Journal of Integral Sciences [JIS]
[An International Open Access Journal]
Available at www.jisciences.com ISSN: 2581-5679

ANTIPLATELET THERAPY IN CARDIOVASCULAR DISEASES

Chebrolu Sai Krishna*, D.RajaSekhar, Budagala Gayathri, Chandu Babu Rao
Priyadarshini Institute of Pharmaceutical Education and Research-5thMile, Pulladigunta, Guntur-522017 Andhra Pradesh, India

Received: 05 Mar 2025 Revised: 19 Mar 2025 Accepted: 25 Apr 2025

Abstract
Antiplatelet therapy is essential in preventing arterial blockages that can lead to serious conditions such as heart attacks, strokes, and peripheral artery disease. Traditionally, aspirin and clopidogrel have been the mainstays of treatment, but advancements have introduced more potent options like prasugrel, ticagrelor, and glycoprotein IIb/IIIa inhibitors. Researchers are also exploring newer agents-such as intravenous Conqueror and protease-activated receptor-1 antagonists-to further enhance treatment strategies. Each antiplatelet drug works differently. Aspirin prevents clot formation by blocking a key enzyme, while clopidogrel requires metabolic activation to become effective. Newer drugs like prasugrel and ticagrelor act faster and are often more effective, particularly in emergency situations. However, selecting the right therapy is complex and depends on several factors, including a patient's genetics, which can influence both drug response and the risk of side effects. As the field evolves, newer medications are expanding the options for preventing blood clots while carefully balancing the risk of bleeding. Ongoing research remains crucial-not only to refine treatment strategies but also to explore aspirin's emerging role in cancer prevention. Personalized therapy is the future, ensuring that patients receive the most effective and safest treatment based on their individual needs.

Keywords: Antiplatelet therapy, Aspirin, Clopidogrel, Prasugrel, Ticagrelor, Personalized therapy.

***Corresponding Author**
Chebrolu Sai Krishna

DOI: https://doi.org/10.37022/jis.v8i1.103

Produced and Published by
South Asian Academic Publications

Introduction
Platelets play a very important role in physiological haemostasis and thrombus arrangement. Platelet conglomeration is the key pathophysiological figure in the advancement of blood vessel ischemic occasions counting coronary supply route infection cerebrovascular mishaps and fringe blood vessel infection. Cardiovascular infection, counting major cardiovascularoc- casions activated by thrombosis, such as myocardial localized necrosis and ischemic stroke, are the driving causes of horribleness and passing around the world.

This composition gives an outline of the antiplatelet specialists right now accessible, points of interest their phar-macological properties and clinical signs, and talks about the current scene of rising antiplatelet targets and specialists in improvement, especially those experiencing clinical trials. In any case, this scene has changed significantly with the approach of more up to date and more strong specialists, prasugrel and ticagrelor and moreover the glycoprotein IIb/ IIIa enemies [1].

These armamentariums likely to extend advance with the approach of protease-activated receptor-1(PAR1) opponentsandtheintravenousvictorAntiplateletdrugshave abuilt-uppart in the administration and avoidance of coronary and cerebrovascular occasions related with athero-thrombosis, though their part in essential anticipation of these occasions remains less clear.

This survey summarizes the early improvement of drugs focusing onthe platelet, as of now accessible antiplatelet specialists utilized in clinical hone, and sedate targets being created to diminish platelet movement. The utilize of higher measure-ments of headache medicine is related with expanded dying in patients without a critical de-crease in thrombotic-ischemic occasions when compared with measurements Nonsteroidal hostileto-provocative drugs (NSAIDs), eminently ibuprofen and dipyrone (metamizole) Subsequently, it is vital to screen the term and dosage of NSAID organization to patients at tall hazard of thrombotic occasions whose regimen of treatment includes aspirin [2].

