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Real World Studies on Undesirable Effects of Some Antithrombotic Drugs in a Tertiary Care Hospital

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Abstract: ***Background: Hemostasis is the cessation of blood loss from a damaged vessel. Platelets first adhere to macromolecules in the sub endothelial regions of the injured blood vessel, where they become activated. Adherent platelets release substances that activate nearby platelets, thereby recruiting them to the site of injury. Activated platelet aggregate to form the primary hemostatic plug. Methods and Materials: It is a hospital based prospective observational study in the inpatient departments of cardiology and neurology for a period of six months. Total 92 patients are included in the study under the guidance of physician. Results: It was a prospective observational study in which total 92 patients were included. Most commonly prescribed drugs were heparin, aspirin and clopidogrel and aspirin-clopidogrel combination which is seen in most of the following diagnosis like myocardial infarction, coronary artery disease, acute coronary syndrome with undesirable side effects like thrombocytopenia, prolonged bleeding, heart burn and tachycardia. Conclusion: Most common drug is heparin which is 50% of the patients. Aspirin 43% mainly for coronary artery disease and myocardial infarction. Remaining 7% either clopidogrel or aspirin-clopidogrel combination (dual therapy).***

Keywords: Myocardial infarction, Coronary Artery Disease, Acute Coronary Syndrome, Hemostasis, Heparin

1. Introduction

An antithrombotic agent is a drug that reduces the formation of blood clots. Antithrombotics can be used for primary prevention or secondary prevention or treatment of dangerous blood clot. There are different types of antithrombotic agents. Anticoagulants drugs would prevent pathologic thrombosis and limit reperfusion injury yet allow a normal response to vascular injury and limit bleeding by coagulation cascade pathway. Indirect thrombin inhibitors include unfractionated heparin, low molecular weight heparin, high molecular weight heparin and synthetic pentasacharide fondaparinux. Oral anticoagulants include warfarin and other coumarin derivaties. Oral direct factor Xa inhibitors includes rivaroxaban, apixaban and edoxaban. Direct thrombin inhibitors includes hirudin, lepirudin, bivalirudin, argatroban and melagatran. Fibrinolytic drugs rapidly lyse thrombi by catalyzing the formation of serine protease plasmin from its precursor zymogen plasminogen. These drugs create generalized lytic state when administered intravenously. Fibrinolytic drugs includes streptokinase, alteplase, reteplase, tenecteplase and urokinase. Antifibrinolytic drugs inhibits the plasminogen activation which includes epsilon amino caproic acid and tranexamic acid. Antiplatelets targets platelet inhibition. Several drugs target platelet inhibition such as inhibition of prostaglandin synthesis (aspirin), inhibition of adenosine diphosphate induced platelet aggregation (clopidogrel, prasugrel and ticlopidine) and blocade of glycoprotein IIb/IIIa receptors on platelets (abciximab, tirofiban and eptifibatide).

The aim of this study is to evaluate the risks and benefits of different antithrombotics, suggestion of better antithrombotic therapy and prevention of thrombosis and to estimate adverse side effects.

2. Literature Survey

The study was a hospital based prospective observational study which was conducted in inpatient facilities of the department of Cardiology and Neurology. Anti platelet medications are considered as first line therapy in preventing cardiovascular thrombotic events. The need of this study brought into light when we observed undesirable effects during regular participation of ward rounds and while assisting patient complications by clinical pharmacist. Multiple studies have demonstrated the effectiveness of dual or triple therapy antiplatelet therapy with aspirin, clopidogrel therapy in patients with acute coronary syndromes. Major cardiovascular adverse events including death, myocardial infarction, stroke and recurrent angina have all been shown to significantly decreased when these agents are employed in the treatment of atherosclerosis, acute coronary syndromes, myocardial infarction and in setting of percutaneous coronary intervention.

3. Methodology and Approach

We have analyzed patients in the departments of cardiology and neurology with a sample size of 92 patients by using patient consent form, patient information leaflet and patient data collection form by using average and standard deviation.

