The Efficacy of Argon Plasma Coagulation versus Carvedilol for Treatment of Portal Hypertensive Gastropathy

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Keywords

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Abstract

Background/Aim: Several treatment options have been developed for portal hypertensive gastropathy (PHG); medications and endoscopic management. The aim of this study was to evaluate the efficacy and safety of argon plasma coagulation (APC) versus Carvedilol in treatment of a cohort of Egyptian patients with severe PHG. **Methods:** A total of 130 patients with severe PHG were enrolled; 10 patients were excluded due to death and failure to complete the treatment sessions accordingly, 120 patients were included. Patients were divided into 2 groups: Group A ($n = 52$) treated with APC; Group B ($n = 68$) treated with oral Carvedilol. Success was defined as stabilization of hemoglobin (Hb) over 100 g/dL or Hb increase $>10\%$ from pretreatment level and reduction of blood transfusion requirements over the following 3 months after the start of therapy. Upper gastrointestinal endoscopy was performed to assess the degree and site of PHG. APC was conducted to areas with mucosal ectatic vascular lesions. **Results:** PHG was mostly fundic (36.35%) in APC group and (36.76%) in Carvedilol group ($p = 0.56$). Throughout follow-up period, there was significant increase

in Hb level, serum iron, and serum ferritin with a significant decrease in total iron-binding capacity (TIBC) in APC group as compared to Carvedilol group ($p < 0.001$). Additionally, there was gradual increase in the mean Hb, serum iron, and serum ferritin and gradual decrease of TIBC in Carvedilol group. Accordingly, there was an overall improvement of iron deficiency anemia (IDA) in both groups; however, it was significantly better in APC group than in Carvedilol group. No major adverse events were detected in both the groups. **Conclusion:** APC significantly improves IDA and decreases transfusion requirements in patients with severe PHG as compared to oral Carvedilol with small risk of adverse events. Furthermore, the combination of APC and Carvedilol unless contraindicated could have a synergistic effect in controlling severe PHG.

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Introduction

Portal hypertension (PH) is an almost unavoidable complication of cirrhosis and provides the driving force for most of its complications, such as esophageal and gastric varices, variceal bleeding, portal hypertensive gastropathy (PHG), ascites, spontaneous bacterial peritonitis, hepatorenal syndrome, thrombopenia, leucopenia,

anemia, and portal-systemic encephalopathy [1]. Because of this, there is a great interest in strategies to revert PH, since these would prevent PH-related complications, clinical decompensation, and death. PHG accounts for 8% of nonvariceal upper gastrointestinal (GI) bleeding in patients with liver disease [2]. The gold standard method of determining portal pressure involves accessing the hepatic vein through a femoral catheter and measuring the wedged and free pressures. The difference of these 2 pressures is called the hepatic venous pressure gradient (HVPG), which is closely related to the development of complications of PH. The elevation of HVPG from a normal of 1–3 mm Hg to >12 is associated with development of ascites and greater chances of variceal rupture. Severe PH is usually defined as an HVPG >15 mm Hg [3]. PHG is classified endoscopically according to McCormack et al. [4] who first described it in 1985; however, it was limited by lack of grading of intermediate endoscopic findings. In 1994, the New Italian Endoscopy Club (NIEC) proposed an alternative classification including a moderate aspect of PHG [5]. Several treatment options have been developed for PHG; medications and endoscopic management. Argon plasma coagulation (APC) has been used to stop bleeding from ectatic vessels, and to attempt to obliterate the vessels, but have limited utility if the disease is diffuse [6]. APC is an electrosurgical technique for the management of bleeding and the devitalization of tissue abnormalities. This is achieved by a noncontact thermal coagulation in which high-frequency current is applied to the target tissue through an argon plasma jet creating effective hemostasis and a homogenous surface coagulation with a limited penetration depth. It was reported that the hemoglobin (Hb) value improved and transfusion requirements decreased in patients with PHG after therapy with APC [7]. Conventionally, the nonselective α - β -blocker, propranolol has been used to lower portal pressure and to avoid variceal rupture and consequent hematemesis. However, two-thirds of cirrhotic patients may not respond to propranolol [8]. Carvedilol is a newer nonselective β -antagonist that also possesses α 1-antagonist receptor properties is currently a mainstay in the treatment of heart failure and hypertension. It is 2–4 times powerful as compared to propranolol in its β -blocking properties [9]. Carvedilol is a potent nonselective beta-blocker with mild anti-alpha 1 adrenergic activity (one-tenth of its beta-blocker activity). It was developed for the treatment of arterial hypertension and heart failure and has US Food and Drug Administration approval for both indications. Milligram for milligram, Carvedilol is 2–4 times more potent than propranolol as

