DEVELOPMENT AND CHARACTERIZATION OF LECITHIN-BASED THE EFFECT OF ORAL ERYTHROMYCIN ON THE QUALITY OF ENDOSCOPY IN PATIENTS WITH UPPER GASTROINTESTINAL BLEEDING

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Abstract:
Background: *Bleeding from the upper gastrointestinal tract is a medical emergency. Endoscopy is the preferred therapeutic and diagnostic procedure after the initial stabilization of the patient. However, the presence of blood, blood products, and other residues retained in the stomach is a major challenge for endoscopists during urgent endoscopy following acute upper gastrointestinal bleeding. Intravenous erythromycin before endoscopy improves the visualization of the gastric and duodenal mucosa in these patients. Since oral erythromycin is easier and more convenient to use,*
Aim: *The aim of our study is to evaluate the effect of oral erythromycin on the quality of endoscopy in patients with upper gastrointestinal bleeding.*
Methods: *This interventional study was conducted in the Medicine department of Lahore General Hospital for the period of six months from January 2021 to June 2021. Patients with clinical signs of acute upper GI bleeding within 12 hours were considered sequentially. Patients were randomized to an oral erythromycin suspension (500 mg) or a placebo three hours prior to endoscopy. The endoscopist performed all procedures with the same two-channel video endoscope. Endoscopic quality was the primary endpoint. Secondary endpoints included the need for a new endoscopy within 48 hours, endoscopic complications, treatment procedure with or without endoscopy, number of blood transfusions, and length of hospital stay.*
Results: *A total of 60 patients were enrolled in the study; 30 received erythromycin and 30 received placebo. Of these, 60% were male and 40% female. The mean age was 53.68 ± 16.64 years. The quality of endoscopy was significantly better in the erythromycin group (83.3%) compared to placebo (40%). Erythromycin did not reduce endoscopic time (15.53 vs 14.33 minutes in the placebo group; p = 0.216) and hospital stay (5.23 for erythromycin vs 5.40 days in the placebo group; p = 0.807). There was no statistically significant relationship between the use of erythromycin and the diagnosis of the cause of bleeding, the need for a new endoscopy, the number of blood transfusions and the number of endoscopic procedures.*
Conclusion: *Oral suspension of erythromycin before endoscopy in patients with acute upper gastrointestinal bleeding resulted in good quality of endoscopy in our study. The visualization of the gastric and duodenal mucosa has been significantly improved. However, this did not shorten the endoscopy or the hospital stay. There was also no significant difference in the number of revision endoscopies and blood transfusions.*
Keywords: *Erythromycin, Endoscopy, Placebo*

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INTRODUCTION:

Bleeding from the upper gastrointestinal tract is a life-threatening condition and a frequent cause of admission to hospital[1-2]. The incidence has decreased with new treatment options, especially for -peptic ulcer disease, but still ranges from 46 to 67 cases per 100,000 [2,3]. In the last two decades, new methods of treating upper gastrointestinal bleeding have been introduced, which improve the prognosis of these patients[3-4]. Nevertheless, upper gastrointestinal bleeding is still associated with significant morbidity, mortality and healthcare costs. In-hospital mortality is approximately 13%, and the probability of re-bleeding is 15%[5].

Endoscopy is the preferred therapeutic and diagnostic procedure after the initial stabilization of a patient with upper gastrointestinal bleeding. Currently, many endoscopic techniques are used to treat this emergency[6]. Endoscopic treatment can improve both immediate and delayed clinical outcomes. However, the presence of blood, blood products, and other residual gastric residues is a major challenge for endoscopists during urgent upper GI endoscopy following acute upper GI bleeding[7-8]. This complicates the visualization and leads to diagnostic and therapeutic problems during the procedure. To solve this problem, various options were used, such as gastric lavage and instillation of 3% hydrogen peroxide, in the case of hydrogen peroxide the results are good, but the sample size is too small and the lavage results are not satisfactory[9-10].

