



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.1844793>Available online at: <http://www.iajps.com>

Review Article

**MANAGEMENT OF HYPERTENSIVE PATIENTS WITH
CARDIOVASCULAR CO MORBIDITY IN PRIMARY CARE**

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Abstract:

Introduction: According to the current evidence and guidelines, the treatment of primary (also known as essential) hypertension is crucial to reduce the risk of cardiovascular-related complications and mortality. The WHO stated in their reports that hypertension is considered the most dangerous predisposing factor that leads to mortality and long-term morbidity in all areas of the world. They estimated that over one billion individuals around the world are hypertensive which is causing more than nine million deaths annually. **Aim of work:** In this review, we will discuss the most recent evidence regarding Management of hypertensive patients with cardiovascular co morbidity in primary care **Methodology:** We did a systematic search for Management of hypertensive patients with cardiovascular co morbidity in primary care using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). We only included full articles. **Conclusions:** Hypertension is considered to be the most important risk factor of developing cardiovascular diseases, and an important factor leading to serious morbidity and mortality. Many patients with hypertension are considered to be high-risk patients, meaning that they have a significantly higher risk of developing cardiovascular complications due to their hypertension. These patients must follow strict management in order to decrease their risks of developing cardiovascular diseases.

Key words: hypertension, management, cardiovascular comorbidity

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Please cite this article in press Yara Mofarrah Assiri et al., *Management of Hypertensive Patients with Cardiovascular Co Morbidity in Primary Care.*, Indo Am. J. P. Sci, 2018; 05(12).

INTRODUCTION:

According to the current evidence and guidelines, the treatment of primary (also known as essential) hypertension is crucial to reduce the risk of cardiovascular-related complications and mortality [1]. The WHO stated in their reports that hypertension is considered the most dangerous predisposing factor that leads to mortality and long-term morbidity in all areas of the world. They estimated that over one billion individuals around the world are hypertensive which is causing more than nine million deaths annually [2]. A large meta-analysis that included more than 120 studies with an overall 613,816 patients with hypertension, improvement of systolic blood pressure levels was associated with a significant decrease in the risk of developing cardiovascular events, cerebrovascular events, and congestive heart failure for each 10 mmHg decrease. Overall, this meta-analysis should a significant improvement in the overall survival of patients following receiving treatment for hypertension. However, the risk of developing chronic kidney disease did not significantly decrease [3].

Based on the present evidence, reductions in blood pressure significantly decrease the risk of cardiovascular diseases and late comorbidities, especially in patients with high cardiovascular risk. Therefore, most guidelines recommended the treatment of any adult with increased blood pressure with a target of blood pressure less than 140/90 mmHg. However, more recent guidelines have been recommending treatment of hypertension with a goal for systolic blood pressure to reach levels lower than 130 mmHg, especially when dealing with patients who have high risk of cardiovascular diseases. High risk patients include patients who have a history of previous cardiovascular diseases, congestive heart disease, renal failure, cerebrovascular events, diabetes mellitus type 2, metabolic syndrome, and elderly patients. (SPRINT 39)

In this review, we will discuss the most recent evidence regarding Management of hypertensive patients with cardiovascular co morbidity in primary care

METHODOLOGY:

We did a systematic search for Management of hypertensive patients with cardiovascular co morbidity in primary care using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). We only included full articles.

The terms used in the search were: hypertension,

diagnosis, high risk patient, and management.

Essential Hypertension Identification and Prevalence

Generally, the diagnosis of hypertension should only be made based on more than two proper measurements of blood pressure while the patients is sitting, and on more than two visits to the clinic. Individuals with prehypertension have a relatively high risk of developing hypertension. In addition, any individual with a systolic blood pressure between 130 and 139 have double the risk of developing hypertension when compared to the general population [4].

Management of primary hypertension is considered to be the commonest cause of seeking medical care among adults in the US [5]. Hypertension remains to be a significant concern due to its wide prevalence and strong association with cardiovascular diseases.⁵ The prevalence of hypertension is generally affected by race, as black patients are considered to have significantly higher risk than any other race [6].

