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Original Article

Endoscopic band ligation versus argon plasma coagulation in management of bleeding from gastric antral vascular ectasia in patients with portal hypertension

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Abstract

Background

Gastric antral vascular ectasia (GAVE) may cause recurrent hemorrhage, and thus, chronic anemia, in patients with portal hypertension. Treatment with argon plasma coagulation (APC) is an effective and safe method in adults but requires multiple sessions of endoscopic therapy. Endoscopic band ligation (EBL) was found to be a good alternative for APC as a treatment for GAVE, especially in refractory cases. The aim of this prospective study was to evaluate the safety and efficacy of EBL, as compared with APC, in treating nonvariceal upper GI bleeding GAVE in patients with portal hypertension.

Patients and methods

A total of 40 patients with bleeding from GAVE were prospectively randomized to endoscopic treatment with either EBL or APC, every 4 weeks, until complete obliteration was accomplished. Hemoglobin level was obtained before and after treatment; then they were followed up endoscopically after 6 months, with documentation of the recurrence of the lesion, if that occurred.

Results

We found that EBL significantly decreased the number of sessions required for complete obliteration of the lesions (1.85 ± 0.81 sessions compared with 4.15 ± 1.22 sessions in the APC group; $P < 0.05$). Moreover, EBL was significantly superior to APC with respect to lower rate of recurrence during the treatment and follow-up period ($P < 0.05$) and a higher rate of endoscopic cure after the follow-up period ($P < 0.05$). Hemoglobin levels increased significantly after obliteration of the lesions in both groups, compared with pretreatment values ($P < 0.05$), but with no significant difference between the two groups; however, the EBL group required a significantly smaller number of units of blood transfusion than the APC group ($P < 0.05$), greater decrease in hospital admissions ($P < 0.05$), and shorter procedure time ($P < 0.05$). Postprocedural abdominal pain and vomiting occurred more frequently in the EBL group, with a significant difference ($P < 0.05$). No major complications or deaths were observed during the study period.

Conclusion

We concluded that GAVE could be safely and successfully managed by EBL or APC. Our study revealed that EBL is more effective, more time saving, and is comparable in safety to APC, in treating nonvariceal upper GI bleeding GAVE in patients with portal hypertension.

Keywords: Anemia, argon plasma coagulation, endoscopic band ligation, gastric antral vascular ectasia

Introduction

We can define gastric antral vascular ectasia (GAVE) as a capillary-type vascular malformation located mainly in the gastric antrum. It has been described as dilated, tortuous mucosal capillaries, which are often occluded by thrombus, and also as dilated, tortuous submucosal veins ([1]). At endoscopy, GAVE may look like multiple longitudinal streaks that converge at the pyloric orifice (stripe type) or as

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multiple erythematous spots (diffuse type) ([2]). Patients with GAVE may be asymptomatic or present with anemia of iron deficiency type or overt gastrointestinal (GI) bleeding. The endoscopic treatment of GAVE with laser, electrocautery, and argon plasma coagulation (APC), which is called thermal therapies, has historically been successful. It provided an alternative to surgical antrectomy, but it has significant limitations such as multiple treatment sessions, persistent bleeding, and occasionally complications [3]. Besides, it is not a very effective therapy for medium and long-term treatment and associated with a high recurrence rate of GAVE [4–6]. Therefore, endoscopic band ligation (EBL) was showed to be an effective management for GAVE, as it may lead to the submucosal vascular plexus obliteration [7] and was recently found to be as a good alternative for APC, especially in refractory cases ([8]).

We aimed, in this prospective, randomized controlled study, at the evaluation of the safety and efficacy of EBL as a new modality, compared with the standard method APC, in treating nonvariceal upper GI bleeding GAVE in patients with portal hypertension.

Patients and methods

Ethical Approval was taken. This prospective randomized controlled study was conducted on 40 patients; these patients had a diagnosis of portal hypertension with overt or occult bleeding from GAVE. The work was carried out at Ahmed Maher Teaching Hospital, Endoscopy Unit, Cairo, Egypt, from March 2016 until September 2017.

