INDIAN SOCIETY OF HYPERTENSION

Hypertension Journal

REVIEW ARTICLE

Linking Evidence-based Management in Hypertension to Real-world Experience for Preventing Stroke: An Indian Perspective

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Abstract

Currently, hypertension is the most critical modifiable risk factor for stroke. The current consensus article describes the clinical views of experts regarding various aspects of the link between hypertension and, stroke, risk assessment of stroke, blood pressure management and consequent stroke prevention, optimal blood pressure targets, along with current antihypertensive approaches. A literature search was performed using databases like PubMed and Google Scholar. Relevant articles were identified using keywords like 'hypertension', 'blood pressure', 'stroke', and, 'antihypertensive therapy.' After the screening, 43 relevant articles were identified and included in the current article. Appropriate blood pressure management with antihypertensive agents is the chief aspect of primary and secondary prevention of stroke. Clinical evidence has strongly established a significant reduction in the risk of first and recurrent stroke with BP-lowering therapy. As the risk of stroke continues to increase, there is a dire necessityto ensure evidence-based management of hypertension to prevent stroke in the Indian population. On similar grounds, the current consensus article aims at providing a collation of evidence-based literature and clinical insights of leading therapy experts of India in the field of neurology, cardiology, and medicine to optimize the management of hypertension and prevention of stroke.

Keywords: Antihypertensive therapy, Blood pressure, Hypertension, Stroke.

doi: 10.61081/htnj/23v9i105

Introduction

Hypertension or raised blood pressure (BP) is a major risk factor for cardiovascular diseases worldwide. It is also a leading cause of premature death. There is a constant association between the level of blood pressure and the risk of complications.[1] One such notable complication is stroke. As established in the literature, the risk of stroke increases at blood pressure levels above 115/75 mmHg.[2] Moreover, high BP is the most vital modifiable risk factor irrespective of geographic location and ethnic background for stroke and shows a link with 54% of stroke episodes globally.[2] There is an evident link between BP and the risk of the first as well as recurrent episodes of cerebrovascular incidents especially in case of ischemic and hemorrhagic stroke.[2] Evidence from clinical trials indicates that antihypertensive therapy enables a significant reduction in the risk of any type of stroke, along with stroke-related disability and death.[2] The current consensus article aims to provide a collation of evidence-based literature and clinical insights from experts to enhance the management of hypertension, and consequently reduce the occurrence of stroke in Indian settings.

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Current Trends in Hypertension: Asian and Indian Perspectives

Epidemiology of hypertension in Asia

In Asia, hypertension is the most prevalent risk factor for stroke. Asian characteristics that differ from the western population are attributable to a higher incidence of stroke. Previous literature assessing the link between ethnicity, BP, and stroke reported that South Asians have a two-fold higher risk of stroke in comparison to Europeans. [3] In addition to ethnicity, systolic blood pressure, diastolic blood pressure, and blood pressure variability are positively associated with the incidence of stroke.[3] As per a recent systematic review and meta-analysis involving the Southeast Asian urban population, the overall pooled prevalence estimate of hypertension was 33.82%.[4] Commonly observed risk factors included ethnicity, education, socioeconomic level, body mass index, waist circumference, smoking, and dyslipidemia.[4] It has been considered that intensive BP control has more benefits in decreasing the risk of cardiovascular events, including strokein Asian hypertensive patients, as Asians have a higher burden of hypertension and stroke compared to Caucasians.[5]

The Indian Scenario

As per the Global Burden of Disease (GBD) study, an age-standardised cardiovascular disease (CVD) death rate of 272 per 100,000 population was reported in India.[6] This was much higher than the global average of 235. Early age of onset, rapid progression, and high mortality rate are the major concerns in CVD. Indians have the highest coronary artery disease (CAD) rates, and the conventional risk factors fail to explain the increased risk. In India, the prevalence of CAD is 21.4% for diabetic individuals and 11% for non-diabetic individuals.[6]

