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EDITORIAL

Early antiplatelet therapy used for acute ischemic stroke and intracranial hemorrhage

Venkata Buddhavarapu, Rahul Kashyap, Salim Surani

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Abstract

In this editorial we comment on the article published by Zhang *et al* in the recent issue of *World Journal of Clinical Cases*. We evaluate their claims on the benefit of use of Aspirin in the early management of patients with ischemic stroke. We also comment on their contention of using aspirin in the early management of patients with intracranial hemorrhage, a practice not seen in modern medicine. Large clinical trials such as the International Stroke Trial and the Chinese Acute Stroke Trial have shown the benefit of Aspirin use within 48 h of patients with Acute Ischemic Stroke. The findings were corroborated in the open-label trial performed by Zhang *et al* in a smaller sample group of 25 patients where they showed improvement in functional scores at 90 days without an increase in adverse events. As such, this intervention is also recommended by the American Heart Association stroke guidelines from 2021. With regard to Intracranial hemorrhage, traditional practice has been to discontinue or avoid antiplatelet therapy in these patient groups. However, no studies have been done to evaluate this management strategy that is more borne out of the mechanism behind Aspirin's effect on the coagulation pathway. Zhang *et al* evaluate the benefits of Aspirin on patients with low-volume intracranial hemorrhage, *i.e.*, less than 30 mL on computed tomography imaging, and show no increase in mortality. The caveat of this finding is that all outcomes were pooled into one group for results, and the number of patients was low. While more studies with larger patient groups are required, the data from Zhang *et al* suggests that patients with small-volume intracranial hemorrhages may benefit from Aspirin administration in the acute phase of management.

Key Words: Aspirin; Ischemic stroke; Intracranial hemorrhage; CVA; Antiplatelet therapy

Core Tip: Clinical trials continue to demonstrate the benefits of Aspirin when given within 48 h of patients with Acute Ischemic Stroke. However, while not standard practice, Aspirin may also have a benefit in patients with Acute Hemorrhagic Stroke with small volume of blood noted on imaging. As aspirin inhibits the coagulation pathway, it may improve blood flow to the ischemic areas surrounding the hemorrhage and improve outcomes without a concomitant increase in mortality.

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INTRODUCTION

The antithrombotic medication Aspirin is one of the most common treatments for patients with acute ischemic stroke. Patients who have received this medication within 24 to 48 h of presentation have been shown to have significant benefits in morbidity and mortality[1]. It has also been shown to increase bleeding risk when compared to placebo, but largely, the benefits have outweighed the risks for measured outcomes at 90 d[2]. There remains a knowledge gap in effectively managing patients with acute hemorrhagic stroke. Antithrombotic and antiplatelet medications are discontinued upon presentation, but data regarding this remains lacking. In this editorial, we further expand on these concepts.

ASPIRIN USE IN ACUTE ISCHEMIC STROKE

Antiplatelet therapy is one of the cornerstones for the treatment of acute ischemic stroke. The International Stroke Trial (IST) and the Chinese Acute Stroke Trial (CAST), both completed in 1997, were the first studies to show mortality benefits in patients with acute ischemic stroke[3,4]. Of note, while both trials administered aspirin within 48 h of suspected onset, the dose of Aspirin was different. Subsequent studies and pooled meta-analyses over the following few years would continue demonstrating mortality benefits from early use regardless of the dose considered[5]. Both IST and CAST also demonstrated that Aspirin use did not significantly increase hemorrhagic complications. The dose of Aspirin used in these trials was different, and the data did not show benefit for patients with severe strokes (National institute of Health stroke scale score greater than 21). The studies that followed included landmark trials such as Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events[6] and Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke[7] would continue to demonstrate the benefits of early Aspirin use especially when used with an antiplatelet drug Clopidogrel. The studies also showed an increase in adverse effects, including hemorrhagic transformation and other bleeding events, which may have some association with the higher dose used.

