Endoscopic Treatment for Gastric Antral Vascular Ectasia: Current Options

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Key Words

Gastric antral vascular ectasia · Endoscopy · Gastrointestinal bleeding · Stomach

Abstract

Gastric antral vascular ectasia (GAVE) is a capillary-type vascular malformation located primarily in the gastric antrum. Patients can present with iron-deficiency anemia, overt gastrointestinal bleeding, or both. Diagnosis and characterization is made at endoscopic examination, and the preferred management of patients with GAVE is endoscopic therapy. Herein, we present a review of the evidence about the efficacy, complications, and outcomes of the most frequently used endoscopic therapies for GAVE.

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Ectasia Vascular do Antro Gástrico (GAVE): Opções Atuais

Palavras Chave

Ectasia vascular do antro · Endoscopia · Hemorragia digestiva · Estômago

Resumo

A ectasia vascular do antro gástrico (GAVE) é uma malformação vascular do tipo capilar formada no antro e que se organiza sob a forma de estrias ou de forma difusa. A GAVE pode causar uma anemia ferropénica com ou sem hemorragia gastrointestinal evidente. O tratamento da GAVE inclui abordagens cirúrgicas e farmacológicas, contudo, a terapêutica endoscópica provou ser a mais eficaz e segura. Várias terapêuticas endoscópicas foram descritas. A coagulação com árgon plasma (APC) tem sido a terapêutica endoscópica mais descrita e utilizada, no entanto, estudos recentes mostram que a laqueação por banda elástica e a ablação por radiofrequência são terapêuticas promissoras com uma eficácia a curto prazo que pode ser superior à APC. O objectivo deste artigo é rever a evidência sobre a eficácia, complicações e resultados a longo prazo das terapêuticas endoscópicas mais frequentemente utilizadas para o tratamento da GAVE.

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Introduction

Gastric antral vascular ectasia (GAVE) is a capillary-type vascular malformation characterized endoscopically by red, angiomatous lesions originating in the antrum and organized either in stripes or in a diffuse pattern [1]

Fig. 1. Gastric antral vascular ectasia. Stripe type (left) and diffuse type (right).

(Fig. 1). Histologically, GAVE presents as dilated, tortuous mucosal capillaries, which are often occluded by thrombus and associated with dilated, tortuous submucosal veins. In general, it is uncommon to see inflammatory changes [2]. GAVE may cause chronic iron-deficiency anemia with or without the presence of overt gastrointestinal (GI) bleeding, manifested commonly by melena. Many patients may require frequent blood transfusions or iron supplementation to maintain adequate hemoglobin levels. GAVE can be isolated or associated with systemic conditions, especially in patients with liver cirrhosis, scleroderma, chronic renal failure, and after bone marrow transplantation. GAVE may account for about 4% of the causes of non-variceal bleeding [3]. The pathophysiology of GAVE is unknown; however, multiple mechanisms have been proposed as the origin of its development. These have included gastric dysmotility leading to chronic mucosal trauma and subsequent fibromuscular hyperplasia and vascular ectasia or an autoimmune reaction to gastric blood vessels among the main contributing factors [4–6].

The management of GAVE has included surgical, pharmacological, and endoscopic therapy. Surgical therapy (antrectomy) carries high morbidity and mortality, especially in patients with liver cirrhosis, and has therefore been reserved for refractory cases only. The evidence for the effectiveness of medical treatment is very limited, there are no studies with comparators, and only 1 case series with a low number of patients has been published (estrogen and progesterone treatment) [7]. Endoscopic therapy has been the mainstay of treatment for GAVE; multiple modalities have been evaluated. Some of these (cryotherapy, Nd:YAG laser) are of limited use, mainly because they are not widely available or have been associated with a higher rate of complications (20–33%) [8–13].

The purpose of this paper is to review the evidence about the effectiveness, complications, and long-term outcomes of the most frequent endoscopic modalities currently used for the treatment of GAVE.

Endoscopic Treatment Options

There is only 1 case series on monopolar coagulation and 1 on heath probe for the treatment of GAVE. These included 6 and 12 patients, respectively. Both studies showed a complication rate of 33% [14, 15]. These endoscopic techniques are not performed routinely, since argon plasma coagulation (APC) has been the traditional method of choice. APC has been the endoscopic therapy most frequently utilized for GAVE; however, recent data shows that endoscopic band ligation (EBL) and radiofrequency ablation (RFA) are new, promising options for the treatment of this condition.

