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STUDY ON ANTI-HYPERTENSIVE DRUGS INDUCED ADVERSE DRUG REACTIONS IN TERTIARY CARE HOSPITAL

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ABSTRACT

This study aimed at analyzing the etiology of hypertension, and to study the type of adverse drug reactions produced by the antihypertensive drugs.80 patients who had admitted in the hospital were taken for the study and were selected randomly in the inpatient in our hospital RMMCH, Chidambaram. The patients type of drug therapy followed by the beta blockers (26)32.5%, calcium channel blockers (20)25%, A-II blockers (20)25% and, ACE inhibitors (14)19.18%.there are some of the ADRs found in the patients using these drugs. The more number of ADRs are observed in the patients using calcium channel blockers. On consultation with prescribers the prescription changes were made respectively. The patients were given counseling regarding their life style change that is smoking, alcohol intake habits and their rationale usage of the drug. Management includes withdrawal of the drug if possible and specific treatment of its effects. Suspected adverse drug reactions were reported.

Key Words: Anti-hypertensive drugs, Adverse drug reactions.

INTRODUCTION

An adverse drug reaction is any undesirable effect of a drug beyond its anticipated therapeutic effects occurring during clinical use. In contrast, an adverse drug event is an untoward occurrence after exposure to a drug that is not necessarily caused by the drug.1When a drug is marketed little is known about its safety in clinical use because only about 1500 patients are likely to have been exposed to it [1,2]. Thus drug safety assessment should be considered an integral part of everyday clinical practice since detection and diagnosis often depend on clinical acumen.

Definition of ADRs

WHO: Any response to a drugs which is noxious and intended and which occur at doses normally used in man for prophylaxis, diagnosis or therapy of disease [3].

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Adverse effects of therapy were recorded by the ancient Babylonians and then William withering describes the benefits of digitalis in the 18th century, he also described the vomiting, alteration of visions, diarrhea, bradycardia, convulsion and death it could cause [3,4].

ADR Risk Factors

Age: The relationship between age and ADR's is ambiguous. The elderly peoples are likely to have more ADRs because of the increased number of medication taken and in addition the metabolism, distribution, excretion of drugs may decrease with age.

Sex: females appear to be more susceptible o ADRs than males. This remained so after consideration of the duration of hospitalization, number of drugs, age, and the presence of liver and renal disease. The increase may be due to pharmacokinetic factors and hormonal influence.

Medical History: patients who have already had an ADR to other drug, butatopy are not a factor either for ADRs in general or allergic ADRs. However, that does not exclude

the possibility that an individual ADR may be more common in atopic patients.

Race and Genetic Polymorphism: race and genetic polymorphism may account for alteration in the handling of drugs and their end –organ effects. May reactions which were previously described as idiosyncratic have now been to have a clearly defined genetic basis.

Drugs: there is a direct relationship between the number of drugs taken and the rate of ADRs.

Disease: there is a high frequency of drug allergy in some of the disease.

1. Clinical pharmacists in teaching hospitals or in any organized health care system are expected to Monitoring, detecting, evaluating, documenting and reporting ADRs
2. Intervening and providing educational feedback to prescribers, other health care professionals and patients.

ADR programs should also focus on identifying problems leading to ADRs, planning for positive changes and analyze the results of these changes [4].

Classification

ADRs may be classified by e.g. cause and severity.

Cause

- Type A: Augmented pharmacologic effects - dose dependent and predictable
  - Intolerance
  - Side Effects
- Type B: Bizarre effects (or idiosyncratic) - dose independent and unpredictable
- Type C: Chronic effects
- Type D: Delayed effects
- Type E: End-of-treatment effects
- Type F: Failure of therapy
- Type G: Genetic reactions

Types A and B were proposed in the 1970s, and the other types were proposed subsequently when the first two proved insufficient to classify ADRs [3,4].

Hypertension

Hypertension is the term used to describe high blood pressure.

Blood pressure is a measurement of the force against the walls of your arteries as your heart pumps blood through your body.

