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Review Paper

Review of Hypertension

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ABSTRACT

Hypertension, defined as persistent systolic blood pressure (SBP) at least 130 mm Hg or diastolic BP (DBP) at least 80 mm Hg, affects approximately 116 million adults in the US and more than 1 billion adults worldwide. Hypertension is associated with increased risk of cardiovascular disease (CVD) events (coronary heart disease, heart failure, and stroke) and death.

INTRODUCTION

Hypertension, commonly known as high blood pressure, is a chronic medical condition characterized by elevated pressure in the arteries. It is a major risk factor for cardiovascular diseases, including stroke, heart attack, and kidney failure. Hypertension often develops without any noticeable symptoms, making it a "silent killer" that can lead to severe health complications if left untreated. Systemic arterial hypertension (hereafter referred to as hypertension) is characterized by persistently high blood pressure (BP) in the systemic arteries. BP is commonly expressed as the ratio of the systolic BP (that is, the pressure that the blood exerts on the arterial walls when the heart contracts) and the diastolic BP (the pressure when the heart relaxes). The BP thresholds that define hypertension depend on the measurement method (Table 1). Several aetiologies can underlie hypertension. The majority (90–95%) of patients have a highly heterogeneous 'essential' or primary hypertension with a multifactorial gene-environment aetiology. A positive family history is a frequent occurrence in patients with hypertension, with the heritability (a measure of how much of the variation in a trait is due to variation in genetic factors) estimated between 35% and 50% in the majority of studies [3,5]

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Pathophysiology:

Hypertension, or high blood pressure, involves the dysregulation of mechanisms that control vascular tone, blood volume, and kidney function, resulting in sustained elevated blood pressure. The pathophysiology is complex and involves multiple organ systems. Here are the key mechanisms involved:

1. **Increased Peripheral Vascular Resistance (PVR):** The most common cause of hypertension is increased resistance in the small arteries and arterioles, leading to elevated systemic vascular resistance. This can be due to structural changes in the blood vessels, such as thickening of the vessel walls (vascular remodeling), or functional factors like vasoconstriction caused by sympathetic nervous system activation, increased levels of vasoconstrictors (e.g., angiotensin II, endothelin), or impaired vasodilation (e.g., reduced nitric oxide production).
2. **Activation of the Renin-Angiotensin-Aldosterone System (RAAS):** The kidneys play a key role in regulating blood pressure. Under conditions of low blood pressure or reduced blood flow to the kidneys, the juxtaglomerular cells release renin, leading to the formation of angiotensin I, which is converted to angiotensin II. Angiotensin II is a potent vasoconstrictor that increases peripheral resistance and stimulates aldosterone secretion from the adrenal glands. Aldosterone promotes sodium and water retention by the kidneys, increasing blood volume and thereby raising blood pressure.
3. **Sympathetic Nervous System (SNS) Hyperactivity:** Chronic activation of the sympathetic nervous system can lead to increased heart rate, vasoconstriction, and increased cardiac output. SNS hyperactivity also contributes to the release of renin from the kidneys, further exacerbating the hypertensive state. In addition, elevated levels of catecholamines (such as norepinephrine) can directly constrict blood vessels, promoting higher blood pressure.
4. **Endothelial Dysfunction:** Endothelial cells, which line the blood vessels, play a crucial role in maintaining vascular tone. In hypertension, endothelial dysfunction is often observed, characterized by a reduced ability to produce vasodilators like nitric oxide. This impairment can promote vasoconstriction and further elevate blood pressure.
5. **Inflammation and Oxidative Stress:** Chronic inflammation and oxidative stress contribute to the pathophysiology of hypertension. Elevated blood pressure can cause endothelial injury, leading to an inflammatory response and the release of pro-inflammatory cytokines. These cytokines can further promote vasoconstriction and vascular remodeling, creating a cycle that perpetuates hypertension. Additionally, oxidative stress can damage the endothelium and decrease nitric oxide bioavailability.
6. **Genetic Factors:** Genetic predisposition plays an important role in hypertension. Several genes involved in salt retention, vascular tone regulation, and sympathetic nervous system activity have been associated with hypertension. Family history and genetic variations can influence the risk of developing hypertension and its severity.
7. **Obesity and Insulin Resistance:** Obesity, particularly visceral fat accumulation, is closely linked to the development of hypertension. Excess adipose tissue contributes to increased sympathetic activity, activation of the RAAS, and inflammation. Insulin resistance often accompanies obesity and can further increase blood pressure through several mechanisms, including

increased sodium retention and vascular remodeling.

