



A practical alternative for salvage therapy in gastrointestinal bleeding: Ankaferd blood stopper

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Abstract

Upper and lower gastrointestinal bleeding is a common medical condition routinely encountered in clinical practice. Endoscopic procedures still constitute the basis of the treatment for hemostasis and the prevention of rebleeding. A variety of endoscopic treatment modalities including hemostatic clipping, argon plasma coagulation, sclerotherapy, heater probe and hemosprays are used alone or in combination. However, these conventional endoscopic therapies are often challenging, so new topical hemostatic agents have been introduced to allow for easier and more effective hemostasis in recent years. In this study, we shared our experience with Ankaferd blood stopper, which is becoming an effective alternative hemostatic medicine for gastrointestinal bleedings, in 64 patients who applied to our clinic with upper or lower gastrointestinal bleeding between January 2019 and April 2020.

Keywords: ankaferd blood stopper, bleeding, endoscopy, gastrointestinal tract

1. Introduction

Gastrointestinal bleeding (GIB) is a very common condition in gastroenterology clinical practice with an incidence of about 61-78 cases per 100.000 population in upper gastrointestinal bleeding (UGIB) (Al et al., 2009) and 33-87 cases per 100.000 population in lower gastrointestinal bleeding (LGIB) (Augustin et al., 2009). In studies, mortality rates are reported as 7-10% for non-variceal UGIB (Barkun et al., 2019), 20% for variceal UGIB (Barkun et al., 2003), and 2.5-3.9% for LGIB (Bilgili et al., 2009). Currently established standard medical and endoscopic therapeutic options are still essential for the management of GIB. Hemostatic approaches including hemoclips, argon plasma coagulation (APC), sclerotherapy, heater probe and hemosprays may serve as an adjuvant and/or primary therapy in endoscopic interventions. Each of these treatment modalities has both advantages and disadvantages, therefore the treatment choice should be specific to the patient.

In addition, the success of the procedure is closely related to the skill and experience of the endoscopist, the type of the bleeding source, the available equipment, the patient's clinical condition and costs. Despite all advances in endoscopic and clinical management, mortality rates are still high for GIBs. Hence, there is an ongoing intensive search for novel techniques or treatments. In recent years, new topical hemostatic agents have been introduced to allow for easier and more effective hemostasis.

Ankaferd Blood Stopper (ABS) is a novel topical hemostatic agent which is a mixture of plants including *Thymus vulgaris*, *Glycyrrhiza glabra*, *Vitis vinifera*, *Alpinia officinarum* and *Urtica dioica* (Farrell and Friedman, 2005). Although the exact mechanism is still unknown, it achieves its basic hemostatic effect through erythroid aggregation by forming an encapsulated protein network (Goker et al., 2008). The aim of our study is to share our experience with ABS which is not widely used in gastroenterology clinical practice.

2. Materials and methods

The records of 9512 patients who underwent endoscopic procedures between January 2019 and April 2020 in our clinic were retrospectively reviewed. A total of 64 patients who applied with UGIB or LGIB and in whom Ankaferd was used for the treatment of bleeding were included in the study. Demographic data of the patients, symptoms at admission, additional risk factors, comorbid diseases, concomitant medications, laboratory tests at the time of admission, causes of bleeding, treatment methods applied, complications and early or late re-bleeding after the procedure were recorded.

SPSS 25 package program (IBM, Statistical Package for Social Sciences) was used for statistical analysis of the data. The results were expressed using the mean±standard deviation, number and percentages depending on whether the data were parametric or not. Kolmogorov Smirnov and Shapiro-Wilk

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tests were used to evaluate the compliance of the quantitative data to the normal distribution. For the comparison of more than two groups, first Fisher exact test and then Bonferroni Correction were used. Values of $p < 0.05$ were considered statistically significant for all tests.

3. Results

A total of 64 patients, 22 (34.4%) female and 42 (65.6%) male, participated in the study. The mean age was 54.32 ± 16.72 years for female patients and 54.3 ± 15.82 years for male patients. Fifty (78.1%) of the patients applied with UGIB, 14 (21.9%) with LGIB, and all patients had an endoscopic procedure within the first 24 hours after admission to the hospital. While the number of male patients with UGIB was higher than female patients, the number of male and female patients with LGIB was equal.

The mean age of patients with LGIB was significantly higher than those with UGIB ($p < 0.001$). There was no significant difference in terms of smoking status and nonsteroidal anti-inflammatory drugs (NSAID) or anticoagulant drug use according to the bleeding locations. Metastatic cancer was observed in most patients with LGIB (57.1%), whereas it was much lower in patients with UGIB (14%). As expected, LGIB was more common in those with diverticulosis ($p = 0.007$). Demographic characteristics, additional risk factors and comorbid diseases of the patients according to the location of GIB are given in Table 1.

