



Reteplase: A promising alternative in acute ischemic stroke management

Muzamil Akhtar¹ · Hajira Karim²

Received: 15 July 2024 / Revised: 15 July 2024 / Accepted: 29 July 2024

© The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2024

Dear Editor,

Acute ischemic stroke (AIS) is a significant global health concern, affecting approximately 15 million individuals annually worldwide, with nearly 87% of all strokes being ischemic [1]. AIS is characterized by a sudden interruption of cerebral blood flow due to arterial occlusion, leading to rapid neuronal damage and severe neurological deficits. Reperfusion therapy is a well-established, evidence-based intervention for ischemic stroke, playing a crucial role in improving patient outcomes. Effective and prompt reperfusion is paramount to mitigate extensive neuronal damage and enhance recovery prospects. The demand for intravenous thrombolysis in acute ischemic stroke has risen significantly alongside advancements in stroke care quality. From 2015 to 2019, the use of intravenous thrombolysis increased by 60.3%, reaching 22.9% among patients treated within 4.5 h of symptom onset [2]. Intravenous alteplase, the internationally approved standard thrombolytic agent, is recommended for use within this critical window [5]. Recent guidelines suggest that either alteplase or tenecteplase can be used for patients with acute ischemic stroke within 4.5 h after symptom onset, with tenecteplase being a genetically modified form of alteplase.

A pivotal study published in the NEJM by Li et al. introduces a promising thrombolytic agent, reteplase, into the discussion of acute ischemic stroke (AIS) management [4]. This trial compared the efficacy and safety of reteplase versus alteplase in AIS patients treated within 4.5 h of symptom onset. The results were noteworthy: an excellent functional

outcome, defined as a score of 0 or 1 on the modified Rankin scale at 90 days, was achieved in 79.5% of patients in the reteplase group, compared to 70.4% in the alteplase group. This indicates a superior efficacy for reteplase. Additionally, the incidence of symptomatic intracranial hemorrhage within 36 h was 1.7% in the reteplase group versus 2.4% in the alteplase group, demonstrating a comparable safety profile. These findings suggest that reteplase may enhance patient outcomes in acute ischemic stroke management.

Furthermore, reteplase is approved for the treatment of acute myocardial infarction (AMI) in several regions. A meta-analysis comparing reteplase with alteplase in AMI patients found no significant differences in terms of mortality or the incidence of disabling stroke between the two treatments [3]. This reinforces the potential of reteplase as an effective thrombolytic agent across different cardiovascular emergencies.

In conclusion, the emergence of reteplase as a potential alternative to alteplase represents a significant advancement in the treatment of acute ischemic stroke. The positive outcomes observed in the clinical trial underscore the need for further research to confirm these findings and possibly revise current clinical guidelines. As the landscape of thrombolytic therapy evolves, reteplase may offer a valuable option for patients, particularly those who are not candidates for alteplase. Continued advancements in stroke treatment are crucial for enhancing patient recovery and overall quality of life on a global scale.

Acknowledgements None.

Author contributions M.A participated in conceptualization, writing and reviewing the manuscript. H.K participated in writing the manuscript.

Funding None.

Data availability No datasets were generated or analysed during the current study.

✉ Muzamil Akhtar
muzamilb112@gmail.com

Hajira Karim
Hajira.karim07@gmail.com

¹ Gujranwala Medical College, Gujranwala, Pakistan

² International School of Medicine, Istanbul Medipol University, Istanbul, Türkiye

Declarations

Competing interests The authors declare no competing interests.

Consent for participation N/A.

Ethics approval and consent N/A.

