Current Trends in Pharmacology and Clinical Trials
ISSN: 2642-0848

Academic Strive
Researcher's perception is our reality

Mini Review *Volume 6 Issue 1*

Need of Dual Antiplatelet Therapy during Percutaneous Coronary Interventions

Chaudhry S*

Director Solutions, Thane & Consultant Edenwell Therapeutics, India

***Corresponding author:** Sunil Chaudhry, Director Solutions, Thane & Consultant Edenwell Therapeutics, Mumbai, India, Email: Sunil.r.chaudhry@gmail.com

Received Date: May 01, 2023; **Published Date:** May 23, 2023

Abstract

Coronary artery disease in Asia is the leading cause of heart failure and is associated low quality of life with poor survival, despite advances in medical therapy. Treating the coronary arteries to improve blood supply (revascularisation) has long been considered as a treatment option. Stent thrombosis (incidence is 0.5-2 %,) is abrupt vessel closure, is one of the fatal complications of percutaneous coronary intervention. The common risk factors include a history of Type 2 diabetes mellitus, acute coronary syndrome, and reduced left ventricular ejection fraction. Drug eluting stents (Zotarolimus and Everolimus eluting stents) are very less likely to cause restenosis, as they are considered for their durable efficacy. DAPT (Dual antiplatelet therapy) is usually prescribed after a heart attack or stent placement to keep the vessels patent and to prevent future heart attacks for period of 12 months, whereas 6 months duration can be considered for those with high bleeding risk. In the first year following PCI, ticagrelor or prasugrel are associated with fewer gastrointestinal bleeds events than clopidogrel which is not perfect match as compared to new options.

Keywords: Drug-Eluting Stents (DES); Dual Antiplatelet Therapy (DAPT); Aspirin; Ticagrelor; Prasugrel

Abbreviations: DES: Drug Eluting Stents; DAPT: Dual Antiplatelet Therapy; MI: Myocardial Infarction.

Introduction

***Recommendations on the use of oral antiplatelet therapy after Percutaneous Coronary Interventions*:** The prevalence of CAD risks in India is 11% for non-diabetic patients and 21.4% for diabetic patients. The mortality in Indian subcontinent is 20–50% higher than other populations [1]. The pioneering work of Laurence Careven in 1950s in California established clinical use of Aspirin in cardiac patients. Aspirin is a cyclooxygenase-1 (COX-1/2) inhibitor which blocks production of an important prothrombotic mediator thromboxane A2. Randomized trials have shown that aspirin is an effective anti-thrombotic agent when used long term at doses between 50 and 100 mg day. Doses of aspirin greater than 75–81 mg per day produced no enhancement in anti-thrombotic efficacy but were associated with increased bleeding events. Thus the marketed formulations came in strength of 75mg, whereas Bayer's Aspirin is marketed with dose of 81mg. Aspirin (loading dose of 160-325 mg orally or 250-500 mg intravenously, followed by an oral maintenance dose of 75 (enteric coated) once daily should be administered in all patients. Enteric coated aspirin may be better tolerated in the event of nausea or dyspepsia

