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LONG-TERM EFFECTS OF ANTIHYPERTENSIVES ON HYPERTENSION MANAGEMENT

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Abstract:

Introduction: *Hypertension is currently considered the major chronic disease affecting the global health, a leading worldwide public health problem; It is considered one the most important risk factors for cardiac, cerebrovascular and kidney diseases by World Health Organization. Many guidelines exist for the management of hypertension. Most of them include Lifestyle modifications and Pharmacologic therapy. If a lifestyle modification fails to to achieve the goal BP, there are several drug options for treating and managing hypertension. In this review, we point out the effect of chronic use of antihypertensive medications on hypertensive patients.****Aim of work:*** *In this review, we will discuss the common effects of antihypertensives on hypertension management.****Methodology:*** *We did a systematic search for appendicitis and appendectomy using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). Our search also looked for effect of antihypertensives on hypertensive patients. All relevant studies were retrieved and discussed. We only included full articles.****Conclusions:*** *Hypertension is currently considered the major chronic disease affecting the global health, a leading worldwide public health problem, It is considered one the most important risk factors for cardiac, cerebrovascular and kidney diseases by World Health Organization. The long-term effect of chronic use of antihypertensive medications on hypertensive patients is an important topic in the management of hypertension. In this review we summarized some of the most important effects of antihypertensive medications on compliance, quality of life, sexual function, and cognitions. It remains a topic of controversy and individualized treatment is often recommended.*

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INTRODUCTION:

Hypertension is currently considered the major chronic disease affecting the global health, a leading worldwide public health problem, It is considered one the most important risk factors for cardiac, cerebrovascular and kidney diseases by World Health Organization [1]. Over the last decade, it has become the number one factor in the global morbidity and mortality. In spite of increased awareness and improved treatment modalities. Recently, there has been an increasing trend in incidence as well as the number of deaths reflected by the incidence-based mortality and morbidity reflected by the disability-adjusted life years related to poorly controlled blood pressure (BP) [2]. It is estimated that one-half (47 %) of adults aged 20 and over with hypertension had uncontrolled high BP in the United States [3]. Resistant hypertension – which is defined as BP that remains above goal regardless of antihypertensives use. It aggravates the morbidity and mortality in hypertensive patients.

Hypertension could be primary, potentially as a result of genetic or environmental causes. Secondary hypertension is due to another medical cause. Primary hypertension accounts for the majority with approximately 90-95% of adult cases, and secondary hypertension accounts for 2-10% of cases. Hypertension is diagnosed when the systolic blood pressure (SBP) is 140 mm Hg or above or a diastolic blood pressure (DBP) of 90 mm Hg or above [4]. Accurate Measurement of blood pressure (BP) is extremely important in the management. It is recommended to regularly measure the blood pressure by using the ambulatory blood pressure monitor to provide an additional assessment of diurnal variation in BP. Multiple readings is recommended to be taken at intervals of at least 1–2 min and then averaged is a better representation of a patient's BP. The optimal BP target in the treatment of hypertension in general is a matter of controversy [5].

Many guidelines exist for the management of hypertension. Most of them include Lifestyle modifications and Pharmacologic therapy. If a lifestyle modification fails to to achieve the goal BP, there are several drug options for treating and managing hypertension. Thiazide diuretics, an angiotensin-converting enzyme inhibitor (ACEI) /angiotensin receptor blocker (ARB), or calcium channel blocker (CCB) are the preferred agents in nonblack populations, whereas CCBs or thiazide diuretics are favored in black hypertensive populations. The standard recommended medical treatment regimen for hypertension is usually a combination of A + C + D. whereas A is angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker; C refers to calcium channel blocker; while D is thiazide-like diuretic [6]. Strong evidence recommends combination regimens to reduce the cardiovascular events in hypertensive individuals [7]. There are many reported side effects of antihypertensive medications on patients.

In this review, we point out the effect of chronic use of antihypertensive medications on hypertensive patients.

METHODOLOGY:

We did a systematic search for appendicitis and appendectomy using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). Our search also looked for effect of antihypertensives on hypertensive patients. All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: hypertension, anti-hypertensive, side effects, diagnosis, management, and treatment.

Hypertension in Chronic Kidney Disease

Chronic kidney disease (CKD) is common and growing worldwide problem. [1] CKD is defined as kidney damage for more than 3 months. Hypertension is the most common comorbidity seen in patients with CKD. Individuals with CKD are more likely to have resistant hypertension.[8] Patients with resistant hypertension are more likely to have target organ damage, including but not limited to carotid intima–media thickening, left ventricular hypertrophy, impaired renal function and microalbuminuria [9]. The relationship between hypertension and CKD is considered bidirectional. CKD can cause hypertension, but it is also a common complication of uncontrolled hypertension [10]. There are many contributing factors in the pathophysiology of CKD associated hypertension. These include but not limited to sodium dysregulation, increased sympathetic nervous system and alterations in renin angiotensin aldosterone system activity. [1] Management of hypertension with CKD should start with non-pharmacological approaches and followed by pharmacologic therapy [11].

Pharmacologic therapy:

The major goal of the medications should be to achieve and maintain BP control using the least number of medications with minimal adverse effects.

Individualization of medications is very critical and should consider both causes and risk factors that commonly exist together. It is also important to consider the cardiovascular risk factors such as age, sex, and ethnicity, any disease associated target organ damage, and risk of drug–drug interactions. ACEI and ARBs are less effective in certain patients especially of the African origin. This might be due to RAAS activation is often absent in elderly patients and in patients of African origin. For these patients, resistant hypertension is a major problem that medications might be ineffective.

