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REVIEW

Management of hypertension in low and middle income countries: Challenges and opportunities

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Summary Hypertension is one of the most important risk factors for cardiovascular morbidity and mortality. More than a quarter of the global adult population (972 million) is currently hypertensive and almost three quarters (639 million) live in developing countries. Hypertension management therefore is of great public health importance in the developing world. In this paper, we review screening, diagnosis and management using lifestyle measures and pharmacotherapy given the resources of developed nations. We then discuss the barriers and challenges to implementing this approach and what can be done regarding prevention, screening, lifestyle modification and pharmacotherapy in developing countries. By adopting a comprehensive population based approach including policy level interventions directed at promoting lifestyle changes; a healthy diet (appropriate calories, low in saturated fats and salt additives and rich in fruits and vegetables), increased physical activity, and a smoke free environment, properly balanced with a high risk approach of cost effective clinical care, developing countries can effectively control hypertension and improve public health. Existing scientific knowledge regarding prevention, treatment and management should be harnessed as a health priority to reduce the disease burden associated with uncontrolled hypertension.

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Introduction

Cardiovascular diseases (CVDs) including strokes are the leading cause of death and disability world wide and in 2005 accounted for about 17.5 million deaths, and 30% of global mortality. About 80% of the deaths occur in developing countries [1]. Hypertension or high blood pressure is the most common risk factor for CVD morbidity and mortality accounting for 7.1 million deaths globally [1]. More than a quarter of the world adult population, 972 million, is currently hypertensive and this figure is projected to rise to 29%, 1.56 billion by 2025. Hypertension is important not only for its high prevalence but also because it is a major modifiable risk factor for cardiovascular and kidney disease. Disconcertingly, almost three quarters of the global population with hypertension (639 million) live in developing countries, which contributes to widening of existing global health disparities [1,2].

Furthermore, the onset of CVD is at an earlier age in developing countries and consequently the age at which people die of CVD is considerably younger than in developed countries, leading to widespread social and economic hardship. In India, an estimated 52% of CVD deaths occur below the age of 70 compared with 23% in developed countries [3]. In the past few decades CVD morbidity and mortality rates have been declining in most developed countries while it has been increasing in developing countries, especially the most populous ones such as China and India [4]. Moreover, the rapidly increasing incidence of diabetes in developing countries of Asia (e.g. India 57.2 million by 2025, China 57.2 million by 2025), Africa (8.3 million by 2025) and Latin America and Caribbean (39.3 million by 2025) [5] and its coexistence with hypertension will further augment the severity of renal, cerebrovascular and cardiac morbidity and mortality [6,7].

Hypertension management therefore is of great public health importance in the developing world, which currently is faced with the dual challenge of concurrently combating communicable diseases and the emerging epidemic of chronic non-communicable diseases. In this paper, we review screening, diagnosis and management using lifestyle measures and pharmacotherapy given the resources of developed nations. Secondly, we will discuss the barriers and challenges to implementing this approach and what can be done regarding prevention, screening, lifestyle modification and pharmacotherapy in developing countries.

Screening and diagnosis

Proper diagnosis with accurate measuring devices is an important first step in the management of hypertension. Screening ideally not only detects hypertension but also provides an opportunity for patient education and therapy [6]. In light of the growing epidemic of CVD in the developing world, a number of world bodies including WHO recommend that opportunistic screening of blood pressure is done at every visit to the physician's office [8].