Scientists also tested erythromycin to improve gastric motility and rapidly remove blood and blood products from the stomach to facilitate endoscopy, with promising results. Erythromycin, when used as an antimicrobial agent, is also a motilin agonist and improves gastric emptying[11-12]. Many studies in America and Europe have shown that intravenous (IV) erythromycin 30 minutes before upper gastrointestinal endoscopy in patients with upper gastrointestinal bleeding improves the visualization of the gastric and duodenal mucosa, shortens endoscopy time and the need for re-endoscopy[13-14]. Based on these findings, the American Society for Gastrointestinal Endoscopy recommended the use of prokinetic drugs, including erythromycin, prior to endoscopy in patients with a high probability of having fresh blood or blood products in the stomach. The European Society for Gastrointestinal Endoscopy also recommends the administration of erythromycin before endoscopy in patients with bleeding from the upper gastrointestinal tract[15].

Since all studies used intravenous erythromycin, both communities recommend that erythromycin be given intravenously prior to endoscopy. Oral erythromycin is more readily available and easier to administer. Oral erythromycin improves gastric emptying, is fast acting, and can be used for rapid gastric emptying when intravenous is not available[16]. With the same rapid gastric emptying mechanism, oral erythromycin can improve endoscopy quality for upper gastrointestinal bleeding. Studies with oral erythromycin have not been conducted in acute upper gastrointestinal bleeding. In our region, no studies have even been conducted to assess the effect of intravenous erythromycin in the local population on acute upper gastrointestinal bleeding. Therefore, it was necessary to study the role of erythromycin, especially orally, to see if it improves the quality of endoscopy in our population. The aim of the study was to evaluate the effect of oral erythromycin on the quality of upper gastrointestinal endoscopy in patients with acute upper gastrointestinal bleeding.

METHODS:

This interventional study was conducted in the Medicine department of Lahore General Hospital for the period of six months from January 2021 to June 2021. Patients over 18 years of age, male or female, with a history of bloody vomiting or tarry stools in the last 12 hours, for whatever reason. Bleeding from the upper gastrointestinal tract was included in the study. Patients with a history of any gastric or duodenal surgery, gastrointestinal drugs such as metoclopramide, use of domperidone in the last 24 hours, gastric lavage after vomiting blood or melaena, and a known allergy to erythromycin were excluded from the study. Pregnant women were also excluded. Informed consent was obtained from the patient or, where applicable, from a family member. The approval of the hospital research ethics committee was obtained prior to the commencement of the study.

All patients were admitted to the intensive care unit and were adequately treated and discharged from hospital in a stable condition. Patients received nothing by mouth (NPO) at least eight hours prior to endoscopy. All patients underwent endoscopy within 12 hours of admission. Since peak erythromycin levels were reached after two hours of oral

erythromycin administration, patients were randomized to an oral erythromycin suspension (500 mg) or placebo three hours prior to endoscopy. Treatments were assigned by means of a computerized randomization list at the hospital pharmacy. Only the hospital pharmacist administered placebo suspension or erythromycin in the same packages. The pharmacist assigned numbers to these packages, and therefore only he knew the result of randomization; neither the endoscopist nor the patients were aware of randomization. The treatment assignment was not released until the computer database was permanently frozen for final analysis.