All patients aged from 24 to 60 years in whom GAVE-associated GI bleeding or GAVE-related iron-deficiency anemia was diagnosed. They were enrolled in the study after written informed consent was obtained. Patients who did not have anemia, who had another possible source of upper GI bleeding or who had GAVE associated with other medical conditions rather than portal hypertension were excluded.

The patients were randomized into two groups: APC group and EBL group; each group included 20 patients. Patient demographics, pretreatment data, and procedure-related data were prospectively recorded.

Patients were advised to come to the endoscopy unit after 6 h of fasting. Upper GI Olympus Medical Systems,Tokyo, Japan was done by a single endoscopist using Olympus endoscope EVIS EXERA GIF-H180 (Olympus).

In the APC group, we used a standard APC equipment, consisting of a high-frequency electrosurgical generator (VIO 200S; ERBE, Tübingen, Germany), an automatically regulated argon source (APC 2), and a flexible APC probe. This probe was a teflon-coated 2.3-mm catheter with a heat-resistant ceramic tip, which could be passed through the working channel of the endoscope. APC coagulation at 40 W and gas flow at 1–2 l/min was used. We applied APC with noncontact technique to the lesion beginning at the pylorus and proceeding proximally in a radiating manner until the endoscopist felt that most of the abnormal-appearing mucosa was treated.

In the EBL group, we used EBL with a multiple band ligator. We applied ligation rubber bands to abnormal-appearing mucosa. We first treated the most distal antrum, adjacent to the pylorus, and then we applied subsequent ligation bands more proximally until as much as possible of the abnormal-appearing mucosa was covered. We applied up to six ligation bands during one procedure, where clean-based ulcers had been developed. In both groups, all patients were re-evaluated after the first endoscopic intervention every four weeks. Endoscopic therapy was done, either APC or EBL, until the endoscopist found satisfactory improvement of the lesion. Patients also were re-evaluated in the event of recurrence of overt bleeding (hematemesis and/or melena) in between treatment sessions. After the procedure, we put all patients under observation for 2 h; then we discharged them, and for 2 weeks after the procedure, we prescribed oral proton pump inhibitor to avoid complication development from possible procedure-induced ulcers and advised to continue on propranolol. A liquid diet was instructed to all patients to be adhered to for 48 h after the procedure and then to advance to their prior diets as tolerated. Follow-up upper GI endoscopy was done after six months to look for recurrence of GAVE.

Treatment outcome data on number of treatment sessions, procedure time, recurrence of bleeding during the follow-up period, endoscopic cure at the end of the follow-up period, hemoglobin level at the end of treatment, number hospitalizations, and transfusion requirements during the follow-up period were recorded for comparison between the two groups and with pretreatment data.

Statistical analysis

Data were analyzed using Statistical Package for Social Science software, version 20 (SPSS, IBM Corp., Armonk, New York, USA), and then processed and tabulated. A frequency distribution was presented as a percentage, and descriptive statistics presented by mean and SD were calculated. χ^2, *t* test, and correlations were done whenever needed. *P* values of less than 0.05 were considered significant.

Results

A total number of 40 patients with GAVE-associated bleeding were enrolled in our study. The age of enrolled cases ranged from 24 to 60 years. The main underlying etiology of portal hypertension was portal vein thrombosis (five cases out of 20 in each group). The main clinical features were pallor (31/40) and splenomegaly (38/40).

The patients in both groups presented before first endoscopic intervention with either overt (hematemesis and/or melena) or occult (+ve occult blood in stools) GI bleeding. There was

no statistically significant difference between the two groups regarding the type of bleeding. ($P = 0.775$) (Table 1).