a beta-receptor antagonist [10]. Carvedilol decreases heart rate and cardiac output and causes splanchnic vasoconstriction. This results in reduced portal blood inflow and in a fall in portal pressure. In addition, through its alpha 1 adrenoceptor blocking effect, Carvedilol decreases the hepatic vascular tone and hepatic resistance resulting in a further decrease in portal pressure [1]. However, the vasodilating activity of Carvedilol may enhance arterial hypotension and sodium retention, a risk which is especially relevant in patients with advanced, decompensated cirrhosis [11]. Some studies suggest that relatively low doses of Carvedilol (12.5 mg/day or 6.25 mg bid) retain a good portal pressure reducing effect with less potential for hypotension which may be relevant when treating decompensated patients with cirrhosis [12].

Materials and Methods

This prospective, observational study was conducted at EL-Hussein university hospital, AL-Azhar University, Cairo, Egypt, between March 2018 and May 2019. This study was approved by Institutional Review Board of the Faculty of Medicine (AL-Azhar Institutional Ethics Committee), and all study subjects provided informed consent.

Study Design

Adult patient's ≥ 18 years old were eligible for recruitment if they had hepatic disease and with severe PHG diagnosed by upper GI endoscopy. The indications of upper GI endoscopy were recurrent episode of upper GI bleeding or during the follow-up after variceal endoscopic therapy and chronic iron deficiency anemia (IDA) resistant to conventional therapy. Patients were excluded if they were in an acute episode of hepatic encephalopathy, severe cardiopulmonary disease, chronic renal failure or hemodynamic instability, or if they had actively bleeding esophageal or gastric varices, or actively bleeding gastric or duodenal ulcers or malignancies and finally, patients with known allergy or contraindication to Carvedilol (bronchial asthma, decompensated heart failure, etc.). Patients were divided into 2 groups: APC Group ($n = 52$) treated with APC; Group B ($n = 68$) treated with oral Carvedilol. The selected groups of patients were subjected to the following: (1) full history taking, (2) complete clinical examination: vital signs, signs of PH such as dilated abdominal veins, or splenomegaly; signs of liver cell failure such as jaundice, ascites, lower limb edema, fetor hepaticus, flapping tremors, or spider angioma; and signs of renal, cardiac, or respiratory diseases; (3) laboratory investigations: liver function tests, prothrombin time, prothrombin concentration (%), and INR; kidney function tests including blood urea and serum creatinine; complete blood count; and iron profile. For each patient, the Child-Pugh score was calculated. Abdominal ultrasonography for all patients was conducted, and cirrhotic echo pattern was determined from the coarse nodular appearance and shrunken size with prominent caudate lobe. The following were also noted: presence of ascites, portal vein diameter, splenic bipolar diameter, hilar varices, and splenic vein diameter.

