

Clopidogrel Induced Left Large Occipital Haemorrhage

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Abstract:

I. Introduction:

Clopidogrel is thienopyridine inhibitor of the platelet P2Y₁₂ adenosine diphosphate (ADP) receptor. Clopidogrel is an agent that irreversibly inhibits adenosine diphosphate (ADP) induced platelet aggregation.¹ The interaction of ADP with the platelet P2Y₁₂ receptor induces platelet shape change, reversible aggregation, initial glycoprotein (GP) IIb/IIIa activation, phospholipase C activation, and calcium flux.¹ Regular use of clopidogrel (75mg daily) can produce 40-50% inhibition of adenosine diphosphate induced platelet aggregation.^{1,2} This function makes it one of the drugs of choice for secondary stroke prevention, and also part of dual antiplatelet therapy in patients undergoing angioplasty and/or stent placement and acute coronary syndromes. The evidence supporting an increased risk of traumatic intracranial haemorrhage in patients receiving Clopidogrel is more limited,³ despite this drug being one of the most commonly prescribed worldwide.⁴ Intracerebral haemorrhage (ICH) is a well-known complication of antiplatelet and antithrombotic therapy. Although the rate and clinical characteristics of ICH with warfarin and aspirin is a well-studied phenomenon, limited information is available regarding the rate, clinical characteristics, and outcome of ICH associated with clopidogrel.¹¹ Gastrointestinal problems including nausea, diarrhoea and constipation are the common side effects of clopidogrel. Serious side effects like intracranial haemorrhage and severe neutropenia have been reported.⁵

II. Case Report:

A 74 year old male patient known case of hypertension, diabetes mellitus, and coronary artery disease – past coronary artery bypass surgery 8 years back was admitted in in General Medicine Department with chief complaints of diminished vision since 2 weeks, and having history of headache & giddiness since 2 weeks, fever on & off since 8 days which is moderate grade not associated with chills. On examination Blood pressure (BP) was 160/100mmHg, pulse rate was 100 Bpm and having imbalance while walking, right homonymous, hemianopia was observed. Cardiovascular sound and per-abdomen were found to be normal at diagnosis (NAD) Past medication history is as follows. Tab. Atorfit CV (atorvastatin 40mg+clopidogrel 75mg) OD , silodosin 8mg H/S, Tab. Telma 80mg+amlodipine 5mg OD, Tab. Glycomet GP1 BD. Complete blood picture (CBP) was done which revealed low RBC and ESR levels, Serum creatinine (Sr.cr), RBS, 2D-Echo, Electrocardiogram (ECG) was done and all those were found to be normal. **MRI brain revealed left large occipital bleed.** Left large occipital bleed due to long term use of Clopidogrel was suspected and the drug was stopped. Drugs on admission was given as follows; Inj. Monocef 1 gm. iv BD, Inj. H. actrapid according to Bl. Sugar , Inj. Pan 40mg iv OD, T. Telma 800mg OD, T. Stamlo 5mg OD, T. Atorva 40mg OD, T. Silodosin 8mg H/S, IV Fluids for 3days and the symptoms was subsided.

III. Discussion:

The risk of occipital bleeding due to clopidogrel is very rare condition. Approximately 7000 intracerebral haemorrhages annually in the United States are estimated to be caused by use of anti-thrombotic therapies.¹² Schalenkamp et al.¹³ suggested that the use of oral anticoagulants in addition to clopidogrel may have similar rates of haemorrhagic complications compared to oral anticoagulants in addition to aspirin. The mortality with clopidogrel related ICH appears to be higher than that observed with aspirin related ICH. The use of clopidogrel is increasing in the general population, especially in patients with previous strokes who suffer recurrent ischemic event who are already on an antiplatelet agent, usually aspirin.^{13,14} A meta-analysis of such treatment strategies have shown the combination of low-dose aspirin plus clopidogrel to be increasing the risks of bleeding as compared with either agent alone.¹⁷ In another randomized, double-blinded and placebo-controlled trial; life threatening bleedings were higher in the group of patients receiving aspirin and clopidogrel versus clopidogrel alone (2.6% vs 1.3%).¹⁸ Clopidogrel inhibits platelet aggregation induced by ADP, resulting in

prolongation of bleeding time and delay of clot retraction. Clopidogrel is at least as effective as aspirin in preventing serious cardiovascular events in patients with stable vascular disease.⁸ Anti-platelet therapy, while efficacious in reducing the incidence of ischemic complications, can cause serious adverse reactions. Several factors are reported which increase the risk of patients developing haemorrhage while receiving clopidogrel, these include advanced age, female gender, hypertension, coagulopathy and usage of other antiplatelet agents. Drug induced adverse effects and drug-drug interactions are commonly seen in the elderly. Total plasma volume decreases and plasma drug concentration increases with aging. The rising plasma concentration of drugs leads to increased efficacy up to a certain level, after which the efficacy of the drug diminishes and there is a concomitant rise in adverse reactions⁵. There was no other medication except clopidogrel that could cause the haemorrhage. Based on the Naranjo's Scale, a score of 6 suggested that the clopidogrel was the probable cause of the left large haemorrhage.

IV. Conclusion:

The treating doctors need to educate the patients while prescribing them such anticoagulant agents regarding lab investigations and potential side effects. If not, the patients become susceptible to fatal bleeding episodes. Both the pros and cons of each treatment modality must be explained in detail to the patient. Further studies need to elaborate the occurrence and risk factors for clopidogrel associated occipital hematomas.

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