University Heart Journal
Vol. 12, No. 2, July 2016

EDITORIAL

Role of Drugs in Coronary Intervention

Coronary artery disease (CAD) remains the leading cause of morbidity and mortality in developed as well as in developing countries. Core pathogenesis of CAD is the development of atherosclerotic plaque in coronary arteries. When these lesion become unstable or clinically significant, they are frequently treated with percutaneous coronary intervention (PCI), which usually involves balloon angioplasty and stent implantation.

Percutaneous transluminal coronary angioplasty (PTCA) expands the arterial lumen, stretching and disrupting the atherosclerotic plaque, vessel wall and redistributing the atherosclerotic plaque along its longitudinal axis. These injure the plaque and vessel wall which denudes endothelium. Moreover the balloons, wires and stents act as foreign bodies, hence PCI is associated with an increased risk of intracoronary thrombosis and thromboembolism. A phase of coordinated proliferation of medial smooth muscle cells and subsequent migration of these cells into the intima in response to the release of chemo attractants such as the platelet derived growth factor (PDGF) which leads to neo-intimal proliferation and post-angioplasty restenosis. So immediate and long-term clinical outcome of PCI depends on effective control of the thrombotic cascade and neo-intimal proliferation. The Achillis heel of angioplasty is restenosis.

Therefore, the drugs used in coronary intervention are predominantly those that act on the thrombotic cascade, which include anti platelet (aspirin, ADP P2Y12 receptor blockers like clopidogrel prasugrel, ticagrelor and glycoprotein IIb/lIIa inhibitors like Eptifibotide, abciximab, tirofiban) and antithrombotic such as intravenous unfractionated heparin, low-molecular-weight heparin (LMWH) and direct thrombin inhibitor bivaluridin. About antiplatelet therapy initial loading dose and maintenance of dual antiplatelet therapy (DAPT) with proper combination, duration, doses and patient compliance should be monitored carefully. Present guidelines recommended DAPT includes aspirin with any one of the ADP receptor blocker.the most widely used DAPT is aspirin with clopidogrel but recent study proves that in certain percentage of patients are inherent resistance to clopidogrel due to some genetic polymorphism of CYP isoenzymes. That's why prasugrel and ticagrelor are now being considered over clopidogrel. ACC/AHA/ESC recommends the maintenance duration of DAPT is minimum 1 month for bare metal stent (BMS) and 1 year for drug eluting stent DES. We consider glycoprotein IIb/IIIa inhibitors and anti-thrombotic drugs during periprocedural period in patients according to indication. Direct thrombin inhibitor has reduced the chances of heparin induced thrombocytopenia(HIT) among patients undergoing PCI. The rate of the composite of death from any cause, myocardial infarction, or major bleeding was not lower among those who received bivaluridin than among those who received heparin monotherapy.

Apart from cholesterol reduction HMG-CoA reductase inhibitors (statins), they have several 'pleiotropic' effects and they modulate inflammatory responses, endothelial function, plaque stability, thrombus formation and apoptosis. So regular dose of statin should according to guideline and target level of cholesterol. Regular high intensity statin therapy is recommended in diabetic patient following PCI. Administration of high loading dose of atorvastatin (80 mg) before primary PCI in STEMI patients has beneficial effect when compared to placebo in the context of microvascular perfusion and arrhythmia. This may provide new insights into the mechanisms of cardioprotection afforded by statins in the setting of PCI.

Few drugs like nitrate, adenosine, verapamil, diltiazem, nicorandil and atropine are kept in hand before the procedure to tackle the difficulties during the procedure. To overcome thromboembolism and prevention of stent restenosis adequate control of risk factors like diabetes, hypertention, dyslipidaemia are of paramountimportance by life style modification and drugs.

At the earliar decade of coronary intervention when only balloon angioplasty were done, abrupt closure of vessel, coronary dissection and restenosis rate was very high. Latter on innovation of stent and subsequent development of drug eluting stent has significantly reduced previous complications of plain old balloon angioplasty (POBA). At present stents are coated with many anti proliferative

drugs which act in-situ. Among those Sirolimus and Paclitaxel are now well recognized. Sirolimus (rapamycin; an immunosuppressive compound derived from a fungus) acts by inhibition mTOR receptor, resulting in the cessation of cell-cycle at G1 to S phases and, consequently, inhibits vascular smooth muscle cell proliferation. Paclitaxel (a well-known anti-cancer drug) inhibits cell proliferation and migration by disturbing cellular microtubule organization. Newer drugs are Everolimus, Zotarolimus and Novolimus which are synthetic form of sirolimus. Myolimus, a macrocyclic lactone in the same family as rapamycin is now being tested in RCTs. New generation DESs with biocompatible or biodegradable polymers (the delivery agent for the drug) are showing safety with shorter duration of DAPT down to 3 months in some cases.

Currently, more than 80% of percutaneous coronary interventions (PCIs) include stenting. Use of antiplatelet, antithrombotic, statin and drug eluting stents have reduced our fear of acute complication as well as improved long-term outcome of our patients.

Syed Ali Ahsan[1], Mohammad Rayhan Masum Mandal[2]
[1]Professor of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka, [2]Assistant Professor of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka,

References:

1. Chandrasekar B, Tanguay JF Platelets and restenosis. J Am Coll Cardiol 2000;35:555–62.
2. Clowes AW, Reidy MA, Clowes MM. Mechanisms of stenosis after arterial injury. Lab Invest 1983;49:208–15.
3. Poon M, Marx SO, Gallo R et al. Rapamycin inhibits vascular smooth muscle cell migration. J Clin Invest 1996;98:2277–83.
4. Axel DI, Kunert W, Goggelmann C et al. Paclitaxel inhibits arterial smooth muscle cell proliferation and migration in vitro and in vivo using local drug delivery. Circulation 1997;96:636–45.