Most of the patients were receiving β-blockade; the only β-blockade received by the patients was propranolol, 16 patients in the APC group and 18 patients in the EBL group were receiving propranolol, with no significant statistical difference between both groups ($P = 0.331$) (Table 1).

Ten patients of twenty in the APC group and 11 out of 20 patients in the EBL group had previously endoscopic variceal ligation for esophageal varices with eradication. However, all varices that were found in patients of both groups had no signs of recent bleeding or impending rupture. The demographic, pretreatment data, and endoscopic profiles of the studied groups are summarized in Table 1.

The number of treatment sessions ranged from one to three sessions in the EBL group, with a mean of 1.85 ± 0.81, whereas in the APC group, the number of treatment sessions had a mean of 4.15 ± 1.22. The EBL group, compared with the APC group, showed a statistically significant lower number of treatment sessions ($P = 0.001$) (Table 1).

EBL had statistically significant lower rate of bleeding recurrence during the 6-month follow-up period as it occurred in 1/20 in EBL group compared with 7/20 in the APC group ($P = 0.022$) and also had statistically significant higher endoscopic cure rate at the end of the follow-up period as it was detected in 19/20 in the EBL group compared with 12/20 in the APC group, with P value of 0.01 (Table 1).

In the EBL group, the mean hemoglobin level increased from 8.71 ± 0.85 g/dl before treatment to 9.2 ± 0.84 g/dl after treatment. This was a statistically significant difference ($P < 0.001$). In the APC group, the mean hemoglobin levels increased from 8.42 ± 1.39 g/dl before treatment to 9.02 ± 1.32 g/dl after treatment. This was a statistically significant difference ($P < 0.001$). Comparison of mean hemoglobin levels between the two groups, both before and after treatment, did not show any significant difference ($P > 0.05$) (Table 2).

EBL group showed a more significant decrease in transfusion requirements and a greater decrease in hospital admissions during the follow-up period in comparison with the APC group, with a statistically significant difference ($P < 0.05$) (Table 1).

We recorded mild postprocedural symptoms like abdominal pain and vomiting in 14 of 20 patients in the EBL group in comparison with two of 20 patients in the APC group, with P value less than 0.001. These symptoms were successfully treated by anti-emetic and a high dose of gastric antacids, with the improvement of all cases (Table 1). No complications or deaths occurred during the study period.

Regarding the nine recurrent cases out of 40, they were scheduled to EBL sessions to obliterate the existing lesions with the same regimen as described before (Fig. 1).

Table 1: The demographic, pretreatment data, and endoscopic profiles of the studied groups

	APC (n=20)	EBL (n=20)	P
Age (mean±SD)	24-60	30-55	0.167
	42±25.4	42.5±17.6	
Sex (male/female)	11/9	13/7	0.374
Type of bleeding [n (%)]			
Occult bleeding	8 (40)	6 (30)	0.776
Hematemesis±melena	8 (40)	10 (50)	
Melena	4 (20)	4 (20)	
Beta blockade administration (yes/no)	16/20	18/20	0.331
Endoscopic findings of EV [n (%)]			
Small	8 (40)	9 (45)	0.425
Eradicated	10 (50)	11 (55)	
No varices	2 (10)	0	
Previous treatment for EV (yes/no)	10/20	11/20	
Before hospitalization (mean±SD)	1.05±0.88	1.93±1.45	0.405
Before transfusion (mean±SD)	1.33±1.25	1.95±1.45	0.708
Treatment sessions (mean±SD)	4.15±1.22	1.85±0.81	0.001*
Mean procedure time (mean±SD)	15.37±1.56	9.4±1.21	0.001*
Postprocedural symptoms (yes/no)	2/20	14/20	<0.001*
Recurrence (yes/no)	7/20	1/20	0.022*
Endoscopic cure (yes/no)	12/20	19/20	0.01*
After hospitalization (mean±SD)	0.95±0.88	0.67±0.15	<0.05*
After transfusion (mean±SD)	1±0.67	0.44±0.1	<0.05*

APC, argon plasma coagulation; EBL, endoscopic band ligation; EV, esophageal varices.. *Significant P value less than 0.05.