In the most recent issue of the *World Journal of Clinical Cases,* Zhang *et al*[8] attempted to replicate the benefits of early-use Aspirin in ischemic stroke patients in a single-center, open-label trial. The study compares administering Aspirin 300 mg once daily vs. no Aspirin in the first 48 h of stroke onset. Total 25 patients were included in the Aspirin group, and 24 patients were included in the No Aspirin group. The primary outcome was a recurrent stroke, myocardial infarction, or vascular event within 90 d, and the secondary outcome was worsening functional outcomes within 90 d, determined by the mRS score, which evaluated functional abilities. The study did not show any difference in primary outcomes (P = 0.33, P = 1.00, and P = 0.55) but did show significance in secondary outcomes of improved mRS scores (P = 0.04). Of note, both ischemic and hemorrhagic stroke patients were pooled into one analysis. Limitations of the study were that it was significantly underpowered, and not-placebo controlled, which limits its conclusions. For generalizing these results, a homogenous cohort of patients is needed in intervention group, as outcomes could be multi-factorial. In terms of ischemic strokes, the studies' results on the primary outcomes are not in line with the major conclusions from the IST and CAST trials. The secondary outcomes do show benefits in concordance with IST and CAST but are difficult to claim due to the low sample size. Therefore, these results should be taken with a grain of salt. The best approach would be to have robust clinical trial design with clean exposure and control groups with appropriate sample for 80% or higher power.

ASPIRIN USE IN HEMORRHAGIC STROKE (INTRACRANIAL HEMORRHAGE)

Aspirin is a potent cyclooxygenase-1 inhibitor, which leads to an irreversible platelet aggregation inhibitor[9]. The effects are maintained at all dosages of Aspirin, leading to a potential increase in bleeding when vascular injury occurs. In patients with acute ischemic stroke, this can manifest as hemorrhagic conversion of the ischemic penumbra, which can lead to worsening neurological outcomes and increased mortality. Consequently, this effect is also thought to potentiate hemorrhage noted in patients dealing with a hemorrhagic stroke[10]. Large-scale systematic reviews have shown an

increase in mortality when Aspirin is continued during the early phases of intracranial hemorrhage, but this intervention did not change functional outcomes in the long term[11,12]. These studies did not differentiate based on the volume of hemorrhage upon presentation. As such, the American Heart Association Stroke guidelines of 2022 recommend discontinuing Aspirin use in acute hemorrhagic stroke and even recommend the use of platelet transfusions in some specific patient population groups[13]. However, there are no studies that evaluate the initiation of Aspirin in patients with small hemorrhagic strokes where the risk of further hemorrhage might be low. Zhang *et al*[8] attempt to evaluate the use of Aspirin within 48 h of patients with acute small-volume hemorrhagic stroke. In the hemorrhagic stroke arm, Aspirin 300 mg daily is given to patients with confirmed small-volume hemorrhagic strokes (Intracranial volume less than 30 mL on computed tomography imaging). A total of five patients received Aspirin, while 6 patients did not. The primary outcome and secondary outcomes remained the same as in the ischemic stroke arm, and the results were pooled into patients with ischemic stroke; therefore, the results were the same. This may question the study methodology. In addition to the earlier mentioned limitations, the study would have benefited if results were reported by stroke type. A low sample size would have continued to limit results, and meaningful conclusions could not have been made.

CONCLUSION

Patients with ischemic stroke continue to demonstrate significant benefits from early Aspirin use, especially when given as early as 24 to 48 h. It remains unclear whether Aspirin should be given to patients with small-volume intracranial hemorrhage. However, studies to evaluate this would be an ethical challenge as, traditionally, antiplatelet medications are discontinued upon presentation. The research does pose an interesting question on whether Aspirin might provide improved blood flow to areas affected by the external compression from small-volume hemorrhages.

FOOTNOTES

Author contributions: Buddhavarapu V, Surani S and Kashyap R designed the research; Buddhavarapu V, performed the research; Buddhavarapu V, Surani S and Kashyap R analyzed the data; Buddhavarapu V wrote the paper; Surani S and Kashyap R edited and revised the paper.

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REFERENCES

1 **Powers WJ**, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauch EC, Kidwell CS, Leslie-Mazwi TM, Ovbiagele B, Scott PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL; American Heart Association Stroke Council. 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke* 2018; **49**: e46-e110 [PMID: 29367334 DOI: 10.1161/STR.0000000000000158]

2 **Kleindorfer DO**, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, Kamel H, Kernan WN, Kittner SJ, Leira EC, Lennon O, Meschia JF, Nguyen TN, Pollak PM, Santangeli P, Sharrief AZ, Smith SC Jr, Turan TN, Williams LS. 2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline From the American Heart Association/American Stroke Association. *Stroke* 2021; **52**: e364-e467 [PMID: 34024117 DOI: 10.1161/STR.0000000000000375]

