

GP1Ib/IIIa Inhibitors: Current Status

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Once thought as inert particles, platelets are found to be pivotal in thrombogenesis, a process that is the core in the pathophysiology of acute coronary syndrome (ACS). Thus platelets are targeted to manage (ACS). For the last 4 decades or so, there is evolving concept of inhibition of platelets – aspirin, cyclooxygenase inhibitor; and then the ADP receptor inhibitors – ticlopidine, clopidogrel, prasugrel and ticagrelor. So many receptors are on the surface of platelets that lead to chance of so many anti-platelets to develop. For the aggregation of platelets the final common pathway is GP1Ib/IIIa receptors. So inhibiting these receptors were lucrative option for effective inhibition of platelets. Whenever there is vascular endothelial damage, platelets adhere to the denuded surface of the endothelium and become activated. GP1Ib/IIIa receptors of activated platelets bind to fibrinogen that leads to aggregation of platelets and thrombus formation. This is what we understand in a simplified way.

In mid nineties, GP1Ib/IIIa inhibitor -abciximab came into clinical use. It became a favorite agent during the procedure percutaneous coronary intervention (PCI). Its upstream use was considered for some time but with little recommendation from scientific bodies. Later eptifibatide and tirofiban were developed. They are advantageous not only due to reduction in cost but also due to reduction in untoward bleeding. No oral preparation can be made and their use is mainly intravenous with intracoronary use in some situations. Due to their prompt and short duration of effect, they gain dearness to the interventionist. One unique effect of this group is “dethrombosis” - they are able to lyse the formed clot by breaking the link between the fibrinogen with platelets.

At the same time, we witness the changing scenario of the ADP receptor blocking anti-platelets. Following ticlopidine and clodidogrel, arrival of prasugrel, an ADP receptor inhibitor, gave support to the interventionist due

to its more rapid platelet inhibition. However, its use has mostly beentaken over by ticagrelor, the more rapid and reversible one. Cangrelor, an ADP receptor blocker with parenteral formulation shows promising role in near-future in the interventional arena.

What the guidelines say about GP1Ib/IIIa inhibitors? At the present time there is no class I indication in European Society of Cardiology (ESC) guideline for their use. In ST-elevation myocardial infarction (STEMI) patients ESC guidelines recommend its use as *bailout therapy if there is angiographic evidence of massive thrombus, slow or no-reflow or a thrombotic complication (IIa); routine use as an adjunct to primary PCI performed with unfractionated heparin without contraindications (IIb); upsteamuse in high risk patients undergoing transfer for primary PCI (IIb)*. All the three available GP1Ib/IIIa inhibitors are listed in the guidelines.

In non ST-elevation acute coronary syndrome (NSTEMI-ACS) patients, GP1Ib/IIIa inhibitors are also recommended in bailout situations or when there are thrombotic complications (IIb). They are not to be used when coronary anatomy is not known (III).

In STEMI, the American College of Cardiology/ American Heart Association (ACC/AHA) guidelines recommend the use of GP1Ib/IIIa receptor inhibitors at the time of *primary PCI (with or without stenting or clopidogrel pretreatment) in selected patients with STEMI who are receiving unfractionated heparin (IIa); in the precatheterization laboratory setting (e.g. ambulance, emergency department) to patients with STEMI for whom primary PCI is intended (IIb); intracoronary abciximab to patients with STEMI undergoing primary PCI (IIb)*. They are not recommended if PCI is not intended (III).

In NSTEMI-ACS patients, ACC/AHA recommends *GP1Ib/IIIa inhibitors in patients with high risk features (e.g. elevated troponin) who are not adequately pretreated with clopidogrel or ticagrelor (class I) and in patients adequately pretreated with clopidogrel and treated with unfractionated heparin (UFH) (IIa)*.

With the advent of newer oral anti-platelets along with intravenous formulation of an ADP receptor blocker - cangrelor with earlier onset of action and use of direct thrombin inhibitor (i.e. bivaluridin) in the cath lab limits the use of GP IIb/IIIa inhibitors in clinical practice as reflected in the recommendation of the guidelines. In the situations where bivaluridin is not available (as in most centres of Bangladesh where UFH is still "popular") and pre-treatment with anti-platelets are not adequate (also in conditions of allergy to aspirin) their use is needed.

One may be reminded of the off-label uses - in patients with drug-eluting stent (DES) during early weeks of PCI who need emergency surgical procedures; GPIIb/IIIa inhibitors may be used as "bridging" antiplatelet after discontinuing oral agents. Some authors showed the beneficial effects in peripheral arterial interventions.

Further Reading:

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