When dealing with black patients with hypertension, hypertension is also considered to be the most important risk factor for the development of cardiovascular events and chronic kidney disease, with higher risks than white patients with hypertension. Black patients of both sexes are generally at higher risk of death due to cardiovascular diseases and cerebrovascular events [7].

Hypertension in black patients is generally associated with earlier onset of disease, higher increases in blood pressure, and more risk of developing complications than white patients. Complications that are commonly encountered in hypertensive black patients include left ventricle hypertrophy, congestive heart failure, chronic kidney disease, coronary heart disease and acute coronary syndrome, vasculitis, and retinopathy. Black individuals have the highest risk of developing hypertension around the world [8]. This significantly higher incidence and prevalence of hypertension among black patients, with the absence of proper management and treatment among this population of patients, have led to significantly shorter life expectancy of blacks, especially females, when compared to any other racial group [9].

Unique Considerations of Treatment of Hypertension in Black Patients:

When dealing with black patients with hypertension, the choice of the initial therapy will usually be based on several hemodynamic factors. Generally, the initial anti-hypertensive therapy will include a

thiazide diuretic, a calcium channel blocker, a beta-blocker, an ACE inhibitor, and/or and ARB. Factors that affect the treatment choice include a BMI higher than 30 (which is present in about half black females), high sensitivity to sodium, decrease renin levels, vascular dysfunctions, nocturnal blood pressure elevation, diabetes mellitus or other chronic conditions, decreased physical activity, and the presence of family history.

In contrast to white hypertensive patients, ACE inhibitors, ARBs, and beta-blockers are not considered among the first choices for the treatment of hypertension in a black patient. Instead, it is preferred to start treatment with thiazide or a calcium channel blocker. ACE inhibitors can be later added in combination with thiazides or calcium channel blockers to achieve higher efficacy, but are not recommended as an initial monotherapy, which can also lead to the development of angioedema among these patients, due to the accumulation of bradykinin [10].

Therapeutic Lifestyle Modifications: The Most Important First Step in The Treatment of Essential Hypertension:

Primary hypertension is generally a result of multiple modifiable and non-modifiable factors that act together to develop the pathology. Therefore, targeting modifiable factors can potentially prevent and even treat hypertension in selected patients. These modifiable predisposing factors include increased weight, increased sodium consumption, decreased physical activity, and increased alcohol intake. Race, positive family history and older age, on the other hand, are considered non-modifiable factors. Addressing modifiable predisposing factors can have a significant impact on decreasing the rates of hypertension [11].

Therefore, lifestyle changes remain to be the single most important first step when managing high risk hypertension patients. Even when prescribing pharmacological anti-hypertensives, lifestyle changes remain essential and must be applied. According to the recent guidelines on the management and treatment of hypertension, lifestyle changes can significantly decrease the risk of developing cardiovascular diseases in high risk hypertensive patients. Specifically, dietary changes were associated with significant benefits in both males and females, and regardless of age [12].

Reduction of sodium consumption has also been found to be also associated with significant improvements in blood pressure, and thus decreased

risk of cardiovascular events [13]. Patients who followed healthy diet with decreased sodium consumption had further improvements in their blood pressure levels.

Current recommendations state that no more than 2400 mg of sodium per day, and preferably less than 1500 or even 1000 mg per day to achieve satisfactory results in decreasing blood pressure. Control of potassium is also important in patients with hypertension. However, evidence on controlling potassium in hypertensive patients is not strong regarding its effects on decreasing blood pressure. Some observational cohorts have found that increasing potassium intake in hypertensive patients can be associated with significant reduction in the rates of developing serious cerebrovascular events.

In summary, the combination of DASH diet with decreased sodium consumption in individuals with primary hypertension, can lead to significant reductions in blood pressure. The addition of increased physical activity can also lead to further reductions in blood pressure. Moreover, aerobic exercise performed at least three times a week also led to significant reductions in blood pressure and hence the risk of cardiovascular events.