References

- Feigin VL, Stark BA, Johnson CO, Roth GA, Bisignano C, Abady GG, Abbasifard M, Abbasi-Kangevari M, Abd-Allah F, Abedi V, Abualhasan A, Abu-Rmeileh NM, Abushouk AI, Adebayo OM, Agarwal G, Agasthi P, Ahinkorah BO, Ahmad S, Ahmadi S, Ahmed Salih Y, Aji B, Akbarpour S, Akinyemi RO, Al Hamad H, Alahdab F, Alif SM, Alipour V, Aljunid SM, Almustanyir S, Al-Raddadi RM, Al-Shahi Salman R, Alvis-Guzman N, Ancuceanu R, Anderlini D, Anderson JA, Ansar A, Antonazzo IC, Arabloo J, Ärnlöv J, Artanti KD, Aryan Z, Asgari S, Ashraf T, Athar M, Atreya A, Ausloos M, Baig AA, Baltatu OC, Banach M, Barboza MA, Barker-Collo SL, Bärnighausen TW, Barone MTU, Basu S, Bazmandegan G, Beghi E, Beheshti M, Béjot Y, Bell AW, Bennett DA, Bensenor IM, Bezabhe WM, Bezabih YM, Bhagavathula AS, Bhardwaj P, Bhattacharyya K, Bijani A, Bikbov B, Birhanu MM, Bolor A, Bonny A, Brauer M, Brenner H, Bryazka D, Butt ZA, Caetano dos Santos FL, Campos-Nonato IR, Cantu-Brito C, Carrero JJ, Castañeda-Orjuela CA, Catapano AL, Chakraborty PA, Charan J, Choudhary SG, Chowdhury EK, Chu D-T, Chung S-C, Colozza D, Costa VM, Costanzo S, Criqui MH, Dadras O, Dagnew B, Dai X, Dalal K, Damasceno AAM, D'Amico E, Dandona L, Dandona R, Darega Gela J, Davletov K, De la Cruz-Góngora V, Desai R, Dhamnetiya D, Dharmaratne SD, Dhimal ML, Dhimal M, Diaz D, Dichgans M, Dokova K, Doshi R, Douiri A, Duncan BB, Eftekhazadeh S, Ekholuenetale M, El Nahas N, Elgendy IY, Elhadi M, El-Jaafari SI, Endres M, Endries AY, Erku DA, Faraon EJA, Farooque U, Farzadfar F, Feroze AH, Filip I, Fischer F, Flood D, Gad MM, Gaidhane S, Ghaneil Gheshlagh R, Ghoshghaee A, Ghith N, Ghozali G, Ghozy S, Gialluisi A, Giampaoli S, Gilani SA, Gill PS, Gnedovskaya E V, Golechha M, Goulart AC, Guo Y, Gupta R, Gupta VB, Gupta VK, Gyanwali P, Hafezi-Nejad N, Hamidi S, Hanif A, Hankey GJ, Hargono A, Hashi A, Hassan TS, Hassen HY, Havmoeller RJ, Hay SI, Hayat K, Hegazy MI, Herteliu C, Holla R, Hostiuc S, Househ M, Huang J, Humayun A, Hwang B-F, Iacoviello L, Iavicoli I, Ibitoye SE, Ilesanmi OS, Ilic IM, Ilic MD, Iqbal U, Irvani SSN, Islam SMS, Ismail NE, Iso H, Isola G, Iwagami M, Jacob L, Jain V, Jang S-I, Jayapal SK, Jayaram S, Jayawardena R, Jeemon P, Jha RP, Johnson WD, Jonas JB, Joseph N, Jozwiak JJ, Jürissom M, Kalani R, Kalhor R, Kalkonde Y, Kamath A, Kamiab Z, Kanchan T, Kandel H, Karch A, Katoto PD, Kayode GA, Keshavarz P, Khader YS, Khan EA, Khan IA, Khan M, Khan MA, Khatib MN, Khubchandani J, Kim GR, Kim MS, Kim YJ, Kisa A, Kisa S, Kivimäki M, Kolte D, Koolivand A, Koulmane Laxminarayana SL, Koyanagi A, Krishan K, Krishnamoorthy V, Krishnamurthi R V, Kumar GA, Kusuma D, La Vecchia C, Lacey B, Lak HM, Lallukka T, Lasrado S, Lavados PM, Leonardi M, Li B, Li S, Lin H, Lin R-T, Liu X, Lo WD, Lorkowski S, Lucchetti G, Lutzky Saute R, Magdy Abd El Razek H, Magnani FG, Mahajan PB, Majeed A, Makki A, Malekzadeh R, Malik AA, Manafi N, Mansournia MA, Mantovani LG, Martini S, Mazzaglia G, Mehndiratta MM, Menezes RG, Meretoja A, Mersha AG, Miao Jonasson J, Miazgowski B, Miazgowski T, Michalek IM, Mirrahimov EM, Mohammad Y, Mohammadian-Hafshejani A, Mohammed S, Mokdad AH, Mokhayeri Y, Molokhia M, Moni