

Study on pathologic mechanism and treatment of hypertension

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Abstract. Hypertension is a cardinal contributor to the global burden of disease due to its widespread prevalence and its insidious ability to instigate life-threatening complications such as stroke, cardiac failure, and renal injury disorders. This discourse reviewed the key drivers of hypertension pathogenesis, emphasizing the role of the renal system, particularly the interplay of angiotensin II and renal impairment. Moreover, hypertension's complex and multivalent management strategies were overviewed, illustrating the salience of lifestyle modifications, a panoply of pharmacological interventions, synergistic combination therapies, and the innovative approach of personalized medicine. Nevertheless, challenges such as medication adherence and balancing side effects remain, alongside the requirement for persistent medical oversight reflective of hypertension's chronic nature. As lethal complications ink the finality of hypertension's narrative, prompt identification and treatment are paramount. This comprehensive account concludes with an urge to further dissect this intricate condition and refine management strategies, propelling us towards a future with more efficacious hypertension control and diminished complication rates.

Keywords: Hypertension; Antihypertensive drugs; Complications; Stroke.

1. Introduction

Hypertension, commonly known as high blood pressure, ranks as one of the predominant chronic diseases affecting a vast segment of the global population. Over a span of 30 years, from 1988 to 2018, there has been a noticeable increase in its prevalence. Specifically, data reveals that the percentage of individuals aged 20 and above diagnosed with hypertension rose from 43% to a concerning 48.4% during this period [1]. This upward trend in hypertension cases is alarming, especially when one considers the associated health risks. Complications such as coronary heart disease, myocardial infarction, and stroke are directly linked to hypertension. These conditions not only deteriorate the quality of life but also pose a severe risk to the very life of those affected by high blood pressure.

At present, the pathogenesis of hypertension has been studied in detail, and the mechanisms of hypertension have been clearly pointed out [2,3]. The pathogenesis of essential hypertension is relatively complex, and many factors have been proven to be closely related to it: sustaining high intake of sodium, while insufficient intake of potassium and calcium; increased sympathetic nerve activity led by long-term exposure to high-intensity psychological stress in the living environment; excessive generation of vasoconstrictors and sodium-retaining hormones; alternations in structure, mechanical properties, and function of blood vessels, especially small arteries; the overreaction of the vascular system, the excessive increase of peripheral vascular resistance. The understanding of these complex pathogenesis is helpful for the research of hypertension treatment and the development of drugs.

Despite significant advancements, the realm of hypertension research still grapples with certain voids. Notably, while numerous plausible avenues elucidate the pathogenesis of hypertension, a cohesive and unified mechanism remains conspicuously absent. The intricate interplay of genetic predisposition, lifestyle factors, and physiological processes offers several conceivable routes through which hypertension may emerge. Yet, the absence of a singular, comprehensive framework hampers a complete understanding of the condition's complexities. This absence of a unified mechanism hinders the ability to develop universally effective interventions and treatments. Consequently, researchers continue to navigate these gaps, diligently exploring the intricate puzzle of hypertension's origins. The pursuit of a holistic comprehension encompasses unraveling the intricate web of

variables that contribute to its onset. As the scientific community delves deeper, bridging these gaps will be pivotal in not only enhancing therapeutic strategies but also shedding light on the broader landscape of cardiovascular health.

This article succinctly outlines five primary categories of hypertension pathogenesis and associated mechanisms. It also introduces corresponding pharmaceutical and therapeutic approaches. By encompassing these varied pathways, the article strives to enhance the understanding of hypertension's multifaceted nature and promote the development of effective treatments. This comprehensive overview serves as a valuable resource for both researchers and medical practitioners, bridging the gap between theoretical insights and practical applications in the realm of hypertension management.

2. The five types pathologic mechanism of hypertension

2.1. Vascular disorder

The predominant mechanism underlying hypertension is vascular dysfunction, which constitutes a multifaceted aspect meriting comprehensive exploration. A key facet within vascular dysfunction is vascular reactivity, wherein the intricate orchestration of the vascular system's responsiveness to specific hormonal and neural stimuli significantly impacts peripheral vascular resistance. The direct correlation between peripheral vascular resistance and blood pressure stems from their reciprocal dependence on blood flow rate. An exaggerated response of the vascular system, wherein peripheral vascular resistance undergoes excessive augmentation in response to specific stimuli, precipitates a noteworthy surge in blood pressure.