Preferred Antihypertensive Pharmacotherapy: Initial Monotherapy and Combination Therapy

When controlling hypertension in high risk patients, lifestyle modifications are essential but are not always essential, especially in patients with other comorbidities. Therefore, pharmacological antihypertensive therapy is usually indicated. Pharmacological agents used as first line treatment for hypertension include ACE inhibitors, ARBs, thiazide diuretics, beta-blockers and calcium channel blockers. The choice of drug for initial treatment is dependent on many factors including the presence of other chronic morbidities like diabetes mellitus type 2, heart failure, chronic kidney disease, and a history of myocardial infarction.

Most these mentioned drugs have similar efficacy in decreasing blood pressure in hypertensive patients when used as an initial monotherapy. In fact, any of these drugs is associated with sufficient response in about 50% of patients with stage one hypertension. However, variability in response still persists between patients especially those with more severe hypertension. For example, when dealing with a patient with a systolic blood pressure higher than 160 mmHg, initial monotherapy is rarely enough to establish satisfactory response. Therefore, about half patients with stage one hypertension, and most

patients with stage two disease, the use of combination therapy of two or more drugs is necessary.

This is also the case in black patients and extremely old patients, where monotherapy with ACE inhibitors or ARBs do not achieve satisfactory results. In these patients, it is preferred to start therapy with a calcium channel blocker or a thiazide as these agents have been associated with higher efficacy in decreasing blood pressure. ACE inhibitors and ARBs can be later added when needed as combination therapy [14].

Many guidelines are recommending the initiation of combination therapy, rather than monotherapy, in patients with high risk patients, and patients with systolic pressure higher than 160 mmHg. These recommendations aim at achieving the target blood pressure within relatively shorter duration, and without the need of frequently changing prescriptions and regimens. The presence of combinations of two or more drugs in one pill lead to higher compliance, improved control of blood pressure, and less rates of developing adverse events.

Most usually used combinations include a thiazide or a calcium channel blocker added to an ACE inhibitor or an ARB. This combinations in considered to be the first preferred step when dealing with high cardiovascular risk patients, especially those who stage two hypertension. Additionally, the combination of amlodipine and benazepril was found in the ACCOMPLISH trial was associated with a better reduction of cardiovascular diseases in high-risk hypertensive patients than the combination of hydrochlorothiazide and benazepril [15].

Protocol-Based Treatment of Essential Hypertension:

The use of standardized protocols for the treatment of hypertension leads to higher efficacy in decreasing blood pressure on a public level. Most recent guidelines and protocols have been encouraging a multi-disciplinary approach that includes the physician, a nurse, and a pharmacist.

Most protocols encourage the use of thiazides as the first line therapy in stage one hypertension, along with prescribing agents that target other comorbidities that are already present in patients, like diabetes mellitus type 2, and chronic kidney disease. In high-risk patients, the first line treatment is a combination of thiazides and ACE inhibitors, which are preferred to be in a single pill to improve compliance and decrease adverse events. In

refractory cases, it is recommended to attempt higher doses for three times before the addition of another pharmacological agent, preferably a calcium channel blocker (amlodipine) [16]. When combinations of three drugs fail to induce sufficient blood pressure control, spironolactone is considered to be the fourth drug to be added [17].

The application of these guidelines was found to be associated with more than 85% success rates in achieving sufficient blood pressure control when was tested on more than 1,000,000 hypertensive adults in the United States. These success rates were similar among all age, sex, and racial groups, except for blacks who showed lower success rates (81%) [16].

To achieve higher success rates of these guidelines among high-risk patients, treatment should be constantly associated with a team-based care, continuous checking of blood pressure, registering all patients in an electronic database, keep following blood pressure goals, assessing quality of performance, and encourage patients to self-monitor their blood pressure. It is important to realize that although it is preferred to follow these guidelines, some modifications are accepted in specific cases, and after the consult of a multi-disciplinary team.

