Digestive hemorrhaging in a patient being treated with anticoagulants

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CLINICAL CASE

The patient was a sixty-five-year-old male with continuous abdominal pain on the left side which had been developing for 12 hours. Towards the end of that period, the patient showed melanemesis, rectal bleeding, hematuria, whimpering, and rectal and bladder tenesmus. An important event in this patient’s background was ischemic heart disease with myocardial revascularization. A coronary stent had been placed six months before. His condition was being dealt with through dual antiplatelet therapy. He had also presented a deep vein thrombosis with pulmonary embolism three months before. Since then, he had been anticoagulated with low molecular weight heparin and warfarin with irregular monitoring. He was also taking metoprolol, enalapril, and lovastatin. He presented chronic alcohol consumption. At the time he was admitted to the hospital, his blood pressure was 130/80 mm Hg and his heart rate was 54 beats per minute. He was sleepy but did not have any other neurological symptoms. There were no cirrhotic or portal hypertension stigmas. His jugular venous distension was level II and his heart beat and respiratory sounds were normal. The abdomen was soft, without pain, and his intestinal sounds were normal. His symmetrical peripheral pulses were also normal.

The patient was hospitalized with a diagnosis of over coagulation, upper and lower gastrointestinal bleeding, and possible urolithiasis.

The initial tests showed the following results: prothrombin time 68.4 with 5.8 INR; hemoglobin 16.7 gr., hematocrit 48.9%, platelets: 250,000. The urinalysis showed proteinuria of 100 mg, and 6-10 red cells per field. The kidney and urinary track ultrasound was normal.

Once hemodynamic stability was achieved, a gastroenterological assessment was requested in order to begin the study and management of gastrointestinal bleeding in an over coagulated patient. Some clinical questions that arose need to be answered by going back to the literature.

INTRODUCTION

Gastrointestinal bleeding is a frequent medical problem. Despite the progress made in its diagnosis and management, it continues to result in significant levels of morbidity and mortality. The more frequent use of anticoagulant therapy has been described as a risk factor that can affect the management and prognosis of gastrointestinal bleeding (1, 2).
Although anticoagulation by itself seems to be a risk factor for patients with gastrointestinal bleeding, it is important to consider that there are often other factors such as old age and comorbidity in patients undergoing anticoagulation treatment. Because of combinations of factors, these patients could be classified as a high risk group for developing complications such as rebleeding and mortality (3).

Most of the available information in the literature about the epidemiology, management, and prognosis of gastrointestinal bleeding in anticoagulated patients comes from descriptive studies, retrospective cohort studies, and recommendations from experts.

Although there are many questions about this clinical condition, we chose five clinical questions that are often considered when dealing with an anticoagulated patient with gastrointestinal bleeding. We reviewed the written resources searching for the best available information that could help us answer these questions. Through a review of the medical materials in the PubMed database, using the keywords: Gastrointestinal Hemorrhage, Gastrointestinal Bleeding, combined with anticoagulants, antiplatelets, antithrombotic therapy and Low molecular weight Heparin, we analyzed review and relevant original articles with the best quality information from among publications from the last 20 years.

**Are there differences in the etiology of digestive bleeding between anticoagulated patients and patients not treated with anticoagulants?**

Several studies with similar results identify the cause of bleeding in 80% to 83% of cases. Among anticoagulated and non-anticoagulated patients, peptic ulcers are the most common etiology, explaining 45% to 58% of the causes of bleeding. Other causes identified in these studies include erosive gastritis, Mallory-Weiss syndrome, erosive esophagitis, gastric polyps and angiodysplasia (4).

Most retrospective studies compare the causes of gastrointestinal bleeding among anticoagulated patients and those who did not receive anticoagulant therapy. No significant differences have been found in the etiologies or locations of the bleeding (5).

**Which factors increase the risk of gastrointestinal bleeding in the anticoagulated patient?**

Risk factors for gastrointestinal bleeding in the patient that chronically receives anticoagulant therapy should be divided into two groups:

1. Related to the patient
2. Associated with the kind of medication, intensity, and combination of medications.

Age is a very important patient related factor. It is estimated that people over 70 years of age have a 3% annual risk of gastrointestinal bleeding. When a person uses 100 mg of acetylsalicylic acid (ASA) daily, the risk can increase to 12%. There are no clear differences related to gender, although some studies suggest that the percentage of bleeding among males could be higher when they receive anticoagulant therapy. A previous history of gastrointestinal bleeding or peptic ulcer increases the relative risk of bleeding from 2.1% to 6.5% (5).

The relative risk of bleeding associated with anticoagulants also increases when there are comorbidities such as chronic kidney disease, heart failure, diabetes mellitus and alcoholism (3).

The most important finding about risk factors associated with these medications is that the combination of two antiplatelet drugs or anticoagulants significantly increases the risk of bleeding above the risk level of monotherapy.