Endoscopic Evaluation

The instruments used in this study were a videoendoscope and an electronic endoscopic system (Olympus EVIS Lucera Ellit CV-290; Olympus Medical Systems, Tokyo, Japan) equipped with 3 imaging modes: high-resolution white light endoscopy, autofluorescence imaging, and narrow-band imaging. Mode switch from white light endoscopy to narrow-band imaging or autofluorescence imaging was controlled by buttons on the control head. All patients were offered conscious sedation with intravenous midazolam (2.5–7.5 mg) and/or propofol (40–200 mg) and then underwent endoscopic assessment of the degree and site of PHG, presence of esophageal varices and their grade, fundal extension or presence of isolated fundal varix, gastritis or duodenitis, erosions, and ulcerations. PHG was assessed according to the NIEC classifications. The elementary lesions of PHG according to the NIEC classification are as follows: (1) mosaic-like pattern is defined as the presence of small, polygonal areas surrounded by a whitish-yellow depressed border. The mosaic is defined as mild when the areola is uniformly pink, moderate if the center is red, and severe if the areola is uniformly red. (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 protrude 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. At a previous International Consensus Conference, it was decided to define PHG as mild when only mosaic-like pattern of any degree was present and severe when RPLs, CRSs, or BBSs were present [5]. Esophageal varices was classified according to Westaby classification of esophageal varices [13], which has been endorsed by the British Society of Gastroenterology in its guidelines [14], Grade 1: Varices appearing as slight protrusion above mucosa, which can be depressed with insufflations; Grade 2: Varices occupying <50% of the lumen; Grade 3: Varices occupying >50% of the lumen and which are very close to each other with confluent appearance. All of the endoscopic examinations were performed by one senior endoscopes with >10 years of experience in diagnostic and therapeutic endoscopy.

Argon Plasma Coagulation

The APC system was consisted of the following: the disposable APC probe with diameters of 1.5 mm, 2.3 mm, and 220 cm long, a foot pedal, 2 tanks of argon gas, and a high-frequency monopole electrosurgical generator current conducted to target tissues through ionized argon gas (argon plasma). Electrical spark could be easily elicited by pressing the blue foot pad connected to APC equipment. The argon gas flow was set at 2.5 L/min, and the electrical power output was adjusted to 60–90 W. APC was applied to all areas of visible red spots of congested gastric mucosa with a depth of penetration of roughly 2–3 mm for about 1–3 s. The session duration was from 15 to 20 min. APC was done in a single session in patients who have localized PHG and in multiple sessions in patients who have diffuse PHG where endoscopy was repeated after 2 weeks. All patients received intravenous antibiotics therapy after the procedure (ceftriaxone 1 g daily) for prophylaxis of infection as well, proton pump inhibitor therapy (lansoprazole 30 mg daily) therapy after the procedure to improve mucosal healing.

Carvedilol Dose

Carvedilol doses were administrated at 12.5–25 mg (mean 19 ± 3.79 mg/day) starting at 6.25 mg and titrated up every 4 days according to blood pressure and heart rate intended to reduce the heart rate by 25% or down to 55 beats/min. The dose should not be increased in patients developing symptoms or with a systolic blood pressure <90 mm Hg or a heart rate <50 bpm. Carvedilol is contraindicated in patients with marked bradycardia, the sick sinus syndrome, and partial or complete heart block (unless a pacemaker is in place). Thus, an electrocardiogram is mandatory before starting therapy. Carvedilol is also contraindicated in patients with asthma. Carvedilol was used cautiously in patients with insulin-dependent diabetes because it can mask the symptoms of hypoglycemia.

Outcome Measures

All patients were followed up after treatment by laboratory evaluation of Hb level and iron profile. Success was defined as; stabilization of Hb over 100 g/dL, or Hb increase >10% from pretreatment level, and reduction of transfusion requirements >50% in transfusion-dependent patients over the following 3 months after the start of therapy.

Statistical Analysis

Data were analyzed by statistical package for social science (version 16.0; SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as mean $\pm$ SD. General linear model was used to test differences at different times using repeated measures analysis of variance. Paired *t* test was used to test before and after paired observations. Qualitative data were expressed as numbers and percentages and analyzed by chi-square test. For the calculation of cutoff values, the receiver operator curve was calculated and the best cutoff was determined. For correlation between 2 parameters, the Pearson's correlation coefficient (*r*) was calculated; it was inverted if the sign is negative and proportional if the sign is positive. Level of significance was set to a *p* value <0.05.