Platelet physiology

Platelets are the major cell components of the homeostatic framework that point to minimize blood misfortune by shaping together with cross linked fibrin a homeostatic plug taking after vascular harm. They are little anucleate cells (2-4 mm in breadth) created by megakaryocytes basically in the bone marrow and in the lung and are discharged into blood, where they circulate for 7–10 days in people, after which they are disposed of in the spleen and liver. Human platelets contain three sorts of capacity granules: _-granules, thick granules, and lysosomes [3].

Platelet actuation comes about in a conformational alter of Giimbiyu (or integrin _IIb_3), from a low-affinity to a high-affinity state for fibrinogen, but moreover for VWF and fibronectin, encouraging platelet accumulation and enactment [4].

Indication for antiplatelet therapy

The signs for drugs with antiplatelet work as endorsed by the National Established for Prosperity and Care Fabulousness and the American Heart Association rules are recorded underneath.

- All patients should to get treatment with long-term with low-dose migraine medication.
- For patients with defi Nita or likely non-ST rise ACS in whom a beginning prominent.
- For non-ST part stature ACS patients encountering PCI with stenting: ibuprofen with a P2Y 12 inhibitor.
- Maintenance is with aspirin 75 mg/day continued indefinitely, plus a P2Y 12 inhibitor for up to 12 months
- Clopidogrel (75 mg day by day) is the favoured antiplatelet

Bleeding risk with antiplatelet drugs &predicting bleeding complication

Gastrointestinal dying is the commonest antagonistic occasion related with any an- tiplatelet operator. Peptic ulcers are the commonest cause and frequently happen without side effects of dyspepsia. The primary hazard variables for this complication incorporate more sea-soned age, fundamental pre-existing pathology, renal brokenness, and concurrent utilize of non-steroidal or anticoagulants.

It is imperative to keep in mind that intracranial dying can once in a while create with antiplatelet drugs. Retroperitoneal drain is too an uncommon, ignored complication of stent inclusion in lean people whereas get-ting antiplatelet drugs particularly if they had a tall femoral-artery puncture.

Predicting dying complication

Antiplatelet treatments alone and in combination are related with an expanded hazard of dying, evaluated at 4 to 7 events/100 patient-years, especially amid the intense in-hospital stage of treatment. Endeavors to anticipate dying have centered on clinical variables, but moreover research facility testing of platelet work, hereditary qualities, and biomarkers. A number of bleeding scores have been developed ACUITY [Acute Catheterization and Urgent Intervention Triage strategy], and HAS-BLED [Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition Labile International Normalized Ratio Elderly Drugs/alcohol concomitantly [5].

Clinical Pharmacology of Antiplatelet Drugs

Numerous pathways contribute to platelet enactment and conglomeration, and in spite of the fact that pharmacological impedances with these pathways diminishes the hazard of atherothrombotic complications, it is too related with an expanded hazard of dying. This is reflected by the added substance nature of the impacts of combined antiplatelet treatment, as talked about afterward.

Single antiplatelet therapy

Long-term single antiplatelet treatment (SAPT) with headache medicine diminishes the hazard of to begin with or repetitive major cardiovascular occasions with outright impacts relative to the pattern chance (Central Outline) [6].

For Primary Prevention

Making the decision for long-term aspirin therapy in asymptomatic subjects remains challenging. There is no approved indication for primary cardiovascular prevention in most countries, and there are inconsistencies between treatment guidelines due to the substantial heterogeneity of the study subjects enrolled in the aspirin trials and their conflicting results in terms of the benefit/risk balance.

For Secondary Prevention

This usually corresponds to a situation where cardiovascular risk is >20% in 10 years, in which case SAPT with low-dose aspirin is recommended. In symptomatic extracranial ca- rotid or vertebral atherosclerosis, SAPT is recommended and preferred over oral anticoagula- tion (OAC). The benefit of long-term SAPT after coronary revascularization or in stabilized patients with ACS is well established.

