

Adverse Effects Associated with the Use of Antihypertensive Drugs: An Overview

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Abstract: Hypertension is one of the most important cardiovascular risk factor but its control is still Challenge for physicians all around the world. Antihypertensive are a class of drugs that are used in medicine and pharmacology to treat hypertension (high blood pressure). All Hypertensive drugs cause dizziness, ankle swelling, headache, fatigue, chest discomfort and cough. This review focus on the adverse effects of Antihypertensive drugs, severity of these adverse effects and attempts made to prevention and treatment of hypertension by non-pharmacological intervention.

Key words: Antihypertensive Drugs

Introduction

Hypertension is a common disorder that, if not effectively treated, results in greatly increased probability of coronary thrombosis, strokes and renal failures¹.

Hypertension, also referred to as high blood pressure, HTN or HPN, is a medical condition in which the blood pressure is chronically elevated. In current usage, the word "hypertension" without a qualifier normally refers to systemic, arterial hypertension².

Hypertension is defined conventionally as a sustained increase in blood pressure $\geq 140/90$ mm Hg, a criterion that characterizes a group of patients whose risk of hypertension-related cardiovascular disease is high enough to merit medical attention. Actually, the risk of both fatal and nonfatal cardiovascular disease in adults is lowest with systolic blood pressures of less than 120 mm Hg and diastolic BP less than 80 mm Hg; these risks increase progressively with higher systolic

and diastolic blood pressures. Recognition of this continuously increasing risk provides a simple definition of hypertension³.

It is estimated that the prevalence of hypertension in India is about 25% among urban adults and 10% in the rural areas⁴. The lifetime risk of developing hypertension is estimated to be 90%⁵.

The aim of antihypertensive therapy is to prevent morbidity and mortality associated with persistently raised BP by lowering it to an acceptable level, with minimum inconvenience to the patient⁶. There are many classes of antihypertensive, which—by varying means—act by lowering blood pressure. Evidence suggests that reduction of the blood pressure by 5-6 mmHg can decrease the risk of stroke by 40%, of coronary heart disease by 15-20%, and reduces the likelihood of dementia, heart failure, and mortality from cardiovascular disease⁷. Some of the widely used drugs in India are shown in Table 1.

TABLE 1: SOME ANTIHYPERTENSIVE DRUGS AVAILABLE IN INDIA'S MARKET⁸

Name	Available Dose	Dosage Form
Thiazide diuretic		
Hydrochlorothiazide	12.5mg, 25mg, 50mg	Tablet
Indapamide	1.25mg, 2.5mg	Tablet
Angiotension-converting Enzyme Inhibitor		
Ramipril	1.25mg, 2.5mg, 5mg, 10mg	Tablet
Captopril	6.25mg, 12.5mg, 25mg, 50mg, 100mg	Tablet
Enalapril	2.5mg, 5mg, 10mg, 20mg	Tablet
Lisinopril	5mg, 10mg, 20mg	Tablet
Angiotensin II receptor blocker		
Candesartan cilexetil	8mg, 16mg	Tablet
Irbesartan	75mg, 150mg, 300mg	Tablet
Losartan potassium	25mg, 50mg, 100mg	Tablet
Valsartan	80mg, 160mg	Tablet
Beta-blocker		
Atenolol	25mg, 50mg, 100mg	Tablet
Metoprolol	25mg, 50mg, 100mg	Tablet
Propranolol	10mg, 20mg, 40mg, 80mg, 120mg	Tablet
Calcium channel blocker		
Felodipine	2.5mg, 5mg, 10mg	Tablet
Nifedipine	30mg, 60mg	Tablet
Amlodipine	5mg, 10mg	Tablet
Diltiazem	30mg, 60mg, 180mg	Tablet

Following adverse effects associated with the use of antihypertensive agents

Thiazide diuretic

Erectile dysfunction is adverse effect of the thiazide-class diuretics, and physicians should inquire specifically regarding its occurrence in conjunction with treatment with these drugs. Gout may be a consequence of the hyperuricemia induced by these diuretics. Hydrochlorothiazide may cause rapidly developing, severe hyponatremia in some patients⁹. Thiazide diuretics have been associated with changes in plasma lipids and glucose tolerance that have led to some concern. The clinical significance of the changes has been disputed.

Angiotension-converting Enzyme Inhibitor

Severe hypotension can occur after initial doses of any ACE inhibitor in patients who are Hypovolemic due to diuretics, salt restriction, or gastrointestinal fluid loss. Other adverse effects Common to all ACE inhibitors include acute renal failure, hyperkalemia, dry cough sometimes accompanied by wheezing, and angioedema. Captopril, particularly when given in high doses to patients with renal insufficiency, may cause neutropenia or proteinuria. Minor toxic effects seen more typically include altered sense of taste, allergic skin rashes, and drug fever, which may occur in as many as 10% of patients¹⁰.

Angiotension II receptor blocker

Infrequent ADRs associated with therapy include: first dose orthostatic hypotension, rash, diarrhea, dyspepsia, abnormal liver function, muscle cramp, myalgia, back pain, insomnia, decreased haemoglobin levels, renal impairment, pharyngitis, and/or nasal congestion¹¹.

