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### RESEARCH ARTICLE

#### CORONARY ARTERY DISEASE SUPERIMPOSED BY INTRACRANIAL HEMORRHAGE; HIGHLIGHTS AND MANAGEMENT.

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#### Manuscript Info

#### Abstract

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#### Introduction:-

Coronary artery disease (CAD), is one of the major causes of death. It is a severe condition of stenosis of a major artery. Percutaneous intervention (PCI) is the common procedure that is done as the initial management of CAD. Dual antiplatelet prophylaxis is then given post PCI, for further prevention of cardiac events. This case report discusses then significance of CAD and management of intracranial hemorrhage (ICH) while of DAPT.

#### Case Report:-

A 63-year-old male, known case of coronary artery disease post PCI to RCA 10 years ago and dyslipidemia, presented to the ER with chest pain radiating to the left arm with sweating for 2 hours, that was relieved by rest.

On examination, patient was conscious, alert, oriented. His BP 135/80 mmHg, pulse rate was 100/min, temperature 36.9 Celsius, Oxygen saturation 100%.

Chest was clear, vesicular breathing, Abdomen soft and lax. The patients Hemoglobin was 12.6, platelets 221, troponin initially 0.06, serum creatinine initially 94, maximum of 107.

ECG showed normal sinus rhythm 2 mm ST depression from V2 to V5, Echocardiography showed normal LV cavity dimension, mild LV systolic dysfunction, regional variability at anterior wall, and ejection fraction (EF) assessed to be 45%.

Patient was admitted initially to ER to treat ACS, patient reserved platelets, Aspirin, Plavix, and intravenous unfractionated heparin . Troponin showed significant increase from 0.06 to 7.8.

The Patient underwent cardiac catheterization, which shows; normal Left main stem, proximal long stenosis 85% in left anterior descending artery, with ostial critical stenosis in the first diagonal. Left Circumflex artery was small and non-dominant with no flow limiting lesions, right coronary artery showed patent old stent. Percutaneous

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Coronary Intervention was done to LAD and diagonal with 2 stents with good final results. ACT was maintained during the procedure from 250-300. then patient was shifted to ICU for observation.

One day after the procedure, patient developed a blurred vision in the left temporal hemianopia, the shortly after he developed on the same day severe sudden complete heart block in the ICU and taken immediately to the Cath Lab and TPM was Inserted. Coronary arteries were clarified and showed patent stents with normal flow in LAD, Urgent CT brain showed intracranial hemorrhage measuring around  $4.6 \times 3.8 \times 2.5$  with mild surrounding hypodense areas indicating vasogenic edema. There was no midline shift, no hydrocephalus, no brain herniation and no acute territorial infarction. Aspirin and Plavix were stopped because of acute cerebral hemorrhage. The second day; CT brain was done showed no significant interval changes and no evidence of increase in size or new bleed seen; therefore, Plavix alone was restarted after the second CT brain because of recent high risk intervention and fear of stent thrombosis.

Neurology advised for Dexamethasone and prophylactic subcutaneous unfractionated Heparin. The patient was followed in ICU for 3 days; then, was shifted to the ward. CT brain was done after 6 days and showed increase in size of hematoma by 2mm; hence, neurologist advised to monitor and continue the patient on single antiplatelet and repeat CT brain after three days. The fourth CT brain showed decrease in hematoma size. After total of ten days hospital observations, we manage to resume Aspirin, Plavix, and discharge the patient in good condition.

#### **Significance Of Coronary Artery Disease:-**

Coronary artery disease (CAD), is a disease due to atherosclerosis, in which plaque builds up in the arteries, that will eventually become blocked.(1) Although mortality rates have fallen the past couple decades, it still remains a major cause of death.(2, 3) Coronary artery disease is accountable for about one-third or more of an individual's death that is over 35 years.(3)

Pathophysiology of CAD has always been somewhat of a complication to comprehend; however, with evolving studies, the understanding of the concept has been greatly enhanced. The global understanding of the cause of CAD is the formation of plaque or atherogenesis. Studies have shown that atherogenesis is usually associate with inflammation(4). Risk factors such as, dyslipidemia, hypertensive states causing vasoconstriction, or proinflammatory cytokines in excess fatty tissue, cause the aggregation of leukocytes in the arterial wall; therefore, causing inflammation. The proliferation of these cells is the major consequence that cause stenosis; hence, lead to CAD. (5)