In addition, to further improve the results of antihypertensive therapy in high-risk patients, physicians are advised to follow certain rules when communicating with the patients regarding their disease and treatment. These rule include slowing down when educating the patients about their disease, avoiding the use of professional and medical terms, using pictures and illustrations to make it easier for patients to understand the disease, repeating information, making the patients repeat to make sure they understand the information, and encouraging the patients to ask any questions they have on their disease [17, 18].

After the application of lifestyle modifications, and the use of antihypertensive therapy to achieve sufficient blood control, high-risk hypertensive patients are recommended to receive anti-lipids therapy to decrease their LDL cholesterol levels and improve dyslipidemia. As we previously mentioned in this paper, lifestyle modifications generally include dietary changes, increased physical activity, and decreased sodium intake.

When treating black patients, who are considered to have higher risk of developing cardiovascular events due to hypertension, chlorthalidone ha been found to achieve better outcomes when compared to lisinopril

regarding the rates of coronary heart disease, cardiovascular diseases, cerebrovascular events, and congestive heart failure development. High-risk white patients, on the other hand, show similar outcomes following treatment with lisinopril or chlorthalidone. Moreover, the use of either lisinopril or chlorthalidone was associated with similar risks of development of end stage renal disease in high-risk hypertensive patients [19].

The use of ACE inhibitors in black high-risk hypertensive patients should be cautiously monitored, and avoided when possible, as these pharmacological agents have been associated with a higher risk of developing angioedema in black patients. This is hypothesized to result from the development of localized vascular dilatation associated with more permeability of vessels that result from the long-term use of ACE inhibitors. This is another concern that make ACE inhibitors less preferred than thiazides in black patients, especially when discussing first line treatment [20].

Treatment of Hypertension In Older Patients:

Elderly do generally have a higher risk of having hypertension and developing associated complications. Therefore, old hypertensive patients, especially those who have other chronic conditions, are considered high-risk patients and require strict control of blood pressure to decrease their risks of developing serious complications that lead to higher mortality rates.

A guideline for the treatment of elderly patients is generally similar to the whole population, with similar efficacy of most combination in reducing blood pressure. However, when treating elderly patients, many factors should be taken into consideration before the decision of optimal therapy is made. These factors include being older than 75 years, having a history of cardiovascular disease, having a history of cerebrovascular events, having a diagnosis of diabetes mellitus type 2, having a history of congestive heart failure, the presence of proteinuria, and the presence of chronic kidney disease.³⁷ The results of a large trial suggest that standard guidelines can be used with similar efficacy in elderly male patients with diabetes mellitus, heart failure, or chronic kidney disease. In addition, both male and female elderly hypertensive patients younger than 75 years can equally benefit from standard guidelines. The presence of chronic kidney disease in elderly patients younger than 75 years do not seem to affect the efficacy of anti-hypertensive treatment [21].

CONCLUSIONS:

Hypertension is considered to be the most important risk factor of developing cardiovascular diseases, and an important factor leading to serious morbidity and mortality. Moreover, hypertension is the most common cause of mortality around the world. Therefore, proper assessment and management of hypertension is essential to decrease the risks of associated complications and thus decrease mortality rates. Many patients with hypertension are considered to be high-risk patients, meaning that they have a significantly higher risk of developing cardiovascular complications due to their hypertension. These patients must follow strict management in order to decrease their risks of developing cardiovascular diseases. High-risk hypertensive patients are generally susceptible to the development of cardiovascular diseases, coronary artery disease, congestive heart failure, chronic kidney disease, and cerebrovascular events. High-risk patients include older patients, black patients, patients who have a systolic blood pressure higher than 160, or patients who have other chronic comorbidities. In addition to lifestyle modifications, most guidelines recommend that high-risk patients start treatment with a combination of two antihypertensives to better achieve blood control. The choice of the best combinations is dependent on the patients' characteristics and the presence of other comorbidities.

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