Empirical investigations have illuminated that individual afflicted with hypertension, as well as normotensive progeny of hypertensive lineage, exhibit a pronounced tendency for their vascular systems to hyperbolically escalate peripheral vascular resistance in reaction to specific stimuli, in contrast to normotensive counterparts. Furthermore, the phenomenon of vascular remodeling emerges as a pivotal participant in hypertension etiology and its associated complications. Vascular remodeling encapsulates a gamut of structural, mechanical, and functional alterations in blood vessels, particularly in the realm of small arteries.

In the context of chronic hypertension, conspicuous instances of vascular remodeling transpire, including the depletion of parallel-connected vessels, constriction of the lumen within resistance vessels, and amplification of arterial rigidity. This conglomerate of alterations collectively augments vascular resistance among hypertensive individuals. By unraveling the intricate nuances of vascular dysfunction, encompassing vascular reactivity and remodeling, a more nuanced comprehension of hypertension's intricate underpinnings is attainable, with the potential to catalyze targeted therapeutic strategies to effectively mitigate its impact [4].

2.2. Sympathetic nervous system disorder

A contributory mechanism to hypertension lies in the disruption of the sympathetic nervous system. Elevated sympathetic nervous system activity engenders heightened blood pressure levels, fostering the genesis and persistence of hypertension by eliciting cardiac, peripheral vasculature, and renal responses. This cascade instigates augmented cardiac output, escalated vascular resistance, and retention of fluids. Substantial evidence underscores the notion that sustained elevation in heart rate within the human context predominantly stems from attenuated parasympathetic influence, bolstering the assertion that autonomic imbalance substantiates the pathogenesis of hypertension [5].

Furthermore, the significance of diastolic blood pressure in relation to vascular resistance rather than cardiac performance comes to the fore. These observations infer that escalated sympathetic tone potentially amplifies diastolic blood pressure by inducing proliferation of vascular smooth-muscle cells and effecting vascular remodeling. As such, unraveling the intricate interplay between the sympathetic nervous system and hypertension not only enriches our comprehension of the ailment's

multifaceted origins but also presents a gateway to targeted interventions, aimed at rectifying the autonomic equilibrium and thereby mitigating the trajectory of hypertension [5].

2.3. Genetics

Moreover, delving into the realm of genetic influence on blood pressure unearths a tapestry of evidence substantiating the intricate links between hypertension and genetics. Predominantly, observational studies targeting genetically related or unrelated individuals offer a compelling vantage point. As anticipated, population-based investigations corroborate a heightened concordance in blood pressure levels within familial clusters compared to those between distinct lineages. Parallely, twin studies illuminate a greater coherence of blood pressure among biological siblings than among adoptive siblings cohabiting the same environment, thereby underscoring the limited role of shared surroundings in explicating elevated blood pressure occurrences.

Delving deeper, the genomic landscape reveals numerous gene segments or genetic loci manifesting correlations with blood pressure variations. A case in point is the M235T variant nestled within the angiotensinogen gene, which has been empirically linked to augmented circulating angiotensinogen levels and elevated blood pressure across diverse populations [6]. Paragons of genetic causality emerge as well, with the Liddle syndrome occupying a pivotal niche. This rare yet clinically significant disorder is characterized by constitutive activation of the epithelial sodium channel, imparting a predisposition to severe, intractable hypertension. The etiology of epithelial sodium channel hyperactivity has been traced back to mutations residing within the β or γ subunits of the channel, exemplifying specific genetic mutations that can precipitate pronounced physiological ramifications. This nexus between genetics and hypertension unfurls a domain of intricate interconnections, underscoring the interplay between individual genomic makeup and the intricate tapestry of hypertension pathogenesis.

