Chapter 3

Recent Advances in Hypertensive Therapy

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Abstract

In addition to being a major risk factor for heart disease, stroke, and kidney problems, hypertension is a substantial worldwide health burden. Despite the fact that traditional antihypertensive medications, including diuretics, beta-blockers, ACE inhibitors, calcium channel blockers, and angiotensin receptor blockers, successfully lower blood pressure, problems such as resistant hypertension, side effects, and poor patient adherence still exist. Novel pharmacological treatments such as enhanced mineralocorticoid receptor antagonists, direct renin inhibitors, and angiotensin receptor–neprilysin inhibitors are the focus of recent developments in hypertension medicine. Treatment results and compliance have improved with fixed-dose combo treatments. Additionally, pharmacogenomics-supported personalized medicine techniques and device-based therapies like renal denervation are showing promise as ways to maximize the control of hypertension and enhance long-term cardiovascular outcomes.

Keywords: Hypertension, Antihypertensive therapy, Resistant

hypertension, Fixed-dose combination, Renal denervation.

1. Introduction

One of the main causes for heart morbidity and mortality worldwide is hypertension, a chronic non-communicable disease. It dramatically raises the risk of heart failure, stroke, myocardial infarction, and chronic renal disease. Many patients still have suboptimal blood pressure control despite the availability of several antihypertensive medication classes, such as diuretics, beta-blockers, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin receptor blockers (ARBs). This is because of resistant hypertension, adverse drug reactions, and poor therapy adherence.

The goals of recent developments in antihypertensive treatment have been to increase patient compliance, safety, and efficacy. Angiotensin receptor–neprilysin inhibitors (ARNIs), direct renin inhibitors, and tailored mineralocorticoid receptor antagonists are examples of novel pharmacological strategies that have shown encouraging clinical results, especially in high-risk groups and resistant hypertension. In order to improve adherence and accomplish quicker blood pressure management, fixed-dose combination treatments are also becoming more and more advised. Renal destruction and baroreceptor activation therapy are two new device-based therapies that are being investigated as potential alternatives for patients who do not respond well to medication. Additionally, chances to customize antihypertensive medication based on individual genetic profiles are presented by breakthroughs in pharmacogenomics and personalized medicine, potentially increasing therapeutic outcomes.

2. Pathophysiology of Hypertension

Multiple physiological systems are involved in the complicated and

ISBN 978-816855389-7

multifactorial condition known as hypertension.

2.1 Renin–Angiotensin–Aldosterone System (RAAS)

RAAS is essential for controlling fluid balance and blood pressure. Increased vasoconstriction and salt retention brought on by excessive RAAS activation raise blood pressure.

2.2 Sympathetic Nervous System Activation

Hypertension is a result of increased sympathetic activity, which also raises heart rate, increases cardiac output, and constricts blood vessels.

2.3 Endothelial Dysfunction

By generating vasodilators like nitric oxide, the endothelium contributes significantly to the control of vascular tone. Vasoconstriction is encouraged, and nitric oxide generation is decreased by endothelial dysfunction.

2.4 Inflammation and Oxidative Stress

Chronic inflammation and oxidative stress have been linked to vascular damage and elevated blood pressure, according to recent research.

2.5 Genetic and Environmental Factors

Major causes of hypertension include genetic susceptibility, excessive salt consumption, obesity, sedentary lifestyles, and stress.

3. Conventional Antihypertensive Therapy

The mainstay of managing hypertension is still conventional antihypertensive medications. Among the main drug classes are:

Diuretics

These drugs promote sodium and water excretion, thereby reducing

blood volume and blood pressure. Examples include hydrochlorothiazide and furosemide.

ACE inhibitors

Angiotensin-converting enzyme inhibitors cause vasodilation and lower blood pressure by preventing angiotensin I from being converted to angiotensin II. Lisinopril and enalapril are two examples.

Angiotensin receptor blockers (ARBs)

ARBs prevent angiotensin II from acting on its receptors. Valsartan and losartan are two examples.

Calcium channel blockers

These medications cause vasodilation by preventing calcium from entering vascular smooth muscle cells. Nifedipine and amlodipine are two examples.

Beta-blockers

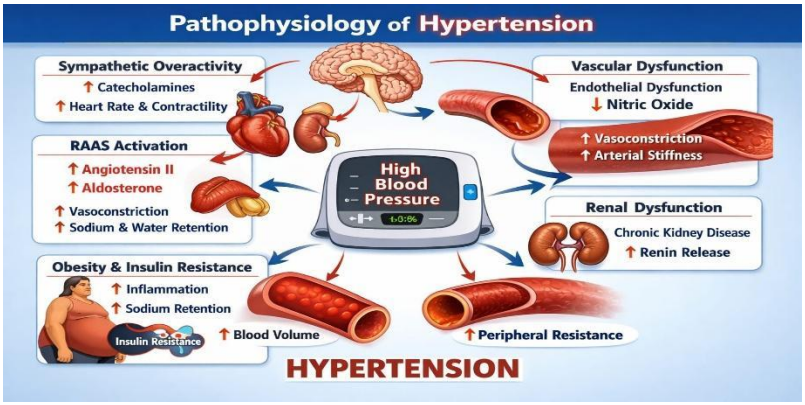

Figure 1: Pathophysiology of Hypertension

Beta-blockers decrease blood pressure by decreasing cardiac output and pulse rate. Propranolol and atenolol are two examples. For the best blood pressure control, combination treatment with two or more medications is frequently necessary.