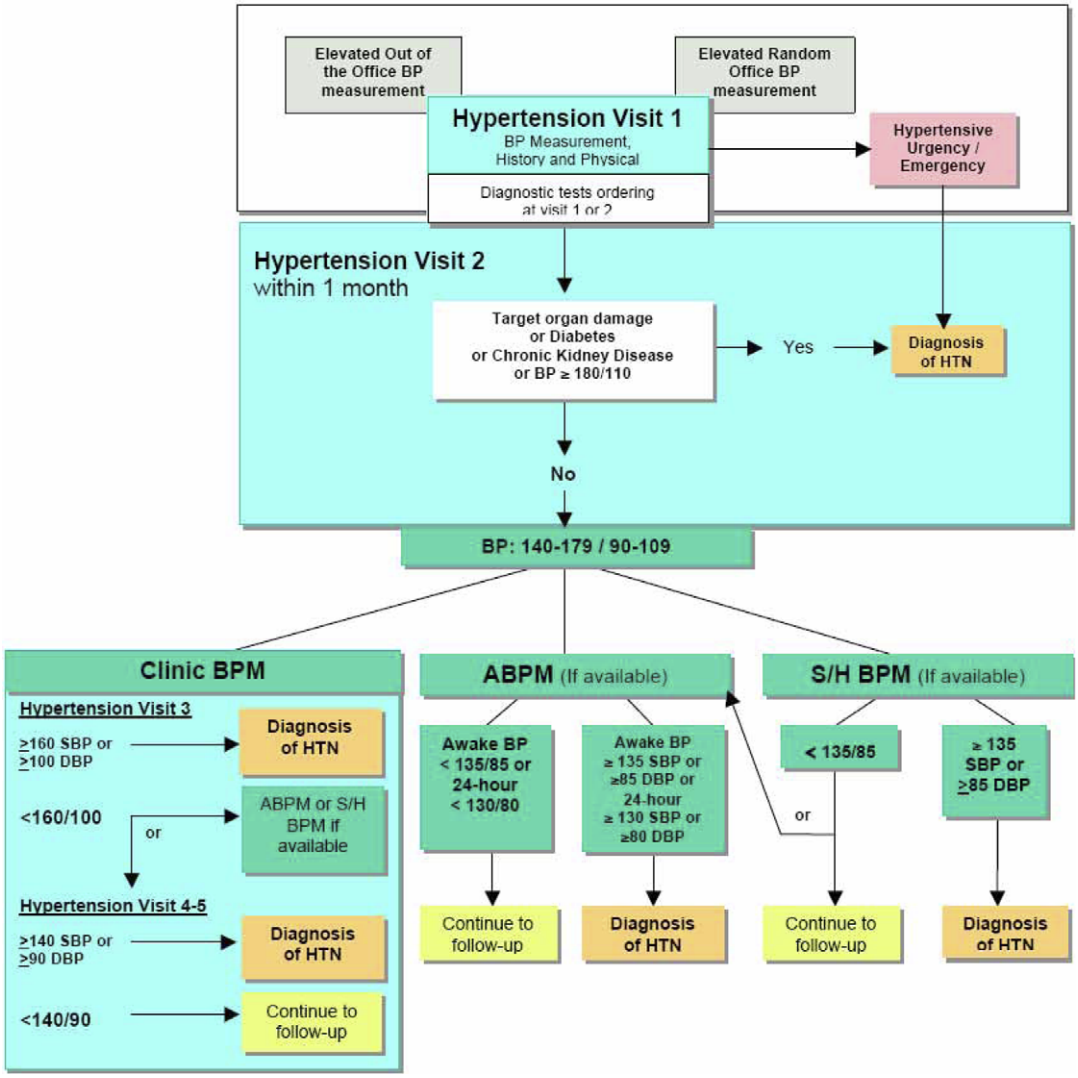

Figure 1 The diagnostic algorithm for hypertension recommended by the Canadian Hypertension Education Program. Reproduced with permission of the Canadian Hypertension Education Program. BPM — blood pressure measurement; ABPM — ambulatory blood pressure measurement; and S/H BPM — self/home blood pressure measurement.

The diagnosis of hypertension should not be made on one single measurement in a physician's office. If the blood pressure is elevated the individual must have the elevated blood pressure reconfirmed at subsequent visits unless there is a hypertensive emergency or urgency [9]. Fig. 1 shows an algorithm for diagnosis of high blood pressure [10].

Assessment of risk

Management of hypertension should be based on global risk assessment considering other concomitant cardiovascular risk factors. Global risk assessment is an important tool to assist physicians and other health care providers to identify hypertensive individuals who are most likely to benefit from management including pharmacotherapy [10]. Well-established models are Framingham [11], CV life expectancy [12] and SCORE [13]. Consideration should be given to lipid lowering therapy and aspirin in patients at high cardiovascular risk [10,14].

Management with lifestyle modifications

Lifestyle modification, is beneficial for both non-hypertensive and hypertensive individuals [15]. When applied on a population-wide basis, lifestyle modification has the potential to reduce cardiovascular risk beyond lowering blood pressure. For patients with hypertension and other cardiovascular

Table 1 Lifestyle modification recommendations to reduce blood pressure

- Maintaining a diet low in salt and saturated fats and high in fresh fruit and vegetables and low fat dairy products (DASH diet)
- 30—60 min of continuous or accumulated moderate intensity dynamic exercise (walking, as well as jogging, cycling or swimming) 4—7 days of the week will lower blood pressure
- Weight reduction in those who are overweight
- Reduction in alcohol consumption in those who drink more than two drinks/day
- Smoking cessation to reduce global cardiovascular risk

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risk factors such a hyperlipidemia, obesity and diabetes, lifestyle measures are even more important [10,16]. Table 1 summarizes the recommendations on lifestyle management of hypertension [17—47].