but does not confer a lower risk of gastrointestinal bleeding. Since Aspirin is administered for long duration proton pump inhibitors (Pantoprazole and Esomeprazole, 20mg to 40mg) are co administered with Aspirin, to prevent GI irritation and bleeds [2-4]. Compared to prasugrel and ticagrelor, clopidogrel has less potent platelet inhibition, slower onset of action and wide interindividual variability in response profiles and requires conversion to active metabolite for its antiaggregatory effect. In CYP2C19 polymorphisms, clopidogrel is ineffective; this appears in 5-30 % population. Clopidogrel genetic testing is therefore is conducted in susceptible patients. The polymorphism in CYP2C19 has been shown to markedly affect the half-life of the common anxiolytic drugs such as benzodiazepines. The current practice is to avoid drugs like Clopidogrel or Dipyridamole. Clopidogrel resulted in less GI bleeds as compared to Aspirin (0.5 % vs 0.7%) [5-8]. Actions of ticagrelor, prasugrel, and clopidogrel mediated by P2Y12 and adenosine. Ticagrelor was found to possess the unexpected property of weak inhibition of the uptake of adenosine by erythrocytes. Ticagrelor is given in a loading dose of 180–270 mg daily and in a maintenance dose of 90-mg twice daily to optimize its efficacy, safety, and tolerability. Two major adverse events are bleeding (20% increased risk of a bleeding event) & dyspnea (10-20 %). Ticagrelor has been shown to cause more ventricular pauses than clopidogrel, and therefore may not be appropriate for individuals with bradycardia. Ticagrelor is administered regardless of coronary angiography, whereas prasugrel administration is recommended only after coronary anatomy has been defined. Prasugrel caused lesser incidence of MI or stroke or even death, than those received Ticagrelor. Prolonged ticagrelor therapy been shown to reduce the rate of major cardiovascular events in patients with a history of MI, regardless of stenting history and stent type, as well as the risk of ST in patients with stents. In Asian patients undergoing PCI, 60 mg ticagrelor was as effective as 90 mg, and reduced the bleeding risk significantly. Prasugrel (Daichi Sankyo & Elli Lilly) was associated with superior clinical outcomes in STEMI patients. Side effects of Prasugrel are irregular heartbeat, patches on skin. Initial dose is 60 mg orally once followed by maintenance dose of 10 mg orally once a day. Prasugrel is not used in elderly more than 75 years of age. The combination of Aspirin and Prasugrel / Ticagrelor is given for minimum period of one year, as evident through results of many multicenter trials, conducted globally by Astra Zeneca, since 2010 [9-12]. DAPT stoppage after 9 months is associated with lower long-term risks of adverse ischemic and bleeding events. DAPT is interrupted, aspirin should be continued if feasible, as it protects against ischemic events, and P2Y12 therapy should be restarted as soon as possible [13,14]. In patients who completed 12 months of DAPT after PCI without suffering an ischemic or bleeding event, continuing DAPT for 18 additional months reduced myocardial infarction and stent thrombosis rates but increased major bleeding and mortality compared with patients taking aspirin and placebo [15-18].

5–10% of the patients for coronary artery stenting take oral anticoagulants, usually for atrial fibrillation. The way for such patients was to put them on Aspirin, Pasugrel or Ticagrelor and an oral anticoagulant such as Rivaroxaban or Dabigatran (triple therapy) for 6 months following the insertion of a drug-eluting stent, and then stop one of the antiplatelet drugs (Tables 1 & 2). P2Y12 antagonists, so as to reduce bleeding episode. Ticagrelor60 MG + Aspirin, is more effective than Aspirin alone, as evident in PEGASUS-TIMI 54 trial (Figure 1), [19-21].

