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Reporting of adverse drug reactions caused while using antihypertensive drugs. A general review

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ABSTRACT

AIM

To study the adverse drug reactions occurred during antihypertensive drugs usage and to report them.

METHODS

The data's are been collected from various reputed journals including international journals and websites. We have analysed the information regarding the adverse drug reactions caused due to use of antihypertensive drugs and reporting them.

RESULTS

Various studies reveal that antihypertensive drugs are a class of drugs that are used in medicine to treat hypertension (high blood pressure). It also states that all hypertensive drugs cause ADRs such as dizziness, ankle swelling, headache, fatigue, chest discomfort and cough.

CONCLUSION

Hypertension is one of the most important cardiovascular risk factor but its control is still Challenge for physicians all around the world. Hence, our study presents the adverse drug reaction profile of antihypertensive medicines prescribed. This review focus on the adverse effects of antihypertensive drugs, severity of these adverse effects and its report.

KEYWORDS: Hypertension, Antihypertensive drugs, Adverse drug reaction, Beta-blockers, Angiotensin-converting enzyme inhibitors, Calcium channel blockers.

INTRODUCTION

HYPERTENSION AND ANTIHYPERTENSIVE DRUGS

Hypertension is high blood pressure; it is caused due to the force of blood moving against the walls of the arteries. Normal blood pressure is in the range of 120/80 mm Hg. Hypertension is the medical condition where the systolic blood pressure is more than 140 mm Hg and the diastolic blood pressure is more than 90 mm Hg. It is a chronic disease which is considered to be one of the major public health problems and a significant cardiovascular risk factor. According to the World Health Organization (WHO), each year, at least 7.1 million people die as a result of increased blood pressure.[1, 8] Primary (essential) hypertension is the most common form of hypertension, accounting for 90–95% of all cases of hypertension. Secondary hypertension accounts for approximately 5-10% of all cases of hypertension, with the remaining being primary hypertension.

Secondary hypertension has an identifiable cause whereas primary hypertension has no known cause (i.e., idiopathic).[2] Hypertension is classified into 4 types according to JNC (Joint National Committee).[7] It is estimated that the prevalence of hypertension in India is about 25% among urban adults and 10% in the rural areas. The lifetime risk of developing hypertension is estimated to be 90%.[1] For the treatment of hypertension, a broad range of antihypertensive medications are currently available. Antihypertensive drugs are frequently associated with adverse drug reactions (ADRs) that may limit treatment options and reduce patient adherence, which may hinder blood pressure control. These drugs are believed to cause ADRs or symptoms that make patients feel worse than they did before beginning drug therapy for their "asymptomatic" disease.[2] 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 patient. There are many classes of antihypertensive drugs, 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 disease. Some of the widely used drugs in India are shown in Table No.1.[3]

Table No. 1: Classification of antihypertensive drugs used commonly in India

CLASSIFICATION OF ANTIHYPERTENSIVE DRUGS	
Thiazide diuretics	Hydrochlorothiazide
	Indapamide
Angiotension converting enzyme inhibitors	Ramipril
	Captopril
	Enalapril
	Lisinopril
Angiotension II receptor blokers	Candesartan cilexetil
	Irbesartan
	Losartan potassium
	Valsartan
Beta blockers	Atenolol
	Metoprolol
	Propranolol
Calcium channel blockers	Felodipine
	Nifedipine
	Amlodipine
	Diltiazem

ADVERSE DRUG REACTIONS (ADRs)

There is no standard definition of an adverse drug reaction (ADR). Early studies used their own definitions, which were indistinct and could be interpreted to include intentional and unintentional overdose, as well as some administration errors. According to World Health Organization (WHO) "An adverse drug reaction (ADR) is any response to a drug which is noxious and unintended and occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or the modification of physiological function". Food and Drug Administration (FDA) defines a serious adverse event as one in which the patient outcome is death, or life threatening, hospitalization, disability, congenital anomaly or required intervention to prevent permanent impairment or damage.[4] ADR can also be defined as 'an appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts

hazard from future administration and warrants prevention or specific treatment or alteration of the dosage regimen or withdrawal of the product'.[5] ADRs are a major universal problem and are one of the leading causes of mortality and morbidity in health care facilities globally. The incidence of ADR varies with studies. A published meta-analysis of the incidence of adverse drug reactions (ADRs) in hospitalized patients concluded that ADRs rank as the fourth to sixth leading cause of death in the United States and the overall incidence of serious ADR accounted for 6.7% of hospitalized patients. According to a study carried out at a private tertiary care hospital in South India, the incidence of ADRs was found to be 1.8%, out of which 12% of suspected ADRs were severe and 49% ADRs were moderate in severity.[4]

REPORTING OF ADRs CAUSED BY DIFFERENT CLASSIFICATION OF ANTIHYPERTENSIVE DRUGS

THIAZIDE DIURETICS

One of the adverse effects of the thiazide-class diuretics is erectile dysfunction. Gout may be a consequence of the hyperuricemia induced by these diuretics. Hydrochlorothiazide may cause rapidly developing, severe hyponatremia and hypokalemia in some patients. Thiazide diuretics have been associated with changes in plasma lipids and glucose tolerance that have led to some concern and can cause hyperglycemia. Thiazides also cause structural kidney damage. [(3, 6)]

ANGIOTENSION CONVERTING ENZYME INHIBITORS

The adverse effects common to all ACE inhibitors include acute renal failure, hyperkalemia, dry cough sometimes accompanied by wheezing and angioedema. 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 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 patients.[3]

ANGIOTENSION II RECEPTOR BLOCKERS

In general, the ARBs are well tolerated. Infrequent ADRs associated with this 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 nasal congestion. 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 + retention. All of the ARBs are pregnancy category C for the first trimester and category D for the second and third trimesters. [(3, 7)]

BETA-BLOCKERS

Beta blockers includes ADRs such as: nausea, diarrhea, bronchspasm, dyspnoea, cold extremities, exacerbation of Reynaud'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 metabolism. A case in point is the development of brownish blue pigmentation of nails of patients on atenolol usage for 3 years.[(3,5)]

CALCIUM CHANNEL BLOCKERS

ADR 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. Amlodipine on 8 years usage develops Schamberg's like purpuric pigmentation. 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 nifedipine. [3, 5]

RESULT

From the above study we have analysed that the ADRs associated with cardio vascular system (CVS) were found to be most frequent followed by gastrointestinal ADRs (abdominal pain, constipation and diarrhoea). Beta-blockers were most frequently associated with ADRs, followed by angiotension converting enzyme inhibitors and calcium channel blockers.

CONCLUSION

We have come to a conclusion that antihypertensive drugs not only treat hypertension but also produce various ADRs. Therefore, these ADRs must be reported and in turn treated as well. The results of the above study would be useful for the physicians in rational selection of drug therapy for treatment in hypertensive patients. The present data suggest that the ADR monitoring needs to be done in hospital settings continuously so that untoward effect caused by different medicines can be identified and documented.

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