Thresholds for therapy

Several trials have shown that certain groups of high-risk patients benefit from blood pressure reduction by pharmacotherapy regardless of their blood pressure [48—50]. This includes patients with overt atherosclerotic vascular disease (e.g. past myocardial infarction or ischemic heart disease, stroke or transient ischemic attack), patients with congestive heart failure and patients with diabetes plus additional cardiovascular risks factors. In patients without any additional cardiovascular risks, drug therapy should be initiated if the blood pressure is sustained above 160 mmHg systolic or 100 mmHg diastolic [10]. For patients with additional risk factors treatment can be initiated for sustained blood pressure greater than 140 mmHg systolic or for diastolic blood pressure greater than 90 mmHg. For patients with diabetes or renal disease, treatment should be initiated if the blood pressure is sustained greater than 130 mmHg systolic or 80 mmHg diastolic. The thresholds for systolic blood pressure in patients with risk factors or with diabetes or renal disease are based largely on expert opinion, while the other thresholds are based on entry criteria to large randomized controlled trials.

Blood pressure targets during pharmacotherapy

In most patients blood pressure should be lowered to less than 140 mmHg systolic and less than 90 mmHg diastolic [10]. For patients with renal disease or with diabetes, the blood pressure target is less than 130 mmHg systolic and less than 80 mmHg diastolic.

Initial pharmacotherapy of uncomplicated hypertension

The reduction in cardiovascular events in uncomplicated hypertension is dependant on the degree of blood pressure lowering and not on the specific blood pressure medication class used to lower blood pressure [10,51—53]. Initial therapy should be selected from classes of drugs proven to reduce cardiovascular events including low dose thiazide type diuretics, beta blockers in patients under age 60, angiotensin converting enzyme (ACE) inhibitors, long acting calcium channel blockers (CCBs) and angiotensin receptor blockers (ARBs). Beta-blockers should not be selected as initial therapy in those over age 60 as they are less effective in the elderly [10,54—56]. Most patients require combinations of lifestyle modification plus two or more antihypertensive medications to achieve current blood pressure targets.

Patients with compelling indications for specific pharmacotherapy

Table 2 outlines initial therapeutic options for patients with specific indications for pharmacotherapy. Dyslipidemia and left ventricular hypertrophy do not modify the recommendations for initial therapy [10].

Management using polypill

Polypill refers to use of a single pill containing six components (thiazide diuretic, ACE inhibitor, beta blocker, statin, aspirin and folic acid) to reduce major risk factors (lipids, blood pressure, homocysteine and platelet function) for primary and secondary prevention of CVDs. The underlying assumption being that these components will have a synergistic treatment effect and combination therapy would be superior to monotherapy [57]. Even if a low cost

Table 2 Considerations in the individualization of antihypertensive therapy

	Initial therapy	Second-line therapy	Notes and/or cautions
Hypertension without compelling indications for other medications	Thiazide diuretics, beta blockers (for patients under 60 years), ACE-inhibitors (in non-blacks), ARBs, or long-acting CCBs (consider ASA and/or statins in selected patients)	Combinations of first-line drugs	Alpha-blockers are not recommended as initial monotherapy. Beta-blockers are not recommended as initial monotherapy in those over 60 years of age. Hypokalemia should be avoided in those who are prescribed diuretics. ACE inhibitors are not recommended as initial monotherapy in blacks. ACE inhibitors and ARBs are contraindicated in women of child bearing potential
Isolated systolic hypertension without other compelling indications	Thiazide diuretics, ARBs, or long-acting dihydropyridine CCBs	Combinations of first-line drugs	Hypokalemia should be avoided in people who are prescribed diuretics
Diabetes mellitus with nephropathy	ACE inhibitors or ARBs	Addition of one or more of thiazide diuretics, cardioselective beta-blockers, long-acting CCBs or use of an ARB/ACE inhibitor combination	
Diabetes mellitus without nephropathy	ACE inhibitors, ARBs, or thiazide diuretics or long acting dihydropyridine CCBs	Combination of first-line drugs or addition of cardioselective beta-blockers and/or long-acting CCBs	
Angina	Beta-blockers (strongly consider adding ACE inhibitors)	Long-acting CCBs	Avoid short-acting nifedipine
Prior myocardial infarction	Beta-blockers and ACE inhibitors (ARBs if ACE intolerant)	Combinations of additional agents	
Heart Failure	ACE inhibitors (ARBs if ACE inhibitor intolerant), beta-blockers, and spironolactone in selected patients	Hydralazine/ isosorbide dinitrate; thiazide or loop diuretics as additive therapy	Avoid nondihydropyridine CCBs
Past cerebrovascular accident or TIA	ACE inhibitor/diuretic combinations		Blood pressure reduction reduces recurrent cerebrovascular events
Chronic kidney disease	ACE inhibitors (diuretics as additive therapy)	Combinations of additional agents (ARBs if ACE inhibitor intolerant)	Avoid ACE inhibitors and ARBs if bilateral renal artery stenosis