Treatment and management of CAD is followed many different strategies that could be either medical or surgical. For instance, successful angiography and revascularization of the target artery by percutaneous intervention (PCI); Nevertheless, it may not be the optimum management as it may not provide protection of any future CVS events. Other than managing the modifiable risks to reduce mortality rates, drugs such as, antiplatelet therapy has been introduced. The Physicians' Health Study (PHS) indicated that aspirin significantly reduces the rates of cardiovascular events, like myocardial infarction and acute coronary syndrome (6). Dual antiplatelet therapy (DAPT) is the treatment with two antiplatelet agents; for example, a combination of aspirin plus ticagrelor or prasugrel, or aspirin plus clopidogrel. It was presented as one of the important managements of CVS disease. Dual antiplatelet therapy is a common remedial option following PCI. (7) Balance between thrombotic risk and bleeding risk generates the effective behavior in management. This case report has made it come to attention about DAPT usage, specifically short term, and any beneficial and associative risks.

#### **Dual Antiplatelet Therapy Safety And Risk Level:-**

Dual antiplatelet therapy (DAPT) carries its own risk of increasing CVS bleeding tendency; as well as, non-CVS bleed, which can be serous and cause irreversible complication, such as, ICH.

Studies have shown that higher or lower dosage of aspirin in DAPT doesn't make a difference in the results of CVS mortalities, Myocardial infarction or stroke. Furthermore, higher dosage implicated the risk of bleeding without any increased remedial benefits.(9) As a result, some studies supported the use of low dose of aspirin in DAPT as there is no statistically significant increase in the outcome between high and low doses. (10)

It has now become the standard care after PCI to provide DAPT; in which, aspirin is either taken with P2Y<sub>12</sub> receptor inhibitor (adenosine diphosphate antagonist - ADP -), ticagrelor or prasugrel, or with clopidogrel.(11) Optimum selection of duration of dual antiplatelet therapy has been discussed by many, as the risks of bleeding or any other adverse effects may occur. Several studies have been evaluating the prime duration of DAPT.(12) Many have concluded that short-term therapy of DAPT reduces bleeding tendency in contrast to long term, which may cause bleeding. Cardiac events may be reduced with long-term; however, bleeding and mortality may increase.(13, 14)

Although a study has suggested, patients receiving DAPT for more than a year will have a 25% reduction of CVS events, many other studies have concluded that there is a greater controversial effect than DAPT usage for a shorter period.(15)

The long-term duration of any drug enhances the ability to cause adversarial results; therefore, reducing the long use of any drug is the ideal way to decrease any misfortunate events. In contrast, the patient should still receive the supreme benefit. To conclude, studies are still going on for the optimum duration for DAPT safety and risk levels, and comparisons between the best combination for lowest risk of bleeding.(16)

#### **Dapt Combinations:-**

DAPT is usually a combination of aspirin plus P2Y<sub>12</sub> receptor inhibitor clopidogrel or ticagrelor and prasugrel. For many years an example of dual antiplatelet therapy, aspirin with clopidogrel has been widely used. Some studies have displayed the combination of aspirin and clopidogrel showed reduction of 20% regarding CVS events in one year use for ACS patients.(17) The new Adenosine diphosphate antagonists (ticagrelor and prasugrel) are progressively used in the current time. They are widely recommended as first-line treatment in patients who have went through PCI.(11, 18) The P2Y<sub>12</sub> inhibitors (ticagrelor and prasugrel) are more potent in reducing ischemic events; however, the side effects that they may cause could be of difference than clopidogrel.

A study stated that there was no significant difference in the frequencies of bleeding according with the use of either ticagrelor or clopidogrel. (19) Despite the fact that there was no difference between the two drugs in the risk of bleeding, ticagrelor however is more prone to cause intracranial bleeding than clopidogrel. (19) Ticagrelor did have other adverse effects that were not seen with clopidogrel. Ticagrelor increases the risk of dyspnea; also, it slightly increases the levels of creatinine and uric acid. Prasugrel also, increases the risk of bleeding; therefore, it should be cautiously used in treating a patient with great threat.(20)

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The adverse effects can be further described according to certain combinations of the drugs with aspirin. The efficacy of ticagrelor and prasugrel is higher than of clopidogrel.(21) These drugs when compared with clopidogrel, have rapid action of onset; hence, they are better in reducing CVS events. Recent findings have displayed the use of aspirin plus ticagrelor or prasugrel, is the modern remedial choice for prophylaxis post PCI. (21) Despite the fast onset of action of these new drugs, they should be avoided in patients with bleeding tendency. (22, 23) While the latest prescribed drugs cause the beneficial action, they should be avoided when a person is susceptible to the different hostile results that they may produce.