The endoscopist performed all procedures with the same two-channel video endoscope. The endoscopist performing endoscopy on these patients did not know if they were in the erythromycin or placebo group. Endoscopy time was recorded. Primary and secondary endpoints were recorded. The primary endpoint was endoscopic efficacy as assessed by objective / subjective scoring system and endoscopic time. This scoring system was developed by Carbonell et al and modified according to our needs. The subjective criteria were based on the endoscopist's decision. He observed whether the gastric and duodenal mucosa was fully visualized. The quality of the visualization was assessed by points (less than 0-25%, 1-26 in 50%, 2-51 in 75%, 3- over 75% of the visible mucosa surface). The objective criteria were the presence or absence of clots in each region of the stomach (fundus, trunk, antrum) and duodenum. Clots were defined as clots that could not be retrieved exclusively from the video endoscope accessory channel. For each area (fundus, trunk, antrum and duodenum), 1 point was scored in the absence of a clot, and no points were obtained in the presence of clots. According to subjective and objective criteria, a total score of 5 or more out of 7 was accepted as good quality, and a score below 5 was considered poor endoscopy quality. It was also noted whether the diagnosis was made at the endoscopy. Secondary endpoints required a new endoscopy within 48 hours of the first, endoscopic complications, blood transfusions, and length of hospital stay. A standard endoscopic report was generated immediately after the endoscopy was completed.

The data was entered and analysed on Statistical Product and Service Solutions (SPSS) version 20 (IBM Corp., Armonk, NY). The t-test was used as the significance of t for quantitative data, and the chi-square test was used to search for a statistically significant relationship between different variables in both groups. A p value of <0.05 was considered significant.

RESULTS:

A total of 60 patients were enrolled in the study; 30 received erythromycin and 30 received placebo. Of these, 60% (n = 36) were men, 40% (n = 24) were women, with a mean age of 53.68 ± 16.64 years, ranging from 18 to 67 years, with a mean age of 53.13 ± 17,7 for the erythromycin group and the placebo group. It was 54.23 ± 15.8. The mean endoscopy time was 14.93 ± 3.7 minutes, and the mean hospital stay was 5.32 ± 2.6 days. While 43.3% (n = 26) had varicose bleeding, 56.7% (n = 34) had non-varicose bleeding. The distribution in both groups is presented in Table 1.

TABLE 1: Distribution of variceal and non variceal bleeding in both groups

		Type of bleeding		Total
		Variceal bleed	Non Variceal bleed	
Drug used	Erythromycin	12	18	30
	Placebo	14	16	30
Total		26	34	60

The bleeding site was 53.3% (n = 32) stomach, 36.7% (n = 22) esophagus, and 10% (n = 6) duodenum. The distribution in both groups is presented in Table 2.

TABLE 2: Site of bleeding

		Site of bleed			Total
		Esophagus	Stomach	Duodenum	
Drug used	Erythromycin	11	17	2	30
	Placebo	11	15	4	30
Total		22	32	6	60

No significant side effects or associated endoscopic complications were observed in any of the groups. There were no deaths during the study period.

Oral erythromycin was associated with better endoscopic quality (better visibility and fewer blood clots) in the erythromycin group (83%) compared to the placebo group (40%) (Table 3).

TABLE 3: Endoscopic quality i.e visibility of mucosa and reduced number of blood clots

		Endoscopic quality		Total	p-value
		good	poor		
Drug used	**Erythromycin**	**25**	**5**	**30**	
	Placebo	**12**	**18**	**30**	**.001**
Total		**37**	**23**	**60**	

Erythromycin did not reduce endoscopic time or hospital stay; similarly, there was no difference in the number of blood transfusions (Table 4).

TABLE 4: Endoscopic duration, length of hospital stay and number of blood transfusions

		Endoscopic quality		Total	p-value
		good	poor		
Drug used	**Erythromycin**	**25**	**5**	**30**	
	Placebo	**12**	**18**	**30**	**.001**
Total		**37**	**23**	**60**	

No statistically significant correlation was found between the use of erythromycin and the determination of the cause of bleeding and the need for revision endoscopy (Table 5).