The GBD study estimated that 1.6 million deaths and 33.9 million disability-adjusted life years were caused due to hypertension and hence, it is the most vital cause of disease burden in India.[7] Ramakrishnan *et al.* reported that the overall prevalence of hypertension among Indian adults was 30.7%.[8] Cardiovascular event-related deaths are experienced by Indians almost a decade earlier than in developed countries. These cardiovascular events were responsible for 52% of all deaths in Indian patients aged <70 years, in contrast to 23% of deaths in developed countries.[8] The SYSTolic blood pressUre in older Patients with hypertension (SYSTUP) study reported that an approximately 4% increase in 5-years, as well as 10-years stroke risk, occurred with each 1-mmHg increase in mean systolic BP (SBP) [p<0:0001]. Moderate-to-severe 5-years stroke risk in 33.9% and 10-years stroke risk in 70% of patients were observed. Additionally, comorbid diabetes andsmoking caused a 2- to 5-fold increase in the 5- and10-years stroke risk. Also, 57% of all stroke deaths and, 24% of all coronary heart disease (CHD) deaths were attributable to hypertension.[9]

Consensus opinion 1

The expert panel agreed that hypertension is a major risk factor for morbidity and mortality. In India, hypertension is responsible for almost 50% of stroke-related deaths. Hence, optimizing the management of hypertension is the need of the hour. The prevalence of stroke has been observed to be higher in rural areas of the country as compared to urban areas. Moreover, experience from the routine practice of an expert depicted a prevalence of 10 to 15% of stroke episodes in the Indian intensive care unit (ICU) settings. Out of these strokes, hemorrhagic strokes were majorly responsible for admissions to the ICU (20 to 30% of the total strokes).

Hypertension: The Major Risk Factor for Stroke

Blood pressure is a vital determinant of ischemic as well as hemorrhagic stroke, which includes intracerebral and subarachnoid hemorrhagic stroke events and is associated with the risk of the first and recurrent episodes of cerebrovascular incidents.[2] Even inindividuals who are not hypertensive, higher blood pressure correlates with a higher risk of stroke. Increased BP, irrespective of hypertension status, increases with age, thus bringing about an upward trend in the lifetime risk of developing hypertension. A study has reported that intra-individual variability in BP measurements, or differences in BP levels taken at different points in time in a person, are related to an increased probability of stroke risk due to elevated mean BP alone.[10]

Pathophysiological Aspects: From Hypertension to Stroke

The strong association of stroke with hypertension is primarily because hypertension is strongly correlated with atheromatous deposits, which block or narrow down arteries in the brain thus, predisposing tolocal clot formation. Atheroma and its ischaemic consequences might cause damage to the cerebral arterioles and the brain tissue they supply. Cerebral infarcts occur more frequently than spontaneous cerebral hemorrhages. High BP itself can not rupture cerebral blood vessels directly owing tothe protection provided by their small size. Intracerebral hemorrhage generally follows previous ischaemic vascular damage.[11]

As per the literature, a delay exists between the onset of hypertension and a hypertensive complication.[12] Hypertension causes changes in the cerebral artery structure and function that can impair blood flow, mainly during an ischaemic insult or periods of low arterial pressure.[13] A series of changes occur in the cardiovascular system, including cerebral circulation throughout this long duration. These changes that may contribute to the pathogenesis of stroke in hypertension include vascular remodeling, inflammation, oxidative stress, and baroreflex dysfunction (Figure 1).[12]

Oxidative stress has an important role in the pathogenesis of hypertension and stroke as long-term complications.[12] Furthermore, inflammation has a key role in the development of secondary brain damage after stroke, and it is correlated with increased infarct size, neuronal loss, and poor clinical outcomes. The peripheral marker of inflammation, C-reactive protein (CRP), has shown a constant association with the risk of recurrent cerebrovascular and cardiovascular events in ischaemic stroke (IS) patients.[14] Lastly, baroreflex dysfunction and BP variability may substantially alter cerebral perfusion and boost perihematomal edema after an ischemic or hemorrhagic stroke. There is an inter-causal relationship among these changes, and if not interrupted, this vicious cycle might ultimately lead to stroke due to secondary morphological and functional alterations of cerebral blood vessels.[12]

Risk Assessment of Stroke

The estimation of stroke risk based on an individual's particular combination of risk factors, specifically for a first stroke event, is

