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Original Article

Evaluation of Endoscopic Mucosal Band Ligation for Treatment of Portal Hypertensive Gastropathy in Cirrhotic Patients

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ABSTRACT

Background: Portal hypertensive gastropathy (PHG) is a clinical condition that can lead to chronic gastrointestinal (GIT) hemorrhage in cirrhotic patients, presented by chronic anemia. The diagnosis is based on the endoscopic features. The aim of the study was to evaluate the safety and efficacy of the use of endoscopic mucosal band ligation for treatment of portal hypertensive gastropathy in cirrhotic patients.

Patients and methods: This prospective study included 80 cirrhotic anemic patients. They divided into four equal groups: Group (A) included patients who were treated with drugs as beta-blockers. Group (B) included patients treated with argon plasma coagulation (APC). Group (C) included patients treated with endoscopic mucosal band ligation and Group (D) included patients treated with combined endoscopic mucosal band ligation and APC in subsequent sessions.

Results: There was statistical significant decrease in TIBC throughout follow up in the four studied groups. And there was statistical significant increase in Hb, and serum ferritin throughout follow up in the four studied groups.

Conclusion: after 2nd follow-up in managing PHG, we have found that there is significant increase in Hb, serum ferritin and significant decrease in recurrent GI bleeding among all groups.

Keywords: Endoscopic; Band Ligation; Ferritin; Portal Hypertension; Gastropathy.

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INTRODUCTION

Portal hypertensive gastropathy (PHG) is marked by typical gastric mucosal lesions in patients with portal hypertension. The typical site is in the gastric fundus and upper part of the stomach. However, it can affect any part of the stomach and even other parts of gastrointestinal (GIT) tract [1].

PHG prevalence in portal hypertension has been reported to range between 20% and 80%. A higher rate of PHG is associated with more severe liver disease or who had previous endoscopic intervention with endoscopic sclerotherapy or variceal ligation [2].

The PHG diagnosis is established on the basis of specific endoscopic findings. It is categorized as mild (the snake-skin mosaic pattern) or severe (the mosaic pattern, and flat or bulging red marks or black-brown spots) [3].

The acute hemorrhage due to PHG is confirmed when active bleeding from gastropathy specific lesions, non-removable clots overlying the lesions or by exclusion when PHG diagnosed and no other sources or causes of acute bleeding can be identified after thorough assessment of the GIT [4].

Treatment of PHG depends on two pillars. The first is the general procedures used in GIT bleeding independent of the etiology should be applied and the second is the specific methods to manage the etiology of the GIT bleeding. The most effective PHG treatment options are those aimed to reduce the portal pressure [4].

In the chronic blood loss, iron-supplementations were provided to counteract the continuous progressive depletion of iron stores. Other treatment maneuvers included non-selective β-blockers that decreases the bleeding due to PHG either acute or chronic [5].

In addition, shunt therapies are evaluated as a treatment option for PHG, as the portal hypertension is the main causes of PHG [6].

Other blood vessels sealing options are introduced, e.g., electrocautery or argon plasma coagulation. The aim is to stop bleeding originating from the ectatic vessels [7].

Sato *et al.* [8] reported that, the recurrent bleeding was significantly reduced by the endoscopic band ligation and lead to reduction of treatment sessions and hospital stay duration than APC.

Endoscopic band ligation (EBL), firstly used to treat esophageal varices and consequently used for management o PHG and GAVE. It is described as the use of multiple elastic bands to mechanically strangulate the lesions. This lead to thrombosis, necrosis, followed by mucosal and submucosal fibrosis [9].

The current work had been designed to assess the safety and efficacy of the endoscopic mucosal band ligation for treatment of PHG in patients with hepatic cirrhosis.

PATIENTS AND METHODS

This prospective study was done in Al-Azhar university hospital at New Damietta, in the period from July 2019 to July 2021.The patients enrolled in this study were taken from inpatient and outpatient clinic of Internal Medicine Department of Al-Azhar university hospital at New Damietta.

This prospective study to evaluate the safety and efficacy of the use of endoscopic mucosal band ligation for treatment of portal hypertensive gastropathy in cirrhotic patients in Damietta.