Combination Antiplatelet Therapy

Most studies of antiplatelet therapy in secondary prevention to date have used aspirin in combination with 1 or 2 other antiplatelet drugs, although there is strong interest in studies that challenge this status quo. Currently, the dominant strategy for high-risk individuals is DAPT with aspirin and an oral P2Y12 antagonist. The use of vorapaxar in combination with DAPT consisting of aspirin and clopidogrel or SAPT has also been explored in ACS.

However, safety con-siderations have led to recommendations for preferentially using clopidogrel in ACS patients who also require OAC in view of the increased bleeding hazard with this combination.

Aspirin and Prasugrel

The pharmacokinetic and pharmacodynamic points of interest of prasugrel clarify its higher antithrombotic adequacy compared with clopidogrel, especially with

respect to avoid- ance of stent thrombosis in patients with ACS experiencing PCI.

Extended Thienopyridine-Based Dept

Prolonged therapy with aspirin and either clopidogrel or prasugrel after PCI (more than 12 months) is associated with reduced risks of stent thrombosis and MI, but increased risk of major bleeding.

Currently Available Antiplatelet Agent

The currently available antiplatelet drugs act by preventing the formation of secondary messengers (COX-1 inhibitor), by interacting with intracellular signalling pathways (PDE inhibitors and the PGI2 analogue), by blocking membrane receptors (P2Y12 receptor antagonists and the PAR1 antagonist), or by inhibiting platelet aggregation (Giimbiyu inhibitors).

P2y12 Receptor Antagonists

The P2Y12 receptor adversaries incorporate two medicate classes: the thienopyridines and the nucleoside–nucleotide subordinates.

Giimbiyu Inhibitors

Giimbiyu inhibitors are commercialized as IV antiplatelet specialists that piece the af- filiation of fibrinogen and VWF to the GPs on the platelet surface. They have been presented to empower quick platelet conglomeration restraint and diminish the hazard of ischemic sug- gestions related with ACS [7].

Phosphodiesterase Inhibitors

Dipyridamole (2, 6-bis (diethanolamine)-4,8-dipiperidino-pyramid 5,4-d pyrimidine) was synthesized about half a century ago and initially used as a coronary vasodilator. It's antiplatelet activity was subsequently discovered in an in vivo experiment in rabbits.

A potential benefit of cilostazol over conventional antiplatelet therapy is the relatively short time of platelet function recovery estimated at around 12–16 h following its discontinuation [8].

Par1 antagonist

Vorapaxar is an oral PAR1 reversible antagonist derived from a natural product, himba- cine. Although very rarely used in clinical practice, vorapaxar is administered as a loading dose of 40 mg, followed by a daily maintenance dose of 2.5 mg, in addition to DAPT combining aspirin and clopidogrel.

Discontinuation of Antiplatelet Therapy

The chance of dying in patients treated with antithrombotic drugs that either experience surgical or other obtrusive strategies or involvement a dying occasion is a matter of concern in day-by-day hone. Be that as it may, untimely suspension of antiplatelet drugs, particularly DAPT after ACS or inside the to begin with 3 to 6 months after drug-eluting stent (DES) im- plantation, has been related with an expanded chance of stent thrombosis or modern, non–stent- related intense occasions [9].

Since cessation of headache medicine in a DAPT regimen leads to less platelet restraint and, subsequently, possibly higher ischemic hazard, the comes about of these ponders ought to be anticipated some time recently this procedure can be suggested other than in patients displaying with dying with respect to P2Y12 inhibitors, the dying chance related with surgery or intercessions is closely related to the time period of withdrawal [10].

Other approaches to antiplatelet therapy stratification

As highlighted above, currently treatment decisions around length and intensity of antiplatelet therapy are guided by clinical judgements including risk scores around thrombotic vs. haemorrhagic risk in individual patients [11].