Blood pressure readings are usually given as two numbers -- for example, 120 over 80 (written as 120/80 mmHg). One or both of these numbers can be too high.

The top number is called the systolic blood pressure, and the bottom number is called the diastolic blood pressure.

- Normal blood pressure is when your blood pressure is lower than 120/80 mmHg most of the time.
- High blood pressure (hypertension) is when your blood pressure is 140/90 mmHg or above most of the time.
- If blood pressure numbers are 120/80 or higher, but below 140/90, it is called pre-hypertension [6].

Pathophysiology

Hypertension is a heterogeneous disorder that may result either from a specific cause (secondary hypertension) or from an underlying pathophysiologic mechanism of unknown etiology (primary or essential hypertension). Secondary hypertension accounts for fewer than 10% of cases, and most of these are caused by chronic kidney disease or renovascular disease. Other conditions causing secondary hypertension include pheochromocytoma, Cushing's syndrome, hyper thyroidism, hyperparathyroidism, primary aldosteronism, pregnancy, obstructive sleep apnea, and coarctation of the aorta. Some drugs that may increase BP include corticosteroids, estrogens, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), amphetamines, sibutramine, cyclosporine, tacrolimus, erythropoietin, and venlafaxine. Multiple factors may contribute to the development of primary hypertension including:

✓ Humoral abnormalities involving the renin-angiotensin-aldosterone system, natriuretic hormone, or hyperinsulinemia;
✓ A pathologic disturbance in the CNS, autonomic nerve fibers, adrenergic receptors, or baroreceptors;
✓ Abnormalities in either the renal or tissue autoregulatory processes for sodium excretion, plasma volume, and arteriolar constriction;
✓ A deficiency in the local synthesis of vasodilating substances in the vascular endothelium, such as prostacyclin, bradykinin, and nitric oxide, or an increase in production of vasoconstricting substances such as angiotensin II and endothelin I;
✓ A high sodium intake and increased circulating natriuretic hormone inhibition of intracellular sodium transport, resulting in increased vascular reactivity and a rise in BP; and
✓ Increased intracellular concentration of calcium, leading to altered vascular smooth muscle function and increased peripheral vascular resistance.

Cardiovascular Disorders

The main causes of death in hypertensive subjects are cerebrovascular accidents, cardiovascular (CV) events, and renal failure. The probability of premature death correlates with the severity of BP elevation.6

There are Two Types

1. Primary hypertension: Patients with uncomplicated primary hypertension are usually asymptomatic initially.
2. Secondary hypertension: Patients with secondary hypertension may complain of symptoms suggestive of the underlying disorder. Patients with pheochromocytoma may have a history of paroxysmal headaches, sweating,

tachycardia, palpitations, and orthostatic hypotension. In primary aldosteronism, hypokalemic symptoms of muscle cramps and weakness may be present. Patients with hypertension secondary to Cushing's syndrome may complain of weight gain, polyuria, edema, menstrual irregularities, recurrent acne, or muscular weakness [7,8].

Non Pharmacological Therapy

All patients with prehypertension and hypertension should be prescribed lifestyle modifications, including (1) weight reduction if overweight, (2) adoption of the Dietary Approaches to Stop Hypertension eating plan, (3) dietary sodium restriction ideally to 1.5 g/day (3.8 g/day sodium chloride), (4) regular aerobic physical activity, (5) moderate alcohol consumption (two or fewer drinks per day), and (6) smoking cessation. Lifestyle modification alone is appropriate therapy for patients with prehypertension. Patients diagnosed with stage 1 or 2 hypertension should
be placed on lifestyle modifications and drug therapy concurrently [6-8].

Pharmacology Therapy

Classification of Antihypertensive Therapy

1. Diuretics:
   - Thiazides: hydrochlorothiazide, chlorothiazide
   - High ceiling diuretics:furesomidE
   - Potassium sparing diuretics: spironolactone, amiloride.
2. Beta blockers:propranolol, metaprolol, atenolol
3. ACE inhibitors: captopril, enalpril, lisinopril
4. Calcium channel blockers: verapamil
5. AII- blocker: losartan
6. Alpha blocker: parazosin
7. Central sympatholytics: clonidine
8. Vasodilators: hydralazine [6,9].

