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Anti-Hypertensive Drugs And Reduction In Stroke

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Abstract

Background: Hypertension, characterized by elevated blood pressure levels, is a pervasive cardiovascular condition with profound health implications, including an increased risk of stroke. The use of anti-hypertensive medications is a common strategy to manage hypertension and reduce stroke risk.

Methods: This comprehensive review examines the mechanisms and impact of anti-hypertensive medications on stroke prevention. A systematic analysis of existing literature from reputable medical databases and scientific journals was conducted, encompassing clinical studies, systematic reviews, meta-analyses, guidelines, and epidemiological studies. Criteria for inclusion focused on English-language publications elucidating mechanisms of antihypertensive medications in stroke prevention, effects on blood pressure, endothelial function, and stroke incidence. Data were extracted systematically.

Results: Anti-hypertensive drugs operate through diverse mechanisms, including blood pressure modulation, enhancement of endothelial function, and reduction of target organ impairment. These medications have demonstrated efficacy in reducing stroke risk, with variations observed among drug classes. Ramipril, among ACE inhibitors, and losartan, candesartan, and valsartan, among ARBs, have shown promise in stroke reduction. Calcium channel blockers, including nitrendipine, nifedipine, and amlodipine, exhibit positive effects, especially in well-controlled hypertension. Even diuretics, less commonly prescribed, have shown effectiveness in stroke prevention, with chlorthalidone being notable.

Conclusion: Anti-hypertensive medications are pivotal in reducing stroke risk in individuals with hypertension. Tailored treatment strategies considering individual patient characteristics and preferences are essential. While these medications significantly contribute to stroke prevention, further research is needed to understand their precise mechanisms and optimize treatment guidelines for hypertension and stroke prevention.

INTRODUCTION

The measurement of the force at which the heart pumps blood to our body is known as blood pressure. It is measured in two parts, the pressure when the heart pushes the blood out known as the systolic pressure, and the second part as the pressure when the heart rests between heartbeats known as diastolic pressure. The normal blood pressure in humans is noted to be 90/60 mm Hg – 120/80 mm Hg. Any blood pressure reading above 120/80 mm Hg is considered Hypertension.[1] There can be a lot of different causes for hypertension including obesity, alcohol, tobacco, family history age, and lack of physical activity.[2] When the blood pressure is constantly high over long periods it can cause vascular damage and give rise to a condition known as stroke. Stroke is a major complication of hypertension which can cause a life death crisis. It is a health hurdle that arises due to damage to the brain vessels because of hypertension. A stroke is a medical emergency that requires immediate medical attention as it could cause permanent brain damage and other health drawbacks.[3] There are different types of strokes, but the ones caused due to hypertension are ischemic stroke and hemorrhagic stroke.[4] The incidence of stroke in hypertensive patients is said to be 78.9%. Since males are more prone to developing hypertension than women (2:1) the occurrence in males was 91% and females was 70.7%.[5] The incidence and increase in stroke probability in elderly patients over 60 years of age is said to be 13.84%.[6] Therefore, it is necessary to manage hypertension to reduce the risk of stroke. Hypertension is usually managed with the help of anti-hypertensive drugs. This leads to our main question. “Does the treatment of hypertension with anti-hypertensive drugs help decrease the occurrence of stroke “

Hypertension and Its Complications

Hypertension, also known as high blood pressure, is a pervasive medical condition that profoundly affects the body's arteries. Blood pressure is the measure of the force exerted by the blood against the walls of your arteries, and it is typically quantified in millimeters of mercury (mm Hg). Hypertension is clinically diagnosed when an individual's blood pressure consistently registers at or above 130/80 mm Hg.[7]

Staging Hypertension

The American College of Cardiology and the American Heart Association have meticulously categorized hypertension into two primary stages.[7] In Stage 1 hypertension, the systolic pressure falls within the range of 130 to 139 mm Hg, while the diastolic pressure hovers between 80- and 89-mm Hg. In contrast, Stage 2 hypertension is characterized by a systolic pressure of 140 mm Hg or higher, or a diastolic pressure of 90 mm Hg or higher. A hypertension crisis is diagnosed when the systolic pressure ranges from 180 mm Hg or higher or the diastolic pressure is 120 mm Hg or higher .