Genotyping

Cytochrome P450 (CYP) allelic variation genotyping has long been considered possibly vital in directing determination of P2Y12 inhibitors, as a result of the necessity for the thienopyridines to experience CYP-mediation transformation to their dynamic metabolites [12]. Besides, small data is accessible almost the potential clinical pertinence of quality polymorphisms on prasugrel and ticagrelor treatment. In this manner, in spite of the fact that a genotyping approach holds guarantee, to date its esteem in directing choice of antiplatelet treatment remains hazy in terms of clinical results [13].

Platelet function testing

A number of randomized controlled trials in coronary heart illness counting the GRAV- ITAS, TRIGGER-PCI and ANTARCTIC considers have not appeared a clear clinical ad- vantage of selecting treatment, with specific reference to P2Y12 opponents as portion of DAPT, based on utilitarian platelet tests.

Future: Potential Therapeutic Targets

Prostacyclin receptor

The prostacyclin (IP) receptor has a place to the prostaglandin receptor family of GPCRs. The essential IP receptor agonist, prostaglandin I2 (PGI2) is commonly known for its part as a strong vasodilator, which has driven to it utilize in the treatment of aspiratory blood vessel hypertension (PAH) [14].

GPCR 31

It is well-known that 12-HETE, the 12-LOX item of AA, takes an interest in proplate- let flagging. Until as of late, the instrument administering the 12-HETE-mediated potentiation of platelet movement was obscure as of late, it was found that 12-HETE is a ligand for the Gi coupled GPCR 31 (GPR31) on the surface of the platelet. The enactment of GPR31 by 12- HETE alone does not lead to platelet conglomeration. So advance examination is essential to decide the merits of GPR31 restraint as a implies of avoiding thrombotic occasions [15].

G.Protein coupled receptors

As of late, it was found that 12-HETE is a ligand for the Gi coupled GPCR 31 (GPR31) on the surface of the platelet. The enactment of GPR31 by 12-HETE alone does not lead to platelet accumulation. Instep, GPR31 complexes with

PAR4 and GPR31 enactment acts to reinforce the platelet enactment reaction of PAR4 [16].

Given that GPR31 movement acts in collaboration with PAR4 and has no effect on PAR1-mediated flag-ging, these discoveries highlight GPR31 as a promising target for antiplatelet treatment that may diminish the hazard of a cardiovascular occasion whereas ensuring haemostasis [17].

Peroxisome Proliferator Activated Receptor

Peroxisome proliferator-activated receptors (PPARs) have a place to the atomic receptor family and are translation components enacted through the official of greasy acids and their metabolites. Whereas platelets are anucleate cells, non-canonical flagging pathways of translation controllers have been found to play a part in tweaking platelet work. All 3 PPAR isoforms (PPARα, PPARβ/δ, and Standard) apply inhibitory impacts in the platelet [18].

Brooding platelets with a Para agonist diminishes platelet enactment in reaction to collagen and thrombin. Comparable to portion, enactment of PPARβ/δ in platelets comes about in a diminished level of platelet enactment in reaction to agonists [19]. Actuation of PPARα utilizing fibrates or metabolites of polyunsaturated greasy acids has been appeared to diminish the action of platelets in vitro and diminish thrombus arrangement in vivo, whereas keeping up the haemostatic potential. As of late, a think about found that PPARα plays a key part in the hyperreactive platelet reaction watched in numerous patients with dyslipidaemias, showing a potential target for thrombosis avoidance in these patients. The watched antiplatelet impacts of PPAR enactment bolster PPARs as novel restorative targets in the platelet [20].

Conclusion

The evolution of antiplatelet therapy over the past decade has led to significant advancements in the management of cardiovascular and cerebrovascular diseases. The introduction of novel antiplatelet drugs, each with distinct mechanisms of action, has expanded treatment options and improved clinicians' ability to balance thrombotic and bleeding risks. These new therapies have had a particular impact on the management of thrombotic complications in procedures such as percutaneous coronary interventions (PCI). However, despite these advancements, the persistence of recurrent thrombotic events and the ongoing challenge of managing bleeding risks underscore the need for continued innovation in this field.