Table 1. Demographic characteristics, additional risk factors and comorbid diseases of the patients according to the location of GIB

Characteristics		Lower GI Bleeding n (%)	Upper GI Bleeding n (%)	p
Gender	Female	7(50.0)	15(30.0)	0.142
	Male	7(50.0)	35(70.0)	
Age (years)		69.29 ± 10.3	50.06 ± 14.7	0.001
Smoking	No	9 (64.3)	28 (56.0)	0.804
	Yes	5 (35.7)	22 (44.0)	
NSAID	No	11 (78.6)	32 (64.0)	0.245
	Yes	3 (21.4)	18 (36.0)	
Anticoagulant Drugs	No	10 (71.4)	36 (72.0)	0.605
	Yes	4 (28.6)	14 (28.0)	
CVD	No	10 (71.4)	40 (80.0)	0.362
	Yes	4 (28.6)	10 (20.0)	
Heart failure	No	14 (100)	49 (98.0)	0.781
	Yes	0 (0)	1 (2.0)	
Metastatic cancer	No	6 (42.9)	43 (86.0)	0.002
	Yes	8 (57.1)	7 (14.0)	
CLiD	No	12 (85.7)	46 (92.0)	0.392
	Yes	2 (14.3)	4 (18.0)	
CKD	No	13 (92.9)	49 (98.0)	0.392
	Yes	1 (7.1)	1 (2.0)	
CLuD	No	13 (92.9)	49 (98.0)	0.392
	Yes	1 (7.1)	1 (2.0)	
Diverticulosis	No	10 (71.4)	49 (98.0)	0.007
	Yes	4 (28.6)	1 (2.0)	

GI: Gastrointestinal, BMI: Body mass index, NSAID: Nonsteroidal anti-inflammatory drugs, CVD: Cardiovascular disease, CLiD: Chronic liver disease, CKD: Chronic kidney disease, CLuD: Chronic lung disease

Forty-nine (98%) of the patients with UGIB had melena, 21 (42%) had syncope, 9 (18%) had hematemesis, whereas all of the patients with LGIB had hematochezia and 3 (21.4%) of those had also syncope. The distribution of symptoms at admission and laboratory results according to the bleeding location of the patients are given in Table 2. When the patients were evaluated according to the etiology of bleeding, the most frequent cause was peptic ulcer in patients with UGIB and malignancies in patients with LGIB. The causes of UGIB and LGIB are given in Table 3.

Table 2. Symptoms at admission and laboratory results according to the bleeding location

		Lower GI Bleeding n (%)	Upper GI Bleeding n (%)
Syncope	No	11 (78,6)	29 (58,0)
	Yes	3 (21,4)	21 (42,0)
Hematemesis	No	14 (100,0)	41 (82,0)
	Yes	0 (0,0)	9 (18,0)
Melena	No	14 (100,0)	1 (2,0)
	Yes	0 (0)	49 (98,0)
Hematochezia	No	0 (0)	50 (100)
	Yes	14 (100)	0 (0)
Blood pressure	>100 mmHg	3 (21,4)	21 (42,0)
	<100 mmHg	11 (78,6)	29 (58,0)
Pulse	> 100bpm	2 (14,3)	21 (42,0)
	< 100bpm	12 (85,7)	29 (58,0)
Hemoglobin	>10	13 (92,9)	37 (74,0)
	<10	1 (7,1)	13 (26,0)
Hematocrit	>35	13 (92,9)	36 (72,0)
	<35	1 (7,1)	14 (28,0)
INR	<1.2	2 (14,3)	6 (12,0)
	>1.2	12 (85,7)	44 (88,0)

GI: Gastrointestinal; INR: International normalized ratio

The ABS method was preferred for bleeding control in all instances because the bleeding could not be stopped completely with standard endoscopic hemostasis methods or these procedures could not be performed technically. ABS solution was applied to the bleeding area by spraying 5-10 cc with endoscopic sclerotherapy needle. ABS was used as the sole method of hemostasis since other methods could not be used in 10 (20%) of 50 patients with UGIB and in 1 (7.1%) of 14 patients with LGIB. Five out of 10 patients with UGIB had esophageal variceal bleeding, which was primarily managed with ABS. In 3 of these patients, ABS was preferred because the esophageal mucosa was highly sclerotic due to multiple variceal ligations, and in two patients the bleeding area could not be visualized due to massive bleeding. Until their control endoscopy, no recurrent bleeding was observed in patients whom only topical ABS was applied. In the control endoscopies performed after 24 hours, no bleeding residue was observed in the esophagus and stomach lumen that would prevent the endoscopic view. Nipple was detected on the sclerosed varicose veins in both patients and sclerotherapy was applied with N-butyl-2-cyanoacrylate (Histoacryl). ABS was

used alone in only one of the patients with LGIB, who was followed-up with diagnosis of hemophilia, since other endoscopic procedures would increase bleeding. The bleeding in the form of leakage from the edge of the rectal ulcer was successfully stopped after ABS application.