Argon Plasma Coagulation

APC is a non-contact thermal method that uses argon gas to deliver plasma of evenly distributed thermal energy to a field of tissue adjacent to the probe with a depth of penetration of roughly 2–3 mm. APC electro-surgical settings vary among studies regarding electrical power, gas flow, and type of APC delivery (pulse, forced coagulation, etc.). There is no data to support specific settings for GAVE; however, last-generation electro-surgical units have a pre-established setting for APC delivery in the stomach. APC has been the endoscopic treatment of choice for GAVE since its introduction; however, most of the published data in the literature are from retrospective case series (Table 1). In some of these studies, patients with angiodysplasias in the stomach were also included, the follow-up period was short, and the evaluation of ef-

Table 1. Results of argon plasma coagulation for the treatment of gastric antral vascular ectasia

First author [ref.], year	Study type	N	Efficacy	Mean number of sessions	Complications	Mean follow-up, months	Comments
Probst [16], 2001	Prospective	17	Improvement in Hb levels	2	Asymptomatic scarring of the antrum	30.4	Recurrence of GAVE in 5 patients (29%)
Yusoff [17], 2002	Retrospective	5	Increase in Hb levels, transfusion dependence ceased in all patients	2.6	Minor bleeding	20	
Roman [18], 2003	Retrospective	21	Increase in Hb levels, only 2 patients required blood transfusion after APC	2.8	2 cases of hematemesis after treatment and 1 of sepsis	15	Recurrent bleeding in 3 patients (14%) at 13 months mean follow-up
Sebastian [19], 2004	Retrospective	12	Increase in Hb levels after treatment ($p = 0.008$) and decrease in number of transfusions ($p = 0.018$)	2	Minor bleeding in 1 patient	24	Only 2 patients with associated cirrhosis
Kwan [20], 2006	Prospective	26	Increase in Hb levels ($p = 0.003$) and decrease in transfusion rate ($p = 0.02$)	2	No	16	In 3 patients with extensive GAVE, the median number of sessions required for eradication was 8
Chaves [21], 2006	Prospective	14	70% with good initial response; however, the rebleeding rate was 35%	3.2	No	9.9	Patients were divided in stripe and diffuse type
Herrera [22], 2008	Prospective	8	Treatment success of 87% based on hematocrit level increase without rebleeding	2.3	No	24	Only patients with active bleeding from GAVE
Lecleire [23], 2008	Retrospective	30	Success in 80% of the patients	2.18	NR	22	Patients without cirrhosis required more APC sessions for eradication (2.1 vs. 3.7)
Batthi [24], 2009	Prospective	50	Patients had an increase in Hb levels and a decrease in blood transfusion requirements	5	NR	8.5	All patients had liver cirrhosis
Fuccio [25], 2009	Prospective	20	Initial response rate of 90% (resolution of transfusion-dependent anemia)	3	Abdominal pain and bloating in 80% of the cases	25	All patients had liver cirrhosis; hyperplastic polyps developed in 15% after treatment
Chiu [26], 2012	Retrospective	19	High rate of recurrent bleeding (78.9%) when compared with gastric angiodysplasia	2.4	No	NR	12 patients had liver cirrhosis

N, number of patients; Hb, hemoglobin; APC, argon plasma coagulation; NR, not reported; GAVE, gastric antral vascular ectasia.

efficacy and/or failure of therapy is not well defined. In general, patients have a good initial response with a low rate of complications. However, the recurrent bleeding rates can be high and in some studies are reported to range from 35 to 78.9% [16–26].

There are 2 studies that have evaluated long-term outcomes after APC treatment for GAVE. Boltin et al. [27] retrospectively identified patients who underwent APC treatment for GAVE with a mean follow-up of 46.9 ± 26.5 months. Treatment success was defined by resolution of the symptoms and stabilization of the hemoglobin level at 30% above baseline. Thirty-one patients were identified; the final analysis showed that treatment success was achieved in only 16 (25.8%) patients [27]. Another retrospective study that included 18 patients showed recurrent bleeding in 7 patients (39%) after a mean follow-up of 42 months [28].