8. **Chronic Kidney Disease (CKD):** CKD is both a cause and a consequence of hypertension. Impaired kidney function results in abnormal regulation of sodium and water balance, promoting fluid retention and increased blood volume. Over time, this leads to worsening hypertension, which in turn accelerates kidney damage. [6,11,15,3]

Non-Pharmacology treatment:

Weight loss:

Weight Loss Weight loss is best achieved by combining calorie reduction and physical activity. The ideal approach is gradual and results in durable weight loss, with a weekly reduction goal of 1 to 2 kg. An SBP reduction of approximately 1 mm Hg is expected for every kilogram of weight lost. Among individuals with obesity and hypertension who meet the appropriate criteria (body mass index >35 [calculated as weight in kilograms divided by height in meters squared] and poorly controlled hypertension), bariatric surgery can induce substantial weight loss and meaningfully improve BP. [5,4,2]

Dietary Sodium and Potassium Intake

Any decrease in sodium intake is helpful because the association between sodium and BP reduction is approximately linear, with a 1000-mg sodium reduction resulting in SBP lowering of approximately 3 mm Hg. As an optimal target, clinicians can recommend sodium intake of less than 1500mg/d. Eating patterns associated with lowering dietary sodium intake include eating fresh rather than processed foods, reducing portion size, avoiding foods especially high in sodium content, reading food labels for packaged and prepared foods, choosing condiments and seasonings with low sodium content, and attempting sodium substitutions by using herbs, spices, or potassium-enriched salt substitutes. [1,5,7,4,6]

Physical Activity

Most clinical trials demonstrating a BP-lowering effect of physical activity have used aerobic exercise such as brisk walking, swimming, dancing, or gym exercises. However, dynamic resistance exercise such as hand grip or yoga is also beneficial. Medium- to highintensity exercise, such as running, and low-intensity aerobic exercise, such as walking, can lower BP. According to clinical trial evidence, an exercise duration of 40 to 60 minutes at least 3 times per week may be optimal for BP lowering. [8,5]

Antihypertensive Pharmacotherapy

Antihypertensive pharmacotherapy has evolved over several decades driven by development of various antihypertensive medication classes and large-scale outcomes trials proving their benefits on CVD morbidity and mortality. Clinicians are now faced with a plethora of antihypertensive medications of different drug classes and a variety of fixed dose combinations. Typically, antihypertensive pharmacotherapy begins with first-line antihypertensive medications either in monotherapy or in combination. Combination therapy may be preferable in patients with higher levels of pretreatment BP. First-line antihypertensive medications include ACE inhibitors, angiotensin II receptor blockers (also known as sartans), dihydropyridine calcium channel blockers, and thiazide diuretics. Beta-blockers are also indicated in patients with heart failure and reduced left ventricular ejection fraction or post myocardial infarction, and some guidelines recommend betablockers as first line antihypertensive medications. The choice should be based on individual efficacy and tolerability. Ethnicity affects the response to antihypertensive medications, and it has been suggested that calcium channel blockers and diuretics may be the first choice in blacks. Further, in specific clinical situations, for example hypertension in pregnant women, other medications such as alpha-

methyldopa (an agonist of alpha adrenoreceptors in the central nervous system that inhibits the sympathetic nervous system) or labetalol (a beta adrenoreceptor blocker) are preferable, whereas some first line antihypertensives, for example ACE inhibitors and angiotensin II receptor blockers, are contraindicated because of increased risk for renal teratogenicity. Divided dosing of antihypertensive drugs tends to decrease adherence and should be avoided when possible (10,15,13,14,12,11)

Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers.

Among medications that inhibit components of the RAAS, ACE inhibitors and angiotensin II receptor blockers are considered first line antihypertensives, whereas other antihypertensive medications targeting RAAS, including direct renin inhibitors and mineralocorticoid receptor antagonists, are usually considered reserve medications because there is less clinical trial evidence supporting their use as first line antihypertensive therapy. ACE inhibitors and angiotensin II receptor blockers have been tested extensively in largescale hypertension trials (16,12).

Dihydropyridine calcium channel blockers.

Dihydropyridine calcium channel blockers elicit vasodilation by blocking vascular smooth muscle L-type calcium channels. They are effective antihypertensive drugs with extensive experience in large clinical trials (16,13)

Thiazide-type and thiazide-like diuretics.

Thiazide-type diuretics (for example, hydrochlorothiazide) have a benzothiadiazine ring, whereas thiazide-like diuretics (for example, chlorthalidone, metolazone and indapamide) lack the benzothiadiazine structure. Both subclasses of thiazide diuretics inhibit Na+ and CI- co-transporters in renal tubules, thereby promoting natriuresis, and have been an important component of pharmacological hypertension management ever since the first trials showing morbidity benefits of antihypertensive therapy (17,14)

Beta-adrenoreceptor blockers.

Beta-adrenoreceptor blockers lower BP reducing cardiac output, heart rate, renin release and adrenergic control nervous system effects. They improve outcomes following acute myocardial infarction and in patients with heart failure with reduced left ventricular ejection fraction, but, in the absence of these comorbidities, beta-adrenoreceptor blockers are inferior to other first line antihypertensives in reducing CVD morbidity and mortality. (18,19,11)

CONCLUSION:

Hypertensive emergencies have the potential for permanent end organ damage and signifi cant morbidity and mortality. Patients with hypertensive crises may require immediate reduction in elevated BP to prevent and arrest progressive end-organ damage. The appropriate therapeutic approach in each patient will depend on the clinical presentation. The best clinical setting in which to achieve this BP control is in the ICU, with the use of titratable IV hypotensive agents. With the development of pharmacological agents in the last decade, the traditional agent, nitroprusside, should be utilized signifi cantly less given that the other agents such as esmolol, nicardipine and fenoldopam are now available and are equally effective with fewer adverse effects. Agents such as nifedipine and hydralazine should be abandoned because these agents are associated with signifi can't toxicities or side-effects and increased mortality.

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