4. Results

1) Segregated Data of Heparin

a) Intended Use V/S Number of Patients

Intended Use	Number of Cases
Cardiology	6
Neurology	2

b) Average Age and Standard Deviation of Patients

Age	
Mean-Age	57.25
SD	6.6

c) Number of Patients V/S Gender

Gender	Number of Cases
Male	7
Female	1

d) Diagnosis V/S Number of Patients

Diagnosis	Number of Cases
CAD	4
CVA	3
AF with CVR	1

e) Undesirable Effects V/S Number of Patients

Undesirable Effects	Number of Cases
Hemorrhage	4
Chest Pain	1
Heavy Bleeding on Cuts of Wounds	2
Information Not Available	1

2) Segregated Data of Clopidogrel

a) Average Age and Standard Deviation of Patients

Age	
Mean-Age	57.9
SD	7.9

b) Diagnosis V/S Number of Patients

Diagnosis	Number of Cases
LVF	2
CAD	2
TIA	2
CVA Ischemic Stroke	3
ACS-NSTEMI	2
CVA	2
AFI, CVA	1
Brain Stroke	1
MI	4
Unstable Angina	4
Stroke	1

c) Drug Dosage and Route of Administration/Number of Cases

75mg	20/po
300mg	2/po
150mg	2/po

d) Indications V/S Number of Patients

Indication	Number of Patients
Reduce the incidence of stroke	4
Reduce the rate of recurrent stroke	10
Reduce the risk of major ischemic stroke	2
Reduction of adverse ischemic incidence	6
To prevent recurrent ischemic event	2

e) Undesirable Effects V/S Number of Patients

Undesirable Effects	Number of Patients
Indigestion	2
Heartburn	2
Prolonged Bleeding	11
Vomiting	6
Dyspepsia	2
Dizziness	1
Headache	6
Stomachache	1
Tiredness	1

3) Segregated Data of Aspirin

a) Average Age and Standard Deviation of Patients

Age	
Mean-age	57.93
SD	6.8

b) Gender V/S Number of Patients

Gender	Number of Cases
Male	35
Female	25

c) Diagnosis V/S Number of Patients

CAD	10
CVA	8
ANGINA	10
MI	11
PERICARDIAL EFFUSION	2
RHD	3
AMOEBIC DYSENTERY	1
LVF	1
LVH	4
MENINGIOMA DECREASED EVALUATION	1
POST PTCA	1
PARKINSONISM	3
ACUTE ISCHEMIC STROKE	1
CHF	1
ISCHEMIC HEART DISEASE	1
GENERALIZED TONIC-CLONIC SEIZURES	1
VERTIGO DECREASED EVALUATION	1

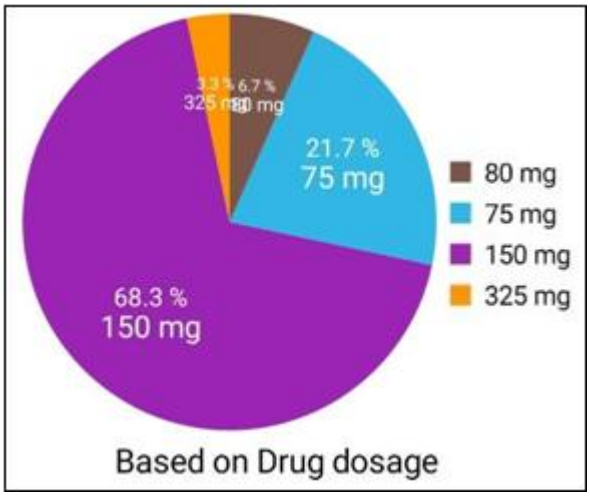
d) Frequency V/S Number of Patients

Frequency	Number of Cases
OD	58
TID	2

e) Undesirable Effects V/S Number of Patients

Undesirable Effects	Number of Cases
Hallucinations	2
SOB	9
Tachycardia	9
Abdominal Pain	1
Diarrhea	1
Heartburn	2
Blood in Stools	4
Blurred Vision	2
Confusion	2

Swelling of Eyes	2
GI Bleeding	6
Ringing Ears	3
Allergic Reactions	1
Nausea	6
Liver Damage Increased Bilirubin Levels	1
Increased Blood Pressure	1
Hemorrhage	1
Thrombocytopenia	1
Ulcers	3
Decreased Urination	1



