Hemodynamic Approach to Antihypertensive Treatment

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SUMMARY :

Hypertension is classified into various individuals profiles based on its pathophysiology and hemodynamics, as devised by Messerli et al. The contemporary hemodynamic approach to antihypertensive treatment is more physiological than the stepped care approach recommended by Joint National Committee.

INTRODUCTION :

Arterial hypertension in adults over 18 years is defined when the diastolic blood pressure on at least two subsequent visits is 90 mm Hg. or higher, or when the average of multiple systolic measurements on two or more subsequent visits is consistently greater than 140 mm Hg.

Over 60 million individuals in the United States have elevated blood pressure or have reported being told by physicians that they have hypertension. About 40 million have diastolic blood pressure in the range of 90-99 mm Hg. The prevalance is twice in blacks than whites. In elderly, age 65 or older, 40-50% have hypertension. Isolated systolic hypertension occurs in 10-31% of elderly patients.

Pathophysiology of Hypertension :

The main determinants of arterial pressure are the Cardiac Output (C.O.), and C.O. are measured and TPR is calculated by dividing the mean arterial pressure by Cardiac Output. See Fig. 1.

$$MAP = C.O. \times TPR$$

$$C.O. = S.V. \times H.R.$$

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MAP = Mean Arterial Pressure; C.O. = Cardiac Output; TPR = Total Peripheral Resistance; S.V. = Stroke Volume; H.R. = Heart Rate

MAP is the pressure differential across the circulation and may be estimated by the diasolic pressure plus one-third pulse pressure. TPR is the sum of the resistance in all the vascular beds of the body. The Systemic arterial hypertension is a hemodynamic abnormality that can be caused by any factors which may alter the relationship between the cardiac output and the total peripheral resistance. The exact mechanism as to how these factors change the hemodynamics, i.e., C.O. and TPR, is still not clear.

Determinants of Cardiac Output (C.O.): Fig. 1

The main determinants of C.O. are heart rate and stroke volume, which are controlled by the autonomic nervous system mainly adrenergic, total blood volume, venous return and myocardial contractility. Alterations in myocardial contractility and heart rate are mediated through adrenergic receptors present in the heart, blood vessels and various tissues of the body. The adrenergic receptors are of two types - Beta and Alpha, which are further sub-classified into Beta $_1$, and Beta $_2$, Alpha 1, Alpha $_2$.

Beta $_1$ Receptors are present in the heart and adipose tissue. Simulation of these receptors in the heart causes increased heart rate, myocardial contractility and lipolysis. Beta $_2$ recep-

tors are present in the kidney, bronchi, uterus and lipolysis. Beta $_2$ receptors are present in the kidney, bronchi, uterus and arterioles. Stimulation of these receptors cause relaxation of the smooth muscles of the uterus and bronchi, vasodilation of the coronary arteries and skeletal muscle blood vessels, and increased renin release. Alpha $_1$ receptors are primarily post-synaptic and their stimulation causes vasoconstriction in the vessels of the skin, mucosa, gut, skeletal muscles and stimulation of sweat gland secretion. Alpha $_2$ receptors are primarily pre-synaptic and deal with auto-regulation of norepinephrine release from the pre-synaptic nerve endings.

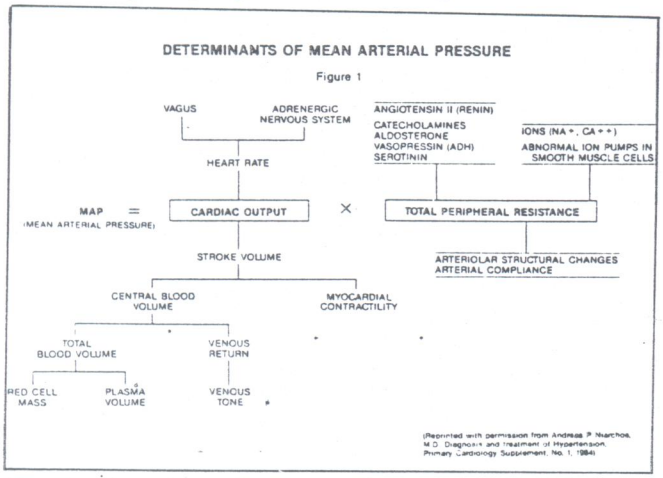

Fig 1. Hemodynamic Approach to Anti-Hypertensive Treatment

Determinants of Stroke Volume (S.V.) :(Fig. 1.)