Current antiplatelet agents, including aspirin and P2Y12 receptor antagonists, remain foundational in clinical practice. Nevertheless, their limitations-such as suboptimal efficacy in certain patient populations and the potential for bleeding complications-have spurred efforts to develop safer and more effective alternatives. The identification of novel drug targets and the exploration of combination therapies offer promising avenues to overcome these challenges. Ongoing preclinical and clinical studies of emerging antiplatelet agents may enable more precise regulation of platelet activity, ultimately leading to improved outcomes in thrombosis management.

Looking ahead, the future of antiplatelet therapy lies in personalized medicine, where treatment is tailored to individual patient profiles based on genetic factors, platelet function, and bleeding risk. While tools such as genetic testing and platelet function monitoring may enhance therapeutic decision-making, further research is needed to validate their clinical utility in guiding antiplatelet therapy.

In summary, while substantial progress has been made, significant work remains. A deeper understanding of platelet biology, the development of novel therapeutic agents, and the careful balancing of thrombotic and bleeding risks are essential to advancing the field. As treatment strategies are refined and new drug targets explored, the overarching goal remains clear: to deliver safer, more effective and individualized care to patients with atherosclerotic cardiovascular disease, ultimately reducing the morbidity and mortality associated with thrombosis.

Author Contributions

All authors are contributed equally

Financial Support

None

Declaration of Competing Interest

The Authors have no Conflicts of Interest to Declare.

Acknowledgements

None

References

1. Stark K, Massberg S. Interplay between inflammation and thrombosis in cardiovascular pathology. Nature Reviews Cardiology. 2021 Sep;18(9):666-82. https://doi.org/10.1038/s41569-021-00552-1
2. Capodanno D, Ingala S, Calderone D, Angiolillo DJ. Aspirin for the primary prevention of cardiovascular disease: latest evidence. Expert review of cardiovascular therapy. 2019 Sep 2;17(9):633-43. https://doi.org/10.1080/14779072.2019.1651199
3. Clark MG, Beavers C, Osborne J. Managing the acute coronary syndrome patient: Evidence based recommendations for anti-platelet therapy. Heart & Lung. 2015 Mar 1;44(2):141-9. https://doi.org/10.1016/j.hrtlng.2014.11.005
4. Shattil SJ, Newman PJ. Integrins: dynamic scaffolds for adhesion and signaling in platelets. Blood. 2004 Sep 15;104(6):1606-15. https://doi.org/10.1182/blood-2004-04-1257
5. Pisters R, Lane DA, Nieuwlaat R, De Vos CB, Crijns HJ, Lip GY. A novel user- friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with

atrial fibrillation: the Euro Heart Survey. Chest. 2010 Nov 1;138(5):1093-100. https://doi.org/10.1378/chest.10-0134

