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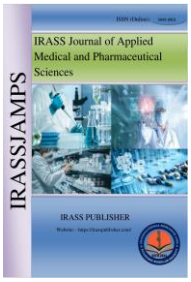

Review: History of Antihypertension

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Abstract: Hundreds of thousands that people worldwide suffering about hypertension, becoming an important risk factor for kidney problems, stroke, and cardiovascular disease. In order to prevent such problems along with improving patient outcomes, blood pressure can only be properly managed. The purpose of this review is to provide an extensive examination of the state of antihypertensive treatments and approaches, including prescription drugs, adjustments to lifestyles, and device-based treatments.To find significant studies and recommendations on the medical management of hypertension, an extensive review of the main databases was carried conducted. The biological makeup of hypertension, risk identification, and treatment modalities—including combo and monotherapy—are all discussed in the review.

Keywords: Hypertension, Antihypertensive Drug, Blood Pressure, Cardiovascular System.

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Introduction

A major medical problem, hypertension raises the risk of kidney, brain, heart, and other illnesses. Globally, it is a leading cause of premature mortality (1).A blood pressure reading that is continuously higher than 130/80 mmHg is referred to as hypertension (5).A third of adults suffer from hypertension, which is the primary cause of early mortality and a reduction in years of disability-adjusted life (6).Over the years, experimental and clinical research have provided consistent and strong support for the idea that essential hypertension may have its roots in changes in the adrenergic regulation of blood pressure homeostasis (7).Systolic blood pressure of 140 mmHg or higher or diastolic blood pressure of 90 mmHg or higher is considered hypertension (9). Antihypertensive medication therapy is commonly used in clinical practice to treat hypertension, because blood pressure reduction lowers cardiovascular risk (10).One of the main risk factors for cardiovascular disease is hypertension.According to a meta-analysis, a 10/5 mm Hg drop in standard office systolic/diastolic blood pressure lowers the risk of coronary artery disease by around 20% and stroke by about 40% (12). Noncompliance with antihypertensive medications (AHDs) is one of the biggest obstacles to controlling blood pressure. An elevated risk of coronary heart disease and end-stage kidney disease is linked to uncontrolled blood pressure and resistant hypertension, or "pseudo-RH," in the event of nonadherence (14). About 3% of pregnancies are complicated by chronic hypertension. Evidence is mounting that the incidence is increasing as maternal age and obesity increase (15).In low-, middle-, and high-income nations, hypertensive problems during pregnancy significantly increase maternal and perinatal morbidity and mortality (18).One of the main causes of death worldwide is hypertension. Many hypertensive patients do not attain goal blood pressure (BP) control, a condition known as resistant hypertension (RH), despite the extensive use of antihypertensive medications and treatment approaches. Because it is linked to an increased risk of hypertension-mediated organ damage (HMOD), which includes chronic kidney disease (CKD) and early cardiovascular diseases (CVD), RH is a significant clinical concern (19). The population's health has been greatly impacted by cardiovascular disease, which includes myocardial infarction, stroke, and coronary heart disease, and for which hypertension is the most modifiable risk factor (20).Following TB and HIV infection, hypertension is the next biggest public health risk and is rising at an alarming rate (22).First, the screening for antihypertensive effects in the identification of medicines from natural materials has mostly been done empirically over the years, using a number of animal model trials (24).Preterm birth, low birth weight, short for gestational age (SGA), perinatal and fetal mortality, and other unfavorable perinatal outcomes are all made more likely by hypertensive disorders of pregnancy. Controlling blood pressure (BP) is crucial to avoiding such negative consequences (25).More than one billion people have hypertension, and it seems to impact about 40% of the general population. As people age, the frequency rises from 7% in younger people (18–39 years old) to 65% in older people (over 59 years old).With an estimated 9.4 million deaths annually, hypertension is the greatest significant risk factor for mortality and disability globally (29).With a prevalence of 24% in men and 20% in women, and 1.1 billion affected persons globally, high blood pressure (BP) has become the primary risk factor for the global

disease burden. An estimated 9.4 million fatalities per year are attributed to hypertension (32).