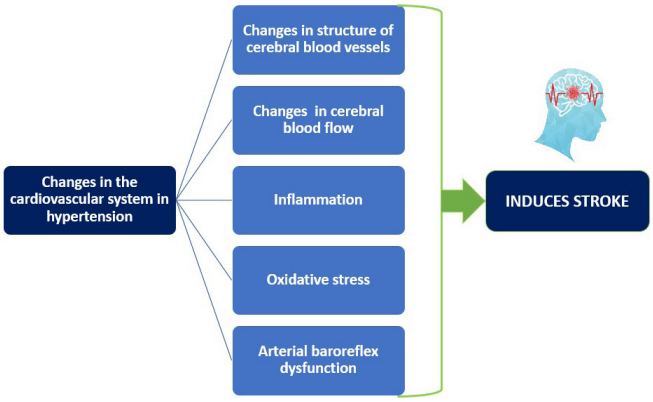

Figure 1. Mechanisms of stroke in hypertension

a crucial aspect of primary care. Certain stroke risk scores like the Framingham Stroke Risk Profile (FSRP) and the American College of Cardiology (ACC)/American Heart Association (AHA) Pooled Cohort 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimator have been developed from various sample populations.[15]

According to the Canadian Stroke Best Practice Recommendations (2020), individuals at risk of stroke and with a history of intracerebral hemorrhage (ICH) should be evaluated for risk factors of vascular diseases such as diet, sodium intake, waist-to-hip ratio, sedentary lifestyle, alcohol intake, blood pressure, and smoking.[16] For the initial clinical evaluation of ICH, a severity score based on neurological examination findings is essential. Patients withan ICH must be evaluated for underlying etiology and risk of recurrence.The evaluation of recurrent risk for an ICH must be based onclinical factors like age, hypertension, ongoing anticoagulation, and previous lacunar stroke, as well as neuroimaging. Neuroimaging would aid in detectingthe lobar location of indexICH suggestive of cerebral amyloid angiopathy, associated convexal subarachnoid hemorrhage, as well as thepresence andnumber of cerebral microbleeds and/or cortical superficial siderosis on susceptibility-weighted or gradientecho magnetic resonance imaging (MRI)sequences.[16]

Significance of Blood Pressure Control in Stroke

Appropriate blood pressure management is a keystone for the prevention of stroke. Clinical trials and observational studies have reported a reduction in the risk of first and recurrent stroke with BP-lowering therapy.[17] Also, intensive BP-lowering has been linkedtoa decrease in the combined risk of dementia and mild cognitive impairment.[17]

Optimal Blood Pressure Targets in Patients with Stroke

Generally, guideline recommendations from various countries are similar concerning the basic recommendations about management. For primary prophylaxis, hypertensive patients must be treated with antihypertensivedrugs to target a BP of <140/90 mmHg.[18] Concerning secondary prophylaxis, BP therapy is indicated for previously untreated patients with ischaemic stroke or TIA who exhibit an established BP ≥140 mmHg systolic or ≥90 mmHg diastolic after the firstfew days.Blood pressure target goals are uncertain and ought to be individualized. However, it isreasonable to achieve a systolic pressure of <140 mmHg and a diastolic pressure of <90 mmHg. Lastly, a systolic BP of<130 mmHg might be a reasonable target for patients with a recent lacunar stroke. These blood pressure levels have been recommended by various guidelines such as Hypertension Canada's 2017 guidelines, 2018 ESC/ESH guidelines for the management of arterial hypertension, and 2017 ACC/AHA/ AAPA/ABC/ ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guidelines for the prevention, detection, evaluation, and management of high blood pressure in adults.[18]

Consensus opinion 2

The benefit of BP-lowering is seen in all age groups, including elderly patients. In young individuals, it is observed as a legacy effect, while in the elderly, it is considered to be a maintenance effect. The optimum blood pressure is 130/80 mmHg, which might need adjustment in vascular stenosis in large arteries of the brain.