The Adverse effects include hypotension, hyperkalemia, and reduced renal function, including that associated with bilateral renal artery stenosis and stenosis in the artery of a solitary kidney. Hypotension is most likely to occur in patients in whom the blood pressure is highly dependent on angiotensin II, including those with volume depletion, renovascular hypertension, cardiac failure, and cirrhosis; in such patients initiation of treatment with low doses and attention to blood volume is essential. Hyperkalemia may occur in conjunction with other factors that alter K⁺ homeostasis, such as renal insufficiency, ingestion of excess K⁺, and the use of drugs that promote K⁺ retention¹⁰.

Beta-blocker

Adverse drug reactions associated with the use of beta blockers include: nausea, diarrhea, bronchospasm, dyspnea, cold extremities, exacerbation of Raynaud's syndrome, bradycardia, hypotension, heart failure, heart block, fatigue, dizziness, abnormal vision, decreased concentration, hallucinations,

insomnia, nightmares, clinical depression, sexual dysfunction, erectile dysfunction and/or alteration of glucose and lipid metabolism¹².

Calcium channel blocker

The most common side effects caused by the Ca²⁺ channel antagonists, particularly the dihydropyridines, are due to excessive vasodilation. Symptoms include dizziness, hypotension, headache, flushing, digital dysesthesia, and nausea. Patients also may experience constipation, peripheral edema, coughing, wheezing, and pulmonary edema. Nimodipine may produce muscle cramps when given in the large doses required for a beneficial effect in patients with subarachnoid hemorrhage. Less common side effects include rash, somnolence, and occasional minor elevations of liver function tests. These side effects usually are benign and may abate with time or with dose adjustment. Worsened myocardial ischemia has been observed in two studies with the dihydropyridine nifedipine¹³.

Non-Pharmacological Intervention

All drugs have side effects. If minor alterations of normal activity or diet can reduce blood pressure to a satisfactory level, the complications of drug therapy can be avoided⁹. Reduction of weight, physical activity, restriction of salt and moderation in the use of alcohol may reduce blood pressure and improve the efficacy of drug treatment³.

Weight reduction

Obesity and hypertension are closely associated, and the degree of obesity is positively correlated with the incidence of hypertension. Obese hypertensive may lower their blood pressure by losing weight regardless of a change in salt consumption¹⁴. The Hypertension prevention trial showed that a 4% reduction in bodyweight over 3 years was associated with a 2.4mm Hg reduction in systolic and 1.8mm Hg reduction in diastolic blood pressures¹⁵. The exact mechanism by which weight reduction lowers blood pressure is not known. There are however certain possible reasons. Obese individuals have been seen to have an over activated renin-angiotensin-aldosterone system with higher renin and aldosterone concentrations than in lean individuals¹⁶. It is therefore important that all patients be advised to maintain weight near optimal by reducing calorie intake and increasing physical activity.

Physical Exercise

Increased physical activity lowers rates of cardiovascular disease in men¹⁷. Lack of physical activity is associated with a higher incidence of hypertension¹⁸. Although consistent changes in blood pressure are not always observed, meticulously controlled studies have demonstrated that regular isotonic exercise reduces both systolic and diastolic blood pressures by approximately 10 mm Hg¹⁹. The mechanism by which exercise can lower blood pressure is not clear. Regular isotonic exercise reduces

blood volume and plasma catecholamines and elevates plasma concentrations of atrial natriuretic peptide. It is recommended that person exercise for at least 30 min on most, if not all, days of the week²⁰.

Alcohol Consumption

Consumption of alcohol can raise blood pressure, but it is unclear how much alcohol must be consumed to observe this effect. Heavy consumption of alcohol increases the risk of cerebrovascular accidents but not coronary heart disease²¹. Alcohol consumption has both acute and chronic deleterious effects on BP. The relationship between high alcohol intake and elevated BP has been documented in many epidemiologic studies²². Hypertensive patients should be advised to restrict consumption of ethanol to no more than 30 ml per day.

Salt Restriction

Dietary salt intake has a linear association with blood pressure. Reduced sodium intake to approximately 100 mmol/day can prevent hypertension, can facilitate blood pressure control in elderly patients on medication²³ and can potentially prevent cardiovascular events in overweight individuals²⁴. In addition, subjects over 40 years of age are more responsive to the hypotensive effect of moderate restriction of salt²⁵. To reduce salt intake, individuals should consume foods low in salt and limit the amount of salt added to food. An additional benefit of salt restriction is improved responsiveness to some antihypertensive drugs.

DASH diet

The DASH diet is recommended to many people with hypertension (high blood pressure) or pre hypertension by their physicians. The DASH diet eating plan has been proven to lower blood pressure in studies sponsored by the National Institutes of Health²⁶. The DASH diet is based on NIH studies that examined three dietary plans and their results. None of the plans were vegetarian, but the DASH plan incorporated more fruits and vegetables, low fat or nonfat dairy, beans, and nuts than the others studied. Not only does the plan emphasize good eating habits, but also suggests healthy alternatives to "junk food" and discourages the consumption of processed foods. The diet reduced systolic blood pressure by 6 mm Hg and diastolic blood pressure by 3 mm Hg in patients with normal blood pressure²⁷.

Conclusions

Anti-hypertensive drugs have become a very important in the management of hypertension. Their use has been limited by their propensity to cause cardiac adverse effects. Research supports the use of pharmacological intervention to reduce and/or avoid hypertension, but these strategies required lifestyle modification. In those with medication-controlled blood pressure, lifestyle modifications can help to

reduce drug dosage or in some cases, even stop drug therapy. Non-pharmacologic measures should be part

of routine management of hypertension.

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