TABLE 5: Need for second look endoscopy and diagnosis established during endoscopy

		Need for second look endoscopy			
		yes	No	Total	p-value
Drug used	Erythromycin	4	26	30	
	Placebo	8	22	30	.333
Total		12	48	60	
		Diagnosis established during endoscopy			
		yes	No	Total	p-value
Drug used	Erythromycin	30	0	30	
	Placebo	28	2	30	.492
Total		58	2	60	

DISCUSSION:

Our results showed that oral erythromycin three hours before endoscopy was associated with better visibility during endoscopy, i.e. 83% good visibility in the erythromycin group compared to 40% in the placebo group. There was no correlation between the use of erythromycin and the diagnosis of the cause of bleeding and the need for a new endoscopy. Endoscopic time and length of hospital stay were also not associated with the use of erythromycin.

Many studies, including randomized trials, have shown that the use of erythromycin before endoscopy in upper gastrointestinal bleeding helps to improve the quality of endoscopy. A meta-analysis published in 2013, including seven randomized controlled trials, showed that administering erythromycin before endoscopy to patients with upper gastrointestinal bleeding significantly improved visualization of the gastric mucosa (odd quotient 3.43, p <0.01) compared to with a lack. erythromycin. Another study in Korea in which patients with upper gastrointestinal bleeding were randomized to erythromycin without gastric lavage, gastric lavage alone, and erythromycin in combination with gastric lavage, showed that more than 90% of patients achieved satisfactory mucosa visualization. in patients in the erythromycin group, but only in 60% of patients without erythromycin. Our results are comparable to previous findings; We found that 83% of the patients in the erythromycin group had good quality endoscopy compared to 40% in the placebo group with p <0.001. The European Society of Gastrointestinal Endoscopy already recommends administering erythromycin prior to endoscopy for non-varicose upper gastrointestinal bleeding for better visualization. All of these previous studies used intravenous erythromycin; We could not find any data on the oral administration of erythromycin to compare our results. Although studies have shown that oral erythromycin significantly reduces gastric transit time in capsule endoscopy, they support our findings.

In our study, the use of erythromycin did not change the duration of endoscopy and hospital stay. The results on this are contradictory in previous studies; Several studies have found the same results as ours, but most studies have found the opposite. Carbonell et al. confirms our findings by showing that erythromycin does not shorten endoscopy or hospital stay. A Swiss study found that, contrary to our results, erythromycin shortens the endoscopy time, but does not affect the length of hospital stay, as do our results. Two meta-analyses published in 2013, including many randomized trials, showed that, contrary to our observations, the use of erythromycin shortens not only the endoscopy time, but also the length of hospital stay.

Many studies have shown that the use of erythromycin reduces the need for revision endoscopy. Coffin et al. and Fossard al. showed that erythromycin significantly reduced the need for revision endoscopy in patients with bleeding from the upper gastrointestinal tract. The same was found in a meta-analysis published in 2016. In our study, although only four patients underwent a second

revision endoscopy compared with eight patients in the placebo group, the statistical difference was not significant (p = 0.33), contrary to the results discussed above. This difference may be due to different administration routes and sample size.

Our study had some limitations as it was mainly a single centre study with 60 patients. Second, all patients with bleeding from the upper gastrointestinal tract, regardless of the cause (varicose or non-varicose bleeding), were included in the study. It is recommended that multicentre studies with appropriate sample sizes be performed comparing the intravenous and oral erythromycin suspension with a separate placebo for varicose and non-varicose bleeding. However, this study opens up a new horizon for the oral use of erythromycin prior to upper gastrointestinal endoscopy, which is the most important finding.

CONCLUSION:

Oral suspension of erythromycin improved the quality of upper gastrointestinal endoscopy in patients with acute upper gastrointestinal bleeding. Indeed, as in other international studies, intravenous erythromycin improved visualization of the gastric and duodenal mucosa, but did not shorten endoscopy or hospital stay. There was also no significant difference in the number of revision endoscopies and blood transfusions.

In patients with a high probability of receiving fresh blood or blood products in the stomach, if intravenous erythromycin cannot be used for some reason, oral erythromycin may be used to improve the quality of upper gastrointestinal endoscopy.

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