Primary Prevention of Stroke

A meta-analysis of 147 randomizedblood pressure difference trials reported that there was a 41% reduction in stroke for a BP-lowering of 10 mmHg systolic or 5 mmHg diastolic. The percentage reductions in stroke were comparable in individuals with and without cardiovascular disease and irrespective of BP before treatment.[19]Another meta-analysis by Ettehad *et al.* which included 54 studies on stroke, reported that a 10 mmHg reduction in systolic blood pressure decreased the risk of stroke by 27%.[20] The Hypertension in the Very Elderly Trial (HYVET) conducted by Beckett *et al.* enrolled 3,845 patients aged≥80 years and with a sustained systolic blood pressure of 160 mmHg or more to receive either Indapamide or a matching placebo.Perindopril or matching placebo was added if required to achieve the target blood pressure of 150/80 mmHg. The findings of this trial reported that active treatment enabled a 30% reduction in the rate of fatal or nonfatal stroke and a 39% reductionin the rate of death from stroke.[21]

The STEP (Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients) study was a multicentre, randomized, controlled trial that enrolled 8,511 patients with hypertension aged 60–80 years in China.[5,22] The findings of this trial established that intensiveBP treatment (systolic BP target, 110 mmHg to <130 mmHg) provided a benefit toolder hypertensive patients aged 60 to 80 years and decreased the incidence of cardiovascular events compared to standard treatment (target 130 mmHg to <150 mmHg). During a median follow-up duration of 3.34 years, the mean systolic BP was 126.7 mmHg in the intensive treatment group compared to 135.9 mmHg in the standardtreatment group. Intensivetreatment decreased the risk of stroke by 33%.[5,22]

Secondary Prevention of Stroke

With regard to the secondary prevention of stroke, intensive antihypertensive therapy has been assessed in various trials.[23-26]The Secondary Prevention of Small Subcortical Strokes (SPS3) trial was a multicentre international trial that included 3,020 patients with recent symptomatic MRI-defined lacunar infarcts. The findings of the SPS3 trial indicated that a target level of <130 mmHg systolic BP reduced intracerebral hemorrhage by 63%.[23] As per the Recurrent Stroke Prevention Clinical Outcome (RESPECT) study, intensive blood pressure control to less than 120/80 mmHg tended to decrease

stroke recurrence than standard blood pressure control (<140/90 mmHg). Intensive blood pressure treatment substantially decreased stroke recurrence by 22% as per the findings ofthe RESPECT study.[24] The PAST-BP (Prevention After Stroke Blood Pressure) randomized controlled trial reported that active BP management after stroke/transient ischaemic attack was more important than the set target.[25] Moreover, the PODCAST (Prevention of Decline in Cognition after Stroke Trial) established that in patients with recent stroke and normal cognition, intensive BP-lowering was feasible and safewithout any changes in cognition over two years.[26] Cumulatively, findings from these trials give significant evidence that a tolerable systolic BP treatment target <130 mmHgis reasonable for secondary stroke prevention.[17]

The Perindopril Protection Against Recurrent Stroke Study (PROGRESS) aimed at assessing the impact of a BP-lowering regimen in hypertensive and non-hypertensivepatients with a history of stroke or TIA in 6,105 patients.Over a follow-up period of 4 years, active treatment with aflexible regimen based on perindopril (with the addition of Indapamide at the discretion of treating physicians) reduced BP by 9/4 mmHg. The relative risk reduction (RRR)was 28%. Perindopril combined with Indapamide reduced bloodpressure by 12/5 mmHg and stroke risk by 43%. The combination of Perindopril with Indapamide enabled larger blood pressure reduction and risk reduction compared to perindopril alone.[27]

The Post-stroke Antihypertensive Treatment Study (PATS) which enrolled 5,665 patients with a history of stroke or TIA reported that a BP decrease of 5/2 mmHg with 2.5 mg Indapamide decreased the first incidence of fatal and nonfatal stroke by 29%. A three-year absolute benefit of 29 events per 1,000 participants was seen. The study established that in such patients, irrespective of the BP, a reduction of 5/2 mmHg by drug therapy decreases the incidence of total stroke.[28] A meta-analysis of 16 randomized controlled trials with 40,292 patients in total, validated that BP-lowering therapy evidently lowered the risk of recurrent stroke (RRR, 18%).[29] Also, a meta-regression analysis reported that each 10mmHg decrease in systolic BP is linked with a 33% decrease in the risk of recurrent stroke.[29] Table 1 provides an overview of the trials on primary and secondary prevention of stroke.