MATERIALS AND METHODS

This study was done in RMMCH, tertiary care teaching hospital, Chidambaram.80 patients who had regular visits for the treatment from period of Aug 2012 to Oct 2012 were taken for the study in the outpatient department. The background details like age, sex, occupations, habits, family history, concurrent illness, and present medical and medication status were collected. The patients were interviewed for the adverse drug reactions and counseled accordingly. Later consultation was made with the physician and the data were documented. The patients were divided in to the two groups accordingly to the class of anti-hypertensive drugs taken.

RESULTS

This study was conducted in the period of 3 months in RMMCH. Out of the 80 patients 30 patients (37.5%) were suffering from hypertension, 15 (18.75%) with diabetic foot ulcer, 19 (26.03%) were hypertension with ischemic heart disease and 16 (20%) were hypertension with Post-operative surgical treatment (like haemorroidectomy, appendectomy, herniplasty).

Table 1. Showing the details of patients taking the anti-hypertensives

Total no. of patients	Beta blockers	Calcium channel blockers	AII blockers	ACE inhibitors
80	26	20	20	14
In Percentage	32.5%,	25%,	25%	19.18%

Table 2. Age Group of the Patients

Total No.	Age Group	No. of Patients	Percentage
80	**0-40**	**3**	**3.75**
	40-50	20	25
	51-60	27	33.75
	61 & above	30	37.5

Table 3. Adverse reactions observed in patients having ACE inhibitors

ADRs	Total no of patients	Total no affected	Percentage
dry cough	14	11	78.57
angioedema	14	3	21.43
headache	14	6	42.86
dizziness	14	8	57.14
nausea	14	7	50
flushing	14	8	57.14

Table 4. Adverse reactions observed in patients having beta blockers

ADRs	Total no. of patients	Total no affected	Percentage
Bronchospasm	26	2	7.69
Cold extremites	26	5	19.23
Vivid dreams	26	10	38.46
constipation	26	13	61.53
Insomnia	26	17	65.38

Table 5. Adverse reactions observed in patients having calcium channel blockers

ADRs	Total no of patients	Total no affected	Percentage
Headache	20	19	95
Ankle edema	20	10	50
Palpitation	20	5	25
Flushing	20	4	20
Fatigue	20	13	65
g.i.t upset	20	10	50
dizziness	20	11	55

Table 6. Adverse reactions observed in patients having alpha II blockers

ADRs	Total no. of patients	Total affected	Percentage
Tachycardia	20	7	35
Dizziness	20	12	60
Angio edema	20	6	30
Dry cough	20	6	30