ACE inhibitors or ARBs if tolerated, are among the most important classes of drugs that are recommended in many guidelines for use in hypertensive CKD patients with or without proteinuria. Because of their efficacy and low side effect profile ACE inhibitors and ARBs are recommended for CKD [12]. Adding low dose spironolactone is recommended as the fourth line of therapy and could effectively lower both systolic and diastolic BP [13].

The side effects of antihypertensive medications are the main cause of non-adherence. It is estimated to occur in about 50% of newly treated hypertensive patients within the first year of treatment [14]. It is estimated that about 20–97% of patients who take antihypertensive medications experience drug side effects [15].

Long-term use of diuretic medications may result in hyponatremia. They can also increase potassium and bicarbonate excretion and decrease calcium excretion and uric acid retention. While the potassium-sparing diuretics interfere with sodium reabsorption at the distal tubules. Amiloride has a black box warning for hyperkalemia which is potentially fatal. ACEIs block the major pathway of bradykinin degradation by inhibiting ACE. Bradykinins are the mechanism for the side effects of cough and angioedema.

ACEIs and ARBs are teratogenic in pregnant patients; ACEIs must be discontinued when the patient becomes pregnant. Hyperkalemia is a critical side effect when using ACEIs and thiazides together. The effect is exacerbated when the patient is taking potassium supplements. While Beta-Blockers, are accused of exacerbating asthma symptoms and severe chronic obstructive pulmonary disease (COPD). Spironolactone can also cause hyperkalemia; Other adverse effects include gynecomastia and impotence which is a major concern in male patients [16].

Antihypertensive treatment and renal protection:

Blood pressure (BP) and kidney function have an opposite relationship, with one aggravating the effect of the other. Hypertension has been considered both a cause and a consequence of kidney disease. The antihypertensive that affect RAAS are considered the most powerful tool to prevent the progression of kidney disease [17]. ACEIs and ARBs have an established record for renal protection and prevention of albuminuria. However, it appears that more profound blockade of angiotensin II obtained by combining multiple RAAS-I provides no additional benefit and possibly more adverse effects. Strong evidence from the literature suggests that CKD patients, an individualized treatment tailored specifically to the patient should be implemented. BP targets and types of antihypertensive drugs should be chosen on the basis of global risk profile as well as on renal phenotype, balancing the risk/benefit ratio for both CV and renal outcome [18].

Effect of long-term treatment with antihypertensive drugs on quality of life of elderly

Long-term treatment with antihypertensive medications has many consequences on the quality of life (QOL) in various ways. The QOL of the elderly is of particularly important because they have multiple interacting risk factors and comorbidity that limit their activities of daily living (ADL)[19] Many risk factors contribute to a decreased QOL in the elder population, these include but not limited to social environment and a decline in ADL due to co-morbid complications or dementia [19]. Therefore physicians must tailor medications to prevent any further deterioration in QOL when treating elderly patients with hypertension.

It is well known that patients tend to have a slightly lower tolerance for the diuretic. A study found that while the calcium antagonist (nicardipine) and the ACE inhibitor (captopril) benefit the QOL, the diuretic (trichlormethiazide) and the /beta-blocker (pindolol) decrease the QOL in many areas. There are many studies that showed improved QOL after calcium antagonist treatment [20].

Long Effects of different antihypertensive medication groups on cognitive function

Hypertension has been linked with an increased risk of cognitive decline. [21] It has also been associated with an increased risk of dementia.[22] In a recent meta- analysis, antihypertensive drugs, especially the CCB and ACEIs were beneficial in preventing cognitive decline and dementia. While other studies, and meta-analysis showed that antihypertensive

medication could significantly decrease the risk of Alzheimer's disease. Some randomized controlled trials revealed a significant positive effect of antihypertensive drugs on prevention of dementia or cognitive decline [23].

Effects of cardiovascular drugs on sexual function

It is well known that many antihypertensive medications have a negative effect on the sexual quality, which lead to diminished quality of life and medications noncompliance.[8] In the united states, the Beta blockers and ACE inhibitors were the 2nd most prescribed. However, some other medications have been described to have positive effects on sexual functions.[24] Diuretics are considered one of the worst side effects regarding sexual dysfunction [25]. While beta blocker is a known cause of Impotence. Angiotensin-converting enzyme (ACE) inhibitors, particularly captopril, have been associated with positive improvement in sexual quality [26]. Thiazide diuretics are responsible for decreased vaginal lubrication. Spironolactone is a common cause of breast tenderness, gynaecomastia and erectile dysfunction can occur in men, whereas menstrual abnormalities may occur in premenopausal women [27]. Literature about the effects of antihypertensive medications in female sexual function is limited.

Long-term effect of antihypertensive drugs on the risk of new-onset atrial fibrillation

Atrial fibrillation (AF) is the most common type of cardiac arrhythmia1 and is responsible for considerable morbidity and mortality worldwide [28]. Many studies have showed that some classes of antihypertensive medications can cause new-onset atrial fibrillation (NAF). The use of ACE inhibitors was independently linked with a decreased risk of NAF. Whereas, Alpha blockers, beta-blockers, calcium channel blockers and ARBs were not associated with NAF. Evidence reveals the blocking the renin–angiotensin–aldosterone system with ACE inhibitors and ARBs has a strong effect in preventing NAF and in maintaining sinus rhythm in patients with recurrent AF [29].

CONCLUSIONS:

Hypertension is currently considered the major chronic disease affecting the global health, a leading worldwide public health problem; it is considered one the most important risk factors for cardiac, cerebrovascular and kidney diseases by World Health Organization. The long term effect of chronic use of antihypertensive medications on hypertensive patients is an important topic in the management of hypertension. In this review we summarized some of the most important effects of antihypertensive medications on compliance, quality of life, sexual function, and cognitions. It remains a topic of controversy and individualized treatment is often recommended.

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