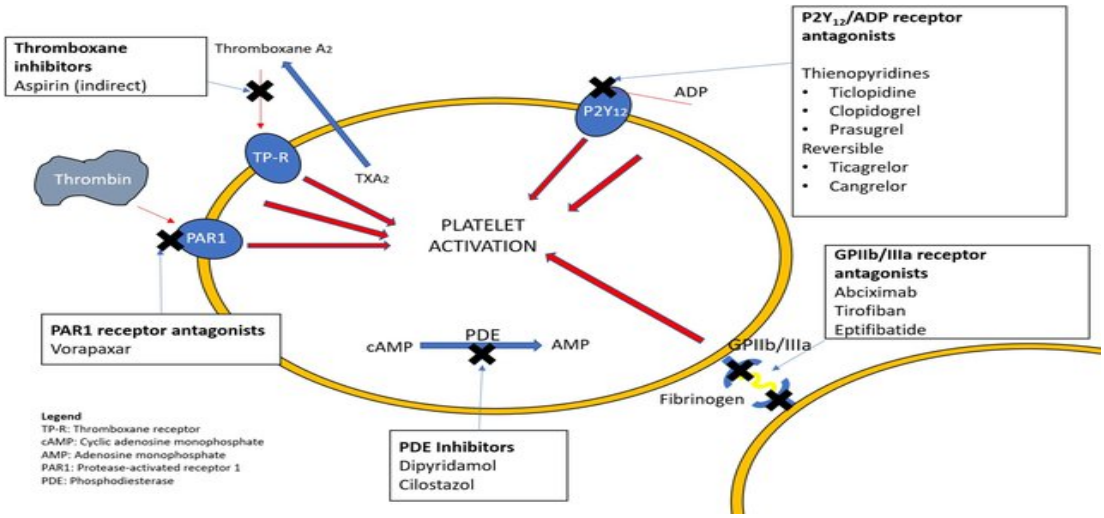

Figure 1: Site of action of Antiplatelet drugs.

Drugs	Actions	Application
Aspirin	Inhibits cyclo- oxygenase, preventing formation of thromboxane A2	Acute coronary syndrome Primary & secondary prevention of cardiovascular disease
P2 Y 12 inhibitors	Acts on ADP receptor, preventing platelet aggregation	Acute coronary syndrome Secondary prevention of stroke
Dipyridamole	Phosphodiesterase 5 inhibition	Secondary stroke prevention Myocardial nuclear imaging
Gb iib/111a inhibitors	Acts on Gb 11b/111a receptors , preventing platelet aggregation	Peri PCI -acute coronary syndrome

Table 1: Mode of action of Antiplatelet drugs.

Features	Clopidogrel	Ticagrelor	Pasugrel
Class	Thienopyridine	Non - Thienopyridine	Thienopyridine
Receptor Binding	irreversibly inhibits P2Y12 receptor	reversibly inhibits P2Y12 receptor	irreversibly inhibits P2Y12 receptor
Metabolism	Prodrug; requires 2-step bioactivation	Direct-acting; active moiety	Prodrug; requires 1-step bioactivation
Loading dose	300–600 mg	180 mg	60 mg
Maintenance dose	75 mg/d	10 mg/d	90 mg twice daily
Stop before surgery	5-7 days	5 days	5-7 days
Avoid in cases			Body weight < 60kg Age >75 year Transient ischemic attack

Table 2: Features of Ticagrelor, Clopidogrel and Prasugrel.

Discussion

In India, nearly 500,000 people undergo angioplasty procedures, with significant success rate. The age for angioplasty procedures in Indian patients, averages to 60 years. 70 % males are affected. The prolonged DAPT duration reduced the incidence of thrombotic complications, including ST and MI, at the cost of increased rates of major bleeding. The severity of CAD is much more severe in India as compared to west. Unhealthy dietary habits, sedentary lifestyle, atherogenic dyslipidemia and high incidence of smoking and diabetes have been major contributory factors. The bleeding risk with antiplatelets increases in advanced age, cardiogenic shock, poor left ventricular function, renal insufficiency, Hypoalbuminemia, alcohol consumption , preoperative low molecular weight heparin & Hereditary coagulopathy. Dual platelet inhibition for a period of 1 year is recommended for patients diagnosed with ACS, especially those who underwent percutaneous myocardial revascularization, regardless of the type of stent; this recommendation is based on the results of randomized clinical trials such as CURE, TRITON-TIMI 38 and PLATO. Abrupt withdrawal of antiplatelet therapy leaves patients at risk for acute in-stent thrombosis, thus single antithrombotic drug, Aspirin is continued lifelong. Extended treatment with dual antiplatelet therapy (DAPT) with ticagrelor 60 mg (twice daily) beyond 12 months in high-risk patients with a history of myocardial infarction (MI) who have previously tolerated DAPT and are not at heightened bleeding risk. Ticagrelor monotherapy after short-term dual-antiplatelet therapy (DAPT) can optimize ischemic and bleeding risks.

References

1. Kumar S, Sinha N (2020) Cardiovascular disease in India: A 360 degree overview. Med J Armed Forces India 76(1): 1-3.

2. Piccolo R, Windecker S (2016) Dual Antiplatelet Therapy in Percutaneous Coronary Intervention. Circulation: Cardiovascular Interventions 9(2): e003587.

