LETTER TO THE EDITOR

RESTARTING ANTIPLATELET AGENTS AFTER INTRACEREBRAL HAEMORRHAGE: A REASSURANCE TO PHYSICIANS

Muhammad Aemaz Ur Rehman[1], Hareem Farooq[2], Muhammad Ebaad Ur Rehman[3]

[1]Department of Neurology, Massachusetts General Hospital, Boston-United States
[2]King Edward Medical University, Lahore, [3]Allama Iqbal Medical College, Lahore-Pakistan

Dear Editor,

Intracerebral haemorrhage (ICH) is the second most common cause of stroke (after ischemic stroke) across the world and has significantly higher morbidity and mortality as compared to ischemic stroke and subarachnoid haemorrhage.[1] Spontaneous (atraumatic) ICH occurs in up to 31 people per 100,000 globally and the incidence is even higher in Asian countries like Pakistan.[2] Most patients experiencing spontaneous ICH have a history of occlusive vascular diseases like myocardial infarction (MI) and are consequently taking antithrombotic therapy (antiplatelets, anticoagulants) at the time of ICH occurrence. Antithrombotic therapy is usually halted for a certain period following ICH but data on the safety of therapy resumption is sparse and physicians largely use clinical judgment to weigh the benefit of therapy resumption against the risk of ICH recurrence.

A randomized controlled trial called RESTART was published in The Lancet in 2019 to assess if restarting the 'antiplatelet therapy only' increased the risk of recurrent ICH. The trial suggested a slightly increased, but nonsignificant, risk of recurrent ICH but the results were limited by a short duration of follow-up. In the latter half of 2021, the extended follow-up of the RESTART trial was published in one of the most reputed Neurology journals i.e., JAMA Neurology.[3] The trial recruited 537 participants with radiologically confirmed ICH and randomly allocated half patients to restart antiplatelets (aspirin, clopidogrel) and half patients to avoid antiplatelets. The primary outcome was the recurrent ICH events during the follow-up time of up to 7 years (mean time = 3 years). Recurrent ICH occurred in 22/268 (8.2%) participants assigned to antiplatelet therapy compared with 25/268 (9.3%) participants assigned to avoid antiplatelet therapy (adjusted HR=0.87; 95% CI, 0.49-1.55; *p*-value = .64). This suggests that re-starting antiplatelet therapy indicated for other occlusive vascular diseases (e.g., MI, ischemic stroke) is safe in patients who suffer from ICH while they are on antiplatelet therapy. This conclusion is in line with some observational studies[4,5] published on the same topic but RESTART remains the only clinical trial to provide credible evidence.

The exact incidence of ICH is not known in Pakistan but trends from Asian countries suggest a higher occurrence as compared to the Western world.[1] The primary reason for such high occurrence is the predisposition of the elderly population to cardiovascular risk factors like hypertension and obesity. Pakistan suffers from a very high burden of coronary artery disease and a significant number of elderly people are on preventive antiplatelet therapy (especially aspirin). Discontinuation of aspirin after an ICH episode in such patients may lead to an increased risk of MI and studies also suggest that survivors of ICH are more likely to suffer from MI and ischemic stroke.[6] This trial provides reasonable reassurance to the medical community about the use of antiplatelet therapy after ICH if indicated for secondary prevention of major vascular events. Therefore, the dissemination of this information to physicians practising in Pakistan is of paramount importance.

REFERENCES

1. Krishnamurthi RV, Feigin VL, Forouzanfar MH, Mensah GA, Connor M, Bennett DA, *et al*. Global and regional burden of first-ever ischaemic and haemorrhagic stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. Lancet Glob Health 2013;1(5):e259–81.
2. Pasquini M, Charidimou A, van Asch CJ, Baharoglu MI, Samarasekera N, Werring DJ, *et al*. Variation in restarting antithrombotic drugs at hospital discharge after intracerebral hemorrhage. Stroke 2014;45(9):2643–8.
3. Salman RA, Dennis MS, Sandercock PA, Sudlow CL, Wardlaw JM, Whiteley WN, *et al*. Effects of Antiplatelet Therapy After Stroke Caused by Intracerebral Hemorrhage: Extended Follow-up of the RESTART Randomized Clinical Trial. JAMA Neurol 202178(10):1179–86.
4. Chong BH, Chan KH, Pong V, Lau KK, Chan YH, Zuo ML, *et al*. Use of aspirin in Chinese after recovery from primary intracranial haemorrhage. Thromb Haemost 2012;107(2):241–7.
5. Flynn RW, MacDonald TM, Murray GD, MacWalter RS, Doney AS. Prescribing antiplatelet medicine and subsequent events after intracerebral hemorrhage. Stroke 2010;41(11):2606–11.
6. Murthy SB, Diaz I, Wu X, Merkler AE, Iadecola C, Safford MM, *et al*. Risk of arterial ischemic events after intracerebral hemorrhage. Stroke 2020;51(1):137–42.

Citation: Rehman MA, Farooq H, Rehman ME. Restarting antiplatelet agents after intracerebral haemorrhage: A reassurance to physicians. J Ayub Med Coll Abbottabad 2022;34(4):907.

DOI: 10.55519/JAMC-04-11095

Muhammad Aemaz Ur Rehman, Post-Doctoral Research Fellow at the Department of Neurology, Massachusetts General Hospital, Boston-United States
Email: MAEMAZURREHMAN@mgh.harvard.edu