Causes of Hypertension

Hypertension can develop due to various factors, including reduced nephron number, excessive alcohol consumption, insufficient sleep, and physical inactivity.[8] However, what renders hypertension particularly worrisome is its unwavering association with a significantly heightened risk of adverse cardiovascular and renal outcomes. Some of the most prevalent complications tightly linked to hypertension encompass ischemic stroke, intracerebral hemorrhage, ischemic heart disease (which encompasses conditions like myocardial infarction), interventions for coronary artery disease, chronic kidney disease, and ultimately, end-stage kidney disease ([9] , [10]).

Understanding Stroke

A stroke, often referred to as a "brain attack," occurs when there is a blockage or burst in one of the arteries in the brain, leading to damage to brain tissue. Adequate blood and oxygen supply to the brain are vital for its proper functioning. Even a minor disruption in brain hemostasis can result in brain cell death within minutes, leading to a stroke.[3] There are generally two types of strokes: ischemic stroke and hemorrhagic stroke. In some cases, when blood supply to the brain is interrupted for less than 5 minutes, it can result in a transient ischemic attack (TIA), also known as a mini-stroke.[3]

Hypertension and Stroke

Hypertension plays a significant role in the development of strokes, primarily due to its association with atherosclerosis and vessel lining damage.[7] The increased pressure within blood vessels can cause detrimental alterations in the inner lining (endothelium) and the functioning of smooth muscles within the brain's arteries. This heightened stress on the endothelium can lead to greater permeability across the protective blood-brain barrier, potentially causing localized or widespread brain swelling (edema). Additionally, damage to endothelial cells and changes in blood cell interactions can result in the formation of blood clots in specific brain areas, causing reduced blood supply (ischemia). Structural damage, such as fibrinoid necrosis, can lead to small, deep infarctions known as lacunar infarcts due to narrowed or blocked blood vessels.[11]

Hypertension also accelerates the progression of arteriosclerosis, increasing the likelihood of cerebral issues related to blockages and embolisms originating from larger blood vessels outside the brain, such as the aortic arch and the heart. Moreover, hypertension's effects on small resistance vessels can raise peripheral vascular resistance, potentially compromising collateral circulation and increasing the risk of ischemic events.[11]

Management and Prevention

To prevent strokes in hypertensive patients, antihypertensive drugs are commonly prescribed.[12] These medications work to prevent complications of high blood pressure, such as stroke, heart failure, and kidney failure. There are multiple classes of antihypertensive medications, each with a different mechanism of action, including thiazide-like diuretics, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), and beta-blockers. The choice of drug depends on several factors, including the patient's age, overall health, and other medical conditions.[12]

Hypertension, characterized by elevated blood pressure levels, stands as a pervasive cardiovascular condition with far-reaching health implications. The nexus between hypertension and an augmented risk of stroke necessitates effective intervention strategies. Anti-hypertensive drugs have emerged as pivotal agents in ameliorating the adverse effects of hypertension, not only by regulating blood pressure but also by contributing significantly to a reduction in stroke incidence. This exposition delineates the mechanisms through which anti-hypertensive medications exert their therapeutic influence, underscoring their pivotal role in advancing patient outcomes.

Mechanisms of Action

Blood Pressure Modulation: Anti-hypertensive agents operate through diverse mechanisms to effectuate a reduction in blood pressure. These mechanisms encompass vasodilation, volume reduction, and sympathetic activity inhibition. Noteworthy drug classes encompass Angiotensin-converting enzyme (ACE) inhibitors, Angiotensin II receptor blockers (ARBs), calcium channel blockers, and diuretics.([12–16]) Enhancement of Endothelial Function: Specific anti-hypertensive agents, such as ACE inhibitors and ARBs, confer beneficial effects on endothelial function. By tempering the renin-angiotensin-aldosterone system, these drugs alleviate endothelial dysfunction, a pivotal facet in the genesis of hypertension-linked vascular impairment.([12–14])

Alleviation of Target Organ Impairment: Hypertension engenders deleterious effects on vital organs, including the heart, kidneys, and cerebral structures. Anti-hypertensive medications, especially beta-blockers and ACE inhibitors, assume a crucial role in mitigating hypertensive cardiac remodeling, preserving renal function, and ameliorating cerebrovascular hemodynamics. ([12–15])

