LETTER TO THE EDITOR

Aprocetentin (Tryvio): A breakthrough in treating Resistant Hypertension

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Dear Editor, According to a scientific statement from the American Heart Association, Resistant hypertension is defined as blood pressure that remains above target levels (i.e., less than 140/90 mmHg, or less than 130/80 mmHg in patients with diabetes or chronic kidney disease) despite optimal use of three different classes of antihypertensive medications, ideally including a diuretic. This definition also covers patients who require four or more medications to achieve blood pressure control.[1]

By 2025, the global prevalence of hypertension is projected to rise from 972 million adults in 2000 to a staggering 1.56 billion - an alarming increase of 60%.[2] Notably, the prevalence of hypertension in Pakistan has risen significantly over recent decades. From 1990 to 1994, a national sampling study reported a prevalence of 19.75%. The National Health Survey of Pakistan (NHSP) later estimated that 18.9% of people aged 15 years and older were hypertensive.[3]

Studies have consistently demonstrated a strong association between hypertension and an elevated risk of mortality, myocardial infarction, heart failure, stroke, and chronic kidney disease.[1] This trend highlights a growing public health concern that requires urgent attention for effective management.[3]

Current interventions for resistant hypertension include: long-acting calcium channel blockers CCB, a blocker of the renin-angiotensin system (ACE inhibitor or ARB), and a diuretic. However, despite these treatments, many patients continue to struggle with blood pressure control, underscoring the need for additional strategies and therapies to manage this condition more effectively.[1]

In March 2024, FDA approved Aprocetentin for the treatment of hypertension as an adjunct with other antihypertensive drugs, to lower blood pressure in adult patients inadequately controlled on existing therapies. Initially studied in Phase 2 as monotherapy, Aprocetentin progressed to Phase 3 (Precision study) as add-on therapy for resistant hypertension. Results showed superior blood pressure reduction indicating potential as a treatment option.[4]

In the human kidney, there are three types of proteins called Endothelin-1, Endothelin-2, and Endothelin-3 that help regulate blood flow and salt balance. These proteins interact with specific receptors in different ways: Endothelin-A receptors cause blood vessels to constrict, while Endothelin-B receptors help release substances that widen blood vessels and regulate fluid levels. Medications known as Endothelin receptor antagonists belong to a class of proteins that can block these receptors to manage conditions like high blood pressure. [5]

Aprocitentan is a dual Endothelin receptor antagonist that inhibits both Endothelin-A and Endothelin-B receptors, thereby preventing binding and reducing the vasoconstrictive and proliferative effects of Endothelin-1, ultimately facilitating blood pressure control.[6]

The most common adverse effect of Aprocetentin is fluid retention. Therefore, to avoid potential serious consequences, close monitoring is necessary for patients with heart failure or kidney disease.[4]

The approval of Aprocetentin marks a significant step forward in offering a new therapeutic option for patients with resistant hypertension. It is therefore essential for medical practitioners to recognise the emerging role of Endothelin receptor antagonists in Pakistan's healthcare landscape.

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References

1. Carey RM, Calhoun DA, Bakris GL, Brook RD, Daugherty SL, et al. Resistant Hypertension: Detection, Evaluation, and Management: A Scientific Statement From the American Heart Association. Hypertension 2018;72:e53-90. doi: 10.1161/HYP.0000000000000084.
2. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data.

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Lancet 2005;365:217-23. doi: 10.1016/S0140-6736(05)17741-1.
3. Shah N, Shah Q, Shah AJ. The burden and high prevalence of hypertension in Pakistani adolescents: a meta-analysis of the published studies. Arch Public Health 2018;76:20. doi: 10.1186/s13690-018-0265-5.
4. Zoccali C, Mallamaci F, De Nicola L, Minutolo R. New trials in resistant hypertension: mixed blessing stories. Clin Kidney J 2023;17:sfad251. doi: 10.1093/ckj/sfad251.
5. Maguire JJ, Davenport AP. Endothelin receptors and their antagonists. Semin Nephrol 2015;35:125-36. doi: 10.1016/j.semnephrol.2015.02.002.
6. Angeli F, Verdecchia P, Reboldi G. Aprocitentan, A Dual Endothelin Receptor Antagonist Under Development for the Treatment of Resistant Hypertension. Cardiol Ther 2021;10:397-406. doi: 10.1007/s40119-021-00233-7.