2.4. Hormone enzyme and angiotensin secretion disorder

Regarding hormone enzymes and the secretion of angiotensin, a realm of intricately woven mechanisms emerges, characterized by their complexity. Central to this intricate landscape is angiotensin II, a potent contributor to blood pressure elevation, orchestrating its impact through a diverse array of pathways. Among its multifaceted actions, angiotensin II effects an increase in blood pressure through the constriction of resistance vessels, fostering the synthesis and subsequent release of aldosterone, and augmenting renal tubular sodium reabsorption. These actions, facilitated both directly and indirectly through aldosterone, collectively culminate in the modulation of fluid balance [7].

Additionally, angiotensin II exerts influence by instigating thirst and the release of antidiuretic hormone, further entrenching its impact on fluid homeostasis [7]. A noteworthy facet resides in its ability to amplify sympathetic outflow from the brain, contributing to the intricate orchestration of blood pressure regulation. A pivotal dimension unfurls as well, wherein angiotensin II fosters hypertrophy and hyperplasia within cardiac and vascular cells. This dual effect stems from its direct engagement with the angiotensin II type 1 receptor, while also indirectly inciting the liberation of an array of growth factors and cytokines. The resultant orchestration of cellular responses underpins angiotensin II's profound influence on the structural and functional dynamics of the cardiovascular milieu.

The intricate interplay between angiotensin II and its multifaceted downstream consequences epitomizes the intricate mechanisms woven within the fabric of blood pressure regulation [7]. This intricate choreography not only underscores the physiological sophistication underpinning hypertension but also elucidates potential nodes for targeted therapeutic intervention aimed at modulating these complex cascades for improved cardiovascular health.

2.5. Renal disorder

A conceptual framework seeking to unify the intricate pathophysiologic underpinnings of hypertension centers around the renal microvascular mechanism. This intriguing proposition, initially put forth by Henke, Lubarsch, and Goldblatt, posits that hypertension may trace its origins to primary renal microvascular abnormalities. Recent research endeavors have furthered this hypothesis, conducting comprehensive investigations within diverse animal models. These endeavors have yielded a coherent trajectory outlining the emergence of hypertension, wherein the kidney sustains progressive injury, ultimately culminating in the manifestation of selective afferent arteriopathy and tubule-Interstitial afflictions [8].

The proposed pathway delineates a multi-faceted initiation, wherein hyperactivity of the sympathetic nervous system or heightened engagement of the renin-angiotensin-aldosterone system may act as instigating factors. The pathway's activation may be potentiated by an array of genetic influences that promote sodium reabsorption or curtail sodium filtration. In addition, primary renal microvascular or tubulointerstitial diseases might serve as catalysts in initiating this trajectory. These cumulative triggers collectively foment renal vasoconstriction, engendering renal ischemia, particularly within the outer medullary regions. This ischemic milieu prompts leukocyte influx and the local generation of reactive oxygen species [8].

An additional dimension hinges on the generation of angiotensin II at sites of renal impairment, invoked as a stimulus for both structural alterations—manifesting as renal microvascular pathology—and attendant hemodynamic shifts, notably elevated vascular resistance, diminished ultrafiltration coefficient, and reduced sodium filtration. Collectively, these repercussions converge to precipitate hypertension. This proposed pathway interlaces harmoniously with established theories expounding on hypertension's pathogenesis, underscoring the intricate interplay between renal microvascular dynamics and systemic blood pressure regulation. Notably, while this framework amalgamates numerous established paradigms, its true resonance necessitates validation within the context of human disease, serving as a bridge between theoretical conjecture and clinical reality.

3. The current treatments of hypertension

3.1. Nonpharmacological method: Lifestyle modification

Hypertension's intricate management hinges on meticulous lifestyle recalibrations that embrace dietary adjustments, regular physical activity, weight management, and temperate alcohol consumption. Dietary Adjustments are instrumental in taming hypertension, and the Dietary Approaches to Stop Hypertension (DASH) diet forms a cornerstone. Comprising fruits, vegetables, whole grains, lean proteins, and low-fat dairy products, this regimen orchestrates a subtle yet profound reduction in sodium intake, pivotal in alleviating blood pressure.

Physical Activity assumes a pivotal role in the hypertension narrative. Beyond cardiovascular fitness, regular exercise fosters vasodilation, contributing to blood pressure modulation. Weight Management, closely linked to physical activity, serves as a linchpin. Even modest weight loss translates to blood pressure reduction, illuminating the intimate interplay between body mass and cardiovascular health. Moderation in Alcohol Consumption parallels these tenets, as excessive alcohol intake can amplify blood pressure, aggravating hypertension. Tobacco Avoidance, another key facet, mitigates the risk of constricted blood vessels, enhancing blood pressure control.