Table 2: Comparison between hemoglobin levels before and after treatment in the studied groups

Hemoglobin level (g/dl)	APC (n=20)	EBL (n=20)	P
Before treatment (mean±SD)	8.42±1.39	8.71±0.85	0.438
After treatment (mean±SD)	9.02±1.32	9.2±0.84	0.447
P	<0.001*	<0.001*	

APC, argon plasma coagulation; EBL, endoscopic band ligation. *Significant P value less than 0.05.

Discussion

APC in GAVE treatment requires multiple sessions for management of vascular ectasia and control of bleeding. EBL is proposed as an option for APC in GAVE treatment in recurrent GI bleeding cases [3].

As EBL is a technique that is easily accessible to many centers, we aimed at comparing the EBL and APC regarding the safety and efficacy in GAVE treatment in patients with portal hypertension.

In 2006, EBL was first reported for the management of GAVE. In one case, EBL was used as a rescue treatment in a patient who presented with recurrent melena, and blood transfusions were required. This was refractory after several APC therapy sessions. After two EBL sessions (the mean number of bands applied was 5.5) with an interval of 2 weeks, there was an

increase in hemoglobin levels, and the case was stable, without further need of blood transfusions [9].

In a second report, as there was no availability of APC at the author's institution, so EBL was performed. The patient presented with anemia and upper GI bleeding signs. Two EBL sessions were performed with a 6-week interval and the application of six bands in each session. As a result, there was a stabilized hemoglobin level and normal serum ferritin [10]. Subsequently, three retrospective comparative studies of EBL versus APC were published [3,7,11] (Table 3).

Abdelhalim *et al.* (2014) [12] did the study on 40 adult patients, where APC was applied to 20 patients and EBL was applied to another 20 patients, whereas Sato *et al.* [7] did the study on 34 patients, where APC group included 22 patients and EBL group included 12 patients. However, Elhendawy and his colleagues in 2016 did a larger study on 88 adult patients who were randomized to be treated with either APC or EBL: 44 patients in the APC group and another 44 patients in the EBL group. Sergio and his colleagues in 2015 did a study on 21 adult patients who were subjected to EBL sessions.

In the present study, GAVE treatment by EBL required significantly fewer treatment sessions, with the mean number of 1.85 ± 0.81 sessions, compared with APC, with the mean number of 4.15 ± 1.22 sessions, with *P* value of 0.001 (Table 1). This is in accordance with a study of Wells *et al.* [3] who concluded that treatment with EBL required significantly fewer treatment sessions, with the mean number of 1.9 ± 0.6 sessions, compared with APC, with the mean number of 4.6 ± 4.6 sessions, with *P* value 0.05. Another study done by Abdelhalim and colleagues concluded significantly fewer treatment sessions in the EBL group, with the mean number of 2.25 ± 0.64 sessions, compared with APC group, with the mean number of 5.5 ± 3.76 sessions, with *P* value 0.001. Moreover, Keohane *et al.* [11] concluded fewer treatment sessions in the EBL group with the mean number of 2.5 sessions compared with APC group with the mean number of 4.1 sessions, but this did not reach a significant value (*P* = 0.24).

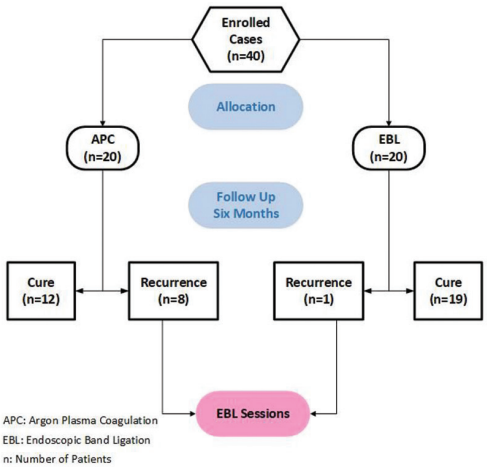

Figure 1: Study flow chart.