As it was discussed, the different side effects that are initiated by the diverse drugs, choosing the optimum combination should be according to the patient's situational stage.

#### **Dual Apt Vs Single Apt / Ich Risk:-**

Intracranial hemorrhage (ICH), specifically spontaneous ICH, is one of the major causes that increases the mortality and morbidity rate in a health care system.(24) Whether ICH was developed due to antiplatelet therapy or not, mortality rates are severe. Despite its serious complications, minor bleeding volumes and small lesions can be managed easily with a good prognostic outcome.(25) Aside from the fact there the management of ICH has been advanced. There is nevertheless no stated proper outcome after ICH. (26)

ICH score is significant in finding the percentage of 30-day mortality. Calculation of ICH score is according to 5 characteristics which is displayed in the table (Table – 1)

A patient who has developed ICH while on antiplatelet therapy has been put through re-evaluation of their situation. Several studies have shown that the progression of ICH is highly due to antiplatelet therapy.(27-29) The presence of spontaneous ICH is commonly due to the use of antiplatelet therapy.

Researchers have been notified and found out that it is essential to signify the difference between DAPT and SAPT in morbidity and mortality; hence, managing a case with ICH would be applicable. It was discovered that mortality rates, between patients who were on SAPT and patients that were not, were in significant; in contrast to those who were on DAPT, mortality rates were higher.(27)

Furthermore, it was acknowledged the usage of DAPT with a case having ICH will make the prognosis worse by 7% that an SAPT. The conclusion has come that SAPT, especially aspirin, has low association with the cause ICH; though, aspirin doses should be taken into consideration.(30) DAPT has higher association with ICH compared to patients that received no antiplatelet therapy. A couple of studies as well analyzed trials, that resulted with the fact, the higher risk of ICH is more probable due to DAPT than monotherapy. (31, 32)

Due to recent findings, patients on DAPT have higher worsening outcomes post ICH. These results suggest that a patient with the development of ICH should receive SAPT; as it does not correlate with ICH.

### Management Of Ich:-

Intracranial hemorrhage is one of the life threatening events that needs a rapid and suitable management. Managing a case of ICH while on antiplatelet therapy (APT). basically lies in the decisions that are taken by the specialized physicians. Furthermore, the first step to control this complication is by neurological and cardiology intervention. A study administered that in order to begin the control of ICH, a patient must interrupt DAPT regimen.(33) As a result, cardiac monitoring at the time of interruption is actively sought. Different methods of ICH management are practiced such as, platelet transfusion, blood pressure control, and surgical intervention. Moreover, platelet transfusion is the presence of CAD, may be thought as a threat to the patient; however, studies showed different opinions about the treatment. It has not been clearly distinct about the role of platelet transfusion for the management of ICH while on DAPT. A study had suggested that there were conflicting results regarding the benefit of platelet transfusion. (34) While another study has displayed positive outcomes in early platelet transfusion.(35)

Evidently, there is not definite time to restart antiplatelet therapy following ICH. ICH score must evaluation to predict mortality with ICH. As per American Heart Association, American College of Cardiology Foundation, and Society for Cardiovascular Angiography and Invention angiography; If DAPT has been interrupted at a later time aspirin only should be restarted. (36) Additionally, the interruption of DAPT at an earlier time results in resuming aspirin; however, P<sub>2</sub>Y<sub>12</sub> receptor inhibitors should be evaluated for the risk of morbidity and mortality of bleeding in which the benefit of the drug should outweigh the risk. (36)

**Table –1 title: ich score**

Compotent	Results	Score
GCS:	3 – 4	2
	5 – 15	1
	13 – 35	0
Age	≥80	1
	<80	0
ICH volume	≥30 cm <sup>2</sup>	1
	<30 cm <sup>2</sup>	0
Intraventricular Hemorrhage	Yes	1
	No	0
Origin of ICH	Infratentorial	1
	Supratentorial	0
Total Score	-	0-6
GSC indicates primary presentation. Initial CT displays ICH volume and origin.		

### Conclusion:-

CAD is a fatal condition in which it is vital to treat the patient insistently. After PCI follows antiplatelet prophylaxis to prevent future thrombosis. DAPT has become the initial regimen post PCI. In this case report the patient has developed ICH; consequently, due to numerous judgments, a person who is receiving DAPT should be converted to SAPT, as SAPT has less association with the mortality of ICH. Furthermore, antiplatelet therapy, DAPT, should be interrupted to manage ICH initially; then, it is restarted according to the opinions of cardiologists.