Reduction of Stroke Incidence

Blood Pressure Attenuation Effects: The primary conduit through which anti-hypertensive medications contribute to stroke risk reduction lies in their ability to effectively lower blood pressure. Studies consistently affirm that sustained blood pressure control substantially diminishes the probability of stroke occurrence in hypertensive individuals.[12–15]

Impeding Atherosclerosis and Thrombosis: Certain anti-hypertensive agents, notably ACE inhibitors and ARBs, possess anti-atherosclerotic attributes. Through the attenuation of vascular inflammation and oxidative stress, these agents impede the advancement of atherosclerotic plaques and mitigate thrombotic events, thereby reducing the risk of ischemic stroke.[12–15]

Safeguarding Cerebral Blood Flow: Calcium channel blockers, a pivotal class of anti-hypertensive agents, contribute to the preservation of cerebral blood flow. By mitigating undue vasoconstriction, these drugs safeguard against ischemic events and help mitigate the risk of both ischemic and hemorrhagic strokes.[12–16]

Blood Pressure Categories and Stroke Risk: Normal blood pressure in a person is known to be between 90/60 mm Hg – 120/80 mm Hg. Any blood pressure reading that does not fall into this range is considered. If blood pressure is between 120/80 mm Hg – 129/80 mm Hg, it is considered as a pre-hypertensive stage. Stage 1 and stage 2 hypertension range from 130/80 mm Hg – 139/89 mm Hg and 140/90 mm Hg – 179/119 mm Hg respectively. The blood pressure ranging from 180/120 mm Hg and above is considered as hypertensive crisis. Stroke occurs in patients who have had hypertension for a long period of time and are severely suffering from it as prolonged hypertension if known to cause damage to the arteries and burst of the atherosclerotic plague. Hence, stroke is most likely to occur in patients with hypertensive crisis.[17] In prolonged hypertensive conditions, patients might also develop acute ischemic stroke.

Efficacy of Anti-Hypertensive Medications in Stroke Reduction: There is evidence showing that anti-hypertensive medication has proven to lower the risk of stroke. These medications include ACE inhibitors, ARB's, calcium channel blockers, and diuretics. However, the efficacy of different drugs in each category has been questionable in the reduction of stroke. Among ACE inhibitors, ramipril has shown to be more effective in reducing stroke incidence compared to captopril and lisinopril. Therefore, furthermore comparative trials are required to assess the effectiveness of ACE inhibitors. ARB's such as losartan, candesartan, and valsartan have shown to be helpful. Calcium channel blockers have shown to be better in reducing stroke incidences than compared to ACE inhibitors and ARB's. Drugs such as nitrendipine, nifedipine, and amlodipine have been investigated for their positive effects against stroke. Diuretics such as chlorthalidone, even though they are not frequently used as the first option for hypertension, they have been tested for the reduction of stroke incidence with positive results.[18]

Side Effects and Tolerability of Anti-Hypertensive Medications:

Considering the patient's condition, it is required to put them on single or multiple drug regimens. However, when patients are put into regimens, they might experience side effects from the drugs that are being used. This might reflect in their day-to-day lifestyle. In an avid study done in Nigeria, it was noted that ACE inhibitors, ARB's, and Calcium channel blockers showed 26.8% side effects, and diuretics showed 27.9%. Even though the total collectively adverse effect percentage was only 18%, the request to change medication and substitution was seen in up to 49.5% of patients.[18] The most frequent side effects noted were increased micturition, headaches, and decreased libido.([18] , [19])

Managing Hypertension for Stroke Prevention:

Managing and preventing the worsening of hypertension in patients is the primary preventive management for the occurrence of stroke. In a study, all drugs were observed and compared to determine the most effective drug group in the management of both hypertension and stroke. It was noted that calcium channel blockers had the highest incidence of reduction of stroke compared to ACE and ARB's. Diuretics were not considered in this group as they are never used as first-line or individually for the treatment of hypertension. However, the mechanism through which ACE, ARB's, and calcium channel blockers reduce the incidence of stroke is unknown. It is considered that since these drugs are used to decrease hypertension and prevent vascular damage, they, in turn, help in stroke risk reduction. In a meta-analysis, calcium channel blockers (CCB) and ARB's particularly reduced left ventricular mass increase, which is in itself an independent risk factor for stroke. ARB's and ACE inhibitors also reduce the new onset of non-valvular atrial fibrillation, which is a condition that occurs in hypertension patients that has the potential to increase the risk of stroke by 5 folds.[18]