Elhendawy and colleagues observed that in the EBL group, the number of treatment sessions ranged from two to five sessions, with a mean of 2.93 ± 0.846, whereas in the APC group, the treatment session number had a mean of 3.48 ± 0.902. The EBL group, compared with the APC group, showed a statistically significant lower treatment session number (*P* = 0.007).

In a study done by Sergio *et al*. [13], a clinical response was achieved in 19 (91%) patients after a mean of 2.28 (range, 1–6) endoscopic sessions. Clinical response was not achieved in two patients, who continued to require blood transfusions. These two patients had chronic renal failure and required additional APC and EBL treatments.

These findings in the previous studies did not match with the study done by Sato *et al*. [7], who concluded that treatment by APC had required fewer treatment sessions compared with EBL. In the study by Sato *et al.* [7], the EBL group had more severe GAVE cases (six out of 12 patients had previously been treated with APC for GAVE).

In our study, we found that APC was time consuming, as the mean procedure time was significantly lower in the EBL group in comparison with the mean procedure time in the APC group, with *P* value of 0.001, and Ripoll and Garcia-Tsao [14] also reported this in Table 1.

Table 3: Results of retrospective comparative studies of endoscopic band ligation versus argon plasma coagulation

References	EBL vs. APC (*n*)	Efficacy	Mean sessions number of EBL vs. APC	Complications	Mean follow-up by months	Comments
Wells *et al*. [3]	9 vs. 13	Higher bleeding cessation rates (*P*=0.046), posttreatment transfusion (*P*=0.008), and hospitalization (*P*=0.015) with EBL	1.9 vs. 4.7 (*P*=0.05)	In the EBL group, 1 patient had postprocedural emesis, and in the APC group, 1 patient had postprocedural bleeding	12.7	In the APC group, ETT such as a bipolar thermal probe was used in a few procedures
Sato *et al*. [7]	12 vs. 22	Recurrence of GAVE: 68.2% for APC vs. 8.3% for EBL (*P*=0.01)	3 vs. 2.3	1 patient had bleeding from ulcer in the EBL group	15.6	All patients had cirrhotic liver
Keohane *et al*. [11]	8 vs. 15	In the EBL group, endoscopic improvement of 100 vs. 46.7% in APC group (*P*=0.01)	2.5 vs. 4.1	None	26	75% in the EBL group had previously failed APC treatment

APC, argon plasma coagulation; EBL, endoscopic band ligation; ETT, endoscopic thermal therapy; GAVE, gastric antral vascular ectasia; *P*, *P* value [12].

During the follow-up period, the APC group showed a significantly higher recurrence of bleeding as it was detected in seven patients out of 20 in comparison with one patient out 20 in the EBL group, and this was in agreement with the study done by Abdelhalim and colleagues, as recurrence of bleeding occurred in seven (35%) patients of 20 in the APC group and one (5%) patient in the EBL group, with *P* value of 0.022, and the study done by Wells and colleagues, who concluded that APC had a higher recurrence rate (56%) compared with EBL (23%).

Sato *et al.* [7] observed recurrence of bleeding in 15 (68.3%) of 22 patients in APC group and one of 12 patients in EBL group, with significant difference ($P = 0.01$).

At the end of our follow-up period, the endoscopic cure was achieved in 19 of 20 patients in EBL group compared with 12 of 20 patients in APC group, with a statistically significant difference ($P = 0.01$). This is supported by the study done by Sato *et al.* [7] who concluded that treatment with EBL had significantly higher cure rate than APC, as well as another study done by Keohane and colleagues, where endoscopic improvement was observed in 100% of patients in the EBL group and 46.7% in the APC group, with a significant difference ($P = 0.01$).