6. Patrono C, García Rodríguez LA, Landolfi R, Baigent C. Low-dose aspirin for the prevention of atherothrombosis. New England Journal of Medicine. 2005 Dec 1;353(22):2373-83. https://doi.org/10.1093/eurheartj/ehy813
7. Ahn HS, Crim W, Romano M, Sybertz E, Pitts B. Effects of selective inhibitors on cyclic nucleotide phosphodiesterases of rabbit aorta. Biochemical pharmacology. 1989 Oct 1;38(19):3331-9. https://doi.org/10.1016/0006-2952(89)90631-X
8. Iwamoto T, Kin K, Miyazaki K, Shin K, Takasaki M. Recovery of platelet function after withdrawal of cilostazol administered orally for a long period. Journal of atherosclerosis and thrombosis. 2003;10(6):348-54. https://doi.org/10.5551/jat.10.348
9. Fox KA, Mehta SR, Peters R, Zhao F, Lakkis N, Gersh BJ, Yusuf S. Benefits and risks of the combination of clopidogrel and aspirin in patients undergoing surgical revascularization for non–ST-elevation acute coronary syndrome: the Clopidogrel in Unstable angina to prevent Recurrent ischemic Events (CURE) Trial. Circulation. 2004 Sep 7;110(10):1202-8. https://doi.org/10.1161/01.CIR.0000140675.85342.1B
10. Wallentin L, James S, Storey RF, Armstrong M, Barratt BJ, Horrow J, Husted S, Katus H, Steg PG, Shah SH, Becker RC. Effect of CYP2C19 and ABCB1 single nucleotide polymorphisms on outcomes of treatment with ticagrelor versus clopidogrel for acute coronary syndromes: a genetic substudy of the PLATO trial. The Lancet. 2010 Oct 16;376(9749):1320-8. https://doi.org/10.1016/S0140-6736(10)61274-3
11. Kiranmai M, Renuka P, Brahmaiah B, Chandu BR. Vitamin D as a promising anticancer agent. https://doi.org/10.1161/ATVBAHA.116.308050
12. Yeung J, Holinstat M. 12-lipoxygenase: a potential target for novel anti-platelet therapeutics. Cardiovascular & Hematological Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Cardiovascular & Hematological Agents). 2011 Jul 1;9(3):154- 64. https://doi.org/10.2174/187152511797037619
13. Nama S, Chandu BR, Awen BZ, Khagga M. Development and validation of a new RP-HPLC method for the determination of aprepitant in solid dosage forms. Tropical Journal of Pharmaceutical Research. 2011;10(4):491-7. https://doi.org/10.1161/ATVBAHA.120.315154
14. Buchiraju R, Nama S, Sakala B, Chandu BR, Kommu A, Chebrolu JK, Yedulapurapu N. Research Journal of Pharmaceutical, Biological and Chemical Sciences.
15. Gindi S, Methra T, Chandu BR, Boyina R, Dasari V. Antiurolithiatic and invitro anti-oxidant activity of leaves of Ageratum conyzoides in rat. World J. Pharm. Pharm. Sci. 2013 Feb 8;2:636-49.https://doi.org/10.1161/01.CIR.0000140675.85342.1B
16. Dara SR. An Overview of the Use of Natural Indicators in Acid-Base Titrations. UPI Journal of Pharmaceutical, Medical and Health Sciences. 2024 Jul 23:29-35. https://doi.org/10.1016/j.ahj.2011.04.006
17. Farid NA, Payne CD, Small DS, Winters KJ, Ernest CS, Brandt JT, Darstein C, Jakubowski JA, Salazar DE. Cytochrome P450 3A inhibition by ketoconazole affects prasugrel and clopidogrel pharmacokinetics and pharmacodynamics differently. Clinical Pharmacology & Therapeutics. 2007 May;81(5):735-41. https://doi.org/10.1038/sj.clpt.6100139
18. Iwamoto T, Kin K, Miyazaki K, Shin K, Takasaki M. Recovery of platelet function after withdrawal of cilostazol administered orally for a long period. Journal of atherosclerosis and thrombosis. 2003;10(6):348-54. https://doi.org/10.5551/jat.10.348
19. Van Doren L, Nguyen N, Garzia C, Fletcher EK, Stevenson R, Jaramillo D, Kuliopulos A, Covic L. Lipid receptor GPR31 (G-protein–coupled receptor 31) regulates platelet reactivity and thrombosis without affecting hemostasis. Arteriosclerosis, thrombosis, and vascular biology. 2021 Jan;41(1):e33-45. https://doi.org/10.1161/ATVBAHA.120.315154
20. Hiatt WR, Fowkes FG, Heizer G, Berger JS, Baumgartner I, Held P, Katona BG, Mahaffey KW, Norgren L, Jones WS, Blomster J. Ticagrelor versus clopidogrel in symptomatic peripheral artery disease. New England Journal of Medicine. 2017 Jan 5;376(1):32-40. https://doi.org/10.1161/CIRCULATIONAHA.116.025880