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Review Article

Primary Hypertension: Historical Context, Current Treatment, Future Direction

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Abstract

It has been 100 years since hypertension was designated as a clinical condition, which resulted in the pursuit of contributing causes and treatment options. Controlling high blood pressure in patients has proved a daunting task: patient compliance with requisite lifestyle modifications and medicines. Many hypertensive patients report that medicines' adverse effects cause them to stop taking their medications as a fundamental reason for non-adherence. The requisite lifestyle changes are challenging to implement: finding time for exercise and quality, unadulterated foods. Nevertheless, in many cases, the patient is in control of the condition's outcome—which can be positively impacted by appropriate lifestyle interventions. This review describes the history of hypertension and outlines specific measurements, parameters, complications, causes, complications, and hypertension treatment.

Keywords: *Gordon Syndrome; Heart Failure; High Blood Pressure; Hypertension; Lifestyle; Sodium*

Abbreviations

ACA: American College of Cardiology; ACE: Angiotensin-Converting Enzyme; AHA: American Heart Association; BP: Blood Pressure; FH-I: Familial Hyperaldosteronism Type I; GRA: Glucocorticoid Remediable Aldosteronism; GWAS: Genome-wide Association Studies; HTN: Hypertension; IDH: Isolated Diastolic Hypertension; ISH: Isolated Systolic Hypertension; JNC: Joint National Commission; NIH: National Institutes of Health; PHA-2: Pseudohypoaldosteronism Type 2; QoL: Quality of Life; SNP: Single Nucleotide Polymorphism

Introduction

Historical perspective

As early as 2600 BCE, it was noted that excess dietary salt could adversely affect the pulse. Venerable physicians treated "hard pulse disease" with acupuncture, venesection and leeches. Ancient Egyptian physicians noted a correlation between the pulse and heart and

brain conditions. In 1628, William Harvey characterized blood flow. In 1733, Stephen Hales invented the manometer. He first measured equine arterial blood pressure [1].

In 1896, hypertension in humans was determined using a cuff-based mercury sphygmomanometer, invented by an Italian physician, Scipione Riva-Rocci [1,2]. In 1905, Russian physician, Nikolai Korotkoff, used a stethoscope to note specific artery sounds, later termed, Korotkoff sounds [1–3].

In the early 1900s, physicians identified essential hypertension, involving elevated blood pressure with no causative agent. Also, they described malignant hypertension, involving severe hypertension, which could result in organ damage or failure and death [1–4].

The perils of hypertension came to public attention, circa 1933, because of U.S. President Franklin D. Roosevelt. Roosevelt had hypertension (188/105) and was eventually treated with phenobarbital and massage therapy [1]. In February 1945, he experienced a blood pressure of 260/150. On the morning of April 12, 1945, he had a blood pressure of 300/190, reporting a severe occipital headache. Subsequently, he lost consciousness and died [1].

Roosevelt's death highlighted that there were few effective antihypertensive drugs before World War II, and available agents were poorly tolerated. Some treatments of that period included salt-restriction, injections of pyrogens, and adrenal surgery [1]. The use of sodium thiocyanate was limited due to high toxicity and low effectiveness [2,4]. Moreover, physicians did not uniformly recognize the need to treat this potentially lethal disease [1,3,4] aggressively.

Despite a known correlation between hypertension and death (from cardiovascular or renal disease), it took another decade for the management of hypertension to be incorporated into medical practice [1,3,4]. The Framingham Heart Study (initiated in 1948) confirmed hypertension as a risk factor in cardiovascular morbidity and mortality and established the need for medical intervention [1].

In the 1940s, hexamethonium, hydralazine, and reserpine were tried as antihypertensive agents. In the 1950s, chlorothiazide (a diuretic) was promoted [1,2]. In the 1960s, beta-blockers were developed, while calcium-blockers followed shortly thereafter. Then came angiotensin-receptor blockers and renin inhibitors [1]. Later, the Joint National Commission (JNC) with the National Institutes of Health (NIH) advanced guidelines for the treatment of hypertension. The American College of Cardiology (ACC) and American Heart Association (AHA) further developed these guidelines [1,4–6].

This paper aims to review important advances in understanding hypertension and its pharmacological management and provide an overview of current pharmacological management's drawbacks.

Discussion

The following provides a broad overview of measurements, parameters, causes, complications, and treatments of hypertension (HTN).