3 The International Stroke Trial (IST): a randomised trial of aspirin, subcutaneous heparin, both, or neither among 19435 patients with acute ischaemic stroke. International Stroke Trial Collaborative Group. *Lancet* 1997; **349**: 1569-1581 [PMID: 9174558]

4 CAST: randomised placebo-controlled trial of early aspirin use in 20,000 patients with acute ischaemic stroke. CAST (Chinese Acute Stroke Trial) Collaborative Group. *Lancet* 1997; **349**: 1641-1649 [PMID: 9186381]

5 **Antithrombotic Trialists' Collaboration**. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002; **324**: 71-86 [PMID: 11786451 DOI: 10.1136/bmj.324.7329.71]

6 **Zhao Y**, Wang C, Hong X, Miao J, Liao Y, Hou FF, Zhou L, Liu Y. Wnt/β-catenin signaling mediates both heart and kidney injury in type 2 cardiorenal syndrome. *Kidney Int* 2019; **95**: 815-829 [PMID: 30770217 DOI: 10.1016/j.kint.2018.11.021]

7 **Johnston SC**, Easton JD, Farrant M, Barsan W, Conwit RA, Elm JJ, Kim AS, Lindblad AS, Palesch YY; Clinical Research Collaboration, Neurological Emergencies Treatment Trials Network, and the POINT Investigators. Clopidogrel and Aspirin in Acute Ischemic Stroke and High-Risk TIA. *N Engl J Med* 2018; **379**: 215-225 [PMID: 29766750 DOI: 10.1056/NEJMoa1800410]

8 **Zhang JQ**, Pan ZB. Efficacy and safety of aspirin antiplatelet therapy within 48 h of symptom onset in patients with acute stroke. *World J Clin Cases* 2023; **11**: 7814-7821 [PMID: 38073696 DOI: 10.12998/wjcc.v11.i32.7814]

9 **Patrono C**, Coller B, FitzGerald GA, Hirsh J, Roth G. Platelet-active drugs: the relationships among dose, effectiveness, and side effects: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004; **126**: 234S-264S [PMID: 15383474 DOI: 10.1378/chest.126.3_suppl.234S]

10 **Qiu J**, Ye H, Wang J, Yan J, Wang Y. Antiplatelet Therapy, Cerebral Microbleeds, and Intracerebral Hemorrhage: A Meta-Analysis. *Stroke* 2018; **49**: 1751-1754 [PMID: 29798835 DOI: 10.1161/STROKEAHA.118.021789]

11 **Thompson BB**, Béjot Y, Caso V, Castillo J, Christensen H, Flaherty ML, Foerch C, Ghandehari K, Giroud M, Greenberg SM, Hallevi H, Hemphill JC 3rd, Heuschmann P, Juvela S, Kimura K, Myint PK, Nagakane Y, Naritomi H, Passero S, Rodríguez-Yáñez MR, Roquer J, Rosand J, Rost NS, Saloheimo P, Salomaa V, Sivenius J, Sorimachi T, Togha M, Toyoda K, Turaj W, Vemmos KN, Wolfe CD, Woo D, Smith EE. Prior antiplatelet therapy and outcome following intracerebral hemorrhage: a systematic review. *Neurology* 2010; **75**: 1333-1342 [PMID: 20826714 DOI: 10.1212/WNL.0b013e3181f735e5]

12 **Apostolaki-Hansson T**, Ullberg T, Pihlsgård M, Norrving B, Petersson J. Prognosis of Intracerebral Hemorrhage Related to Antithrombotic Use: An Observational Study From the Swedish Stroke Register (Riksstroke). *Stroke* 2021; **52**: 966-974 [PMID: 33563019 DOI: 10.1161/STROKEAHA.120.030930]

13 **Greenberg SM**, Ziai WC, Cordonnier C, Dowlatshahi D, Francis B, Goldstein JN, Hemphill JC 3rd, Johnson R, Keigher KM, Mack WJ, Mocco J, Newton EJ, Ruff IM, Sansing LH, Schulman S, Selim MH, Sheth KN, Sprigg N, Sunnerhagen KS; American Heart Association/American Stroke Association. 2022 Guideline for the Management of Patients With Spontaneous Intracerebral Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. *Stroke* 2022; **53**: e282-e361 [PMID: 35579034 DOI: 10.1161/STR.0000000000000407]

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