EPEDIMEOLOGY:

SBP ≥ 140 mm Hg, mean DBP ≥ 90 mm Hg, and/or the administration of antihypertensive medication within the six months before to the clinical examination were considered indicators of hypertension.With a prevalence of 31.3%, males were substantially more likely than women to have hypertension (38.6% vs. 25.8%, P <.0001), and this difference persisted even after controlling for age and BMI (P <.0001). As people aged, the prevalence rose, reaching 68.8% of those aged 65-74 (P <.0001). Of those with hypertension, 56.3% said they were aware of their condition.Less than one in two adults with hypertension received treatment. The percentage of persons with hypertension who received treatment increased to 74.7% when the group was limited to those who were aware of their condition.Of the hypertensives treated, 37.9% received two or more antihypertensive classes, while 62.1% received just one. In terms of polytherapy treatment, there is no discernible difference between men and women (40.4% vs. 34.6%, P =.197).38.4% of treated hypertensives received prescriptions for angiotensin II receptor blockers (ARBs), 32.9% for diuretics, 25.2% for angiotensin converting enzyme inhibitors (ACEI), 25.2% for beta-blockers (BB), 19.3% for calcium-channel blockers (CCB), and 2.2% for other antihypertensive medications. 49.7% of persons with treated hypertension had uncontrolled hypertension.Men were substantially more likely than women to have uncontrolled hypertensives (58.2% vs. 39.8%, P =.001). For geographical and chronological comparisons, studies on the prevalence of hypertension that use a single set of measurements are helpful. However, due to differences in the age groups examined and a lack of standard technique, comparisons are challenging for the more recent years.Although France's awareness rate is better than the average for the US and Europe (51%), it is lower than that of England (71.0%), Portugal (76.6%), Germany (82.3%), and Portugal (76.6%).20 Regarding hypertension awareness, certain sex disparities have been noted.Our study's percentage of hypertensives treated with medication is lower than the percentages seen in Germany (71.8% of hypertensives treated) and England (58.0% of hypertensives treated). 18.4% of individuals with hypertension and 38.5% of those receiving treatment The 2013 French guidelines, which suggested that initiation should be preferred with thiazide diuretics, CCB, ARB, or ACEI—the latter two classes being primarily associated with higher persistence and tolerance compared to BB and diuretics—were in conflict with the high percentage of BB in patients treated with monotherapy.(122).One of the most common chronic conditions, hypertension is present in practically every nation and has grown to be a global public health concern. The World Health Organization's Global Health Observatory [(GHO)] reports that hypertension kills millions of people annually and affects approximately 1.13 billion people worldwide.A diagnosable disorder, hypertension puts the kidneys, heart, brain, and other organs at risk for harm. Higher blood pressure levels are linked to heart failure, atrial fibrillation, and stroke.The majority of hypertension can be treated, despite the fact that it is difficult to cure. After hypertension develops, it needs to be controlled for the remainder of a person's life.Hypertensives' blood pressure can be effectively controlled with follow-up care (123).

PATHOPHYSIOLOGY

Blood pressure can be determined by a number of cardiovascular system characteristics, including cardiac output, blood volume, arterial tone balance, etc.(1).Raised vascular resistance, primarily identified by decreasing vascular diameter due to increased vascular contraction and arterial remodeling, is one of the pathophysiological pathways implicated in the development of hypertension. Increases in the renin-angiotensin-aldosterone system (RAAS), sympathetic nervous system stimulation, vasopressin, disrupted G protein-coupled receptor signaling, inflammation, various T-cell functions, and the variety of vasoactive peptides released by other endothelial cells and smooth muscle cells are just a few of the many variables that contribute to the pathophysiology of hypertension.(86).

The majority of secondary hypertension's underlying causes are now well understood. Conversely, those associated with essential (main) HTN are far less well-known. Total peripheral resistance (TPR) is normal in the early stages of the disease, although cardiac output is increased. TPR increases when cardiac output recovers to normal. This could be explained in one of three ways:

- Natriuretic factors, such as atrial natriuretic factor, are released to increase salt excretion and raise TPR when the kidneys are unable to eliminate sodium.
- An overactive renal angiotensin system causes vasoconstriction, which leads to fluid and salt buildup in the circulation. An increase in blood volume is the cause of hypertension.
- An overactive sympathetic nervous system results in elevated stress responses.
- Since HTN is known to be polygenic (produced by multiple genes) and heritable, a few candidate genes have been put forth as its aetiology (91).