We included 80 patients with portal hypertensive gastropathy (PHG) due to Chronic liver disease, selected from outpatient clinic and Internal Medicine Department of Al-Azhar University Hospital – Damietta – Egypt, from July 2019 to July 2021.

Institutional Review Board (IRB) approval was acquired, and all patients were aware of the study and signed informed consent forms.

Patients were divided to four groups. ***Group A*** for patients treated with medical treatment as beta-blocker. ***Group B*** for patients treated with APC. ***Group C*** for patients treated with endoscopic mucosal band ligation. ***Group D*** for patients treated with combined endoscopic mucosal band ligation and APC in subsequent sessions.

Inclusion criteria:

Chronic liver disease, and severe PHG.

Exclusion criteria:

Patients on non-steroidal anti-inflammatory drugs (NSAIDs) in the last month; presence of esophagitis, gastritis or duodenitis; esophageal, gastric, duodenal ulceration, mass or tumor and hiatus hernia.

All study patients were subjected to the following:

Full history and thorough physical examination including age, sex, treatment history, smoking, family history, other chronic illnesses, and causes of cirrhosis.

Laboratory investigations were also studied as the following: complete blood count (CBC), liver function tests (serum bilirubin (total and direct), serum albumin, serum glutamic pyruvic transaminase (SGPT), and serum glutamic oxalacetic transaminase (SGOT)), coagulation profile (PT and INR), Serum Iron, Serum ferritin, TIBC.

Radiological investigation included Pelvi-abdominal ultrasonography.

Upper gastrointestinal endoscopy:

PHG diagnosis was built according to the NIEC classifications. The simple lesions of PHG are

(1) Mosaic like pattern (the presence of small, polygonal areas surrounded by a whitish yellow depressed border).

(2) Red point lesions (RPLs) are small, flat, red point like lesions, 1 mm in diameter.

(3) Cherry red spots (CRSs) are red colored, round lesions about 2 mm in diameter, and slightly protruded into the lumen of the stomach

(4) Black brown spots (BBSs) are irregularly shaped flat spots, black or brown, persistently present after washing, and caused by intramucosal hemorrhage.

Statistical methods:

The results were collected, tabulated, and statistically analyzed using IBM personal computer and statistical package SPSS version 11.

Frequencies and percentages were used in description of categorical data, while means and standard deviations were used for presentation of quantitative data.

Chi-squared test was used to test for association between two categorical variables. Also, independent samples t-test was used to test for statistical difference of normally distributed quantitative data. P value < 0.05 was considered significant.

RESULTS

We included 80 cirrhotic patients with portal Hypertensive Gastropathy into our study. Patients were divided into four groups: Group A: Cirrhotic anemic patients treated with medical treatment as beta blocker. Group B: Cirrhotic anemic patients treated with Argon Plasma Coagulation (APC). Group C: Cirrhotic anemic patients treated with endoscopic mucosal band ligation. Group D: Cirrhotic anemic patients treated with combined endoscopic mucosal band ligation and Argon Plasma Coagulation (APC) in subsequent sessions.

There was no statistically significant difference between the studied groups regarding age and gender. (Table 1).

There was no observed significant difference between study groups in all studied clinical parameters which included palpable spleen, ascites, Previous intervention (P > 0.05). (Table 2).

Regarding laboratory parameters, there was no statistically significant difference between the studied groups regarding white cell count, hemoglobin, and platelet count (P > 0.05. Moreover, liver enzymes and albumin and bilirubin level INR, there was no statistically significant difference between the studied groups (P >0.05). Also There was no statistically significant difference between the studied groups regarding iron, TIBC, ferritin level (Tables 3).

There was no statistically significant difference between the studied groups regarding distribution of portal hypertensive gastropathy and fundal varices. (P >0.05). There was no statistically significant difference between studied groups regarding distribution of PHG lesions and OV grade.

There was statistical significant increase in hemoglobin throughout follow up in the studied groups. At first follow up, hemoglobin level was significantly lower in group A compared to group B and group D. At second follow up, hemoglobin level was significantly lower in group A compared to group B, group C and group D (Table 4).

There was statistical significant increase in iron, serum ferritin, TIBC throughout follow up in the four studied groups (P < .001) (Table5).

