Current Antiplatelet Agents in Acute Coronary Syndrome

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Acute coronary syndrome (ACS) comprises of ST segment elevation myocardial infarction (STEMI), non-ST segment elevation myocardial infarction (NSTEMI) and unstable angina (UA). Dual antiplatelet therapy with aspirin (ASA) and clopidogrel (P2Y12 receptor inhibitor) reduces cardiovascular (CV) death, MI and stroke. However, 5-44% of studied patient population showed high platelet activity despite use of clopidogrel. Ticagrelor and prasugrel (new P2Y12 receptor inhibitors) have shown to reduce level of platelet activation as compared to clopidogrel.

While clopidogrel and prasugrel are irreversible inhibitors of P2Y12 receptors on platelet surface, ticagrelor is reversible and non competitive antagonist and is not a prodrug as it is with clopidogrel and prasugrel. Therefore, the platelet inhibited by clopidogrel or prasugrel are affected for rest of their lifespan and platelet function returns to normal by 5-10 days after stoppage of these agents. Prasugrel is contraindicated in patients with previous stroke, transient ischaemic attack (TIA), age of 75 years or above and weight below 60 Kg. Ticagrelor is contraindicated in patients with history of intracranial haemorrhage and patients taking strong CYP3A4 inhibitors.

TRITON-TIMI 38 (Trial to assess improvement in therapeutic outcomes by optimizing platelet inhibition with prasugrel-thrombolysis in myocardial infarction) compared prasugrel (60 mg loading dose, 10 mg maintenance dose) to clopidogrel (300 mg loading dose, 75 mg maintenance dose )in double blind randomised control trial. 13,604 (10074-UA/NSTEMI and 3534-STEMI) moderate to high risk ACS patients were enrolled and followed for a minimum of 6 months and maximum of 15 months. Results suggest a superiority of prasugrel over clopidogrel in preventing composite cardiac end points mainly in preventing non fatal MI when used in moderate to high risk patients. It also suggests a small statistically significant increase in fatal bleeding. The dose of clopidogrel in this trial was questioned as to why not 600 mg loading dose was used which may have biased the outcomes.

A comparison of prasugrel and clopidogrel in acute coronary syndrome subjects (TRILOGY ACS) study was to assess the efficacy of prasugrel (10 mg daily dose) versus clopidogrel (75 mg daily dose) in long term medical therapy of ACS under patients of 75 years of age with composite end points same as TRITON-TIMI. It showed no statistically significant change in primary end points between clopidogrel and prasugrel group. ACCOAST (A Comparison of prasugrel at PCI or Time of Diagnosis of Non-ST elevation myocardial infarction) trial investigating the risks and benefits of pretreating with 30 mg of prasugrel at the time of ACS diagnosis and 30 mg more at time of percutaneous coronary intervention (PCI) versus 60 mg at the time of PCI only was stopped prematurely as it showed that pre-treatment with prasugrel was associated with an increased risk of major and life-threatening bleeding, although no increased rate of mortality.

The platelet inhibition and patient outcome (PLATO) trial was done to determine whether ticagrelor is superior to clopidogrel for preventing vascular events and death in patients with ACS. This multicentre, randomised double blind, double dummy trial compared ticagrelor (180 mg loading dose and 90 mg bid maintenance dose) against clopidogrel (300-600 mg loading dose, 75 mg daily) in 18,624 patients. It suggested...
a clinical superiority of tecagrelor over clopidogrel. However patients on tecagrelor had higher rates of major bleeding and showed that using lower dose of ASA with tecagrelor is preferable for better outcomes. Also, ticagrelor can cause dyspnoea as an adverse effect in 10-14% of patients early in the course but is self-limited.

References