ISBN 978-816855389-7

4. SGLT2 Inhibitors in Hypertension

A relatively recent family of medications called sodium-glucose cotransporter-2 (SGLT2) inhibitors was first created to treat type 2 diabetes. Recent research, however, has shown that these medications also have positive effects on the kidneys and heart. Dapagliflozin, empagliflozin, and canagliflozin are a few examples of SGLT2 inhibitors. Through a number of processes, including osmotic diuresis, natriuresis, and enhanced endothelial function, these medications lower blood pressure. SGLT2 inhibitors lower cardiovascular events and enhance results among individuals with hypertension and cardiac failure, according to clinical trials like the DAPA-HF and EMPEROR-Reduced investigations.

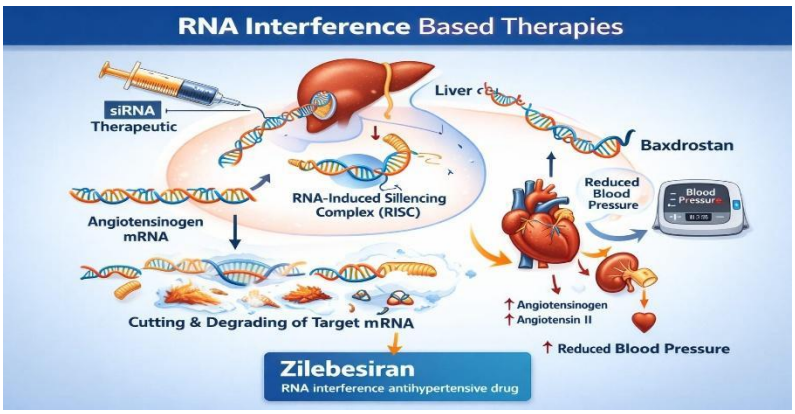

Figure 2: RNA Interferences

5. Non-Steroidal Mineralocorticoid Receptor Antagonists

The treatment of hypertension has traditionally involved the use of mineralocorticoid receptor antagonists. However, adverse effects, including hyperkalemia and hormonal imbalances, are linked to conventional medications like spironolactone. A new non-steroidal mineralocorticoid receptor antagonist with better selectivity and fewer side effects are finerenone. Finerenone lowers cardiovascular and renal problems in people with diabetes and hypertension, according

to clinical trials like the FIDELIO-DKD research.

6. Aldosterone Synthase Inhibitors

Aldosterone is crucial for controlling blood pressure and salt retention. Resistant hypertension is linked to excessive aldosterone production. Aldosterone synthesis is decreased by the selective aldosterone synthase inhibitor baxdrostat. Baxdrostat dramatically reduces blood pressure in patients with treatment-resistant hypertension, according to recent clinical studies. A potential strategy for treating individuals who don't react well to traditional treatments is this new class of medications.

7. RNA Interference-Based Therapies

One new therapeutic approach that can specifically silence genes linked to illness is RNA interference (RNAi) technology. Zilebesiran is one of the most promising RNA-based medications for hypertension. The gene that produces angiotensinogen, a crucial part of the RAAS pathway, is the target of zilebesiran, a small interfering RNA. This medication successfully decreases blood pressure by lowering angiotensinogen levels. Zilebesiran may be a long-acting treatment for hypertension since clinical research has shown that a single injection can lower blood pressure steadily for several months.

8. Device-Based Therapies

For individuals with resistant hypertension, device-based therapies are becoming more popular.

Renal Denervation

A catheter-based technique called renal denervation damages the sympathetic nerves in the renal arteries. This process decreases blood pressure by decreasing sympathetic activity. Renal denervation

ISBN 978-816855389-7

dramatically lowers blood pressure in individuals with resistant hypertension, according to recent clinical trials.

Baroreceptor Activation Therapy

Baroreceptors in the carotid sinus are electrically stimulated during this treatment. Reflex processes that lower blood pressure are triggered when these receptors are activated.

9. Precision Medicine in Hypertension:

The goal of precision medicine is to customize medical care based on a patient's genetic profile, way of life, and surroundings. Numerous genetic variations linked to hypertension have been found because of advancements in genomics. These findings might aid in the creation of individualized treatment plans. Wearable blood pressure monitors, smartphone apps, and telemedicine platforms are examples of digital health technology that are enhancing patient monitoring and treatment compliance.

10. Future Perspectives

Future studies in the treatment of hypertension will concentrate on finding novel pharmacological targets and creating cutting-edge therapeutic approaches. Long-acting injectable medications, microbiome-targeted therapeutics, and gene-based medicines may be crucial to the treatment of hypertension in the future. Predicting illness risk and improving treatment strategies may potentially be aided by artificial intelligence and big data analytics. To enhance treatment results and lessen the impact of hypertension worldwide, further research and clinical trials are necessary.

11. Conclusion

Patients now have a far wider range of treatment choices because of recent developments in hypertension management. SGLT2 inhibitors,

finerenone, and aldosterone synthase inhibitors are examples of novel pharmaceuticals that have demonstrated encouraging outcomes in lowering cardiovascular problems and enhancing blood pressure control. Patients with resistant hypertension have fresh hope thanks to RNA interference-based treatments and device-based interventions such as renal denervation. In the future, managing hypertension may be significantly enhanced by the combination of digital health technology and precision medicine.

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ISBN 978-816855389-7