Review Article

Epidemiology, Pathophysiology, and Treatment of Hypertension in Ischaemic Stroke Patients

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Stroke continues to be one of the leading causes of mortality and morbidity worldwide. There are 2 main types of stroke: ischaemic strokes, which are caused by obstruction of the blood vessels leading to or within the brain, and haemorrhagic strokes, which are induced by the disruption of blood vessels. Stroke is a disease of multifactorial aetiology that may develop as an end state in patients with serious vascular conditions—most notably, uncontrolled arterial hypertension—thereby necessitating the effective control of this risk factor to prevent stroke or its recurrence. This paper focuses specifically on the epidemiology and pathogenesis of ischaemic stroke mainly in chronically hypertensive patients and pays particular attention to the efficacy of a select group of routinely used major antihypertensive drugs (i.e., angiotensin-converting enzyme inhibitors, angiotensin II type 1 receptor blockers, and calcium channel blockers) in the treatment of strokes. **Key Words:** Angiotensin-converting enzyme inhibitors—angiotensin II type 1 receptor blockers—calcium channel blockers—hypertension—ischaemic stroke.

Introduction

Stroke constitutes the third leading cause of mortality in the United Kingdom after coronary heart disease and cancer. Each year, approximately 140,000 people in the United Kingdom have a first stroke, and there are close to 60,000 deaths caused by stroke.[1] There are 2 main types of stroke; haemorrhagic and ischaemic. Haemorrhagic stroke involves bleeding within the brain and results from a variety of conditions including uncontrolled hypertension and aneurysms. Two types of haemorrhagic strokes exist: intracerebral and subarachnoid, which are associated with brain tissue damage emerging from the rupture of a cerebral artery within or on the surface of the brain, respectively. Similarly, there are 2 types of ischaemic stroke: thrombotic and embolic; together, the 2 types account for approximately 85% of all strokes. Thrombotic strokes usually occur at night or in the early morning and are caused by a thrombus (blood clot) forming in an artery inside or leading to the brain, chiefly as a result of atherosclerosis. Thrombotic strokes are further stratified into lacunar and nonlacunar strokes. Lacunar infarcts are small infarcts of <20 mm in diameter that are observed in the deep cerebral white matter, basal ganglia, or pons. They are thought to stem from the occlusion of a single small perforating artery feeding the subcortical areas of the brain.[2] Embolic strokes, on the other hand, occur when an embolus (a piece of intravascular itinerant object) breaks loose and travels through the bloodstream to a part of the brain that is too narrow to let it pass, thereby occluding a small cerebral artery and cutting off the blood supply to the brain. Most emboli are caused

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by atrial fibrillation, endocarditis, mitral stenosis, or atherosclerosis.

Other than being one of the main causes of mortality, stroke makes up the single most common cause of morbidity in the United Kingdom, where >250,000 people live with disabilities inflicted by stroke. Major medical complications after a stroke include cardiac problems, venous thromboembolism, pneumonia, fever, pain, headache, dysphagia, faecal and urinary incontinence, and hip fractures.[3] One-third of all stroke survivors also develop poststroke depression, which negatively affects participation in rehabilitative therapies, adherence to treatment, short-term recovery, and contributes to an increased risk of death in the poststroke period.[3,4] In terms of economic burden, stroke costs covering all direct (diagnosis, inpatient and/or outpatient cares), indirect (income loss and social benefit payments to stroke patients), and informal costs (home nursing for disabled stroke survivors) amount to approximately £9 billion per annum in the United Kingdom.[5]

Age, gender, low birth weight, race, and genetic predisposition are enumerated amongst the nonmodifiable risk factors for stroke; modifiable risk factors include hypertension, diabetes mellitus, atrial fibrillation, smoking, dyslipidaemia, sickle cell disease, carotid artery stenosis, postmenopausal hormone therapy, physical inactivity, and obesity.[6,7] This review aims to discuss and summarise the evidence regarding selectively the prevalence, pathophysiology, and treatment of hypertension in ischaemic stroke.

Epidemiology of Hypertension in Stroke Patients

Compared to all known modifiable and nonmodifiable risk factors, hypertension is more closely associated with the risk and severity of stroke. Indeed, a cohort study designed to assess the predictive value of stroke risk factors measured in midlife (47-55 years of age) and over a follow-up period extending to 28 years revealed hypertension as being a perpetually important risk factor from middle into old age. Additional risk factors apart from diabetes mellitus, including atrial fibrillation, tobacco smoking, stress, and chest pain, did not appear to be independently associated with the increased risk of stroke for the entire period.[8]

Hypertension is one of the most common significant diseases, affecting approximately 1.4 billion people worldwide. The prevalence of essential hypertension steadily increases with age. As the world population ages, the prevalence of hypertension is expected to increase even further. Despite extensive translational and clinical research, concerted patient education with regard to vascular risk factors and lifestyle modifications, and a serious effort on the part of health care professionals over the last few decades, only one third of hypertensive patients have blood pressure (BP) controlled to recommended levels of <140/90 mm Hg for uncomplicated hypertension and <130/80 mm Hg for patients with diabetes mellitus or renal disease. For those with uncontrolled hypertension, the risk of stroke is dramatically increased. In a US population–based study, the estimation of population attributable risks has revealed that 9% to 16% of all ischaemic stroke cases can be avoided by eliminating hypertension alone.[9] Table 1 shows the classification of hypertension with reference to recent recommendations of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC).[10] In light of this particular specification, a 2005 survey in the United States found that in the population aged ≥20 years, approximately 42 million men and 28 million women have prehypertension, 13 million men and 12 million women have grade 1 hypertension, and 4 million men and 7 million women have grades 2 or 3 hypertension.[11]

Pathophysiology of Hypertensive Stroke

The role of hypertension in the pathogenesis of stroke is complex and multifaceted. Chronic hypertension contributes to the pathogenesis of stroke via the initiation and acceleration of intracerebral vasculopathy. Hypertension also facilitates the development of a full-blown stroke through the promotion of microatheroma or lipohyalinosis in small arteries and atherosclerotic disease in medium to large arteries.[12,13] Microatheroma is typically defined by the infiltration of lipid-laden macrophages and subintimal cholesterol deposits in small-sized cerebral arteries between 300 μm and 700 μm in diameter. The extent of vascular occlusion in these arteries is further exacerbated by endothelial cell proliferation and smooth muscle cell hypertrophy. Lipohyalinosis constitutes the main pathologic change in cerebral arteries of diameters <200 μm and is associated with sustained arterial hypertension and microaneurysmal dilatation.[13] Atherosclerotic plaques form in the regions of the vascular system with perturbed flow and are characterised by subendothelial lipid deposits, smooth muscle layer thickening, leukocyte infiltration, and the accumulation of collagen in the vascular

Table 1. *Classification of blood pressure*

	Blood pressure (mm Hg)	
Category	Systolic	Diastolic
Normotension		
Desirable	<120 and	<80
Normal	120-139 and/or	80-89
Hypertension		
Grade 1 (mild)	140-159 and/or	90-99
Grade 2 (moderate)	160-179 and/or	100-109
Grade 3 (severe)	≥180 and/or	≥110