

Treatment of the Acute Coronary Syndrome: A Quick Clinical Perspective

While the initial treatment of patients with unstable angina and non-ST segment elevation myocardial infarction includes prompt antiplatelet therapy with aspirin (or Clopidogrel for patients with hypersensitivity reactions to aspirin), it is not always clear what role low molecular weight heparin and intravenous platelet glycoprotein IIb IIIa antagonists have in this syndrome. When should they be used? First, it is important to note that there is a delay in onset of antiplatelet activity with thienopyridines – several days for Ticlopidine (though now rarely used) and several hours for Clopidogrel compared with the effect of platelet inhibition which begins within 15-20 minutes with chewed aspirin. Heparin should be used in patients who present with unstable angina. Heparin inactivates factors IIa (thrombin) and factors IXa and Xa. Unfractionated heparin binds to several plasma proteins and also may activate platelets. The advantages of low molecular weight heparin (LMWH) includes less plasma protein binding, more predictable and sustained anticoagulation affect, and subcutaneous administration without the need for monitoring. Though these properties make low molecular weight heparin particularly attractive in ease of administration, the level of anticoagulant activity cannot be easily measured (measuring Xa activity is required). This is at least a theoretical concern for patients undergoing percutaneous coronary interventional procedures within 0-6 hours after LMWH administration, especially when intravenous glycoprotein inhibitors are being used.

While several studies have demonstrated the effectiveness of intravenous glycoprotein inhibitors for the treatment of acute coronary syndromes (ACS), these studies have had variable enrollment protocols and end points. A meta-analysis of six large randomized placebo controlled trials of glycoprotein IIb/IIIa receptor antagonists in patients with ACS not routinely scheduled to undergo coronary revascularization did not achieve statistical significance for the individual end-points of death and nonfatal myocardial infarction. In addition, bleeding complications are increased in patients receiving a combination of aspirin, heparin, and glycoprotein inhibitor therapy, which may especially be an issue in unstable patients found to need urgent coronary artery bypass surgery. These combined trials of intravenous glycoprotein inhibitor therapy suggest that these agents are effective in the initial periods of medical stabilization for patients with unstable angina and this effect appears to be magnified if early catheterization and percutaneous coronary intervention is performed. It is important to note that the use of glycoprotein inhibitors appears to be of modest benefit *in patients who are not routinely scheduled to undergo percutaneous coronary intervention (PCI) (but who may do so), and they are of questionable benefit in patients who do not undergo PCI.*¹ Therefore, some general recommendations about anticoagulant therapy in the acute coronary syndrome could be stated as follows:

1. All patients with acute coronary syndromes should receive a chewable non-enteric coated aspirin (165-325 mg.) as soon as possible with Clopidogrel used only for significant aspirin allergic reactions due to its delayed onset of action.

2. Patients should be anticoagulated with intravenous unfractionated heparin. Low molecular weight heparin may also be used, especially in patients who present with unstable angina pectoris and are pain free at the time of presentation and in whom cardiac catheterization is contemplated several hours after admission, such as the following morning.

3. In most other patients who present with ACS and become stable on aspirin and heparin, this combination can be continued alone in preparation for early cardiac catheterization – which in most contemporary medical practices includes a large proportion of patients who present with acute coronary syndromes. Intravenous glycoprotein inhibitors could be considered in those individuals with underlying active ischemia or high risk clinical features as indicated in the table below. It would appear from the available evidence of several large studies though, that patients at low risk or who quickly stabilize probably derive little or no additional benefit from the “upstream” (prior to cardiac catheterization) addition of intravenous glycoprotein inhibitors.

References

- 1 ACC/AHA Guideline Update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction. *Braunwald et.al* 2002.
- 2 Cadroy Y, Bossavy JP, Thalamas C, Sagnard L, Sakariassen K, Boneu B. Early potent antithrombotic effect with combined aspirin and a loading dose of clopidogrel on experimental arterial thrombogenesis in humans. *Circulation* 2000;101:2823-8.
- 3 Boersma E, Harrington RA, Moliterno DJ, et al. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomized clinical trials. *Lancet* 2002;359:189-98.

Table I

High Risk of Death or Non Fatal MI in Patient with Unstable Angina

- 1) accelerating symptoms
- 2) prolonged and ongoing rest pain, especially with transient ST segment changes
- 3) new mitral regurgitant murmur
- 4) ischemic induced pulmonary edema
- 5) Hypotension, bradycardia, tachycardia
- 6) age > 75 years
- 7) sustained VT

Adapted from #1