Endoscopic Band Ligation

EBL was first reported for the treatment of GAVE in 2006. In 1 case, EBL was utilized as a salvage therapy in a patient who presented with recurrent melena and required blood transfusions. This was refractory after several sessions of APC therapy. After 2 sessions of EBL (the mean number of bands applied was 5.5) with an interval of 2 weeks, the hemoglobin levels increased and were stable without the need of further blood transfusions [29]. In a second report, EBL was performed as there was no availability of APC at the author's institution. The patient presented with signs of upper GI bleeding and anemia. Two sessions of EBL were performed with an interval of 6 weeks and application of 6 bands in each session. The hemoglobin levels stabilized, and the serum ferritin normalized [30]. Subsequently, 3 comparative studies of EBL versus APC were published; 1 study also included endoscopic thermal therapy along with APC [31–33]. The

Table 2. Results of retrospective comparative studies of endoscopic band ligation versus argon plasma coagulation

First author [ref.], year	EBL vs. APC, n	Efficacy	Mean number of sessions EBL vs. APC	Complications	Mean follow-up, months	Comments
Wells [31], 2008	9 vs. 13	Higher rates of bleeding cessation ($p = 0.046$), post-treatment transfusions ($p = 0.008$) and hospitalizations ($p = 0.015$) with EBL	1.9 vs. 4.7 ($p = 0.05$)	1 patient in the EBL group had post-procedural emesis, and 1 in the APC group had postprocedural bleeding	12.7	Endoscopic thermal therapy, such as bipolar thermal probe, was used in a few procedures in the APC group
Sato [32], 2012	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 an ulcer in the EBL group	15.6	All patients had liver cirrhosis
Keohane [33], 2013	8 vs. 15	Endoscopic improvement of 100% in the EBL group vs. 46.7% in the APC group ($p = 0.01$)	2.5 vs. 4.1	None	26	75% of the patients in the EBL group had previously failed APC treatment

n, number of patients; APC, argon plasma coagulation; EBL, endoscopic band ligation; GAVE, gastric antral vascular ectasia.

Fig. 2. Gastric antral vascular ectasia with active bleeding at the endoscopic examination (left) and after treatment with endoscopic band ligation (right).

overall results of these studies showed better outcomes for the groups treated with EBL, including less transfusion requirements and stabilization of hemoglobin levels. However, these studies included a low number of patients and are all retrospective (Table 2).

The first prospective study about the efficacy of EBL in GAVE was published in 2015 [34]. This study included 21 consecutive patients. The clinical response to therapy was defined by eradication or near-eradication of GAVE along with stabilization of hemoglobin levels and/or a decrease in blood transfusion requirements. Patients received endoscopic treatment every 2 months and were under treatment with proton pump inhibitors during the study period. Clinical response was achieved in 91% of the patients after a mean of 2.2 sessions of endoscopic therapy (Fig. 2). Nine patients (43%) had previously failed endoscopic treatment with APC. The 2 patients who did not achieve complete clinical response had chronic renal failure as well as diffuse-type GAVE. Regarding complications, 2 patients experienced mild-to-moderate abdominal pain that disappeared 24 h later. Finally, a ran-

domized controlled trial of EBL versus APC for GAVE has recently been published [35]. Eighty-eight patients (all cirrhotic) were included and randomized to receive endoscopic treatment every 2 weeks. The results showed a significantly lower number of endoscopic sessions required for eradication (2.98 vs. 3.48, $p < 0.05$) and a significant decrease in blood transfusion requirements ($p < 0.05$) in the EBL group. Both groups had a significant increase in hemoglobin levels, but without differences between them. In the EBL group, 13.6 % of the patients had adverse events, including fever, mild bleeding from a post-banding ulcer, and epigastric pain in 3 cases. In the APC group, 20.5% of the patients experienced adverse events: fever occurred in 2, abdominal distention in 4, and epigastric pain in 2 patients. There was no statistically significant difference between the groups.

Radiofrequency Ablation

RFA is a technique that delivers rapid pulses of radio-frequency energy at a constant power of 40 W with variable energy densities, depending on the pathology being

Table 3. Results of radiofrequency ablation treatment in gastric antral vascular ectasia patients