Table 3. The causes of upper and lower GI bleeding

Causes of UGIB	Number (%) n= 50	Causes of LGIB	Number (%) n= 14
Duodenal ulcer	22 (44)	Colon Cancer	8 (57,1)
Gastric Cancer	8 (16)	Post polypectomy	2 (14,2)
Gastric Ulcer	10 (20)	Post ESD	1 (7,1)
Mallory Weiss tears	2 (4)	Rectum Ulcer	2 (14,2)
Variceal bleeding	5 (10)	Hemorrhoidal bleeding	1 (7,1)
Post sphincterotomy	2 (4)		
GAVE	1 (2)		

UGIB: Upper gastrointestinal bleeding, LGIB: Lower gastrointestinal bleeding, GAVE: Gastric antral vascular ectasia, ESD: Endoscopic submucosal dissection

The patients were evaluated in terms of early and late re-bleeding after ABS application. Recurrent bleeding within the first 24 hours from the same location was considered as early re-bleeding. Recurrent bleeding within the first month was considered as late re-bleeding. Early re-bleeding was not observed in any of the patients. Late re-bleeding occurred in only 1 (1.5%) of 64 patients who had stomach cancer. No mortality was observed in any of the patients after ABS application during the study.

4. Discussion

There are numerous studies about the application of ABS for bleeding control in dental and surgical procedures and in hemorrhages due to gastroenterological and hematological disorders. (Strate and Gralnek, 2016) All these studies have demonstrated that ABS is highly safe and an effective alternative method in the treatment of bleeding. Endoscopic therapy in clinical practice has some drawbacks that limit its efficacy. For instance, despite being highly effective in achieving hemostasis in acute UGIB, in 5%-10% of patients this bleeding will not be initially controlled or they will experience a recurrence (Gralnek et al. 2008). In patients with severe acute bleeding, hemorrhagic diathesis and bleeding due to gastrointestinal tract cancers, endoscopic therapy can be challenging, often requiring a high level of technical expertise. Therefore, new topical hemostatic agents in the control of GI bleedings refractory to conventional antihemorrhagic measures seem promising. The reason for using ABS in all patients included in our study was that the hemostasis could not be achieved with standard endoscopic methods. It was an important finding that bleeding was primarily managed with ABS in all. ABS, technically, seems to be a practical treatment alternative with its easy applicability. Therefore, its ease of use reduces the need for highly skilled expertise compared to other

endoscopic techniques.

Our study is one of the studies involving the highest number of patients in whom ABS is used for the control of GI bleeding. It is also remarkable that only one patient had re-bleeding and no patient was died due to bleeding in one month follow-up considering the fact that the mortality rate due to GIB is 2.5%-20% despite current treatments. Variceal bleeding still carries a significant mortality of 7%-15%, as well. Endoscopic interventions are very difficult to perform, especially in patients who have recurrent band ligations, due to fibrosis in the esophageal mucosa at the ligation site. In our study, it was observed that ABS was applied to five patients for variceal bleeding at their admission and hemostasis was successfully achieved in all. This is very important regarding the high mortality rates in variceal bleeding. Another finding that should be taken into account is that there was no obstacle in the lumen of two patients in early endoscopic re-evaluation and intervention, after application of ABS due to massive bleeding with poor visualization.

ABS is a medicinal product that can be applied endoscopically like Hemospray which is also used as a topical hemostatic agent in the management of GI bleeding. ABS and Hemospray may be helpful in the control of bleeding alone or in combination with other endoscopic techniques. They are effective options in various clinical situations such as salvage therapy, massive bleeding with poor visualization and bleeding from luminal malignancies due to their ease of use, noncontact/nontraumatic application and ability to cover large bleeding areas. (Chen and Barkun, 2015). The liquid form of ABS is superior to the powder form of Hemospray cause it can be applied with standard endoscopic equipments and the treatment cost is cheaper. Further controlled studies are needed to establish ABS as an effective and safe treatment option in the management of all types of GI bleeding

Conflict of interest

None.

Acknowledgments

No competing financial interests exist.

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