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Review Article

A REVIEW ON CAUSES AND MANAGEMENT ON HYPERTENSION

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ABSTRACT

Self-reported incident hypertension was defined as not having physician-diagnosed hypertension nor taking antihypertensive medications at baseline and reporting a diagnosis / treatment of hypertension at follow-up. High-risk categories for six lifestyle risk factors were defined as: a BMI ≥ 25 kg/m^2, physical activity levels <150 min/week, consuming ≥14 alcohol drinks/week, being a current smoker, consuming <2 fruit and/or <3 vegetable serves/day, and being at high risk of psychological distress (Kessler-10 score ≥ 22). The association between baseline risk factors. The present review gives an overview on complications of hypertension in AS, how these can be diagnosed, and potentially may be managed. Expert commentary: Hypertension-mediated cardiovascular damage in AS is associated with increased morbidity and a 2-fold higher mortality even in asymptomatic patients, and also limits the symptomatic and survival benefit from valve replacement. Data from registries and post-hoc analyses from outcome studies in AS suggest that treatment with angiotensin converting enzyme inhibitors, angiotensin receptor blockers and β-blockers, respectively, is safe and associated with improved survival and reduced cardiovascular events in these patients. However, optimal blood pressure target in AS patients is not documented.

Key Words: *Hypertension, stroke, beta-blockers, ACE inhibitors, thiazides, metoprolol, diltiazem, verapamil.*

INTRODUCTION

Hypertension is one of the leading causes of global burden of disease. Approximately 7.6 million deaths (13 to 15% of total) and 92 million disability-adjusted life years worldwide were attributable to high blood pressure in 2001. Hypertension doubles the risk of cardiovascular diseases, including coronary heart disease (CHD), congestive heart failure (CHF), ischemic and haemorrhagic stroke, renal failure and peripheral artery disease. In a few patients, markedly elevated levels clearly indicate serious disease requiring immediate treatment. However, in most cases, initial readings are not high enough to indicate immediate danger, and the diagnosis of hypertension should be substantiated by repeated readings. The reason for such caution is obvious: The diagnosis of hypertension imposes psychological and socioeconomic burdens on an individual and usually implies the need for commitment to lifelong therapy.

Both transient and persistent elevations in pressure are common when it is taken in the physician office or hospital. To identify "white coat" hypertension, more widespread use of out of the office readings, either with semiautomatic inexpensive devices or with automatic ambulatory recorders, is encouraged both to establish the diagnosis and to monitor the patient's response therapy[1]. A large body data provides normal ranges for home self-recorded[2] and autonomic ambulatory measurements [3], both average about 10/5 mmhg lower than the average of multiple office readings. A closer correlation between the presences of various type of target organ damage especially left ventricular hypertrophy (LVH), carotid wall thickness, proteinuria, and retinopathy, has been noted with ambulatory levels than with office levels[4].

Hypertension in special group:

Blacks: Although, on average, blood pressure in blacks is not higher than that in whites during adolescence[5], adult blacks have hypertension more frequently, with higher rates of morbidity and mortality. These higher rates may reflect a higher incidence of low birth weight from intrauterine growth retardation[6], a lesser tendency for the pressure to fall during sleep[7], greater degree of LVH [8], and impaired NO- induced vasodilatation[9], but lower socioeconomic status and lesser access to adequate, health care of blacks as a group are probably more important[10]. In particular, blacks suffer from renal damage, even with effective blood pressure control, which leads to a significantly greater prevalence of end- stage disease[11]. When given a high sodium diet, most blacks but not whites tend to have renal vasoconstriction[12]. And increase in glomerulofiltration rate (GFR)[13]. Thus providing a possible mechanism for increased glomerular sclerosis[13].

Women: Women suffer less cardiovascular morbidity and mortality than men do for any degree of hypertension[14]. Moreover, before menopause, hypertension is less common in women than men, perhaps reflecting the lower blood volume afforded women by menses. However, more women than men have a hypertension- related cardiovascular complication because there are more elderly women than elderly men and hypertension is both more common and more dangerous in elderly[15].