First author [ref.], year	Study type	N	Efficacy	Mean number of sessions	Complications	Mean follow-up, months	Comments
Gross [36], 2008	Prospective	6	Increase in Hb levels in all patients; 1 patient remained transfusion dependent	1.6	No	2	Five patients had liver disease; the mean duration of treatment sessions was 28.6 min
McGorisk [37], 2013	Prospective	21	Clinical success achieved in 86%, no need for subsequent blood transfusions, and significant increase in Hb levels ($p = <0.001$)	2	1 patient with a superficial ulcer and another with a bleeding ulcer discovered at repeat endoscopy	6	All patients had previous APC treatment; technical success was achieved in 90% of the cases
Dray [38], 2014	Retrospective	24	Significant decrease in the mean number of blood transfusions and increase in Hb levels ($p = <0.001$)	1.8	No	6	Previous treatment with APC in 15 patients; the mean duration of treatment sessions was 77 min
Jana [39], 2015	Prospective	7	Clinical success of 71% based on requirement of post-treatment blood transfusions	2	No	6	All patients had previous APC treatment; technical success achieved in 100% of the cases
Raza [40], 2015	Prospective	9	Clinical success in 67% of the patients based on blood transfusion requirements	3	No	11	All patients with previous APC treatment; 2 patients had recurrent bleeding at 11 months; technical success was 100%

N, number of patients; Hb, hemoglobin; APC, argon plasma coagulation.

treated. This results in a uniform ablation depth of 0.5–1 mm, which involves only the superficial layer of the mucosa. RFA has been used for the ablation of dysplastic mucosa in Barrett's esophagus and recently for the treatment of GAVE. RFA is a method that requires further training to familiarize with the technique. A pilot trial of RFA for the treatment of GAVE with the HALO90 ablation catheter that included 6 patients was published in 2008. This showed improvement of the hemoglobin levels after 1–3 treatment sessions, and 5 patients did not require subsequent blood transfusions [36]. Since then, 4 additional studies on the usefulness of RFA treatment in GAVE have been published. Table 3 shows a summary of the results of these trials [36–40]. The patients included in these trials had previous endoscopic treatment for GAVE, mainly APC. The overall clinical success rate ranged from 67 to 86%. Complications were mild; however, there is a recent report of a patient that experienced bacteremia and sepsis after RFA treatment for GAVE [41].

Discussion

Multiple types of endoscopic treatment have been used for GAVE. A recent systematic review regarding therapies for angiodysplasia and GAVE has shown a lack

of good-quality studies (prospective and randomized trials) about endoscopic therapy for this condition [42]. Traditionally, APC has been the most frequently used modality; however, a considerable number of patients will not have a good initial response or will experience recurrence of anemia or bleeding at follow-up. This is also true for other GI angiodysplastic lesions, as shown in a recent systematic review that excluded patients with GAVE. The authors found that the pooled recurrence rate of bleeding was 36% [43]. Endoscopic therapy with EBL and RFA has recently shown promising results regarding efficacy and safety, but the long-term outcome of these modalities is still unknown. EBL may have the advantage over RFA that it is more widely available and is an easier technique to perform.

One of the drawbacks when analyzing the information from the current literature regarding endoscopic therapy for GAVE is that the definition of treatment success or clinical response varies widely among studies. Clinical response to endoscopic therapy should be defined by the increase or stabilization of hemoglobin and iron levels, along with a decrease or elimination of blood transfusions when patients are transfusion dependent. Complete or near-eradication of GAVE at the endoscopic examination should also be part of the definition. However, it is important to understand that near-eradication of GAVE does not mean failure to endoscopic therapy if the other

endpoints are achieved. There is also a need for further information about the long-term response to therapy. Patients with GAVE will need regular determinations of hemoglobin and iron levels after endoscopic therapy to confirm response to treatment and to identify cases of recurrent bleeding and/or anemia from refractory GAVE. Patients with recurrence of symptoms may need to undergo further endoscopic examination and therapy. The clinical response to this approach needs to be established with a prospective, long-term follow-up study.

There is also not sufficient information about subgroups of patients with GAVE regarding differences in clinical response. For example, patients with comorbidities such as chronic renal failure or liver cirrhosis and patients under treatment with anticoagulation or antiplatelets may, in theory, have a poor clinical response when compared to patients without these conditions. In summary, GAVE can be a challenging condition when pa-

tients do not respond well to traditional endoscopic therapy. New endoscopic modalities for GAVE are available and promising. Nonetheless, there is need for high-quality, randomized prospective studies to confirm their efficacy and safety in the short and long term.

Statement of Ethics

The author declares that no experiments on humans or animals were performed for this study. Furthermore, he declares that they have followed the protocols of their work center on the publication of patient data and that no patient data appear in this article.

Disclosure Statement

The author has no conflicts of interest to declare.

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