S.V. is dependent on the central blood volume and myocardial contractility. Central blood volume is indirectly dependent on the plasma volume and venous tone or capacity. Plasma volume is determined by solium balance and arterial pressure. With negative sodium balance, plasma volume falls; and with positive sodium balance, plasma volume increases. Sodium balance is determined not only by the sodium intake but also by the ability of the kidney to excrete sodium. Plasma volume is diminished in established hypertension due to increased natriuresis which is believed to be partly due to arterial hypertension. The classic example of increased sodium balance and plasma volume is aldosteronism. In labile, borderline or early hypertension, there is evidence of diminished venous capacity or increased tone and therefore increased cardiac output causing hypertension.

Determinants of Total Peripheral Resistance (TPR) : Fig. 1.

Renin Angiotension System

Intracellular Sodium and Calcium

Arterial Structural Changes

Arterial Compliance

Vasopressin, Seratonin and Prostaglanins

Aortic Impedence and Diastolic Arterial Volume

Renin, a proteolytic enzyme, is released from the kidney. It converts angiotensinogen to angiotensin I and then II. Angiotensin II is a powerful vasoconstrictor, is the main controlling mechansim for aldosterone release, increases the activity of the sympathetic nervous system, and has an inhibitory effect on sodium excretion. Intracellular sodium in vascular smooth muscle is currently considered important in increasing vascular resistance that characterizes hypertension. Vasconstriction is also mediated through intracellular calcium and is blocked by calcium channel blockers. Structural changes in the arteriolar wall diminish the arteriolar diameter and renders resistance vessels more sensitive to exogenous vasoconstrictors and less sensitive to vasodilators.

Classification of Essential Hypertension based on Hemodynamic Profile:

(Cardiac output, total blood volume, total peripheral resistance, and plasma renin activity) is as follows: (Fig. 2.)

1. Labile, borderline or early mild
2. Established mild, moderate and severe
3. Hypertension in blacks and obese
4. Hypertension in elderly

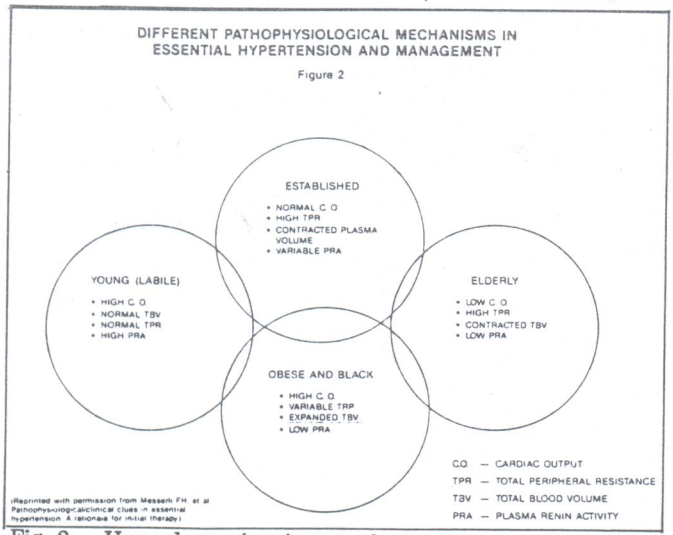

Fig. 2 Hemodynamic Approach to Anti-Hypertensive Treatment

Labile Hypertension:

In labile, borderline or early mild hypertension, with diastolic blood pressure < 105, these patients have hyperkinetic circulation and seem to be in an early developmental stage of hypertension manifested by increased C.O., increased myocardial contractility, increased catecholamines, normal blood volume, normal total peripheral resistance, increased plasma renin activity and decreased venous capacity. These patients also have other symptoms and signs of an imbalaned automomic nervous system such as hyperhydrosis, palpitations, acrocyanosis, headaches, chest pain or mitral valve proplapse. According to Australian studies, 12% of these patients over a 3 year period progressed to a more severe stage of hypertension.