**Are there differences in morbidity and mortality rates associated with gastrointestinal bleeding between anticoagulated and non-anticoagulated patients?**

Mortality rates associated with upper gastrointestinal bleeding among patients who receive anticoagulants vary between 3.5% and 13%. Mortality rates for patients with lower gastrointestinal tract hemorrhaging range from 1% to 5%.

A study published in 2005 shows that anticoagulated patients that were admitted because of gastrointestinal bleeding had a slightly higher mortality rate (3.6%), although not statistically significant, than the one found in patients that were not anticoagulated (3.3%). Other variables also differed: 2.3% of anticoagulated patients needed transfusions vs. 1.6% of other patients; hospital stays of anticoagulated patients averaged 7.7 days vs. 5.9 days for others, and 5.4% of anticoagulated patients required emergency surgery vs. 3.8% of other patients. The average age of the patients admitted was 62.9 years for anticoagulated patients and 67.2 years for non-anticoagulated patients (4).

The results of other studies are similar. They allow us to conclude that mortality rates associated with gastrointestinal bleeding among patients receiving anticoagulants does not significantly vary from those for patients who are not anticoagulated. However, there are other issues such as morbidity rates and increased costs related to patients who receive anticoagulation.

**What level of anticoagulation is safe for performance of endoscopy on a patient with gastrointestinal bleeding?**

Controlled studies have shown that anticoagulation reversion between 1.5 and 2.5 International Normalized Ratio
(INR), combined with early diagnostic and therapeutical procedures, is a safe strategy. No differences regarding mortality, hospital stay, and need for transfusion were found when comparing the anticoagulated group of patients with the control group (6).

A retrospective cohort study of 233 patients with upper gastrointestinal bleeding found that 95% of the anticoagulated patients had between 1.3 to 2.7 INR at the time of admission. It also found that the level of INR was not associated with higher risk of rebleeding, need for surgery, hospital stay or mortality. Also, if an adequate reversion to safe levels of anticoagulation is achieved, a supratherapeutic INR level at the time of admission does not have a negative impact on the prognosis of the patient (7).

Early endoscopy in anticoagulated patients with gastrointestinal bleeding can often reveal lesions that require endoscopic therapy, and injuries not previously identified. In cases of bleeding ulcers, the endoscopic hemostasis after partial reversal of INR to 1.5 to 2.5, is not associated with a higher risk of uncontrollable bleeding, emergency surgery or mortality (8).

In a small series of cases of anticoagulated patients, variceal ligation for primary or secondary prophylaxis intervention was safe and well tolerated (9).

Based on these results we can support the international consensus recommendation on non variceal upper gastrointestinal bleeding which proposes correcting anticoagulation in patients with gastrointestinal bleeding. However, this corrective process should not delay performance of therapeutic and diagnostic endoscopy except for patients who are over anticoagulated. These patients should reach safe INR levels ranging between 1.5 and 2.5 before treatment (10).

**When, and in what kind of patient, should anticoagulation be restarted after an episode of gastrointestinal bleeding?**

Although continuation of antiplatelet and anticoagulation treatment in patients with clinically significant gastrointestinal bleeding is associated with high risk of persistence or recurrence of bleeding, the appropriate amount of time for suspension of anticoagulants is not clear. Two issues which remain unclear are whether reversal should be partial or complete, and whether partial or complete reversal is the best option (10).

Usually the decision is based on assessment of risks and benefits if the possibility of thromboembolic events and risk of bleeding must be considered. Classifying patients according to high and low risks for thromboembolism if anticoagulation is partially or totally reversed is a useful decision making tool.

Patients are considered high risk patients if they have had a pulmonary embolism or arterial embolism within the last six months. They are also considered to be at high risk if they have had valvular heart disease with atrial fibrillation, a mechanical mitral valve, any mechanical valve with previous embolic events, previous arterial or venous thromboembolism, and conditions of thrombophilia with at least one thromboembolic event.

Patients are considered to be low risk patients when they have had one isolated arterial or venous thromboembolic episode of more than six months duration, atrial fibrillation without valvular disease, and a mechanical valve or bioprosthetic aortic valve. In these cases, the complete suspension of anticoagulation is associated with low risks of thromboembolic events (11).

**Evolution of the clinical case**

The group treating the patient diagnosed upper digestive tract bleeding associated with over-anticoagulation with warfarin and requested an esophagogastroduodenoscopy (EGD). The gastroenterology department considered that the patient needed to have the over-anticoagulation addressed prior to conducting the EGD. Ten mg of Vitamin K were administered intravenously to control INR levels. After six hours the INR level was 2.4, a level which is considered to be safe for performance of an EGD. When the procedure was conducted, it was found that the patient has the following conditions:

1. The patient had gastric antral vascular ectasia (GAVE)
2. Erosive antral gastritis
3. Erosive and erythematous gastritis of the antrum
4. Elevated lesion in the bulb

**Note:** There were no endoscopic stigmas from active or recent bleeding. The patient was monitored for 72 hours without evidence of stigmas or rebleeding. Oral management with PPIs was continued because of patient’s chronic consumption of aspirin, and the patient was treated with argon plasma for gastric ectasia.

**REFERENCES**