Posttreatment hemoglobin levels improved in comparison with pretreatment hemoglobin levels in both APC and EBL groups, with a statistically significant difference, and this was in agreement with the studies done by Abdelhalim and colleagues and Elhendawy and colleagues.[12]

In the current study, a comparison of the treatment outcomes between the EBL group and the APC group demonstrated a numeric improvement in the mean posttreatment hemoglobin level but did not reach statistical significance (Table 2). This is in agreement with the studies done by Keohane *et al.* [11] and Elhendawy and colleagues. However, in our study, the EBL group showed a significantly greater decrease in a number of hospitalizations owing to bleeding and significantly fewer requirements for transfusions (Table 1), similarly to a study done by Wells and colleagues, who concluded that EBL showed a significantly greater decrease in hospitalizations and transfusions compared with APC.

No complications occurred in our study in both treatment modalities, and this finding matched with the studies done by Wells *et al.* [3], Keohane *et al.* [11], and Abdelhalim and colleagues who reported no complications in their studies, but Sato *et al*. [7] reported bleeding from the ulcer after EBL in only one patient, where APC was successfully carried out on this oozing ulcer.

In a study done by Elhendawy and colleagues, mild adverse events were observed in nine (20.5%) of 44 patients who were included in the APC group. These events were fever in two patients, abdominal distension in four patients, and epigastric pain in three patients, whereas six (13.6%) of 44 patients who were included in the EBL group had mild adverse events, which were fever in two patients, mild bleeding from a postband ulcer in one patient, and epigastric pain in three patients. The study found no statistically significant difference between the two groups.

In contrast, most of our patients (14/20) in the EBL group and two of 20 patients in the APC group had postprocedural symptoms in the form of abdominal pain and vomiting, which were easily treated by medications. This finding was in agreement with a study done Sergio *et al*. [12], as patients experienced mild to moderate abdominal pain immediately following the procedure, which was managed by over-the-counter pain medications, taken for a few days, in combination with oral proton pump inhibitors. Wells *et al.* [3] and Keohane *et al.* [11] reported that 10% of the patients in the EBL group had postprocedural vomiting. The difference in incidence may be attributed to the ability of the large adult stomach to deal with gastric banding.

We followed up the patients for six months that ended by endoscopic evaluation, and this was in agreement with studies done by Sergio and colleagues and Elhendawy and colleagues who followed up the patients for the same period. During the follow-up period, no deaths were recorded in our patients, and this was in agreement with Abdelhalim and colleagues[12] who recorded no deaths in patients during the follow-up period (mean 6 months), whereas Wells and colleagues recorded deaths in patients during the follow-up period (mean 10 months), which were three (33%) patients in the EBL group compared with five (39%) patients in the APC group, although there were no bleeding-related deaths. Moreover, Keohane and colleagues recorded deaths in patients during the follow-up period (mean 26 months), which were 12.5% in the EBL group compared with 20% in the APC group, although they died from unrelated causes.

Sato *et al.* [7] recorded deaths in patients during the follow-up period (mean 15 months), which were two (16.6%) patients in the EBL group (no bleeding-related deaths) compared with seven (31.8%) patients in the APC group (two cases with bleeding-related deaths). The difference in mortality between our study and the other studies may be owing to their more prolonged period of follow-up; the old age, as these studies were done in adults; and the associated liver cirrhosis, which was the main etiology of portal hypertension.

Conclusion

We concluded that both APC and EBL are effective and safe in the management of GAVE-associated bleeding in patients with portal hypertension. However, EBL had fewer significant statistically number of treatment sessions, had a lower bleeding recurrence rate during the period of follow-up, had a higher rate of cure at the end of the period of follow-up, had a more significant decrease in transfusion requirements, had a more significant decrease in hospital admissions, and showed greater time saving. In the EBL group, abdominal pain and vomiting postprocedurally were significantly more frequent, and this was successfully controlled by medications.

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Conflicts of interest
There are no conflicts of interest.

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