Results

A total of 130 patients were recruited over the study period; 10 patients (8.33%) were excluded due to either death (*n* = 5) caused by hepatic encephalopathy and hepatorenal syndrome or did not complete the treatment sessions (*n* = 5); therefore, 120 patients completed the study (92.30%). Table 1 presents the baseline demographic and clinical characteristics for the 2 groups. Of the 120 patients, 90 (75%) were referred to the emergency endoscopy unit due to either melena or hematemesis and 30 (25%) were referred for elective upper GI endoscopy as a follow-up after variceal endoscopic therapy. The mean Hb level at the start of therapy of both APC and Carvedilol groups was 7.95 ± 0.52 , 7.42 ± 0.33 , respectively, without significant difference (*p* = 0.17). The most common cause of PHG was viral hepatitis 57 (47.5%) including HCV 44 (36.6%) and HBV 13 (10.8%) followed by viral hepatitis mixed with bilharziasis 51 (42.5%) and finally bilharziasis alone 12 (10%).

Table 1. Baseline characteristics of the study groups

Variable	APC group (<i>n</i> = 52)	Carvedilol group (<i>n</i> = 68)	<i>p</i> value
Age, years, mean ± SD	45.9±8.6	46.5±7.6	0.18
Gender, <i>n</i> (%)			
Male	33 (63.46)	42 (61.76)	0.67
Female	19 (36.53)	26 (38.23)	0.68
ALT, IU/L	44.05±10.34	46.04±8.7	0.87
AST, IU/L	37.92±12.52	39.76±11.54	0.95
INR, mean ± SD	2.05±0.44	1.06±0.32	0.92
Bilirubin (total), mg/dL	3.30±1.53	3.29±1.64	0.45
Albumin, mean ± SD, g/dL	2.70±0.70	2.60±0.65	0.89
Urea, mean ± SD, mg/dL	65±15	66±14	0.78
Creatinine, mean ± SD, mg/dL	1.23±0.3	1.21±0.4	0.96
Hb, g/dL	7.95±0.52	7.42±0.33	0.17
WBCs	4.69±3.87	3.9±1.95	0.28
Platelets	89.27±45.87	90.8±25.11	0.67
Iron, µg/dL	51.37±2.72	50.40±3.75	0.88
TIBC, µg/dL	476.64±19.34	478.28±20.04	0.62
Ferritin, µg/dL	9.12±0.45	8.96±0.57	0.29
Ascites, <i>n</i> (%)	43 (82.69)	56 (82.35)	0.58
Spleen, <i>n</i> (%)			0.67
Normal	3 (5.35)	4 (5.88)	
Splenectomy	4 (7.14)	5 (7.35)	
Splenomegally	45 (86.53)	59 (86.76)	
Previous intervention, <i>n</i> (%)	42 (80.7)	56 (82.35)	0.86
Cause of PHG, <i>n</i> (%)			0.37
Viral	25 (48.07)	32 (47.05)	
Bilharzial	5 (9.61)	7 (10.29)	
Mixed	22 (42.30)	29 (42.64)	
Child classification, <i>n</i> (%)			0.76
Child A	8 (15.38)	11 (16.17)	
Child B	17 (32.69)	22 (32.35)	
Child C	27 (51.92)	35 (51.47)	

No significant differences between the 2 groups regarding the baseline characteristics.

APC, argon plasma coagulation; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; Hb, hemoglobin; WBC, white blood cells; TIBC, total iron-binding capacity; PHG, portal hypertensive gastropathy.

Our results revealed that there were 27 (22.5%) patients with no esophageal varices; 20 patients of them were eradicated previously; and 7 had no esophageal varices. Regarding the severity of PHG according to NIEC, Bus accounts to about 58 (48.3%), CRSs 53 (44.1%), and Rolls 9 (7.5%; Table 2). Furthermore, the fundus is the most affected site of the stomach 44 (36.6%) followed by corporeal 41 (34.1%) and finally pan gastric 35 (29.1%). With regard to hepatic functional reserve, 19 (15.8%) had Child class A, 39 (32.5%) had Child class B, and 62 (51.6%) had Child class C; this indicated that most patients with PHG had decompensated hepatic disease. In APC group, there was significant increase of Hb, serum iron, serum ferritin and significant

