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ACENOCOUMAROL (NICOUMALONE) INDUCED GASTROINTESTINAL BLEEDING

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ABSTRACT

Nicoumalone is an oral vitamin K antagonist prescribed for the prevention and treatment of venous thromboembolism. The major challenge faced during the therapy were control of bleeding and identification of risk factor with cause associated with bleeding. Here we report a case study of 58 years old male presented to ICU with the complaints of hematemesis, hematuria, malena, and breathlessness. The plausible correlation of the GI bleeding is due to chronic consumption of acitrome 0.5mg orally since last one year. The blood investigation revealed anemia (hb 7g/dl). He was immediately provided with plasmolyte and kabilyte intravenously to reserve body fluids. INR/prothrombin time were measured and alternative anticoagulant from novel oral anticoagulant was started replacing acitrom. Furthermore, this case highlights the importance of regular INR/Prothrombin time monitoring in patients on oral anticoagulants to avoid further risk of bleeding.

Keywords: Acenocoumarol, GI Bleeding, INR, Prothrombin time, Genetic polymorphism.

INTRODUCTION

Superior mesenteric vein thrombosis is a condition in which a blood clot is form within mesenteric veins that drain blood from intestine into the liver. This can eventually expedite ischemia of the digestive system hence causing ischemia of intestinal tissue.[1] Anticoagulants are widely used for prevention of thrombosis. Before prescribing anticoagulants, speculation of its complications is imperative. Bleeding is the predominant complication of anticoagulants.[2] Monitoring of INR and prothrombin time is crucial for assessing the risk of bleeding in susceptible individual. The severity of anticoagulants adverse effects have increased with the advent of direct oral anticoagulants(DOACs) as they directly inhibit either thrombin or activated coagulation factor ten (GI endoscopy in patient on anticoagulant therapy).one such anticoagulant associated with anticoagulant bleeding is acitrome an acenocoumarol derivative. It works by inhibiting enzyme vit K reductase that is involved in reduction of Vit K. [3-5]

Risk factors for Vitamin K antagonist associated GI bleeding comprises of advance age, co morbid conditions like hypertension, diabetes mellitus, congestive cardiac failure, hepatic failure, renal failure, and cancer etc. Apart from the above risk factors variability in genetic polymorphism, contribute largely for bleeding risk. Alteration in VK0RC1 and CYP2C9 genes demands the adjustment in dos of

acenocoumaroul and other VKA.VK0R1 encodes for epoxide reductase responsible for effective clotting. Mutations in this gene can be associated with deficiencies in vit K dependent clotting factors that demands lower dose of acenocoumarol. While, CYP2C9 is associated with metabolism of acenocoumarol. several variant of this gene alleles (such as CYP2C9*2 and CYP2C9*3) have reduced metabolism leading to higher acenocoumarol concentrations requiring lower than normal dose in such subjects.[6-10]

Case Presentation

A 58 yrs old male patient admitted in the tertiary care hospital on 17/11/2017 with chief complaints of Hematemesis, Hematuria 4-5 episodes, malena, and breathlessnesss. Patient has a history of DM with HTN for which he is on regular treatment of vildagliptin/metformin (50/500) twice daily He was admitted 1 year ago and has been operated for Superior mesenteric vein (SMV) thrombosis-underwent jejunal resection. His past medication history illustrates the use of tab acitrom 0.5 mg orally once daily for prevention of thrombosis. Patient was shifted to ICU upon admission for the above complaints and was immediately held on inj ethamsylate 250mg IV for the bleeding complaints. BP of 70/45 mm/hg lead to the starting of IV fluids that includes IV kabilyte 500ml and IV plasmolyte. Vitals were monitored thereafter and oesophago-gastroduodenoscopy (OGD) with colonoscopy and chest Xraywas performed on 18/11/2017 once the patient was stabilized.

Observations of CT scan included: -

1. Chronic thrombosis in the form of severe narrowing of right branch of portal vein

2. Small sub capsular area in segment 6 of right lobe of liver showing progressive enhancement mostly suggestive of benign etiology like haemangioma

3. Small and atrophic right kidney with multiple scars in left kidney.

While chest X-ray showed fibrotic band in left lower lobe and prominent vascular markings. Nevertheless, rest of the visualized lung fields appeared clear. During colonoscopy procedure; scope was passed until the caecum. Although antral gastritis was seemed, the entire colonic mucosa was normal.lab values were suggestive of increased bleeding due to increase in prothrombin time (21.2 sec) and INR (1.94 sec) on 18/11/2017.since bleeding time was increased acitrom was withdrawn after which INR and prothrombine time were regularly monitored. A decrease in prothrombine time (12.2 sec) and INR (1.14sec) was found on 20/12/2017. Acitrom was replaced by rivaroxaban. On hospitalization tab cardarone 100 MG twice daily was prescribed for atrial fibrillation.[11]

Discussion

Acitrom contains nicoumalone as an active ingredient. It is one of the oral acenocoumarol derivative functioning as a vit K antagonist. Acenocoumarol inhibits vitamin k reductase that is involved in generation of reduced form of vit K. This substantially inhibits carboxylation process and hence impeding synthesis of vit k dependent coagulation factors. Severity of anticoaulant induced bleeding depends on dose and duration of treatment. high dose and longer duration of treatment along with other risk factors increases the risk of bleeding in susceptible individual. Other risk factors include advanced age; hepatic disease, renal failure, and low body weight etc are other risk factors contributing to increase risk of bleeding. Malnourished people with low plasma protein are susceptible to bleeding since 97% of acenocoumarol is bound to plasma protein albumin.

The most perennial symptoms observed are: cutaneous bleeding, hematuria, hematomas, gastrointestinal bleeding, haematemesis, epistaxis, uterine bleeding, and gingival bleeding. This increased bleeding leads to hypotension due to loss of blood. Tachycardia results due to compensatory mechanism involving sympathetic activation in response to hypotension. Considering acenocoumarol predominant action as vitamin K antagonist, 5-10 mg of slow Vit k infusion over 30 min is the first treatment approach for controlling bleeding (Franco et al., 2015). To avert bleeding while on acenocoumarol derivative assessment of risk factors including genetic testing is necessary. Monitoring of INR and prothrombin levels determine the risk of bleeding. INR levels >3 suggests bleeding risk.

Conclusion

Assessment of risk factors for bleeding while prescribing anticoagulants aids in rational prescribing of anticoagulants. This lessens further bleeding complication with increase effectiveness of anticoagulant therapy.

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