### References:-

1. National Heart L, and Blood Institute. Coronary Heart Disease [Available from: <https://www.nhlbi.nih.gov/health-topics/coronary-heart-disease>.
2. Rosamond W, Flegal K, Furie K, Go A, Greenlund K, Haase N, et al. Heart disease and stroke statistics--2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2008;117(4):e25-146.
3. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, et al. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. *Circulation*. 2017;135(10):e146-e603.
4. Libby P. Inflammation in atherosclerosis. *Nature*. 2002;420(6917):868-74.
5. Libby P, Theroux P. Pathophysiology of coronary artery disease. *Circulation*. 2005;111(25):3481-8.
6. Steering Committee of the Physicians' Health Study Research G. Final report on the aspirin component of the ongoing Physicians' Health Study. *N Engl J Med*. 1989;321(3):129-35.
7. Dual Antiplatelet Therapy Acetylsalicylic Acid Dosing: A Review of the Clinical Effectiveness and Harms. 2017 Mar 14. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470792/>.
8. Task Force on Myocardial Revascularization of the European Society of C, the European Association for Cardio-Thoracic S, European Association for Percutaneous Cardiovascular I, Kolh P, Wijns W, Danchin N, et al. Guidelines on myocardial revascularization. *Eur J Cardiothorac Surg*. 2010;38 Suppl:S1-S52.
9. Mehta SR, Tanguay JF, Eikelboom JW, Jolly SS, Joyner CD, Granger CB, et al. Double-dose versus standard-dose clopidogrel and high-dose versus low-dose aspirin in individuals undergoing percutaneous coronary intervention for acute coronary syndromes (CURRENT-OASIS 7): a randomised factorial trial. *Lancet*. 2010;376(9748):1233-43.
10. Hanna EB, Glancy DL, Saucedo JF. Antiplatelet and anticoagulant therapies in acute coronary syndromes. *Cardiovasc Drugs Ther*. 2010;24(1):61-70.
11. Yaron Arbel M, a,b Maria C. Bennell, MSc,b Shaun G. Goodman, MD, MSc,c and, Harindra C. Wijeyesundera M, PhD,b,d,e. Cost-Effectiveness of Different Durations of Dual-Antiplatelet Use After Percutaneous Coronary Intervention. *Canadian Journal of Cardiology*. 2018;34(1):31-7.
12. Valgimigli M, Campo G, Monti M, Vranckx P, Percoco G, Tumscitz C, et al. Short- versus long-term duration of dual-antiplatelet therapy after coronary stenting: a randomized multicenter trial. *Circulation*. 2012;125(16):2015-26.
13. Palmerini T, Benedetto U, Bacchi-Reggiani L, Della Riva D, Biondi-Zoccai G, Feres F, et al. Mortality in patients treated with extended duration dual antiplatelet therapy after drug-eluting stent implantation: a pairwise and Bayesian network meta-analysis of randomised trials. *Lancet*. 2015;385(9985):2371-82.
14. Navarese EP, Andreotti F, Schulze V, Kolodziejczak M, Buffon A, Brouwer M, et al. Optimal duration of dual antiplatelet therapy after percutaneous coronary intervention with drug eluting stents: meta-analysis of randomised controlled trials. *BMJ*. 2015;350:h1618.
15. Savarese G, Savonitto S, Lund LH, Paolillo S, Marciano C, Dellegrattaglie S, et al. Efficacy and safety of prolonged dual antiplatelet therapy: a meta-analysis of 15 randomized trials enrolling 85 265 patients. *Eur Heart J Cardiovasc Pharmacother*. 2016;2(4):218-28.
16. Bhatt DL, Fox KA, Hacke W, Berger PB, Black HR, Boden WE, et al. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. *N Engl J Med*. 2006;354(16):1706-17.
17. Wilson SJ, Newby DE, Dawson D, Irving J, Berry C. Duration of dual antiplatelet therapy in acute coronary syndrome. *Heart*. 2017;103(8):573-80.
18. Gandhi S, Zile B, Tan MK, Saranu J, Bucci C, Yan AT, et al. Increased uptake of guideline-recommended oral antiplatelet therapy: insights from the Canadian acute coronary syndrome reflective. *Can J Cardiol*. 2014;30(12):1725-31.
19. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med*. 2009;361(11):1045-57.

