**Drug Eluting Stents: A new era in Interventional Cardiology**

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**INTRODUCTION**

Over the last decade or so, no other subspecialty of medicine has seen such technological innovations, as interventional cardiology. These advances have revolutionized the management of coronary artery disease. From statin drugs to oral platelets inhibitors like clopidogrel and ticlopidine, intravenous platelet glycoprotein IIb/IIIa receptor blockers like Abciximab (Reo-Pro), Eptifibatide (Integriillin) and Tirofiban (Aggrastat) and finally drug eluting stents, it has truly been a success story. (Rawal Med J 2005;30:36-37).

**HISTORICAL PERSPECTIVE AND RESTENOSIS**

Starting from the first balloon coronary angioplasty in 1977 by Andreas Gruntzig,¹ percutaneous coronary intervention has now become a viable and sustainable alternative to CABG surgery. What initially started as plain old balloon angioplasty (POBA), matured into stenting in most cases. By 2002 more than 80 % of coronary interventions
were employing stents. However, the problem of restenosis has plagued the interventional community for years. Restenosis is a complex process involving vessel recoil, vessel remodeling and neo-intimal proliferation (smooth muscle growth) leading to reduction in vessel lumen and hence eventual loss of the beneficial effects of angioplasty. Restenosis after balloon angioplasty has been as high as 40-50%. And though restenosis rates with stent implantation were much lower than with plain balloon angioplasty, primarily because of reduction in vessel recoil and remodeling, they remained at an alarming rate of 15-30% due to continuing neo-intimal proliferation.² The rates are even higher in diabetics and those with complex coronary lesions.

**DRUG ELUTING STENTS (DES)**

Research over the last several years has particularly focused on strategies to reduce restenosis due to neo-intimal proliferation after coronary intervention and has finally culminated, for the time being, in the marketing of drug eluting stents (DES). The concept is simple; coat the metal surface of the stent with an antiproliferative drug and aim to reduce the smooth muscle proliferation. The drug is slowly released inside the coronary artery over several days to weeks. The initial success of drug eluting stents came about in the form of First in Man (FIM) study, which was the first study to employ the cypher stent (by Johnson & Johnson).³ The study showed remarkable reduction in restenosis at one-year follow-up. The stent was coated with an immunosuppressive drug Sirolimus (rapamune by Wyeth-Ayerst). Sirolimus was already available in oral form for use in transplant rejection and works as a cell cycle inhibitor at the G1 phase. These initial positive results were confirmed in a larger randomized trial; RAVEL⁴ which
randomized 238 patients to either a bare metal stent or a drug eluting stent. The results were remarkable; at 6 months, vessel luminal loss was virtually eliminated in patients receiving the sirolimus stent and restenosis rate was 0% in the sirolimus group vs. 26.6% in the bare metal stent group. Since then there has been active research at finding other drugs that will reduce restenosis. Equally impressive results have been shown by stents coated with Paclitaxel (TAXUS by Boston Scientific). Paclitaxel interferes with microtubule function, suppressing cell division which intern reduces intimal smooth muscle proliferation.

Though RAVEL included patients with simple coronary lesions, multiple subsequent randomized trials comparing drug eluting stents (including both rapamycin and paclitaxel) to bare metal stents have shown similar beneficial results in complex (i.e. small vessels, longer lesions, diabetic patients etc) coronary lesions as well. These included the SIRIUS, E-SIRIUS, C-SIRIUS, new-SIRIUS, TAXUS II, TAXUS IV etc.\textsuperscript{5}

But as with any new emerging technology, the interventional community is critically reviewing the positive results as well as the potential complications of drug eluting stents. Unlike bare metal stents which require 4-6 weeks of specific antiplatelet therapy i.e. clopidogrel or ticlopidine, after implantation, drug eluting stents require prolonged therapy up to 6 months and perhaps even longer. This is primarily due to increased incidence of thrombosis, particularly late thrombosis.

The other vital issue regarding drug eluting stents is their significantly higher cost compared to bare metal stents. This becomes even more critical in economically constrained societies such as Pakistan. However, it has been argued that this cost
difference may be partially offset by the significantly reduced need for repeat revascularization.

**A SIGNIFICANT ADVANCE**

As long-term i.e. 2-4 yr results of some of these trials become available, it is apparent that the initial beneficial effects are sustainable. It is becoming clear that although the problem of restenosis has not completely disappeared (approximately 5-7% at 2 years), drug-eluting stents have clearly emerged as the most dramatic improvement to-date in the management of coronary artery disease.

**REFERENCES**


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