3.2. Pharmacological Interventions: Antihypertensive drugs

Pharmacological interventions surge forth when lifestyle measures falter. Diuretics manifest as frontline defenders, heightening sodium and water excretion to curtail blood volume and pressure. Beta-Blockers quell heart rate by impeding beta-adrenergic receptors, leading to reduced cardiac output. Calcium Channel Blockers, while targeting the heart, diminish arterial smooth muscle calcium influx, inducing vasodilation, and attenuating peripheral resistance.

Angiotensin-Converting Enzyme (ACE) Inhibitors mitigate angiotensin II synthesis, forestalling vasoconstriction and sodium reabsorption. Similarly, Angiotensin II Receptor Blockers (ARBs) obviate angiotensin II's effects via receptor blockade. Direct Renin Inhibitors are a nascent addition, stifling renin, thereby curtailing angiotensin II generation. Alpha-Blockers, by intercepting alpha-adrenergic receptors, usher arterial and venous dilation, reducing resistance and expediting blood pressure reduction. These pharmacological engagements are pivotal in hypertension management, tackling diverse pathophysiological pathways. Harnessing the synergy between diverse medication classes, Combination Therapies epitomize comprehensive blood pressure control. These amalgamated regimens amplify antihypertensive effects through the orchestrated modulation of multiple physiological factors. Combination therapies underscore the dynamic interplay between varied mechanisms, often outperforming singular interventions.

Personalized Medicine, an emergent paradigm, propels hypertension management into the era of precision-oriented care. Tailoring interventions to an individual's genetic and physiological traits augments treatment efficacy. This paradigm shift, aligning treatment strategies with unique patient profiles, optimizes outcomes, showcasing the potential for precision medicine in hypertension management. Nevertheless, challenges persist. Ensuring Medication Adherence, vital for sustained control, requires patient commitment. Balancing medication-induced side effects against therapeutic efficacy remains a delicate task. Consistent Medical Oversight underscores the chronic nature of hypertension management, necessitating ongoing healthcare engagement.

4. The Complications of hypertension

4.1. Stroke as a Complication of Hypertension

The classic definition of a stroke refers to a neurological deficit of cerebrovascular cause that persists beyond 24 hours or is interrupted by death within 24 hours. Hypertension is a leading risk factor for the development of stroke [9]. It contributes to stroke by accelerating the process of atherosclerosis - a pathological condition that causes the arteries to harden and narrow. Chronic high blood pressure also weakens the blood vessels in the brain, making them more likely to rupture and bleed, leading to hemorrhagic stroke. Clinical manifestations of hypertension-induced stroke depend on the area of the brain affected and include sudden numbness or weakness of the body, confusion, trouble speaking, visual disturbances, dizziness, loss of balance, and severe headache. The probability of experiencing a stroke double for each increment of 20/10mm Hg in blood pressure levels from a baseline of 115/75mm Hg [9]. Treatment of stroke typically hinges on swift intervention. Fibrinolytic therapy using tissue plasminogen activator (tPA) within the acute phase is beneficial. Preventive measures include the control of high blood pressure primarily through nonpharmacologic methods and medication.

4.2. Cardiac Failure as a Complication of Hypertension

Cardiac failure, commonly known as heart failure, signifies the heart's inability to pump efficiently [10]. Long-standing hypertension fosters left ventricular hypertrophy, a compensatory mechanism by which myocardial cells enlarge to manage increased workload. Over time, alternative remodeling occurs, curtailing the heart's pumping capacity and triggering heart failure. Manifestations of heart failure may include breathlessness, fatigue, fluid build-up, and reduced exertion capability. Hypertension-induced cardiac failure may be particularly resistant to therapy due to persistent afterload excess [10]. Treatment encompasses lifestyle modifications, high blood pressure control, and the use of medications like angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and beta-blockers to improve heart function. More severe cases may necessitate cardiac devices or transplantation [10].

