



International Journal of Cardiovascular Diseases & Diagnosis

Short Communication

Focus on Less Spoken Trials in Hypertension & Stroke: HYVET-PATS-PROGRESS -

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Submitted: 02 July 2022; **Approved:** 01 August 2022; **Published:** 02 August 2022

Cite this article: Chaudhary G, Kohli G, Bhattacharyya S. Focus on Less Spoken Trials in Hypertension & Stroke: HYVET-PATS-PROGRESS. Int J Cardiovasc Dis Diagn. 2022 Aug 02;7(1): 009-011.

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Stroke is a major health concern and is a second leading cause of mortality globally [1]. Among all the global stroke patients, India accounts for 60% with approximately 4000 cases occurring every day. Further, the reported age of presentation in India is three decades earlier than the global average age of 80 years and above [2]. The earlier age of presentation has a direct impact on the economic, social, and psychological well-being of the patient's family and on society. The most important and common modifiable risk factor for stroke is uncontrolled blood pressure levels which is responsible for both types of strokes ischemic and hemorrhagic. It is thus critical to control hypertension in patients reducing incidences of stroke and minimizing morbidity and mortality in the Indian population [3]. Blood pressure can be controlled by using antihypertensive medications, which also lowers the risk of stroke [4]. The international guidelines from the American College of Cardiology (ACC) and the American Heart Association (AHA) have now proposed the use of thiazide-like diuretics over thiazides, for hypertensive patients [5].

What is less spoken about is the evidence from trials -Hypertension in the Very Elderly Trial (HYVET) [6], The Perindopril Protection against Recurrent Stroke Study (PROGESS) & Post-Stroke Antihypertensive Treatment Study (PATS) which had a base of antihypertensive therapies in the form of Indapamide ± Perindopril and prevention of stroke [7].

Looking at the HYVET trial, a double-blind, randomized, placebo-controlled clinical trial, with a median duration of follow-up of 1.8 years, which involved 3845 patients 80 years of age or older with hypertension, where they evaluated the effect of stepped-care therapy, beginning with indapamide and adding perindopril as needed. The authors found that active treatment, as compared with placebo, was associated with a 21% reduction in the relative risk of death from any cause, a 64% reduction in the relative risk of heart failure, and a 30% reduction in the relative risk of stroke. This did confer that using stepped care in the form of Indapamide ± Perindopril demonstrated primary prevention of stroke in elderly patients with hypertension [8].

Now the first major trial to demonstrate the effectiveness of hypertension treatment for secondary prevention of stroke was the PATS, which was a randomised, double-blind placebo-controlled trial, in patients with a history of stroke or TIA, conducted in China in 44 centers, with Indapamide based therapy in the active group & showed a reduced risk of stroke by -29% [9].

This was subsequently confirmed in PROGRESS-The perindopril protection against recurrent stroke study, with about 4 years of follow up which was designed to determine the effects of a blood-pressure lowering regimen in 6105 hypertensive and non-hypertensive patients with a history of stroke or transient ischaemic attack and looked at the primary outcome of total stroke (fatal or non-fatal). Combination therapy with perindopril plus indapamide reduced blood pressure by 12/5 mm Hg and stroke risk by 43%. The paper's interpretation did mention that treatment with these two agents should now be considered routinely for patients with a history of stroke or transient ischaemic attack, irrespective of their blood pressure [10].

The combination would be expected to be metabolically neutral and to confer significant reductions in blood pressure and its-related morbidity, but also significant benefits are attributable to the targeting of blood-pressure-independent pathways. Thiazide-like diuretics are longer-acting drugs with a demonstrated potential for cardiovascular event reduction [5]. Indapamide is an orally-administered thiazide-like diuretic and antihypertensive drug chemically distinct from

regular thiazides, it lacks the thiazide ring system and contains a single sulfonamide group [11].

Indapamide exhibits a dual mechanism of action: a diuretic effect occurs at the proximal segment of the distal tubule in the nephrons, in addition to a direct vascular effect. Together, these mechanisms serve to improve the drug's antihypertensive efficacy [12].

Indapamide has been demonstrated to be metabolically neutral in a range of patients. The beneficial microvascular and macrovascular effects of indapamide extend beyond blood pressure reduction [13].

CONCLUSION

The burden of stroke in India is huge. It is essential that clinicians show consider enhancing awareness for patients for timely intake of their antihypertensive treatment in order to avoid a devastating complication like stroke. In terms of evidence for primary and secondary prevention of stroke with anti-hypertensive therapy with Indapamide ± Perindopril have conferred benefits in landmark trial like HYVET, PATS the first major anti-hypertensive trial for secondary prevention of stroke and similar emphasis being depicted in PROGRESS study.

It would be worthwhile to have an extensive review on trials done till date with anti-hypertensive therapies both in primary & secondary prevention of stroke to have guidance in clinical settings for better management of patients. This write-up is just an attempt to consider all available evidences while choosing an anti-hypertensive to prevent a dreadful condition like stroke.

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