Figure 1. Adverse reactions observed in patients having ACE inhibitors

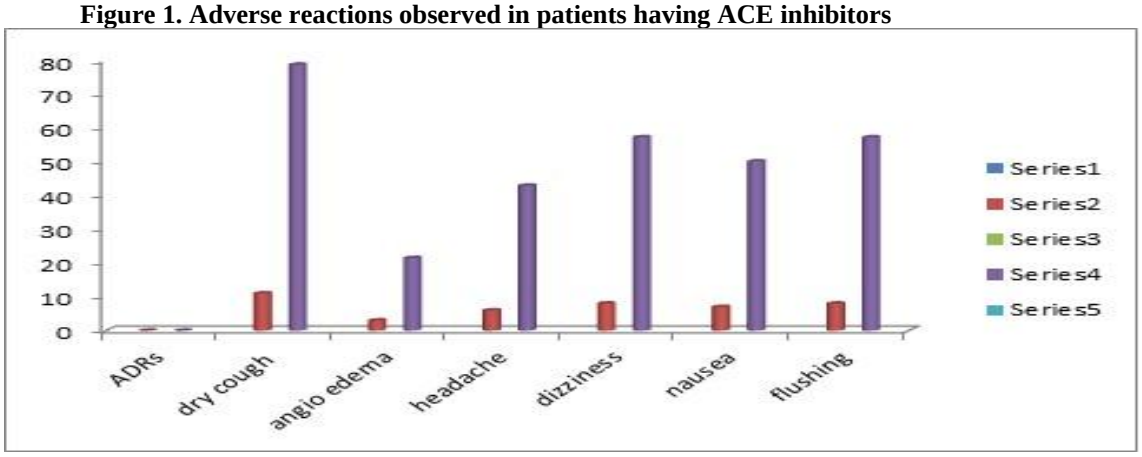


Figure 2. Adverse reactions observed in patients having beta blockers

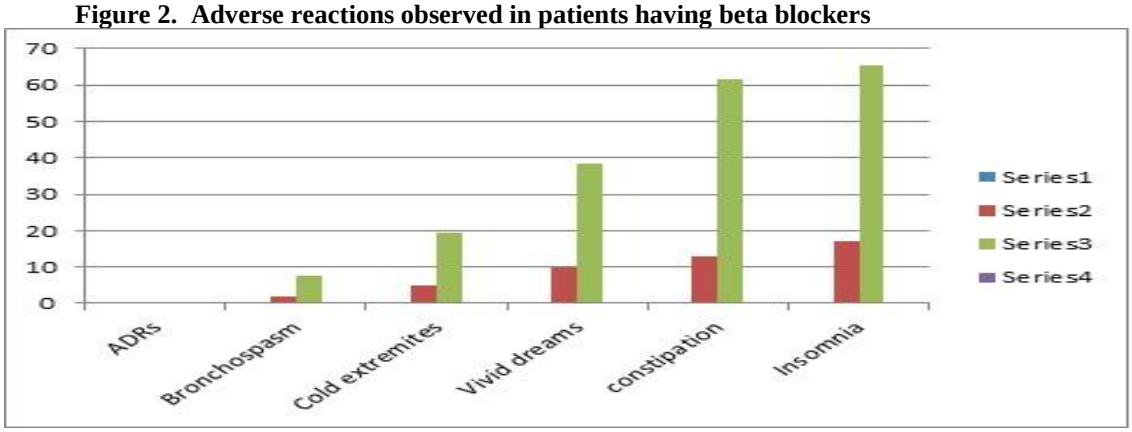


Figure 3. Adverse reactions observed in patients having calcium channel blockers

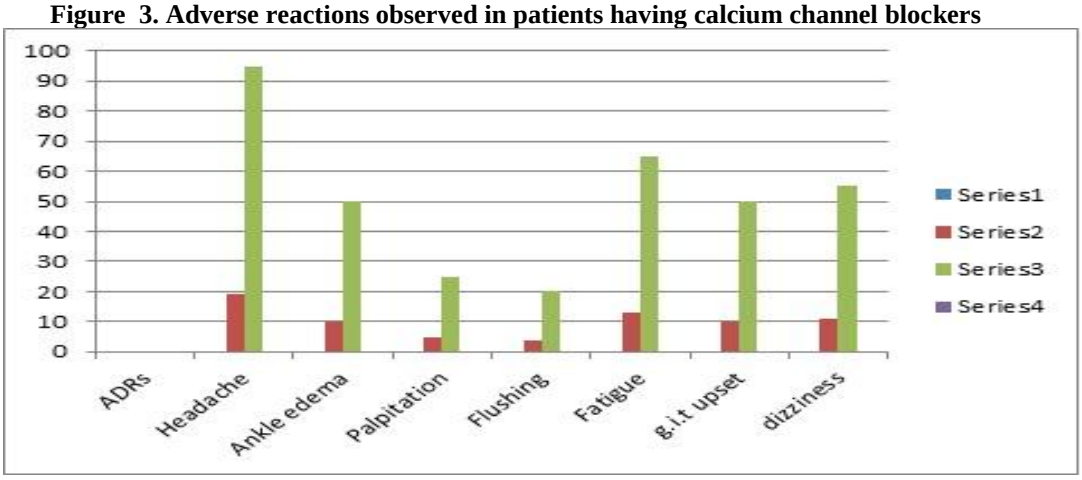
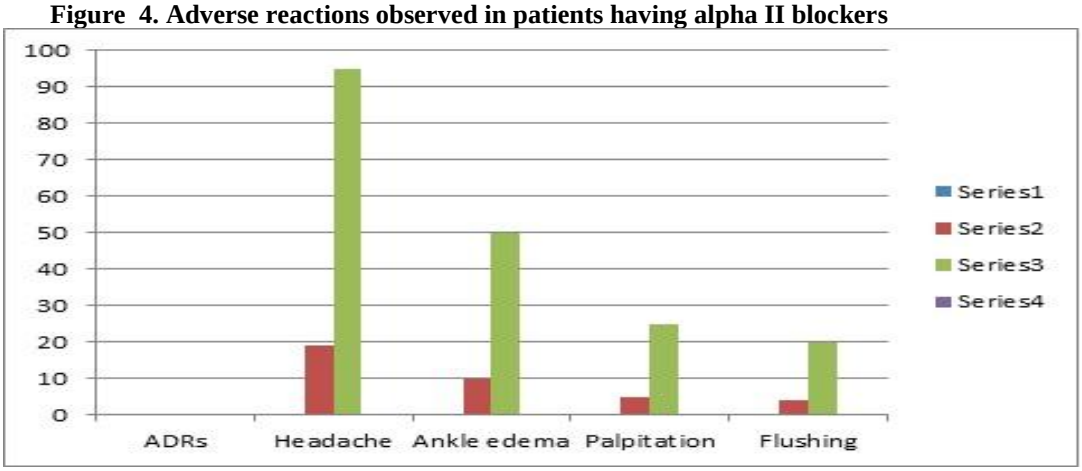


Figure 4. Adverse reactions observed in patients having alpha II blockers



DISCUSSION

In this study most of the patients were alcoholic and smokers, which could be precipitated hypertension. All those patients are suffering from hypertension for 2-3 years, this shows that they do not take drugs patients regularly or though they take drugs but don't have a control over the diet. On analysis among the 80 patients, 15 patients were diabetes developed hypertension, these patients should be carefully monitored, counseled, to be treated because they have a risk of developing renal failure. And the patients who undergone the surgery had also developed the hypertension, those patients should be kept in observation and regular monitoring of blood pressure and taking strict diet should be maintained. The study shows that many of the patients are above 40 age group those patients must go for regular checkup. They must be maintain the good health and diet control must be followed and should have some changes in life style like doing physical exercises etc. The patients type of drug therapy followed by the beta blockers (26) 32.5%, calcium channel blockers (20) 25%, A-II blockers (20) 25% and, ACE inhibitors (14) 19.18%. Among the patients using those four types of drugs it was observed that more number of ADRs was found in patients using calcium channel blockers, mainly the adverse reactions reported are headache, ankle edema, palpitation, flushing, fatigue, g.i.t upset, and dizziness.

And in patients taking beta blockers the adverse reactions reported are bronchospasm, cold extremities, vivid dreams, constipation, insomnia.

And in patients taking ACE inhibitors were suffering from dry cough, angioedema, headache, dizziness, nausea and flushing.

And in patients taking angiotensin II blockers adverse reactions reported are tachycardia, angioedema, and dry cough.

The most of the adverse drug reactions can be treated by the drugs but some of the adverse reactions cannot be treated.so adverse reactions should be carefully monitored, observed and should be reported. Clinical pharmacists in teaching hospitals or in any organized health care system are expected to

1. Monitoring, detecting, evaluating, documenting and reporting ADRs
2. Intervening and providing educational feedback to prescribers, other health care professionals and patients.

CONCLUSION

Further clinical and laboratory tests should be done at least once in three months to assess the progress in the treatment. Where there is no improvement, drug could be changed, dose alteration could be done, instead of asking the patients to take same drugs continuously, because every drug has its own complications on the patient body when it is used for a long time.

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