A STUDY TO MONITOR THE ADVERSE DRUG REACTIONS OF ANTI-HYPERTENSIVE DRUGS

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Summary

A study on 'Adverse Drug Reactions (ARDs)' of antihypertensive drugs in patients of selected hospitals and clinics in Nashik City was conducted.

A prospective, hospital based study was carried out in 4 selected hospitals of Nashik city in an inpatient as well as outpatient setting. A voluntary ADR reporting form given by Central Drugs Standard Control Organization (CDSCO) was filled. The seriousness of the ADRs was graded as per the WHO scale. The data obtained was studied and analyzed further.

A total of 350 hypertensive patients were screened of which 25 patients (7.14%) were diagnosed for ADRs. The maximum numbers of ADRs were observed in the age group 51-60 years with 28% in all the age groups. The ADRs mainly observed were dizziness, cold and headache amongst the potentially non-serious, while edema, hypotension, and bronchospasms were among the potentially serious category. The ADRs observed were maximum for the 'Combination' class of antihypertensive medications.

ADRs have a major public health and economic implication. This data suggests that there are limitations to the therapeutic safety of the antihypertensive drugs. More drug safety studies are needed to evaluate all possible ADRs and their mechanisms.

Key words: hypertension, adverse drug reaction, Nashik patients

Introduction

'Hypertension' is one of the most widespread cardiovascular disorders with approximately one billion people suffering from it world over [(1)]. Various epidemiological surveys carried out have shown that about 57% of the elderly Indian population suffers from Hypertension, with more prominence in urban parts of the country. It is expected that in 2010 about 2 million Indians will be suffering from Hypertension [(2-3)]. Some associated complications of hypertension include hyperlipidemia, diabetes mellitus, bradycardia and bronchospasms. A large number of drugs in various combinations are prescribed for the therapy. Multidrug therapy is a treatment of choice to counter hypertension. The classes of drugs commonly used are Angiotensin converting enzyme (ACE) inhibitors, β – adrenergic blockers, α – adrenergic blockers, calcium channel blockers, Angiotensin receptor blockers and diuretics [(4)]. A combination of any two is generally prescribed. More than 1500 formulations of the above categories are available in the market [(5)]. In spite of a high therapeutic index of these drugs, a substantial number of 'Adverse Drug Reactions' (ADR) are encountered each year. Studies have shown that ADRs of Anti Hypertensive and cardiovascular drugs are among the most commonly observed. They are a frequent cause of mortality and morbidity to the patients, with great associated costs to healthcare providers [(6-7)]. The primary objective of the study was to conduct a survey on Adverse Drug Reactions (ADRs) reported by patients using antihypertensive drugs in Nashik city.

Materials and methods

The study was conducted by one to one patient interaction based on a questionnaire (ADR monitoring form) drafted according to Central Drug Standard Control Organization (CDSCO) - ADR monitoring guidelines. The study included inpatients as well as outpatients. It was carried out in consultation with doctors and other healthcare professionals. A few prominent hospitals that were selected to carry out the study were The Civil Hospital,Triambak Road, Nashik, Bytco Hospital, Nashik Road, Nashik, MUHS Medical College, Adgaon, Nashik,Dr. Kunal Gupte's Centre for Cardiac Care, Nashik.

All the above hospitals had specialized units devoted for the cardiovascular diseases and a bed capacity of more than 25 beds. Everyday around 100 – 250 patients visited the hospitals for diagnosis or treatment relating to hypertension. The study was also carried out in private clinics in addition to hospitals. The college provided a written letter of authorization of the project and permission was obtained from the hospital authorities to carry out the survey. The actual study consisted of consultation with the physician in- charge of the hospital department, the medical interns and the paramedical hospital staff. The protocol was devised according to the voluntary ADR reporting form given by the CDSCO [(8)]. If a sign or symptom of the suspected ADR was observed then the form was filled. The patient consent regarding his inclusion in the project was obtained and only those patients who were willing to cooperate were selected. During the whole project the patient's identity was held in strict confidence. A one to one interaction with the patient with help from the medical interns was carried out. The patient demographics were noted, paramount amongst these were the patient's sex and age. The other data obtained were the pre-existing diseases and other medication or therapy the patient was undertaking. Relevant history of patient like – allergies, pregnancy, tobacco or alcohol use, and hepatic/renal dysfunction were also considered.