5. Discussion

From the segregated data of heparin 8 cases out which cardiology 6 cases and neurology 2 cases were using heparin. Among them 7 are male and 1 is female patient. The average age of the patients which as noted as 57.25. Most commonly patients were diagnosed with coronary artery disease with undesirable effects of hemorrhage, chest pain and cuts of wounds. From the segregated data of clopidogrel with a sample size of 92 patients mostly used clopidogrel in myocardial infarction and unstable angina with least prescribed in diagnosis of atrial fibrillation and cerebrovascular accident. Among dosage 75 mg was most commonly prescribed with about 20 patients and least prescribed as 150 mg dosage form seen in 2 patients only. In the indications clopidogrel was mainly used for reduce the rate of recurrent stroke and least to prevent recurrent ischemic event. Most undesirable effects of clopidogrel are prolonged bleeding and least with dizziness, stomach ache and tiredness. The average mean of age is 57.9. From the segregated data of aspirin 60 patients are using aspirin. Among them 35 are male and 25 female patients. The average age of the patient which was noted as 57 years. Most commonly patients was diagnosed with coronary artery disease, cerebrovascular accident, angina, myocardial infarction, left ventricular hypertrophy with observed undesirable effects like shortness of breath, tachycardia, gastrointestinal bleeding.

6. Conclusion

Heparin: In the current study there were 8 cases were 50% of the patients complained of hemorrhage/bleed. Though the patient group is small it is quite evident common undesirable effects of bleeding to heavy bleeding are noted in patients. Intravenous administration of heparin is advised than subcutaneous route.

Clopidogrel: In the current study 92 cases data of 24 patients who are on clopidogrel was studied. Of them 19 patients are in cardiology and 5 patients are in neurology. The study clearly shows that prolonged bleeding was observed in 40% of patients on clopidogrel mainly while administering high doses or with concomitant medication.

Aspirin: In the current study 60 patients are on aspirin.43 patients are in cardiology and 17 in neurology. Important undesirable effects noted in the study include shortness of breath, tachycardia. It is advised from the current study that antiulcer drugs should be made mandatory for the patients on aspirin based on undesirable effects. Most of the adverse effects are found in patients taking more than 75 mg and more than once a day.

7. Future Scope of Antithrombotics

Antithrombotic therapy including antiplatelet and anticoagulation therapy represents an essential component in the treatment of ST segment elevated myocardial infarction. Early onset of antithrombotic effect may attenuate and even reverse the process of thrombus formation in a coronary artery prior to mechanical revascularization. The current recommended antiplatelet treatment for patients with ST segment elevated myocardial infarction who are planned to undergo primary percutaneous coronary intervention involves the combination use of the cycloxygenase 1 inhibitor aspirin and an adenosine diphosphate receptor antagonist targeting the P2Y1212 receptor (ticagrelor, prasugrel, clopidogrel or cangrelor), also referred to as dual antiplatelet therapy. The first generation thienopyridine ticlopidine is no longer being used for the treatment of ST segment elevated myocardial infarction, due to rare but severe side effects such as neutropenia. Anticoagulant therapy is an essential prerequisite for primary percutaneous coronary intervention to avoid thrombotic complications. Fondaparinux has been associated with significant rates of catheter thrombosis, it is no longer recommended in the treatment during primary percutaneous coronary intervention. Early trials have demonstrated an important ischemic benefit of glycoprotein therapy in acute coronary syndromes patients but with an additional unwanted significant increase in major bleeding. Interestingly, with the development of novel antithrombotic agents, more recent trials have shown less ischemic benefit with the routine use of glycoprotein IIb/IIIa inhibitors.

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Author Profile

Mudigonda Sai Krishna, Diploma in Medical Lab Technician (Telangana State Paramedical Board), Doctor of Pharmacy (Pharm D) from Omega college of pharmacy has done research article in real world studies on undesirable effects of some antithrombotics from Continental Hospitals (JCI) and St. Theresa Hospital, Hyderabad. This article mainly focus on adverse effects of antithrombotic drugs which can cause life threatening complications. Main conclusion is to bring newer drugs and Novel anticoagulants are better choice of drugs in many cardiovascular and stroke diseases.