(*continued on next page*)

Table 2 (*continued*)

	Initial therapy	Second-line therapy	Notes and/or cautions
Left ventricular hypertrophy	ACE inhibitors, ARBs, CCBs, thiazide diuretics (beta-blockers for patients under 60 years)		Avoid hydralazine and minoxidil
Peripheral arterial disease	Does not affect treatment recommendations		Avoid beta-blockers with severe disease
Dyslipidemia	Does not affect treatment recommendations		

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polypill using generic components is available, it would still be unaffordable to most in developing countries. For instance, a conservative estimate of the median annual retail cost of the standard polypill for CVD prevention in India was reported to be 4383 Indian Rupees or US$100, [58] which compares disproportionately to the per capita income of US$440 in India [68]. Even though this might appear to be low in comparison to developed countries, other associated expenses such as hospital costs, consultant's fees, and investigation costs would substantially increase costs, making the polypill economically unviable [58]. Thus, it might be useful for secondary prevention in those with pre-existing CVD and increasing adherence in high risk patients rather than for primary prevention efforts and broad population level application in countries with limited resources.

Barriers, challenges and potential solutions in developing countries hypertension management gap

Despite convincing evidence about the benefits of lowering blood pressure and existence of national and international guidelines on detection and management, management of hypertension has remained suboptimal. Less than a third of hypertensive patients receive recommended levels of treatment even in resource rich developed nations [59]. Low levels of awareness and inadequacy of treatment are of an even greater magnitude in the developing world [60—64]. In Chennai, India among the 22.8% of adult male and 19.7% of adult female hypertensives, only 8.3% and 8.2%, respectively, were aware of their hypertensive status and just 3.8% and 4.4% were on treatment [61]. Similar results have been reported in sub continental Asia [62]. In China, where hypertension prevalence is on the rise, similar findings of low overall awareness (43%), under treatment (31%) and inadequate control (6%) of hypertension were reported [63]. In Africa, which accounts for one sixth of the global population, control rates of hypertension have been reported to be as low as 2% [64]. This underscores the large gap between available evidence and clinical practice that could be improved to reduce the widespread health consequences of uncontrolled hypertension [65,66], particularly in the developing world.

Health system barriers

A major impediment to effective detection, management and control of hypertension in the developing world is the constrained, ill equipped and low capacity of the public health systems [67,68]. Much of public health systems is still directed towards communicable diseases. National policies to combat the emerging epidemic of chronic diseases including hypertension are virtually absent and developing countries spend a low proportion of their resources on health care.

Need for context specific guidelines

The absence of specific national hypertension treatment guidelines based on country specific circumstances also adds to the challenges in hypertension management. The development of BP guidelines for sub-Saharan Africa could serve as an example for developing countries [69]. The absence of treatment guidelines in most developing countries is accentuated by the sale of drugs without prescription by providers who may not have adequate qualifications or who have financial incentives for certain prescribing patterns. For instance in India, up to 70% of drug expenditures was reported to be unnecessary [70].

Existing state of the art guidelines such as the Canadian Hypertension Education Program (CHEP), which is a dynamic therapeutic knowledge translation program, that annually updates evidence-based hypertension management recommendations and has an extensive implementation program designed to enhance guideline uptake, are a potential ideal. But they are very unlikely to be directly relevant or feasible for implementation in most developing countries. However, such guidelines could provide invaluable insights and a scientific literature review for developing countries, that they could leverage while developing their context specific national guidelines.