Causes of hypertension:

Acute Glomerulonephritis	Chronic Nephritis	Polycystic disease
Diabetic nephropathy	Hydronephrosis	Renal artery stenosis
Intrarenal vasculitis	Acromegaly	Hypothyroidism
Hyperthyroidism	Hypercalcemia	Cushing syndrome
Primary aldosteronism	Congenital adrenal hyperplasia	Pheochromocytoma
Extraadrenal chromaffin tumors	Estrogen	Glucocorticoids
Mineralocorticoids	Coarctation of the aorta	Pregnancy induced hypertension
Brain tumor	Encephalitis	Respiratory acidosis
Sleep apnea	Quadriplegia	Acute porphyria
Familial dysautonomia	Lead poisoning	Guillain barr'e syndrome
Psychogenic hyperventilation	Burns	Pancreatitis
Alcohol withdrawl	Sickel cell crisis	Aortic volvular insufficiency
Arteriovenious fistula	Patent ductus arteriousis	paget disease of bone
Beriberi	Hyperkinetic circulation	

Hypertensive crisis:

A number of clinical circumstances may require rapid reduction of blood pressure. These circumstances may be separated into emergencies, which require immediate reduction of blood pressure (within 1 hour) and urgencies, which can be treated more slowly. A persistent diastolic pressure exceeding 130 mmHg is often associated with acute vascular damage; some patients may suffer vascular damage from lower level of pressure.

Secondary hypertension:

Among the large number of people with hypertension, it is helpful to know whether some secondary process- perhaps curable by surgery or more easily control by specific drugs. Most survey determines the relative proportions of various secondary diseases are biased as a result of the selection process, with only the increasingly suspect population. Thus, estimates as high as 20% for the certain secondary form of hypertension have been reported. Estimates more likely to be indicative of the situation in usual clinical practice[16-18].

Screening for secondary hypertension:

Because of relatively low frequency of various secondary diseases, the clinician should be selective in carrying out various screening and diagnosis tests. The presence of features inappropriate for the usual

uncomplicated primary hypertension is an indicated for additional tests. However, for the 9 in 10 hypertensive patients without these features, a haematocrit, urine analysis, automated blood biochemical profile (including plasma glucose, potassium, creatinine, and total and high density lipoprotein cholesterol) and electrocardiogram are all that is required.

Natural history of untreated hypertension:

A meta-analysis of nine major prospective observational studies involving 420,000 individual free of known coronary or cerebral vascular disease at baseline who were monitored for 6 to 25 years (mean of 10 year) shows a "direct, continuous and apparently independent association" of diastolic blood pressure with both stroke and coronary heart disease[19]. The data indicate that prolonged increases in the usual diastolic pressure of 5 to 10 mmHg were associated with at least 34 to 56 percent increases in stroke and with at least 21 and 37% increases in coronary heart disease risk, respectively.

Symptoms and signs:

Uncomplicated hypertension is almost always asymptomatic; a person may be unaware of the consequent progressive cardiovascular damage for as long as 10 to 20 years. Only if blood pressure is measured frequently and people are made aware that hypertension may be harmful even if asymptomatic will the majority of people with unrecognized or inadequately treated hypertension be managed effectively. Symptoms often attributed to hypertension- headache, tinnitus, dizziness, and fainting may be observed just as commonly in the normotensive population. Moreover, many symptoms attributed to the elevated blood pressure are psychogenic in origin, often reflecting hyperventilation induced by anxiety over the diagnosis of a lifelong, insidious disease that threatens wellbeing and survival [20]. Even headache, long considered a frequent symptom of hypertension, is poorly related to level of blood pressure, as noted 10 to 20% of those of diastolic blood pressure levels from below 90 to above 120 mmhg[21].

Role of oral contraceptive (OCP) induced hypertension and its mechanisms of hypertension:

Estrogen-containing oral contraceptive pills are probably the most common cause of secondary hypertension in young women. most women who take them experience a slight rise of blood pressure, and hypertension develops in about 5%(i.e. blood pressure above 140/90 mmHg) within 5-year oral contraceptive use. This incidence is more than twice that seen among women of the same age who do not use these agents. Although the mild hypertension is usually mild, it may persist after oral contraceptive use is discontinued, it may be severe, and it is almost certainly a factor is increased cardiovascular mortality seen among the young women who take these agents[22]. In USA at a rate equal to that noted among American men. Moreover, the risks appeared to have been lessened by more careful selection of users and lowers doses of hormones[23]. Most adverse effects occur in women who smoke and have other cardiovascular risk factor and who take formulation with more than 50mcg of estrogen.

Incidence of OCP induced HTN:

The incidence of hypertension was 2.6 times greater among 23,000 pills users than 23,000 nonusers, with pills users having a 5 percent incidence over 5 years oral contraceptive use[24]. In addition, this incidence increased with longer duration of pills use, being only slightly higher than that in controls during the first year but rising almost 3 times higher by fifth year. In a much smaller, but more carefully performed, prospective study of 186 Scottish women, systolic pressure rose in 164 (by more than 25 mmHg in 8) and diastolic pressure rose in 150 (by more than 20 mmHg in 2) during the first two years' oral contraceptive in use[25].