decrease of total iron-binding capacity (TIBC), at all post-operative check points as compared to pretreatment values in both per-protocol and intention-to-treat analysis ($p < 0.001$; Table 3; Fig. 1). Additionally, there was gradual increase in the mean of Hb, serum iron, and serum ferritin and gradual decrease of TIBC in Carvedilol group. Accordingly, there was overall improvement of IDA in both groups; however, it was significantly better in APC group than in Carvedilol group. Furthermore, there was reduction of transfusion requirements >50% in transfusion-dependent patients over the following 3 months after the start of therapy in APC group in comparison to Carvedilol group. With regard to rebleeding in APC group, it was

Fig. 1. Treatment outcomes after 3 months. Hb, hemoglobin; TIBC, total iron-binding capacity; APC, argon plasma coagulation.

28.84, 17.30, and 9.61%, respectively, at 1, 2, and 3 months after treatment; while in Carvedilol group, it was 41.17, 34.61, and 11.76%, respectively, with significant difference between the 2 groups $p = 0.02$, $p = 0.03$, $p = 0.05$, respectively, these results indicated that Carvedilol take long time to get a full benefit in preventing reloading in PHG. As regard to complications in APC group, gaseous distension was reported in 57.6% and pain at treatment site in 38.4%. Concerning the APC sessions, the initial session duration extended from 22 min (fundic or corporeal) up to 30 min (pan gastric). The mean number of sessions was 1.65 ± 0.8 , and the range of sessions was 1–4; 8 (15.3%) of patients needed 4 sessions, 12 (23.07%) needed 3 sessions, 10 (19.2%) patients needed 2 sessions, and 22 (42.30%) needed only 1 session. The number of sessions varied according to PHG distribution; fundic and corporeal PHG needed 1 or 2 sessions, while pan gastric PHG needed 2, 3, or 4 sessions; therefore, patients with fundic and corporeal PHG required the lowest number of sessions, on the other hand, more sessions were needed for pan gastric PHG.

Discussion

This study investigated the efficacy and safety of APC versus Carvedilol in the treatment of patients with severe PHG. PHG is one of the clinical conditions that can cause

Table 2. Endoscopic evaluations of the study groups

Variable	APC group (n = 52)	Carvedilol group (n = 68)	p value
PHG distribution, n (%)			0.56
Fundic	19 (36.53)	25 (36.76)	
Corporeal	18 (34.61)	23 (33.82)	
Pangastric	15 (28.84)	20 (29.41)	
Severity of PHG, n (%)			0.69
MLP	0 (0)	0 (0)	
RPLS	4 (7.69)	5 (7.35)	
CRSs	23 (44.23)	30 (42.64)	
BBSs	25 (48.07)	33 (48.52)	
OV grade, n (%)			0.88
Eradicated	12 (23.07)	15 (22.05)	
Grade I	14 (26.92)	18 (26.47)	
Grade II	20 (38.46)	26 (38.23)	
Grade III	6 (11.53)	9 (13.23)	
Fundal vascis, n (%)	8 (15.38)	10 (14.70)	0.30

The fundus is the most affected site of the stomach 44 (36.6%) followed by corporeal 41 (34.1%) and finally pangastric 35 (29.1%).

APC, argon plasma coagulation; PHG, portal hypertensive gastropathy; MLP, mosaic-like pattern; RPLs, red-point lesions; CRSs, cherry-red spots; BBSs, black-brown spotsare.