Hypertension is a blood regulation disorder; the overactive renin-angiotensin system results in vasoconstriction and the buildup of water and salt; the kidneys' inability to release sodium encourages the excretion of natriuretic factors, such as atrial natriuretic factor. HTN is influenced by blood volume development (92).

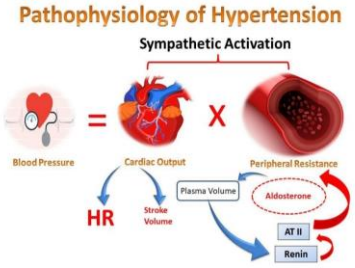


Figure 1: Pathophysiology of Hypertension.(92).

Factors That Influence Hypertension (127).

Certain traits, including age and underlying or pre-existing illnesses like diabetes, are associated with hypertension. Other significant variables that affect hypertension include:

- Age: People are more likely to develop hypertension as they get older. Most often, adults over 45 experience the

onset of hypertension. Additionally, there is a chance that some will get it earlier in life.

- Diabetes: It is possible for diabetes and hypertension to be related. Diabetes is a disease that causes the arteries to stiffen, which leads to hypertension.
- Hereditary: The likelihood of developing hypertension is increased if it runs in your family because it is a disorder that can be passed down through the generations.
- Other Medical Conditions: A person may be more susceptible to hypertension if they have a history of kidney disease, congenital adrenal hyperplasia, or disorders of the adrenal glands such as pheochromocytoma. A healthy heart is linked with a good lifestyle, thus incorporating smoking, alcohol, salt, and fatty foods into your diet may cause high blood pressure or cardiac problems.
- Obesity: Your lifestyle choices regarding food and exercise also have a significant impact on your risk of hypertension. Conditions like being overweight or obese, which result in hypertension, are brought on by a poor diet and a lack of exercise. Weight gain puts stress on the arteries' ability to pump blood, which leads to resistance and elevated blood pressure.
- Salty Diet: Including too much salt in your diet may cause you to harm your health. The human body retains more water in order to flush away salt; consuming more salt raises water levels, which might result in hypertension.
- Disturbed sleep cycle: Hormonal imbalances brought on by an inconsistent sleep schedule can result in hypertension.

Communication:

Antihypertensive drug:

Antihypertensive drugs, also known as blood pressure medications, are used to treat high blood pressure (hypertension). There are many different types of antihypertensive drugs, and they work in different ways to lower blood pressure.

Antihypertensive drugs, also known as blood pressure medications, are used to treat high blood pressure (hypertension). There are many different types of antihypertensive drugs, and they work in different ways to lower blood pressure. Some common types of antihypertensive drugs include:

- Diuretics: These medications help the body remove excess fluid and salt through the urine.
- Beta-blockers: These medications block the effects of adrenaline, a hormone that can raise blood pressure and heart rate.
- Calcium channel blockers: These medications relax blood vessels and make it easier for blood to flow.
- Angiotensin-converting enzyme (ACE) inhibitors: These medications block the production of angiotensin II, a hormone that narrows blood vessels.
- Angiotensin receptor blockers (ARBs): These medications block the effects of angiotensin II, a hormone that narrows blood vessels.

Antihypertensive drugs are typically taken orally, but some may be given by injection. The dosage and type of medication will depend on the individual's condition and other factors.

It is important to talk to your doctor abouandt the risks benefits of antihypertensive drugs before taking them. You should also tell your doctor about any other medications you are taking, as well as any allergies or medical conditions you have.

Here are some additional things to keep in mind about antihypertensive drugs:

Do not stop taking your medication without talking to your doctor first. Stopping your medication suddenly can cause your blood pressure to rise sharply.

Take your medication at the same time each day. This will help you remember to take it and will help keep your blood pressure under control.

Do not take more or less medication than your doctor prescribes. Taking too much medication can be dangerous, and taking too little medication may not be effective.