Consensus opinion 3

As per the experts, for primary prevention of stroke, 140/90 mmHg should be the average cut-off for the majority of adults. For high-risk adults, particularly, those with CKD, type-2 diabetes, and coronary artery disease which is revascularized, the cut-off should be 130/85 mmHg. A systolic BP below 120 mmHg in elderly individuals above the age of 60 years, results in more fractures and falls. In cases of isolated systolic hypertension, thiazide-like diuretics like Indapamide are the best drugs to be used. In cases of isolated diastolic hypertension, Chlorthalidone could be considered. At a dose of 6.25 mg, Chlorthalidone does not lower systolic BP excessively. However, it lowers the diastolic BP by 5-7 mmHg without resulting in considerable electrolyte imbalances.

Role of Antihypertensive Therapy in thePrevention of Stroke

For controlling BP, majority of the hypertensive adults ought to be treated with two or more antihypertensive drugs, combined with lifestyle modification. Drugs with complementary mechanisms of action, like a diuretic and renin-angiotensin system (RAS) blocker, are favored for combination therapy and could be given as a single-pill combination when possible.[17]

According to the Ministry of Health and Family Welfare Government of India, starting drug therapy should be considered even with Grade 1 hypertension in patients with a history of stroke or TIA. A systolic BP of <140mmHg must be targeted. An ACEI or ARB can be the initial drug of choice.[30]A fewclinical trials reporting the clinical efficacy of antihypertensive therapy in the prevention of stroke are mentioned in Table 2.[31-38]

In recent times, an important topic of interest is the interchangeability of thiazide-type diuretics hydrochlorothiazide and thiazide-like diuretics, including Indapamide and Chlorthalidone, for the treatment of hypertension. The evidence establishes that using thiazide-like diuretics is superior to thiazide-type diuretics in decreasing BP without causing an increase in the incidence of hypokalaemia, hyponatremia, and any alteration of blood glucose and serum total cholesterol.[39]

It has been shown that Indapamide is more effective in decreasing a cardiovascular outcome relative to Hydrochlorothiazide.[40]

Consensus opinion 4

Consistent withthe clinical experience of the experts, a combination of a CCB and a diuretic like Indapamide works optimally in reducing systolic BP. ACE inhibitors like Perindopril should be an integral part of the antihypertensive regimen in majority of the hypertensive patients to reducethe occurrence of fatal and non-fatal stroke. Patient tolerance with respect to ACE inhibitors and diuretics is significant. Also, they are effective in the prevention of recurrent strokes. In patients with high systolic BP, Amlodipine is quite effective. It is the most effective drug among all the CCBs but is associated with minor occurrences of pedal edema. Indapamide has been recommended by the majority of experts as the preferred thiazide-like diureticowing to itshigh efficacy in reducing systolic BP. Additionally, this drug does not causeany major electrolyte imbalances.

Hyponatremia is a very common emergency in neurology, and as per local clinical practice observations, most of these patients are prescribed Chlorothiazide. Indapamide is a vascular diuretic as it shows more antihypertensive effects compared to diuretic effects. For similar efficacy benefits, higher doses of ARBs are essential as compared to ACE inhibitors. In cases ofuncontrolled hypertension with dual-drug therapy, a treatment regimen of triple-drug therapy may be essential. An ideal triple-drug combination of antihypertensives would include a RAAS blocker, preferably an ACE inhibitor, a CCB like Amlodipine, and a thiazide-like diuretic like Indapamide.

Blood Pressure Management in Specific Patient Profiles

In cases of recent small vessel ischaemic stroke, reducing systolic BP by <130 mmHg could lower the risk of a future intracerebral hemorrhage. In cases of hemodynamically significant large artery disease, BP lowering must be done with caution as tolerated, with no specific goal other than a minimum lowering of 10/5 mmHg. In patients who develop recurrent neurologic symptoms referable to a stenotic artery when the BP is reduced below a threshold, maintaining BP above that threshold is suggested.[18]