Table (1): Age distribution among the studied groups

		Group A (n=20)	Group B (n=20)	Group C (n=20)	Group D (n=20)	P-value*
Age	Mean± SD	46.20± 8.65	45.12±8.73	43.44± 8.97	43.08± 7.25	0.617
	Range	31.31- 62.96	26.79- 58.62	24.03- 59.93	28.02- 55.73	

Table (2): Characteristics and clinical parameters in study groups.

			Group A (n=20)	Group B (n=20)	Group C (n=20)	Group D (n=20)	P-value*
Ascites (n,%)	Negative		11 (55.0%)	9 (45.0%)	10 (50.0%)	9 (45.0%)	0.908
	Positive		9 (45.0%)	11 (55.0%)	10 (50.0%)	11 (55.0%)	
Spleen	Normal		3(15.0%)	5(25.0%)	2(10.0%)	3(15.0%)	0.892
	Splenectomy		11 (55.0%)	8 (40.0%)	11 (55.0%)	11 (55.0%)	
	Splenomegaly		6 (30.0%)	7 (35.0%)	7 (35.0%)	6 (30.0%)	
Previous intervention	Negative		20 (100.0%)	20 (100.0%)	20(100.0%)	19(95.0%)	0.801
	Positive		0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	
Cause	Bacterial	n	6 (30.0%)	10 (50.0%)	10 (50.0%)	9 (45.0%)	0.784
	Viral	n	5(25.0%)	4(20.0%)	4(20.0%)	6 (30.0%)	
	Mixed	n	9 (45.0%)	6 (30.0%)	6 (30.0%)	5(25.0%)	

Table (3): Laboratory parameters in study groups.

Parameter	Group A (n=20)	Group B (n=20)	Group C (n=20)	Group D (n=20)	P-value*
ALT (IU/L)	41.29 ± 15.07	42.48 ± 10.49	45.38 ± 10.33	43.46 ± 12.79	0.757
AST (IU/L)	36.96 ± 12.12	34.33 ± 9.97	34.13 ± 12.82	38.31 ± 11.04	0.600
INR	2.00 ± .49	2.13 ± .49	1.95 ± .43	1.91 ± .46	0.470
Bilirubin (mg/dl)	3.51 ± 1.33	3.06 ± 1.15	3.24 ± 1.31	2.78 ± 1.46	0.371
Albumin (g/dl)	2.60 ± .61	2.88 ± .84	2.60 ± .75	2.68 ± .81	0.611
Urea (mg/dl)	65.10 ± 11.50	65.23 ± 13.84	66.06 ± 17.82	68.54 ± 17.66	0.887
Creatinine (mg/dl)	1.33 ± .23	1.18 ±.30	1.20 ± .33	1.16 ± .38	0.333
Hb (g/dl)	7.93 ± .56	8.00 ± .64	7.84 ± .62	7.90 ± .57	0.878
WBCs	5.17 ± 1.71	4.16 ± 2.44	4.80 ± 2.21	4.78 ± 2.95	0.599
Platelets	90.65 ± 10.42	88.28 ± 12.72	87.81 ± 10.45	84.39 ± 10.45	0.359
Iron	50.48 ± 3.44	52.25 ± 2.81	50.87 ± 3.03	50.84 ± 2.67	0.265
TIBC	470.2 ± 22.53	476.0 ± 26.74	484.5 ± 22.03	472.04 ± 20.62	0.218
Ferritin	9.13 ± .51	9.20 ± .35	9.22 ± .40	9.13 ± .29	0.827

Table (4): comparison between the studied groups regarding Hb at different follow-up periods

		Group A (n=20)	Group B (n=20)	Group C (n=20)	Group D (n=20)	P-value
Hemoglobin concentration (g/dl)	Before	7.93 ± .56	8.00 ± .64	7.84 ± .62	7.90 ± .57	0.878
	first follow up	8.06 ± 1.43	9.20 ± 1.29	9.02 ± 1.18	9.33 ± 1.54	0.018
	second follow up	8.90 ± 1.63	10.16 ± 1.53	10.12 ± 1.30	11.21 ± 1.25	<0.001
P-value		<0.001	<0.001	<0.001	<0.001	

Table (5): Comparison between the studied groups regarding serum iron at different follow-up periods