Tell your doctor about any side effects you experience. Some side effects are mild and may go away on their own. However, if you experience any serious side effects, such as chest pain, shortness of breath, or swelling of the face or throat, seek medical attention immediately.

If you have high blood pressure, it is important to see your doctor regularly for checkups. Your doctor will monitor your blood pressure and may adjust your medication as needed.

Examples of synthetic Antihypertensive drug (22).

Diuretics:

- Hydrochlorothiazide
- Furosemide
- Spironolactone

Beta-blockers:

- Atenolol
- Metoprolol
- Propranolol

Calcium channel blockers:

- Amlodipine
- Nifedipine
- Verapamil

Angiotensin-converting enzyme (ACE) inhibitors:

- Captopril
- Lisinopril
- Ramipril

Angiotensin receptor blockers (ARBs):

- Losartan
- Valsartan
- Candesartan

Example of natural Antihypertensive drugs are

- Rauwolfia
- Garlic
- Sesame seeds
- Linseed
- Fish oil
- Vitamin C

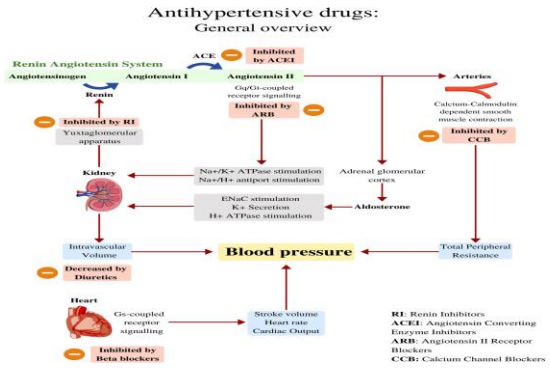
Plants profile:

Drugs name	Rauwolfia
Synonym	Sarpagadah, chootchand
Source	Dried roots and rhizomes of rauwolfia serpentia belonging to Family Apocynaccae
Chemical constituents	Mainly alkaloids
Uses	Antihypertensive agents,tranquilizers, angina pectoris,cardiac arrhythmias.

Drugs name	Garlic
Synonym	Adrak, Aala
Source	Ripe bulbs of Alium sativum belonging to family Liliaceac
Chemical constituents	Allin, Allinlysase, Allicin
Uses	Antihypertensive agents, falovring agents, antibacterial.

Drugs name	Linseed
Synonym	Flex seeds
Source	Dried ripe seeds of Linium Usitatissium belonging to family Linaceccae.
Chemical constituents	Fixed oils, Linamarin, protein,Mucilage
Uses	Antihypertensive agents, poulticc, demulcent ,laxatives

General Mechanisms of action of Antihypertensive drugs: (23)



Approach to Therapy:

Both non-pharmacologic and pharmacologic methods are part of a logical strategy for treating hypertension in people with chronic kidney disease. A generalized strategy for the pharmacologic treatment of hypertension in chronic renal disease is shown in Figure 3. The Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure is now reviewing an eighth (JNC 8) report, however current JNC 7-based guidelines recommend that people with CKD aim for a blood pressure goal of 130/80 mm Hg. Numerous studies support this objective by indicating that lowering blood pressure may decrease the course of CKD. A meta-analysis in 2003 reported a lowered risk of CKD progression with a blood pressure goal of 110–129 mm Hg, and an increase in the relative risk for CKD progression at blood pressures 1 130 mm Hg. The beneficial results were most notable in those with proteinuria exceeding 1 g/d. (121)

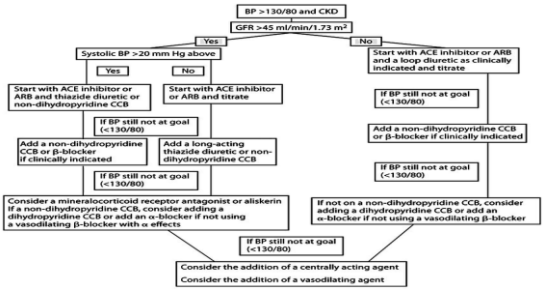


Fig.3: Pharmacologic approach to hypertension management in CKD. BP = Blood pressure; CCB = calcium channel blocker; ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker. (121)

Challenges of Hypertension (122)

Challenge 1: Fulfillment of the Responsibility for Treatment

It is obvious that if the basic knowledge is not applied to routine clinical practice, no new understanding of the disease's processes and therapy can be fully grasped. The latest national statistics from the United States are identical to those from other countries: Our communities' hypertension problems are not being adequately controlled by organized medicine.