20. Clemmensen P, Dridi NP, Holmvang L. Dual antiplatelet therapy with prasugrel or ticagrelor versus clopidogrel in interventional cardiology. *Cardiovasc Drugs Ther.* 2013;27(3):239-45.
21. Testa L, Biondi Zoccai GG, Valgimigli M, Latini RA, Pizzocri S, Lanotte S, et al. Current concepts on antiplatelet therapy: focus on the novel thienopyridine and non-thienopyridine agents. *Adv Hematol.* 2010;2010:595934.
22. Schuler J, Maier B, Behrens S, Thimme W. Present treatment of acute myocardial infarction in patients over 75 years--data from the Berlin Myocardial Infarction Registry (BHIR). *Clin Res Cardiol.* 2006;95(7):360-7.
23. Montalescot G, Wiviott SD, Braunwald E, Murphy SA, Gibson CM, McCabe CH, et al. Prasugrel compared with clopidogrel in patients undergoing percutaneous coronary intervention for ST-elevation myocardial infarction (TRITON-TIMI 38): double-blind, randomised controlled trial. *Lancet.* 2009;373(9665):723-31.
24. Hemphill JC, 3rd, Greenberg SM, Anderson CS, Becker K, Bendok BR, Cushman M, et al. Guidelines for the Management of Spontaneous Intracerebral Hemorrhage: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke.* 2015;46(7):2032-60.
25. Zahuranec DB, Gonzales NR, Brown DL, Lisabeth LD, Longwell PJ, Eden SV, et al. Presentation of intracerebral haemorrhage in a community. *J Neurol Neurosurg Psychiatry.* 2006;77(3):340-4.
26. Broderick JP, Adams HP, Jr., Barsan W, Feinberg W, Feldmann E, Grotta J, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: A statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. *Stroke.* 1999;30(4):905-15.
27. Nadeem I. Khan MFMS, MD; Joshua N. Goldstein, MD, PhD; Marguerite Cox, MS; Ying Xian, MD, PhD; Roland A. Matsouaka, PhD; Paul A. Heidenreich, MD, MS; Eric D. Peterson, MD, MPH; Deepak L. Bhatt, MD, MPH; Gregg C. Fonarow, MD; Lee H. Schwamm, MD; Eric E. Smith, MD, MPH. Association Between Previous Use of Antiplatelet Therapy and Intracerebral Hemorrhage Outcomes. <http://strokeahajournalsorg/>. *Stroke.* 2017.
28. He J, Whelton PK, Vu B, Klag MJ. Aspirin and risk of hemorrhagic stroke: a meta-analysis of randomized controlled trials. *JAMA.* 1998;280(22):1930-5.
29. Ducrocq G, Amarenco P, Labreuche J, Alberts MJ, Mas JL, Ohman EM, et al. A history of stroke/transient ischemic attack indicates high risks of cardiovascular event and hemorrhagic stroke in patients with coronary artery disease. *Circulation.* 2013;127(6):730-8.
30. Serebruany VL, Malinin AI, Eisert RM, Sane DC. Risk of bleeding complications with antiplatelet agents: meta-analysis of 338,191 patients enrolled in 50 randomized controlled trials. *Am J Hematol.* 2004;75(1):40-7.
31. Lee M SJ, Hong KS, Rao NM, Wu YL, Ovbiagele B. Risk benefit profile of long-term dual versus single antiplatelet therapy among patients with ischemic stroke: a systematic review and meta-analysis. *Ann Intern Med.* 2013;159:463-470.
32. Chen S SQ, Tang Y, He L, Li Y, Li H, et al. Efficacy and safety of adding clopidogrel to aspirin on stroke prevention among high vascular risk patients: a meta-analysis of randomized controlled trials. 2014;9:e104402.
33. Naik BI, Keeley EC, Gress DR, Zuo Z. Case scenario: a patient on dual antiplatelet therapy with an intracranial hemorrhage after percutaneous coronary intervention. *Anesthesiology.* 2014;121(3):644-53.
34. Nishijima DK ZS, Berrong J, Legome E. . Utility of platelet transfusion in adult patients with traumatic intracranial hemorrhage and preinjury antiplatelet use: a systematic review. *Trauma Acute Care Surg* 2012;72:1658-63.
35. Naidech AM LS, Rosenberg NF, Lindholm PF, Bernstein RA, Batjer HH, Alberts MJ, Kwaan HC. . Early Platelet Transfusion Improves Platelet Activity and May Improve Outcomes After Intracerebral Hemorrhage. *Neurotic care* 2012;16:82-7.
36. Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, et al. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *J Am Coll Cardiol.* 2011;58(24):e44-122.