Iron	Group A (n=20)	Group B (n=20)	Group C (n=20)	Group D (n=20)	P-value
Before	50.48 ± 3.44	52.25 ± 2.81	50.87 ± 3.03	50.84 ± 2.67	0.265
First follow up	55.84 ± 1.40	60.79 ± 1.90	69.25 ± 1.28	73.49 ± 1.56	<0.001
Second follow up	64.89 ± 1.49	70.52 ± 1.78	81.26 ± 1.41	81.37 ± 1.57	<0.001
P-value	<0.001	<0.001	<0.001	<0.001	

DISCUSSION

The results of the current work showed that, all groups were comparable regarding demographic characteristics. **Hashim *et al.*** [10] reported in comparable results, as there was no significant difference between their groups regarding demographics. They included 67 (59.8%) males and 45 (40.2%) females and 92.1% of patients coming from rural and 17.9% of from urban areas.

In addition, laboratory investigations, spleen status, previous interventions, splenomegaly, PHG and fundal varices or esophageal varices grade were comparable between groups. These results are comparable to **Milić *et al.*** [11] reported no significant differences groups with liver cirrhosis. However, they reported significant increase of men in the group of alcoholic cirrhosis, which is different than the current work. This could be attributed to the absence of alcohol drinking in our patients. Only minorities drink alcohol due to prohibition of it by religious instruction. But, groups were comparable as regard to sex distribution. They didn't find significant difference between two groups regarding OV (p=0.396) and hepatic encephalopathy. Their patients had severe degree of the disease and laboratory findings were comparable, except significant lower values of RBCs and longer prothrombin time in alcoholic than non-alcoholics.

We had a significant increase of hemoglobin and iron stores during follow up in all four groups. This explained by the control of esophageal hemorrhage associated with PHG. However groups differ in each visit of follow up (for example, at first visit, hemoglobin was significantly lower in group A than groups B and D. But at the second visit, hemoglobin significantly reduced in group A than groups B, C and D.

Elhendawy *et al.* [12] in the EBL group, the average hemoglobin increased from 6.73 ± 0.991 before to 10.31 ± 1.01 after treatment, with significant differences; and the difference was statistically significant ($p < 0.001$). In the APC group, hemoglobin increased from 6.72 ± 0.905 before, to 9.85 ± 0.906 after treatment; and the difference was significant.

Wells *et al.* [13] performed an observational study and included nine patients managed by EBL and 13 patients managed with endoscopic thermal therapy (ETT). They reported superiority of EBL over ETT, regarding to reduction of treatment sessions, bleeding control, duration of hospitalization, need for blood transfusion and increase in hemoglobin values. **Zeped-Gomez *et al.*** [14] published a study on a number of patients treated by EBL for PHG. They found a significant increase in hemoglobin and a significant reduction of the need to transfusion.

McCarty *et al.* [15] in their meta-analysis reported that patients need about 2.76±2.74 units of blood for transfusions and were hospitalized for 2.06±0.31 times before EBL. Mean pre-EBL hemoglobin was significantly increased after treatment. The need for blood transfusions were significantly reduced after than before-EBL. The pooled mean hemoglobin increased 1.48 gm/dL after EBL treatment.

The TIBC were significantly reduced while serum ferritin significantly increased after treatment than before therapy in all groups and it was steady during follow up. In line with these findings, **Hashim *et al.*** [10] reported significant increase in hemoglobin concentrations, serum iron and ferritin with a significant reduction of TIBC after than before treatment. This indicates an overall improvement of anemia and iron deficiency.

Finally, in the current study, we found statistically significant differences between the four studied groups regarding recurrent bleeding at the first and the second follow up visits.

McCarty *et al.* [15] reported that EBL was associated with a significant reduction of re-bleeding).

Chalhoub *et al.* [16] included a 207 patients (EBL: 93 vs APC 114) and reported comparable results regarding the effectiveness of EBL vs APC, with significantly reduced transfusion needs and number of treatment sessions to achieve eradication with no significant differences in adverse events.

Conclusion:

The hemoglobin concentrations, and serum ferritin were significantly increased after than before treatment in

all groups, and recurrent attacks of PHG were significantly reduced among all groups. These results indicating effectiveness and absent major side effects indicating safety of studied procedures.

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