Mechanism of OCP induced hypertension:

Oral contraceptive use probably causes hypertension by volume expansion since both estrogen and the synthetic progesterone used in oral contraceptive pills cause sodium retention. Although plasma rennin level rise in response to increased level of angiotensinogen, angiotensin- converting enzyme(ACE) inhibition did not alter blood pressure any more in women with oral contraceptive induced hypertension[26] .In keeping with the probable role of hyperinsulinemia in other hypertensive states, hyperinsulinemia may be involved oral contraceptive induced hypertension as well because plasma insulin levels are increased after the start of oral contraceptive use, a finding reflection of peripheral insulin resistance[27].

Treatment and Management of Hypertension:

A. Benefit of Therapy: The treatment of hypertension is aimed not at simple reduction of blood pressure but at prevention of the cardiovascular complications that are known to accompany the high pressure. During the past 30 years, many randomized, control trials (RCTs) have tested the ability of antihypertensive drugs- primarily diuretics and adrenergic inhibitors to prevent strokes and heart attacks. Although the RCTs have limited ability to aid in clinical decisions about the individual patients [28], few other aspects of clinical practice have as strong an evidence base as does the treatment of hypertension. A series of eta-analysis have portrayed the effects of therapy in the progressively enlarging number of completed trials[29-31]. They have shown a uniform and persistent reduction in morbidity and mortality from stroke averaging 40%, a reduction that exactly fits that was predicted from epidemiological evidence if the attributable risk had been completely reversed[32].

B. Threshold for therapy: Systolic pressure in elderly- "generally have a higher absolute risk of cardiovascular disease and therefore derive greater benefit from treatment"[33]. The elderly achieved even greater protection from coronary disease in three trials. Furthermore, protection from congestive heart failure was even more impressive, therapy during the incidence by over 50 %[34,35].

C. Goal of therapy: Most physicians assumed that the effects of reduction of blood pressure on the cardiovascular risk would fit straight line downward [36]. Justifying the opinion "the lower, the better" however as noted, data from large trials indicated a more gradually decline in risk when pressures were reduced to moderate levels, DBP approximately 95 mmHg in the IPPPSH trial[37]. Subsequently, Cruick-shank[38] called attention to J curve, reflecting a progressive fall in risk of pressure is lowered, but only to a

certain level; below that level, the risk for coronary ischemic events rises again.

D. Life style modifications:

1. **Avoidance of tobacco:** The major pressure effect of tobacco is easily missed because patients are not allowed to smoke in places where blood pressures are recorded. With automatic monitoring, the effect is easy to demonstrate[39], and blood pressure immediately falls when smokers quit[40].
2. **Weight reduction:** Relatively small increases in body weight increase the incidence of hypertension[41], and even small decreases in excess weight lower blood pressure[42]. A 1kg decrease in body weight was accompanied by an average reduction of 1.6/1.3 mmHg in blood pressure[43].
3. **Dietary sodium restriction:** By cutler and colleagues of 32 well-controlled intervention studies in which daily intake (based on urinary sodium excretion) was reduced by a median of 77 mmol/24 hours, blood pressures fell an average of 4.8/2.5 mmHg hypertensive individual[44]. There is probably a dose- response relation – the more sodium reduction, the greater the blood pressure decline. In a small but well controlled study, the reduction in the blood pressure was shown to be 8/5 mmHg on the daily sodium intake of 100mmol and 16/9 mmHg on a 50 mmol/day intake [45].

E. Antihypertensive Drugs Therapy: Drugs therapy is recommended for individuals with blood pressures > or equal to 140/90 mmHg. The degree of benefit derived from antihypertensive agents is related to the magnitude of the blood pressure reduction. Lowering systolic blood pressure by 10 – 12 mmHg and diastolic blood pressure by 5- 6 mmHg confers relative to risk reduction of 35 to 45% stroke and 12 to 16% CHD with 5 years of initiation of treatment.

Diuretics: Diuretics useful in the treatment of hypertension may be divided into four major groups by their primary site of action within the tubule, starting in the proximal portion and moving into collecting duct [46a,b],clinical effects with continuous diuretic therapy, blood pressure usually falls about 10 mmHg, although the degree depends on various factors, including the initial height of the pressure, the quantity of the ingested, the adequacy of the renal function, and the intensity of counter regulatory rennin aldosterone response [47a].The antihypertensive effect of the diuretic persists indefinitely, although it may be overwhelmed by dietary sodium intake exceeding 8 gm/day.

Thiazides: bendroflumethiazide, benzthiazide, chlorothiazide,cyclothiazide, hydrochlorothiazide, hydroflumethiazide etc.