Challenge 2: Cardiac Failure

The most frequent cause of heart failure is still hypertension, just as it was during the early years of the Framingham Heart Study, before any of the benefits of antihypertensive medication were realized. In fact, heart failure is currently the leading cause of hospitalization for Medicare-eligible patients in the US. However, we still don't fully grasp the primary causes, the underlying disease mechanisms, or how to treat them.The majority of multicenter, controlled clinical trials studies currently focused on heart failure limit patient admission to nonhypertensive patients who have recently experienced myocardial infarction and intentionally try to avoid patients with high blood pressure. However, we are aware that we can undoubtedly lower the number of patients admitted to hospitals with heart failure based on other publications that address the more recent and successful classes of antihypertensive medication.

Challenge 3: End-Stage Renal Disease

Once more, epidemiological data from the present day indicate that this complication of hypertension is becoming more

common in our society and most others. The three main causes of end-stage renal disease (ESRD) are diabetes mellitus, hypertension, and the poorly known pathophysiological pathways that affect black individuals, according to an effective presentation of the most recent demographic and epidemiological data. Nevertheless, it is evident that hypertension is the primary underlying cause of ESRD, even when we take into account that it is a significant cardiovascular issue in both diabetic patients and Black individuals. Furthermore, when we concentrate on this issue, the majority of the large clinical trials that have been carried out or are currently underway are mainly focused on the issue of diabetes in patients with end-stage renal disease (ESRD). The hope is that the researchers and clinicians will apply the lessons learned from these expensive observational efforts to the problem of hypertension, which is a much more common disease.

Challenge 4: Obesity

We all know that obesity is becoming a big global concern, whether we are scientists, clinicians, or laypeople. However, our understanding of the basic and further clinical data has not clarified the reasons behind the close connection between the pathophysiological mechanisms of obesity and hypertension. Once more, our understanding of this significant cardiovascular risk factor is really basic and unsophisticated, especially in relation to hypertension. Furthermore, there isn't much information or effort available regarding the effective treatment and control of this risk factor, aside from the knowledge that diet therapy has a high recidivism rate and that the majority of potential pharmacological interventions are typically not recommended due to side effects, such as further raising the patient's blood pressure. Pharmacological treatment drugs that do not negatively impact arterial pressure are long overdue, and the development of effective behavioral modification strategies is just one of the essentials.

Challenge 5: Atherosclerosis

As we are all well know, atherosclerosis and hypertension are closely related conditions that exacerbate and feed off one another. The common targets of the disease, the heart, blood arteries, and the endothelium, have been the focus of fundamental and clinical research. At this time, we are discovering intriguing areas for freshly targeted research. This is based on very recent experiences with the very new family of drugs known as "statins," which suggests both their new actions on producing endothelium superoxides and free radicals as well as their original purpose as treatments to lower LDL cholesterol. As a result, we now have preliminary evidence that these substances may possibly have additional metabolic effects on oxidative metabolism and vascular smooth muscle tone regulation. Undoubtedly, more thorough research in this field will yield a wealth of fascinating new data that ought to be quickly incorporated into clinical practice. The pharmaceutical business, clinicians, and laboratory workers will all need to put in a lot of work and focus on this. **Limitations** (123)

- Patient education is necessary.
- Absence of blood pressure while sleeping at night
- Patients' stated blood pressure readings are not reliable.
- Anxiety induction that leads to over-monitoring
- The potential for patients to self-modify their medication
- Inaccurate blood pressure measurement in arrhythmia patients
- Insufficient clinical research evidence regarding therapeutic goals and normalcy threshold

Conclusion

Blood pressure regulation in hypertension may be impacted by the vascular, renal, and inflammatory effects of bioactive lipids. We calculated minor variations in the impact of antihypertensive medication classes on the course of dementia. Additionally, we demonstrate that the size of the drug class disparities is less than what has been previously documented.

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