4.3. Renal Injury and Disorder as a Complication of Hypertension

Persistent hypertension exerts a systemic impact, including renal dysfunction [11]. Hypertension disrupts renal autoregulation and inflicts direct vascular damage, fostering renal ischemia, nephron loss and, eventually, chronic kidney disease. Clinically, renal damage may be subtle initially, presenting as microscopic hematuria or slight proteinuria. As the disorder advances, symptoms of chronic kidney disease and end-stage renal disease develop. Hypertension remains a leading cause of end-stage renal disease, emphasizing the grim reality of this complication. Management of hypertensive nephropathy hinges on strict blood pressure control. ACE inhibitors or angiotensin II receptor blockers demonstrate beneficial effects, especially for those with proteinuria. Ultimately, prevention through optimal control of high blood pressure remains the gold standard to avoid these complications [11].

5. Limitations and future development

The comprehension and management of essential hypertension, while progressing significantly, are encumbered by various limitations that demand exploration for the advancement of therapeutic strategies. Presently, the field grapples with constraints stemming from the intricate interplay of genetic predispositions and environmental influences that underlie hypertension. Additionally, the etiology of essential hypertension remains multifactorial and complex, with no singular identifiable cause. This inherent complexity contributes to variations in patients' responses to available antihypertensive interventions.

A substantial research gap exists in the mechanistic understanding of essential hypertension, where there is a dire need to unravel the intricate molecular pathways contributing to the condition. Investigating the long-term implications of prevalent antihypertensive medications is also necessary to refine treatment approaches. Delving into the intricacies of angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers, and beta-blockers could unearth unforeseen effects that could guide clinical decisions more effectively. Furthermore, there is a persistent challenge in identifying precise targets for intervention, necessitating comprehensive studies to pinpoint novel therapeutic avenues.

Promisingly, technological advancements provide a ray of hope in surmounting these hurdles. Personalized medicine, an emerging paradigm, holds potential to revolutionize hypertension management. By integrating genetic profiles with clinical data, treatment plans can be tailored to an individual's unique genetic predisposition, optimizing therapeutic outcomes. The convergence of advanced imaging techniques and wearable devices enables continuous monitoring of blood pressure patterns, facilitating proactive interventions before complications manifest.

Anticipating the future, ongoing research endeavors are focused on unraveling the genetic tapestry of essential hypertension. The journey to uncover the intricacies of genetic determinants that contribute to hypertension susceptibility seeks to shed light on personalized treatment strategies. By identifying gene variants that confer higher risks of hypertension, researchers aim to implement preventive measures and deploy precision medicine with greater efficacy.

Collaborative efforts are pivotal to surmounting the multidimensional challenges posed by essential hypertension. Converging experts from diverse domains such as genetics, pharmacology, cardiology, and data science are essential to holistically comprehend the condition. This multidisciplinary approach paves the way for innovative interventions that address both genetic susceptibilities and environmental triggers, fostering a comprehensive and nuanced management approach.

In conclusion, the journey to understand and manage essential hypertension confronts intricate limitations rooted in the complex genetic and environmental landscape. While the challenges persist, ongoing research is driven by the promise of technological advancements and collaborative endeavors. By bridging these domains, the field inches closer to a future where precision medicine, targeted interventions, and interdisciplinary collaboration collectively redefine the boundaries of essential

hypertension management. It is this confluence of innovative research and shared expertise that holds the potential to transform the outlook for patients grappling with this pervasive cardiovascular disorder.

6. Conclusion

Hypertension, a pervasive condition characterized by elevated systemic blood pressure, exerts detrimental systemic implications, exacerbating the risk of serious complications like stroke, cardiac failure, and renal disorders. The pathogenesis of hypertension intertwines with an array of multifaceted components, from renal microvascular dynamics to complex genetic interactions, signifying its intricate and multifactorial nature. The successful mitigation of hypertension hinges on comprehensive strategies ranging from proactive lifestyle adjustments to advanced pharmacological interventions and personalized treatment plans. However, managing hypertension remains an enduring challenge due to non-adherence to medication, side effects, and the need for constant medical supervision. Future research aimed at illuminating the complexities of the disease and refining therapeutic interventions can present strategies for more effective management and mitigation of complications.

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