Table 3. Treatment outcomes

Posttreatment	Test	APC group (<i>n</i> = 52)	Carvedilol group (<i>n</i> = 68)	<i>p</i> value
1 month	Hb	8.60±0.72	7.75±0.49	<0.001
	Iron	68.81±4.54	56.10±3.95	<0.001
	TIBC	450.13±22.77	480.50±19.88	<0.001
	Ferritin	11.52±0.55	9.24±0.66	<0.001
	Rebleeding	15 (28.84)	28 (41.17)	0.02
2 months	Hb	9.51±0.60	8.23±55	<0.001
	Iron	78.75±4.12	67.95±4.19	<0.001
	TIBC	409.15±27.87	465.26±19.05	<0.001
	Ferritin	11.95±0.85	9.51±0.4	<0.001
	Rebleeding	9 (17.30)	18 (34.61)	0.03
3 months	Hb	10.12±0.86	8.7±0.75	<0.001
	Iron	86.80±	73.68±4.51	<0.001
	TIBC	387.56±28.24	440.16±19.23	<0.001
	Ferritin	12.51±0.67	9.95±0.5	<0.001
	Rebleeding	5 (9.61)	8 (11.76)	0.056

Values are expressed as mean ± SD or *n* (%).

Throughout follow-up period, There was significant increase in hemoglobin level, serum iron, and serum ferritin with a significant decrease in TIBC in APC group as compared to Carvedilol group.

There was gradual increase in the mean of hemoglobin, serum iron, and serum ferritin and gradual decrease of TIBC in Carvedilol group.

APC, argon plasma coagulation; Hb, hemoglobin; TIBC, total iron-binding capacity.

chronic GI hemorrhage in patients with cirrhosis and is manifested by chronic anemia [15]. A reduction in portal pressure is the main target of treatment in PHG. Nonselective beta-blockers are the most thoroughly investigated drugs for a sustained reduction in portal pressure. They should be continued on a long-term basis because discontinuing the drug frequently leads to recurrence of bleeding [16]. APC is an effective and safe method to stop bleeding in patients with PHG [7]. Our results revealed that most common cause of liver disease was HCV infection either alone or associated with bilharziasis. Our results do agree with the Egyptian Demographic Health Survey, who conducted survey including HCV biomarkers in 2008 on a large nationally representative sample and estimated that HCV prevalence among the 15–59 years age group to be 14.7% [17]. Therefore, Egypt has the highest HCV prevalence in the world [18]. In the current study, the number of patients with Child B and C scores was 84.16%, which was higher than the number of patients with Child A score (15.83%), and this finding was similar to Bang et al. [19] who reported that PHG is more frequently observed in patients with more severe liver disease. Our results demonstrated that PHG was higher in the fundus and body than the antrum. These

results were found to be close to those reported by Bang et al. [19] who stated that PHG lesions are most often typically found in the fundus and body (proximal to antrum). Our results revealed also that 20% of cases had history of variceal intervention (sclerotherapy or band ligation) and this was similar to Elwakil et al. [20] who reported that variceal obliteration aggravates PHG. Furthermore, El-Khayat et al. [21] documented that endoscopic therapy has been associated with an increased incidence of PHG. On the other hand, another study observed no difference in the natural history of PHG whether or not previous endoscopic sclerotherapy therapy was performed [22]. APC is a new, efficacious, safe, and easy-to-use method for the noncontact application of high-frequency current through ionized and electrically conductive argon gas. It has been used successfully to treat vascular bleeding of the upper digestive tract including GAVE, sporadic angiodysplasia, hemorrhagic telangiectasia, and radiation-induced enteropathy [23]. We applied APC to all areas of visible red spots of congested gastric mucosa, and the end point of successful endoscopic therapy was production of a white coagulum. On comparing laboratory investigations in 1st visit then 1, 2, and 3 months of APC group, there was a highly sig-