Defining HTN

HTN involves high blood pressure (BP), and is a major cause of medical visits and prescription use [5,6]. Roughly half of hypertensive individuals do not have adequate BP control.

Primary hypertension, known as essential hypertension, is challenging to identify. The majority of people with this type of hypertension seem no different than anyone with normal BP. Secondary hypertension results from other medical problems or medications, for example, kidney and liver disease. HTN may go unnoticed for years, damaging the body's systems, such as the lungs, blood vessels, brain,

kidneys, liver, and heart [7]. Resistant hypertension is elevated BP that does not respond well to aggressive medical treatment, including 3–4 BP medicines (at maximum dose), one of which is a diuretic [5–7].

Parameters of HTN

- Stage 1: systolic 130–139 mmHg; or diastolic: 80–89 mmHg.
- Stage 2: systolic, starting at 140 mmHg; or diastolic, starting at 90 mmHg.

  Note: The higher value of systolic versus diastolic governs the stage of HTN [7].

Complications of HTN

HTN can harm the body before overt symptoms appear. Uncontrolled HTN results in impairment, low quality of life (QoL), or death (from a heart attack or stroke). HTN can damage the arteries, heart, brain, liver, kidneys, and eyes [8]. The inflammatory response as a contributing factor, often accompanies HTN. The inflammatory process does not cause HTN; instead, it results in kidney and vasculature disorders [9,10].

Aging and HTN

Aging has been correlated with increased systolic BP, reduced diastolic BP, and broadened pulse pressures, due to a loss of tractability of the arteries. Isolated systolic hypertension (ISH) presents widely in the older adult population, with a systolic BP ≥ 140 mmHg and diastolic BP ≤ 90 mmHg; ISH ≥ 130/< 80 mmHg; isolated diastolic hypertension (IDH) < 130/≥ 80 mmHg [8].

Genetic causes of HTN

Monogenic disorders (which are rare), result in excess renal sodium reabsorption, inducing low-renin hypertension. Syndromes with elevated aldosterone levels include glucocorticoid remediable aldosteronism (GRA) or familial hyperaldosteronism and apparent mineralocorticoid excess [11]. Syndromes with low aldosterone levels include Liddle syndrome or pseudoaldosteronism [11,12]. Syndromes with low aldosterone levels with unique features include congenital adrenal hyperplasia. A defective NR3C2 gene can cause autosomal dominant hypertension (which is exacerbated in pregnancy). Hypertension and brachydactyly syndrome involve the mutated gene PDE3A [11–13].

To date, gene-linkage studies have yielded few reproducible results. Nonetheless, genetic factors are posited for 30–50% of the deviations in BP [13].

Non-pharmacological treatment of primary HTN

Pharmacological treatments for HTN are well documented, and information regarding utilized pharmaceuticals is readily available [13–15] and thus, will not be repeated herein (although the evolution of treatments is outlined in the Introduction). Medicines do not cure HTN; thus, the emphasis is on non-pharmacological interventions, such as lifestyle changes. Nonpharmacologic interventions include the following:

- Dietary salt restriction
- Potassium supplementation
- Weight loss

- DASH diet
- Exercise
- Limiting alcohol intake [5,6].

The benefits of these healthy lifestyle interventions in lowering high blood pressure have been well documented in the literature. A healthy lifestyle can help lower BP, allowing a person to stop or reduce medications. For example, in excess body weight and high blood pressure, losing 5–10% of body weight can significantly decrease BP [5,6].

Conclusion

More than a century of research has sought a cure for hypertension. Maintaining healthy blood pressure levels has proved elusive. Patient compliance with requisite lifestyle modifications and medicines is problematic. Many hypertensive patients report that the adverse effects of medicines cause them to stop taking their medications. Also, the requisite lifestyle changes are challenging to implement. In today's society, access to proper exercise and quality, unadulterated foods is demanding for most persons and impossible for others. Nonetheless, in many cases, the patient is in control of the condition's outcome—in lowering blood pressure. Appropriate lifestyle interventions positively impact hypertension. So, although the future of medical research should continue to seek more useful and efficacious medicines in controlling (and perhaps curing) hypertension, the onus is squarely on the individuals affected (to effect the necessary lifestyle changes) and society (to provide a social structure, work environment, and food sources more conducive to a healthier lifestyle).

Conflict of Interest Statement

The authors declare that this paper was written in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

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