Table 1: Overview of trials on primary and secondary prevention of stroke

Trial	Number of patients	Patient profile	Medications used	Duration of trial	Outcomes
Primary prevention of stroke					
Hypertension in the Very Elderly Trial (HYVET)[21]	3845	Patients ≥80 years with sustained SBP of ≥160 mm Hg or more	Indapamide (sustained release, 1.5 mg) [Perindopril (2 or 4 mg) was added if required]	2 years	• 30% reduction in the rate of fatal or nonfatal stroke • 39% reduction in the rate of death from stroke
STEP (Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients) study[5,22]	8511	Hypertensive patients aged 60–80 years	Olmesartan or Amlodipine as initial therapy	3.34 years	• 33% reduction in risk of stroke
Secondary prevention of stroke					
Secondary Prevention of Small Subcortical Strokes (SPS3) trial[23]	3020	Patients ≥ 30 years with a recent (≤180 days) symptomatic lacunar stroke who were without surgically-amenable ipsilateral carotid artery stenosis or major-risk cardioembolic sources	Thiazides, ACEIs/ARBs, calcium channel blockers, and betablockers	3.7 years	• Reduction in intracerebral haemorrhage: 63%
Recurrent Stroke Prevention Clinical Outcome (RESPECT) study[24]	1263	Hypertensive patients with a history of stroke	ACEIs/ARBs, thiazides, and calcium channel blockers	3.9 years	• Substantial decrease in stroke recurrence by 22%
Perindopril Protection against Recurrent Stroke Study (PROGRESS)[27]	6105	Patients with a history of stroke or transient ischaemic attack within the previous 5 years	Perindopril (4 mg daily) combined with Indapamide	4 years	• Reduction in BP by 12/5 mmHg • Reduction in stroke risk by 43%
Post-stroke Antihypertensive Treatment Study (PATS)[28]	5665	Patients with a history of stroke or transient ischaemic attack	Indapamide (2.5 mg)	2 years	• Reduction in the first incidence of fatal and nonfatal stroke by 29%

Abbreviations- BP: Blood pressure, SBP: Systolic blood pressure

Need for an ASCVD Scoring System for the Asian Population

Regional and national differences exist in the incidence and mortality of ASCVD, which are attributable to the variations in the prevalence of ASCVD risk factors andaccess to high-quality health services.[41] Race and ethnicity are vital parameters thatcan impactthe risk algorithm. The ASCVD risk algorithm was developed mainly from a White and Hispanic cohort. Hence, this calculator substantially overestimates the overall CVD risk in the non-white and non-Hispanic populations. Recent evidence from China and Korea have reported that additional correction factor or recalibration of the pooled cohort risk equation is essential to correctly estimate the short-term and lifetime CVD risk in their population.[42]

Consensus opinion 5

The ASCVD risk score does not take into account the family history of premature coronary artery disease. Also, the score appliesto individualsaged 40 years and above. As per the experts, there is a need for an ASCVD score tailored to the characteristics of the Asian population. A lower age limit would be necessary for the Asian population owing to the early onset of vascular events.

MANAGEMENT OF ACUTE STROKE

In patients with acute ischaemic stroke and elevated BP eligible to be treated with IV Alteplase, BP must be carefully lowered to a systolic BP <185 mmHg and diastolic BP <110 mmHg before starting IV

Table 2: Clinical trials on antihypertensive therapy used for the prevention of stroke

Trial	Number of patients	Patient profile	Medications used	Trial duration	Results
Nordic Diltiazem (NORDIL) study (2000)[31]	10,881	Patients aged 50–74 years with DBP of ≥100 mm Hg	Diltiazem	4.5 years	Fatal and non-fatal strokes were experienced by 159 patients in the diltiazem group and by 196 patients in the diuretic and β-blocker group (6.4 *vs.* 7.9 events per. 1000 patient-years; 0.80; p=0.04)
The Losartan Intervention For Endpoint Reduction (LIFE) study (2002)[32]	9193	Patients aged 55–80 years with essential hypertension (sitting BP 160–200/ 95–115 mm Hg) and left ventricular hypertrophy	Losartan	4.8 years	Significant reduction of 25% in the rate of fatal and nonfatal stroke while BP dropped by 30.2/16.6 mmHg.
Study on Cognition and Prognosis in the Elderly (SCOPE) [2004][33]	4,964 .	Patients aged 70-89 years with isolated systolic hypertension	Candesartan	3.6 years	BP was decreased by 22/6 mmHg and there was a 42% relative risk reduction in fatal or non-fatal stroke versus placebo.
Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA) [2005][34]	19,257	Patients with hypertension aged 40–79 years and with at least 3 other cardiovascular risk factors	Amlodipine (Perindopril was added as needed)	5.5 years	Fewer patients on the Amlodipine-based regimen had fatal and non-fatal strokes (327 vs 422; 0.77, p=0.0003) versus the atenolol-based regimen.
Antihypertensive and Lipid-Lowering treatment to Prevent Heart Attack Trial (ALLHAT) [2007][35,36]	42,418	High-risk hypertensive patients without symptomatic HF or known left ventricular ejection fraction 35%	Chlorthalidone; Amlodipine	8.9 years	Chlorthalidone had a lower risk of stroke versus Doxazosin (RR 0.84) and Lisinopril (RR 0.87). Amlodipine had a lower risk of stroke (odds ratio [OR] 0.82) versus Lisinopril.
Prevention Regimen for Effectively Avoiding Second Strokes (PRoFESS) study (2008)[37]	20,332	Patients with a recent ischemic stroke (mean BP at entry was 144.1 mmHg systolic and 83.8 mmHg diastolic)	Telmisartan	2.5 years	Telmisartan started soon after an ischaemic stroke and continued for 2.5 years did not significantly lower the rate of recurrent stroke.
Perindopril Plus Indapamide Combination Blood Pressure Reduction (PICASSO) study (2013)[38]	9257	Patients with primary hypertension who did not reach the BP goal (<140/90 mmHg) with antihypertensive therapy	Fixed-dose Perindopril 10 mg/ Indapamide 2.5 mg (switched from ongoing therapy)	3 months	Mean BP reduced from 159/93 mmHg to 132/80 mmHg in patients with uncontrolled hypertension and cerebrovascular events.