3. Horiuchi H (2006) Recent advance in antiplatelet therapy: The mechanisms, evidence and approach to the problems. Annals of Medicine 38(3): 162-172.

4. Andrade PBD, Borges LSR (2017) Antiplatelet Agents

in Acute Coronary Syndromes. International Journal of Cardiovascular Sciences 30(5): 442-451.

5. Goldstein JA (2001) Clinical relevance of genetic polymorphisms in the human CYP2C subfamily. Br J Clin Pharmacol 52(4): 349-355.

6. Curtin R, Fitzgerald DJ (2002) Pharmacogenetics of Antiplatelet Drugs. Scientific World Journal 2: 791- 800.

7. Patrono C, Andreotti F, Arnesen H, Badimon L, Baigent C, et al. (2011) Antiplatelet agents for the treatment and prevention, of atherothrombosis. European Heart Journal 32(23): 2922-2932.

8. Younis LS, Mohammed IM, Najah HT, Haider AM (2020) Antiplatelet drugs overview. GSC Biological and Pharmaceutical Sciences 10(1): 81-89.

9. Jourdi G, Lordkipanidzé M, Philippe A, Bachelot Loza C, Gaussem P (2021) Current and Novel Antiplatelet Therapies for the Treatment of Cardiovascular Diseases. Int J Mol Sci 22(23): 13079.

10. Konduru J, Vanita P (2014) A Review on Antiplatelet Drugs and Anticoagulants. Advances in Pharmacoepidemiology & Drug Safety 3:3.

11. Metharom P, Berndt MC, Baker RI, Andrews RK (2015) Current State and Novel Approaches of Antiplatelet Therapy. Arterioscler Thromb Vasc Biol 35: 1327-1338.

12. Howard TM, Khot UN (2021) Dual antiplatelet therapy after percutaneous coronary intervention: Personalize the duration. Cleveland Clinic Journal of Medicine 88 (6): 325-332.

13. Feres F, Costa RA, Abizaid A, Leon MB, Marin Neto JA, et al. (2023) Three vs Twelve Months of Dual Antiplatelet Therapy After Zotarolimus-Eluting Stents The OPTIMIZE Randomized Trial. JAMA 310(23): 2510-2522.

14. Jayasinghe R, Markham R, Adsett G (2013) Dual antiplatelet therapy Management in general practice. Australian Family Physician 42(10): 702-705.

15. Magnani G, Valgimigl M (2016) Dual Antiplatelet Therapy After Drug-eluting Stent Implantation. Interv Cardiol 11(1): 51-53.

16. Chua D, Nishi C (2013) New antiplatelet agents for cardiovascular disease. CMAJ 185(16): 1405-1411.

17. lessen E, Hewitt C, Giannitsis E, Hedberg J, Jernberg T, et al. (2021) Extended dual antiplatelet therapy with ticagrelor 60 mg in patients with prior myocardial infarction: The design of ALETHEIA, a multi-country observational study. Clin Cardiol 44(10): 1333-1343.

18. Mayor S (2007) Drugs are as good as PCI in stable coronary artery disease. BMJ 334(7596): 713.

19. Schellenberg A, Shmyr D, Koziol K, Martens B, Kosar L (2016) Duration of dual antiplatelet therapy after coronary stent insertion. Canadian Family Physician 62 (11) 905-911.

20. Lin Luo, Wang S, Tang K, Yang X, Wu J, et al. (2022) Efficacy and safety of dual antiplatelet therapy after percutaneous coronary drug-eluting stenting: A network meta-analysis. Medicine (Baltimore) 101(42): e31158.

21. Xu JJ, Jia SD, Jiang L, Song Y, Zhu P, et al. (2023) Prolonged dual antiplatelet therapy after drug-eluting stent implantation improves long-term prognosis for acute coronary syndrome: five-year results from a large cohort study. World J Emerg Med 14(1): 25-30.