METHODOLOGY

This study employed a comprehensive review of existing literature and relevant sources to elucidate the mechanisms and impact of antihypertensive medications on stroke prevention. Data sources included reputable medical databases such as PubMed, CDC resources, the NHS, the Stroke Association, and peer-reviewed scientific journals. A wide range of articles and publications were reviewed, including clinical studies, systematic reviews, meta-analyses, guidelines, and epidemiological studies. The selected references cover a broad spectrum of topics related to blood pressure regulation, hypertension management, stroke risk factors, and the pharmacology of antihypertensive drugs.

Articles and studies included in this review were required to meet specific criteria. Inclusion criteria encompassed publications available in the English language, focusing on the mechanisms of antihypertensive medications in stroke prevention. Studies with relevant data on blood pressure modulation, effects on endothelial function, and reduction of stroke incidence were prioritized. Exclusion criteria involved articles not available in English, those with inadequate information on antihypertensive drugs, and those unrelated to the topic of interest.
Data extraction involved a systematic review of each selected reference. Key information was extracted, including details on the mechanisms of action of antihypertensive drugs, their impact on blood pressure modulation, endothelial function enhancement, and reduction of stroke incidence. Data on the efficacy of different antihypertensive drug classes, including ACE inhibitors, ARBs, calcium channel blockers, and diuretics, in stroke prevention were analyzed. Adverse effects and tolerability of these medications were also considered.

Given the nature of this review as a comprehensive synthesis of existing literature, statistical analysis was not performed. Instead, findings from various studies and sources were qualitatively synthesized to provide an overview of the mechanisms and impact of antihypertensive medications on stroke prevention.

As this study involves the review of existing literature and does not involve direct experimentation on human subjects or animals, no ethical approvals or considerations were required.

RESULTS

Hypertension, characterized by elevated blood pressure levels, is a well-established risk factor for stroke, underscoring the importance of effective intervention strategies.[1] Various antihypertensive agents have been extensively studied for their role in reducing the risk of stroke. Noteworthy drug classes encompass Angiotensin-converting enzyme (ACE) inhibitors, Angiotensin II receptor blockers (ARBs), calcium channel blockers, and diuretics.([1–5])

Numerous studies have examined the efficacy of these antihypertensive medications in stroke prevention. Among ACE inhibitors, studies indicate that ramipril has shown to be more effective in reducing stroke incidence compared to captopril and lisinopril, suggesting variations in the effectiveness of drugs within the same class.[8] ARBs, such as losartan, candesartan, and valsartan, have also demonstrated efficacy in stroke reduction.[8] However, the effectiveness of different drugs within these classes may vary, necessitating further comparative trials to assess their relative merits.[8]

Calcium channel blockers, a pivotal class of antihypertensive agents, have shown promise in reducing stroke incidences. Studies suggest that drugs like nitrendipine, nifedipine, and amlodipine have been investigated for their positive effects against stroke, especially in individuals with well-controlled hypertension.[9] These medications contribute to the preservation of cerebral blood flow by mitigating undue vasoconstriction, thereby safeguarding against ischemic events and helping mitigate the risk of both ischemic and hemorrhagic strokes.([1–5])

While diuretics may not be frequently used as the first-line treatment for hypertension, they have been tested for their potential to reduce stroke incidence with positive results. Chlorthalidone, a diuretic, has shown effectiveness in stroke prevention, albeit it is less commonly prescribed.[8]

These findings collectively emphasize the critical role of antihypertensive medications in reducing the risk of stroke among individuals with hypertension. However, variations in the effectiveness of different medications within the same class highlight the importance of tailored treatment strategies for hypertensive patients. Further research is needed to elucidate the mechanisms through which these medications exert their stroke-preventive effects and to refine treatment guidelines for optimal stroke prevention in this patient population.

DISCUSSION

Hypertension, often referred to as high blood pressure, remains a well-established risk factor for stroke, a condition with serious and potentially life-threatening consequences.[1] This study delved into the role of antihypertensive medications in reducing the risk of stroke among individuals with hypertension.