Establised Hypertension :

Individuals with established hypertension, i.e., diastolic blood pressure > 105,have normal cardiac output, contracted total blood volume, increased total peripheral resistance and variable plasma renin activity. It has been shown by Dr. John Laragh that renin profile in essential hypertension falls into three major groups (Low renin - 30%; Normal renin - 55% and High renin-15%). High Plasma renin profile enhances the antihypertensive efficacy of beta-blockers and convertaing enzyme inhibitors, whereas a low plasma renin profile may improve the efficacy of diuretics and calcium channel blockers.

Hypertension in Blacks :

Established, longstanding hypertension in blacks is different from whites. Blacks more often have expanded total blood volume and lower plasma renin activity, lower renal blood flow and higher renal vascular resistance. In blacks compared to whites for any given level of arterial pressure, the systemic vascular resistance and target organ disease such as hypertensive heart disease, stroke and nephrosclerosis is more rapid and severe with the exception of coronary artery disease.

Hypertension in Elderly :

Fifteen percent of whites and twenty-five percent of black elderly have isolated systolic hypertension between 65-74 years of age and the incidence increases with age. One possible explanation seems to be a loss of distensibility of the aorta and large arteries. Elderly hypertensives have low cardiac output, with markedly increased total peripheral resistance, contracted total blood volume and low plasma renin activity. There is no controversy about treating diastolic in edlerly, but in case of isolated systolic hypertension, the answer is not very clear. However, recent data suggests that low dose diuretic thereay is well-tolerated and effective in reducing the elevated systolic pressure.

Hypertension in the Obese :

Obesity alone causes increased toal blood volume, decreased total peripheral resistance, which is opposite to what hypertension effects are increased peripheral resistance and decreased total blood volume.

Obesity increases preload and increased cardiac output causes eccentric hypertrophy. Hypertension increases afterload, causing concentric hypertrophy. This double burden leads to early left ventricular dysfunction and premature congestive heart failure. Also, the risk of sudden death is increased in obsesity with hypertension, according to the Framingham study. Obese hypertensives have lower renin activity compared to lean hypertensives.

Management :

VA (Veterans Administration) Cooperative Study, Hypertension Detection and Followup Program (HDFP), Australian study and Oslo study, have shown the benefits of lowering blood pressure even in mild hypertension (diastolic blood pressure <100), that it dose significantly reduce the hypertensive complications of cerebrovascular disease, aortic dissection, renal damage, congestive heart failure and left ventricular hypertrophy. But only the HDFP study have shown the reduction of mortality and mordibity due to coronary artery disease (CAD). The joint National Committee recommendations for hypertensive treatment are to use drug therapy in individuals who have persistantly high diastolic blood pressure greater than 95 mm Hg. , or those who have 90-94 with target organ damage, diabetes and other major risk factors for CAD. In individuals with 90-94 mm Hg. diastolic pressure, without target organ disease or risk factors, should be carefully monitored and nonpharmacological therapy tried for 3 to 6 months.

The Joint National Committee drug treatment recommendations are to use step care approach in antihypertensive treatment; i.e., start with diuretic or beta blocker and go to other Steps 2, 3, or 4 drugs. I prefer the hemodynamic approach by Messerli et al which is more physiological, with minimal side effects and increased patient compliance. (Fig. 2.)

In patients with labile, borderline and early mild hypertension with hyperkenetic circulation, to use a beta blocker which will reduce the heart rate, myocardial contractility and plasma renin activity. In established mild, moderate to severe hypertension, the basic pathology is high total peripheral resistance; start with either Methyl-dopa, Clonidine, Reserpine, Prazosin or Captopril. All of these decrease peripheral resistance but increase fluid retention; hence a diuretic may be added. In blacks with established hypertension, the main pathophysiological defect is expanded total blood volume and low plasma renin activity. Start theraphy with a diuretic to reduce total blood volume and then add adrenergic blockers if necessary. In the elderly, the main hemodynamic abnormality is very high total peripheral resistance, and markedly contracted blood volume. Drug treatment preferably with centrally acting adrenergic blockers, like clonidine, guanabenz or Methyldopa, low dose diuretics, vasodilators or calcium channel blockers. In obese patients, the basic defect is expanded total blood volume; the recommended treatment is a diuretic and then adrenergic inhibitors.

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