MA, Montasir A Al, Moradza-deh R, Morawska L, Morze J, Muruet W, Musa KI, Nagarajan AJ, Naghavi M, Narasimha Swamy S, Nascimento BR, Negoi RI, Neupane Kandel S, Nguyen TH, Norrving B, Noubiap JJ, Nwatah VE, Oancea B, Odukoya OO, Olagunju AT, Orru H, Owolabi MO, Padubidri JR, Pana A, Parekh T, Park E-C, Pashazadeh Kan F, Pathak M, Peres MFP, Perianayagam A, Pham T-M, Piradov MA, Podder V, Polinder S, Postma MJ, Pourshams A, Radfar A, Rafiei A, Raggi A, Rahim F, Rahimi-Movaghar V, Rahman M, Rahman MA, Rahmani AM, Rajai N, Ranasinghe P, Rao CR, Rao SJ, Rathi P, Rawaf DL, Rawaf S, Reitsma MB, Renjith V, Renzaho AMN, Rezapour A, Rodriguez JAB, Roever L, Romoli M, Rynkiewicz A, Sacco S, Sadeghi M, Saeedi Moghaddam S, Sahebkar A, Saif-Ur-Rahman K, Salah R, Samaei M, Samy AM, Santos IS, Santric-Milicevic MM, Sarrafzadegan N, Sathian B, Sattin D, Schiavolin S, Schlaich MP, Schmidt MI, Schutte AE, Sepanlou SG, Seylani A, Sha F, Shahabi S, Shaikh MA, Shannawaz M, Shawon MSR, Sheikh A, Sheikhbahaei S, Shibuya K, Siabani S, Silva DAS, Singh JA, Singh JK, Skryabin VY, Skryabina AA, Sobaih BH, Stortecky S, Stranges S, Tadesse EG, Tarigan IU, Temsah M-H, Teuschl Y, Thrift AG, Tonelli M, Tovani-Palone MR, Tran BX, Tripathi M, Tsegaye GW, Ullah A, Unim B, Unnikrishnan B, Vakilian A, Valadan Tahbaz S, Vasankari TJ, Venketasubramanian N, Vervoort D, Vo B, Volovici V, Vosoughi K, Vu GT, Vu LG, Wafa HA, Waheed Y, Wang Y, Wijeratne T, Winkler AS, Wolfe CDA, Woodward M, Wu JH, Wulf Hanson S, Xu X, Yadav L, Yadollahpour A, Yahyazadeh Jabbari SH, Yamagishi K, Yatsuya H, Yonemoto N, Yu C, Yunusa I, Zaman MS, Zaman S Bin, Zamanian M, Zand R, Zandifar A, Zastrozhin MS, Zastrozhina A, Zhang Y, Zhang Z-J, Zhong C, Zuniga YMH, Murray CJL (2021) Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Neurol* 20:795–820. [https://doi.org/10.1016/S1474-4422\(21\)00252-0](https://doi.org/10.1016/S1474-4422(21)00252-0)
- Gu H-Q, Yang X, Wang C-J, Zhao X-Q, Wang Y-L, Liu L-P, Meng X, Jiang Y, Li H, Liu C, Wangqin R, Fonarow GC, Schwamm LH, Xian Y, Li Z-X, Wang Y-J (2021) Clinical characteristics, management, and In-Hospital outcomes in patients with stroke or transient ischemic attack in China. *JAMA Netw Open* 4:e2120745. <https://doi.org/10.1001/jamanetworkopen.2021.20745>
- Jinatongthai P, Kongwatcharapong J, Foo CY, Phrommintikul A, Nathisuwan S, Thakkestian A, Reid CM, Chaikunapruk N (2017) Comparative efficacy and safety of reperfusion therapy with fibrinolytic agents in patients with ST-segment elevation myocardial infarction: a systematic review and network meta-analysis. *Lancet* 390:747–759. [https://doi.org/10.1016/S0140-6736\(17\)31441-1](https://doi.org/10.1016/S0140-6736(17)31441-1)
- Li S, Gu H-Q, Li H, Wang X, Jin A, Guo S, Lu G, Che F, Wang W, Wei Y, Wang Y, Li Z, Meng X, Zhao X, Liu L, Wang Y (2024) Reteplase versus Alteplase for Acute ischemic stroke. *N Engl J Med* 390:2264–2273. <https://doi.org/10.1056/NEJMoa2400314>
- 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 (2019) Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke* 50. <https://doi.org/10.1161/STR.0000000000000211>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.