Economic impediments

Multiplicity of health care providers including alternative care givers, lack of capacity and affordability of physician services in most developing countries adversely impacts hypertension care. Patients often pay out-of-pocket for their health care (up to 80% of total spending on health In India) [67,68]. Besides imposing considerable economic burden, this often drives many families into poverty particularly those with chronic conditions such as hypertension requiring life long care. Consequently, many forgo treatment altogether or become non-adherent. Studies from India have reported that up to a quarter of the 17% of rural residents, who did not seek care, cited financial reasons while in China 30% of poor households attributed their poverty to health care costs [68,69].

Recommendations

Developing countries cannot afford the resource intensive management of established hypertension and associated CVD that has been shown to be of limited success even in developed countries [6,71,72]. Substantially, greater gains in population health can be achieved by even a modest lowering of the population mean blood pressure. Such gains could be sustainable over time and can yield greater reductions in associated CVD events. Therefore, the major thrust of management of hypertension in such settings should be on primary prevention efforts through a comprehensive population based approach directed at lifestyle changes (a healthy appropriate calorie diet (low in saturated fat and salt additives and rich in fruits and vegetables), increased physical activity, and a smoke free environment), properly balanced with a high risk approach of cost effective clinical care. The health care delivery system needs to emphasize early detection and treatment of individual patients at high risk with the most cost effective drugs.

Comprehensive population approaches based on low cost strategies of risk factor modification from developed nations like USA, UK, and Finland [73—75] as well as developing nations such as Mauritius, China, Poland and Cuba [76—79] provide good models that can be adopted and applied with appropriate country specific modifications. Mass screening is not usually economically viable nor sustainable, therefore opportunistic screening within the existing health system during routine consultation with a health care provider should be utilized for blood pressure measurement. Adequate risk screening could be based on simple assessment of age, sex, immediate family history of CVD, measured blood pressure, waist and hip circumference, tobacco use, alcohol use and past CVD events. This approach requires no additional material resources. Low cost risk reduction strategies such as brief intervention for tobacco cessation, nutritional advice for a healthy diet (a diet low in salt additives, saturated fats and alcohol and increased in fruit and vegetables) and increased physical activity could be integrated without much difficulty and resources into existing public health systems.

Existing networks of primary health care centres in developing nations should be optimally utilized and categories of healthcare providers, who can detect, educate and monitor hypertensive patients can be expanded to include nurses and multi purpose health workers. Though the current networks focus primarily on communicable diseases and reproductive health, networks could be used for opportunistic screening for hypertension and CVD risk assessment. A good model in optimal use of existing services for hypertension management was reported from South Africa, where a nurse-led clinical protocol based in primary care clinics succeeded in achieving hypertension control in 68% of patients [80].

Policy interventions

Policy-level interventions are effective in bringing about substantial population-wide behavioral change and risk reduction. Policy change helps create enabling environments for making healthy choices. National legislation directed at reducing the addition of salt to foods and appropriate content labeling is a cost effective policy that needs to be implemented globally as a priority. Healthy

foods, particularly fresh fruits and vegetables need to be easily available and affordable while production and marketing of unhealthy foods should be regulated and taxed. As policy interventions will have limited success if the community is unwilling to accept them, the top—down approach of enabling legislation and regulation must be complemented by a bottom—up approach of community mobilization through health education and promotion. This can be accomplished through community empowerment focused on enhancement of knowledge, motivation and skills. Policies should also address urban planning to provide adequate safe spaces and recreational areas for promoting physical activity and recreation. Governmental policies directed at tobacco control including effective implementation and enforcement of landmark global public health agreements such as the Framework Convention on Tobacco Control (FCTC) and the Global Strategy on Diet, Physical Activity and Health, are also of utmost importance and could make a huge impact on hypertension prevention and control. For example if government policy or regulations to reduce salt additives to food reduced diastolic blood pressure by 2 mmHg this could reduce the prevalence of hypertension by 17% and reduce strokes by 15% [81].

Conclusion

Hypertension is a major cause of CVD morbidity and mortality in developing countries and presents an important opportunity to improve public health. Adequate scientific knowledge exists regarding prevention, treatment and management to reduce the disease burden associated with uncontrolled hypertension. Important initiatives that require consideration include organization of medical societies in developing nations to create region specific management recommendations, a sharing of knowledge, expertise and tools by developed nations and development of national policies and regulations to facilitate healthy environments.

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