fibrinolytic therapy. Patients who are not treated with IV thrombolytic therapy will be treated with intra-arterial therapy, maintaining a BP level of ≤185/110 mmHg before the procedure is rational. For acute hemorrhagic stroke, in patients with systolic BP of 150–220 mmHg and an absence of contraindications to acute BP treatment, it is safe to lower systolic BP to 140 mmHg. It may be rational to consider aggressive BP-lowering with continuous IV infusion and regular BP monitoring in patients with systolic BP >220 mmHg and acute hemorrhagic stroke.[18] BP-lowering therapy must be considered in patients with stable neurological status, 72 hours after onset of neurologic symptoms, or immediately after a transient ischaemic attack (TIA), for formerly treated or untreated hypertensive patients, excluding patients presenting with large vessel occlusion and fluctuating clinical symptoms.[18,43] Reducing BP by 15% during the first 24 hours after the onset of stroke could be reasonable. During hospitalization, initiating or reinitiating antihypertensive therapy in neurologically stable patients with a BP of more than 140/90 mmHg is safe and rational for improving long-term BP control unless contraindicated.[43] The detailed discussion on acute stroke is beyond the scope of this article.

Conclusion

In conclusion, hypertension is a major risk factor for morbidity and mortality. Blood pressure is a critical determinant of the risk for stroke. In Indian settings, hypertension leads to many stroke-related deaths, which makes it essential to optimize its management. The benefit of BP-lowering is seen in all age groups, including the elderly. In cases of hemorrhagic strokes, rapid BP-lowering to 140 mmHg systolic is advised. Evidence strongly suggests that lowering BP to individualized target levels with antihypertensive drugs like ACEIs, diuretics, CCBs, or ARBs reduces the risk of stroke. In cases where hypertension remains uncontrolled with dual-drug therapy, a treatment regimen of triple-drug therapy may be essential. An ideal triple-drug combination of antihypertensives would include a RAAS blocker, preferably an ACE inhibitor, a CCB like Amlodipine, and a thiazide-like diuretic like Indapamide. The management of BP in patients with stroke is a challenge owing to its varied causative factors and hemodynamic consequences. Future research must emphasize optimum targets for lowering BP.

Conflict of Interest

There is no conflict of interest among the authors.

Acknowledgment

We would like to acknowledge Scientimed Solutions Pvt. Ltd. for assistance in developing the manuscript.

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How to cite this article: Nirmal Surya, Subhash Kaul, Virendra Atam, C K Ponde, S Ramesh, Mangesh Tiwaskar, T K Banerjee, Puneet Saxena, R Nandakumar. Linking Evidence-based Management in Hypertension to Real-world Experience for Preventing Stroke: An Indian Perspective. Hypertens J. 2023; 9(1): 15-22.

Source of support: Nil, **Conflicts of interest:** None