nificant increase in Hb level, serum iron, and serum ferritin with a significant decrease in TIBC as compared to Carvedilol group ($p < 0.001$) due to discontinuing of chronic blood loss from PHG. Additionally, these results may be attributed to coagulation of mucosal vessels, thus prevention of bleeding and improvement in gastric perfusion due to decrease in gastric congestion and therefore enhances absorption of the nutrients through gastric mucosa. Therefore, APC proved to be efficacious in controlling bleeding from PHG with no complications and with a significant improvement in Hb levels and a decrease in blood transfusions requirements. Another study evaluated the role of APC in treating different types of gastric vascular ectasia lesions in patients admitted for upper GI tract hemorrhage and revealed that the overall success of APC was 86%, with only one recurrence of upper GI tract bleeding during the follow-up period. The total number of APC sessions was 1.9 ± 1.3 , and the treatment success for PHG was 81% with a rise in hematocrit from baseline values ($p = 0.01$) [24]. Furthermore, there was gradual increase in the mean of Hb, serum iron, and serum ferritin and gradual decrease of TIBC in Carvedilol group. Accordingly, there was overall improvement of IDA in both groups; however, it was significantly better in APC group than in Carvedilol group. Therefore, the combination of APC and Carvedilol, unless contraindicated, may have a synergistic effect in controlling PHG. The effect of nonselective beta-blockers may take longer time so in case of acute bleeding APC is a rapid, effective method for the control of PHG-induced bleeding, especially when beta-blockers are hazardous or contraindicated. Our results were found to be close to Abd El-Ghany et al. [25] who reported that the mean Hb pre-APC was 8.3 ± 1.1 , which gradually elevated to become 10.72 ± 1.54 , this elevation showed significance throughout treatment follow-up. Moreover, our results do agree with that reported by Gonzalez-Suarez et al. [7] that studied the effect of APC on bleeding from PHG, where out of 22 cirrhotic patients, 16 patients had PHG with chronic anemia and 6 patients had PHG with acute bleeding episode. APC was applied to the area of PHG. Patients were followed up for a mean of 36 months. Hb value was significantly improved after APC. Another study has challenged the traditional consideration that lesions associated to PHG do not benefit from endoscopic therapy by evaluating the use of APC in the treatment of PHG [24] in this study, 11 patients with bleeding from PHG were included. APC sessions were aimed to ablate the greatest area of mucosal surface as possible, at least 80% in diffuse lesions. Sessions were repeated every 2–4 weeks. The end

point, which was defined by the absence of upper GI bleeding or a reduction in transfusion requirements, was achieved in 81% of the patients who were bleeding from PHG. In the current study, there were no reported APC complications among the studied groups of patients apart from mild gaseous distension and local pain at epigastrium although these effects are temporary and mild. This do agree with Abd El-Ghany et al. [25] who reported that there were no complications related to APC throughout 4 months' treatment follow-up. After performing the APC and follow-up for 1 year, APC proved to be efficacious in controlling bleeding from PHG with no complications and with a significant improvement in Hb levels and a decrease in blood transfusions and ICU admissions ($p < 0.0001$). On the other hand, there has been several studies on the use of Carvedilol for PH in patients with cirrhosis. Most of these studies assessed the effects of Carvedilol on HVPg. The results show that Carvedilol causes dose-related and marked decreases in HVPg (of about 20% from baseline) significantly greater than those caused by propranolol [26]. Banares et al. [27] reported the longest follow-up trial of 11.1 ± 4.1 weeks in 51 cirrhotic patients (26/carvedilol, 25/propranolol). The Carvedilol doses were administrated at 12.5–50 mg (mean 31 ± 4 mg/day) starting at 6.25 mg and titrated up every 4 days according to blood pressure and heart rate. Chronic Carvedilol administration resulted in 58% hemodynamic response rate compared to 23% response rate in the propranolol group. Chronic Carvedilol administration at lower doses of 12.5 mg was studied in 2 clinical trials [12, 28]. Both trials reported a reduction in HVPg by 23–43% from baseline measurements without a significant effect on the mean arterial blood pressure. Regarding our limitations in the current study, we included an adequate number of patients; however, it should be confirmed with a larger sample size. Additionally, the follow-up period of our study was short and it was better to extend to sufficient follow-up period. In conclusion, after 3 months follow-up in managing PHG, we have found that APC significantly improve IDA and decrease transfusion requirements in patients with severe PHG as compared to oral Carvedilol with small risk of adverse events. Additionally, the combination of APC and Carvedilol, unless contraindicated, may have a synergistic effect in controlling PHG.

Disclosure Statement

The authors declared that they have no conflict of interest.

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