Related sulfonamide compounds: chlorthalidone, indapamide, metolazone, quinethazone.

Loop diuretics: bumetanide,ethacrynic acid, furosemide,torsemide.

Potassium sparing agents: Amiloride, spironolactone, triamterene.

Adrenergic Inhibitor:

Methlydopa: The primary site of action of methyldopa is within the central nervous system, where alpha-methlynorepinephrine, derived from methyldopa, is released from adrenergic receptors, reducing the sympathetic outflow from the central nervous system[48]. The blood pressure mainly falls as a result of a decrease in peripheral resistance with little effect of cardiac output.

Clonidine: As an alpha – adrenergic receptor agonist, the drug also acts on presynaptic alpha receptors and inhibits norepinephrine release, and plasma catecholamine levels fall [49].

Alpha – Adrenergic Receptor antagonists: Phenoxybenzamine and phentolamine are effective in acutely lowering blood pressure, but their effects are offset by an accompanying increase in cardiac output and side effect and frequent and bothersome. These drugs blockade of presynaptic alpha – adrenergic receptors, which interferes with feedback inhibition norephinephrine release.

Prazosin: First group of selective antagonists of the postsynaptic alpha1 receptors. By blocking alpha mediated vasoconstriction,prazosin induces a decline in the peripheral resistance with both venous and arterial dilation.

Beta – Adrenergic Receptors Antagonists: Beta- adrenergic receptors blockers become the most popular form of antihypertensive therapy after diuretics, reflecting their relative effectiveness and freedom from many bothersome side effects. Beta- blockers have been found to reduce mortality if taken either before or after acute myocardial infarction [50] (i.e. secondary prevention), it was assumed that they might offer special protection against initial coronary events, i.e., primary prevention. However, in four large clinical trials, beta blockers provided less protection than did a low dose of diuretic[51]. Nevertheless, their efficacy in treatment of congestive heart failure will likely stimulate their use[52].

Beta Receptor Blockers: Acebutolol, Atenolol, Betaxolol, Bisoprolol, Carteolol, Metoprolol, Nadolol, Penbutolol, Propanolol, Timolol.

Calcium Antagonists: These drugs have become the most popular class of agents used in the treatment of hypertension. They differ in both their sites and mode of action, with major pharmacological differences between the various dihydropyridines[53]. Dihydropyridines have the greatest peripheral vasodilation action[54] with the little effect of cardiac automaticity, conduction or contractility. However, comparative trials have shown that verapamil and diltiazem which do affect these properties are also effective antihypertensives, and they may cause fewer side effects related to vasodilation, such as flushing and ankle edema. Calcium antagonists are effective in hypertensive patients of all ages and races [55] and in hypertensive diabetic [55a]. In the large comparative trail, verapamil is more effective than chlorthalidone in promoting regression of carotid intima – media thickness and preventive cardiovascular events [56]. Similar case control studies claiming that the use of reserpine was associated with three-fold increase in breast cancer was subsequently shown to be erroneous

because of exclusion bias [57]. The decrease in coronary events in large randomized controlled trials with long-acting dihydropyridines [58, 59, 60] is the best proof of safety of these agents. Similar claims based on case control studies that calcium antagonists increase cancer and gastrointestinal bleeding also have not been confirmed [61, 62].

Renin – Angiotension Inhibitors: Activity of the rennin-angiotensin system may be inhibited in four ways, three of which can be applied clinically. The first, use of beta-adrenergic receptor blockers to inhibit the release of rennin, was discussed earlier. The second direct inhibition of rennin activity by specific rennin inhibitors is being investigated[63]. The third, inhibition of enzyme that converts the inactive decapeptide angiotensin 1 to the active Octapeptide angiotensin 2, is being widely used with orally effective ACE inhibitor. The fourth approach to inhibiting the Renin- Angiotension system, blockade of angiotension's action by competitive receptor blocker, is now the basis for the fastest growing class of antihypertensive agents[64].

For examples: Captopril,Enalapril, lisinopril, Perindopril,Ramipril, Fosinopril, etc

CONCLUSION

Hypertension is one of the leading causes of global burden of disease approximately 7.6 million deaths (13 to 15% of total). Hypertension doubles the risk of cardiovascular diseases, including coronary heart disease (CHD), congestive heart failure (CHF), ischemic and hemorrhagic stroke, renal failure and peripheral artery disease. It often is associated with additional cardiovascular disease risk factors, and risk of cardiovascular disease increases with the total burden of risk factors although antihypertensive therapy reduces the risks of cardiovascular and renovascular disease.

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