A CASE REPORT OF CLOPIDOGREL-ASPIRIN INDUCED UGI BLEED

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ABSTRACT

Non-variceal bleeding is associated with peptic ulcer disease (PUD) or other causes of UGIB Drug-induced. Clopidogrel, another form of antiplatelet agent, has been approved by the US-FDA for use in secondary prevention of heart attacks, valve replacement and stroke. The risk of gastrointestinal bleeding generally increases by a factor of two to three with the use of even low-dose aspirin by substantially inhibiting gastric cyclooxygenase and causing gastric ulceration. The major adverse event of the combination of heparin, aspirin and Clopidogrel is bleeding, particularly from the gastrointestinal tract. Combined anti-thrombotic drug treatment confers particular risk and is associated with high incidence of gastrointestinal bleeding. This can be prevented with the use of regular PPI treatment, esomeprazole was found to be most effective.

Key words: Upper gastrointestinal bleeding, Clopidogrel, PPI, Esomeprazole.

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Available online: www.ijipsr.com August Issue 1181
INTRODUCTION

Upper gastrointestinal bleeding is defined as bleeding from a source proximal to the ligament of Treitz and can be categorized as either variceal or non-variceal. Variceal haemorrhage results from complications of end stage liver disease, and non-variceal bleeding is associated with peptic ulcer disease (PUD) or other causes of UGIB Drug-induced [1].

Upper gastrointestinal bleeding (UGIB) is a potentially life-threatening condition that requires prompt and appropriate management. UGIB annually produces a hospitalization rate of 165 per 100,000 adults (more than 300,000 hospitalizations) at an estimated cost of 2.5 billion. More people are hospitalized for UGIB than for congestive heart failure or deep venous thrombosis [2]. Bleeding from the upper gastrointestinal (GI) tract is 4 times as common as bleeding from the lower GI tract. The annual incidence of UGIB ranges from 48 to 160 cases per 100,000 individuals [3].

Despite the advances in therapeutic management, mortality has remained unchanged at 10% to 14%, which may be related to longer life expectancy and the higher number of co-morbidities in the aging population [4].

The risk of UGIB is also significantly higher in patients with concomitant use of serotonin reuptake inhibitors and NSAIDs. Clopidogrel (Plavix, Bristol-Myers Squibb Co.), another form of antiplatelet agent, has been approved by the Food and Drug Administration for use in secondary prevention of heart attacks, valve replacement and stroke [5].

The major adverse event of the combination of heparin, aspirin and Clopidogrel is bleeding, particularly from the gastrointestinal tract. However, information on gastrointestinal bleeding is scarce [6]. The gastrointestinal tract figures as one of the most common sites of a bleeding complication during high dose of anti-platelet therapy is an adverse drug effect [7]. It was suggested that the GI side effect among ischemic patients is being influenced by the dosage of the aspirin used. Even though, 80mg is considered as a low dose of aspirin, the data still suggests that there are side effects due to its administration to the heart failure patient [9].

CASE PRESENTATION

A 35 years old female known case of hypertension and mitral valve replacement (MV) 3yrs back was admitted in General Medicine Department with chief complaints of hematemesis since 2days, history of malena positive. On examination Blood pressure (BP) was 100/70mmHg low, Cardiovascular sound and per-abdomen were found to be normal at diagnosis NAD) Past
medication history is as follows. Tab.Clopitab A (Clopidogrel 75mg + Aspirin 80mg) & Tab. Acitram (Lorazepam) 3mg/OD since long time, without use of any proton-pump inhibitors.

**Laboratory investigations:** Complete blood picture (CBP) was done which revealed low RBC and hemoglobin levels, Serum creatinine (Sr.cr), Blood urea (BU), 2D-Echo, Electrocardiogram (ECG) was done and all those were found to be normal. Endoscopy has revealed perforation in UGI.

**Treatment:** GI bleed due to long term use of Clopitab-A was suspected and the drug was stopped. Drugs on admission was given as follows; Inj.Ceftriaxone 1g IV BD, Inj.Pantoprazole 40mg IV OD, Tab.Atorvastatin 40mg OD HS, Inj.Tranexamic acid 500mg IV OD, IV Fluids for 5 days and the symptoms was subsided.

**DISCUSSION**

The risk of gastrointestinal bleeding generally increases by a factor of two to three with the use of even low-dose aspirin by substantially inhibiting gastric cyclooxygenase and causing gastric ulceration [7]. It is for this reason that Clopidogrel as an alternative to aspirin has been sought. It is anticipated from the mechanism of action of the two drugs that aspirin is more likely to cause GI bleeding than Clopidogrel. Aspirin prevents thrombosis and blocks platelet aggregation through inhibition of the cyclooxygenase enzyme. It induces GI ulceration also through the same mechanism. The antithrombotic effect of Clopidogrel is by blocking the platelet activation of adenosine diphosphate (ADP) which prevents the activation of the glycoprotein IIb/IIIa complex [8]. Contrary to current literature, Chan et al showed that patients receiving Clopidogrel had an astonishing increase in the rate of recurrent upper gastrointestinal bleeding from ulcers, as compared with those in the group taking aspirin plus esomeprazole (8.6 percent vs. 0.7 percent, P=0.001). Impairment of healing induced by Clopidogrel may be the primary mechanism which may explain the increased bleeding by this antiplatelet agent. Apart from the aspirin and Clopidogrel issue, possibility of previous esophageal surgery as a cause of the bleeding was also evaluated. It did not seem to the authors that that was the cause of the bleeding 3 years later [8].

**CONCLUSION**

Combined anti-thrombotic drug treatment confers particular risk and is associated with high incidence of gastrointestinal bleeding. This can be prevented with the use of regular PPI treatment, esomeprazole was found to be most effective.
Hence, PPI should be added to the treatment regimen when Clopidogrel-aspirin is used for long term, because which will lead to an adverse drug reaction (drug induced UGI bleed) as seen in this case.

**AUTHOR’S CONTRIBUTIONS**

VA: investigation of the patient, literature research, drafting of the manuscript, corresponding author. AM: literature research, drafting of the manuscript. SM: drafting of the manuscript. All authors read and approved the final manuscript.

**REFERENCES**