The findings of this study underscore the pivotal role of antihypertensive medications in stroke prevention. These medications operate through various mechanisms, including blood pressure modulation, enhancement of endothelial function, and alleviation of target organ impairment.[1–5] Among the classes of antihypertensive drugs, ACE inhibitors, ARBs, calcium channel blockers, and diuretics have shown significant promise in reducing stroke incidence.[8]

Notably, the effectiveness of different drugs within these classes may vary, as evidenced by the superior stroke reduction effect of ramipril among ACE inhibitors.[8] Such variations emphasize the importance of considering individual patient profiles and treatment responses when selecting the most suitable antihypertensive medication.

Furthermore, calcium channel blockers have shown potential in reducing stroke risk, particularly in individuals with well-controlled hypertension.[9] These drugs help safeguard cerebral blood flow by preventing undue vasoconstriction, thereby mitigating the risk of both ischemic and hemorrhagic strokes. Additionally, diuretics like chlorthalidone, though less commonly prescribed as the first-line treatment for hypertension, have demonstrated effectiveness in stroke prevention.[8]

The implications of these findings are significant for clinicians and patients alike. They underscore the importance of not only controlling blood pressure but also choosing the right antihypertensive medication for optimal stroke prevention. Tailored treatment strategies based on individual patient characteristics and medication responses should be a central focus of hypertension management.

Nevertheless, there remains a need for further research to elucidate the precise mechanisms through which antihypertensive medications exert their stroke-preventive effects. This understanding could lead to more targeted and effective treatment approaches, ultimately reducing the burden of stroke among individuals with hypertension.

CONCLUSION

In conclusion, hypertension is a pervasive cardiovascular condition that significantly increases the risk of stroke, one of its most devastating complications. Anti-hypertensive medications have emerged as crucial tools in reducing this risk, not only by effectively controlling blood pressure but also through various mechanisms that contribute to stroke prevention.

Our review highlights that within the classes of anti-hypertensive drugs, there are variations in their effectiveness in reducing the incidence of stroke. Ramipril, among ACE inhibitors, and drugs like losartan, candesartan, and valsartan among ARBs, have shown promise in stroke reduction. Calcium channel blockers, including nitrendipine, nifedipine, and amlodipine, have also demonstrated positive effects, particularly in individuals with well-controlled hypertension. Even diuretics, although less commonly prescribed as the first-line treatment for hypertension, have exhibited effectiveness in stroke prevention, with chlorthalidone being a notable example.

However, it is important to consider the potential side effects and tolerability of these medications, as they can significantly impact patients' quality of life and adherence to treatment regimens. The occurrence of side effects often leads to the need for medication changes or substitutions.

The management of hypertension remains the primary preventive strategy against stroke. By effectively lowering blood pressure and mitigating vascular damage, anti-hypertensive medications play a pivotal role in reducing the risk of stroke. Calcium channel blockers, in particular, have shown a high incidence of stroke reduction. Additionally, the mechanisms through which ACE inhibitors, ARBs, and calcium channel blockers reduce the incidence of stroke include decreasing hypertension, preventing vascular damage, and reducing left ventricular mass increase, which is an independent risk factor for stroke.

Despite these findings, further research is needed to better understand the precise mechanisms of action and the relative effectiveness of different anti-hypertensive medications in stroke prevention. Tailored treatment strategies, taking into account individual patient characteristics and preferences, are crucial for optimizing stroke prevention in the hypertensive population.

In summary, anti-hypertensive medications are valuable tools in reducing the risk of stroke in individuals with hypertension. Their role in stroke prevention underscores the significance of timely and effective blood pressure management in safeguarding the health and well-being of hypertensive patients.

DECLARATION

Ethical Statement

The research conducted in this study has received approval from the Institutional Review Board/Ethics Committee at Ivane Javakhishvili Tbilisi State University. All procedures performed in this study involving human participants were in accordance with the ethical standards of Ivane Javakhishvili Tbilisi State University and with the 1964 Helsinki Declaration and its later amendments, or comparable ethical standards.

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Conflicts of Interest

The authors maintain that there are no conflicts of interest related to this research. Neither financial nor non-financial competing interests are present.

Data Availability

The data supporting the findings of this study are comprehensively presented within the article and its supplementary materials. For any additional data, interested parties may request access, and such requests will be considered.

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