The problem or the abnormal reaction the patient was facing was described in brief. If the patient was not in a condition to converse, then the consulting physician explained the problem. The name - preferably generic name of the medication, dose, route and frequency used were entered in the form. Therapy dates were also included; if unknown then the duration of therapy was stated. The brand name of a drug and its manufacturers name were also held in confidence. The seriousness of the reaction was assessed by the WHO definition [(9)], which involved ADR's resulted in death, life threatening situation, hospitalization – initial or prolonged, disability or birth defect. The outcomes were noted in as fatal, recovering, recovered or unknown. The analysis of the data and its interpretation was carried out.

Results

A total 350-hypertensive patient was screened of which 25 patients (7.14%) were diagnosed for ADRs; of which 16 were males while 9 were females (Table 1). The maximum numbers of ADRs were observed in the age group 51-60 years (Table 2). The ADRs mainly observed were dizziness, cold and headache amongst the potentially non-serious, while edema, hypotension, and bronchospasms were among the potentially serious category (Table 3). The ADRs observed were maximum for the 'Combination' class of antihypertensive medications (Table 4).

Table 1: Demographic distribution of hypertensive patients in selected hospitals/clinics of Nashik city

Age(Years)	Males N=224	Females N=126	Total N=350 (%)
21-30	9	5	14 (4%)
31-40	26	9	35 (10%)
41-50	30	18	48 (13.71%)
51-60	46	32	78 (22.28%)
61-70	56	34	90 (25.71%)
71-80	46	23	69 (19.71%)
80 +	11	5	16 (4.57%)

N= number of patients

Table 2: Demographic distribution of ADRs observed in hypertensive patients in selected hospitals/clinics of Nashik city

Age(Years)	Males N=16	Females N=9	Total N=25(%)
21-30	Nil	Nil	0 (0%)
31-40	Nil	1	1 (4%)
41-50	5	1	6 (24%)
51-60	4	3	7 (28%)
61-70	3	3	6 (24%)
71-80	3	1	4 (16%)
80 +	1	Nil	1 (4%)

N= number of patients

Table 3: Frequency of individual ADRs observed in hypertensive patients of selected hospitals/ clinics in Nashik city

Sr. No.	Adverse Reaction	Number of Patients
1	Sore Gums	1
2	Fatigue	4
3	Vertigo	2
4	Dizziness	8
5	Headache	6
6	Edema	3
7	Cold	6
8	Bronchospasm	2
9	Nausea/Vomiting	3
10	GI - Disorders	3
11	Tachycardia	2
12	Hypotension/Syncope	4
13	Cough	5
14	Insomnia	1
15	Dysgeusia	3
16	Drug Fever	1
17	Electrolyte Imbalance	1
18	Diarrhoea	1
19	Muscle Pain	3

Table 4: Percentage of ADRs according to Class of Antihypertensive medication

Sr. No	Class of Antihypertensive Drug	% of ADRs
1	Diuretics	4
2	β - Blockers	16
3	ACE - Inhibitors	16
4	Calcium Channel Blockers	16
5	Angitensin II Receptor Blockers	4
6	α - Blockers	12
7	Combination	36

Discussion

The present study gave an idea about the number, type and the seriousness of the ADRs encountered with antihypertensive therapy in Nashik city. The study also assessed the therapeutic effectiveness and safety of antihypertensive medication and provided a statistical database regarding ADR's. The prominent ADRs observed were Vertigo and Dizziness caused by α- blockers; first dose hypotension, dry cough and dysgeusia caused by ACE Inhibitors [(10)], Ca Channel Blockers and α – Blockers.

The ADRs of a particular drug can be linked to its in vivo activity or pharmacological actions of the active components. However, individual concrete explanations are not established for each and every precipitated ADR. Nor can every ADR be justified as a cause of the drug action alone as various other parameters like the interaction of drug with patient's body, other medications and the co-morbid diseased states are also to be considered.

The male to female ratio of ADRs of antihypertensive patients observed in this survey was 16: 9 for 25 patients. Moreover the age group 51-60 years showed maximum number of ADRs. The ADRs like first dose hypotension, muscle fatigue and dry cough are seen in these patients. This may be linked to the intolerance of the newly introduced antihypertensive medication in the body. However these adverse reactions subside spontaneously over a period of time or sometimes a reduction in dose was required. Our work has supported that blood pressure could be adequately controlled with the help of combinational therapy, as this therapy seems to be a rational approach to reduce cardiovascular mortality [(4-12)]. However maximum number of adverse reactions was observed in combinational therapy than in monotherapy. The frequency of ADRs reported was least with patients on diuretics or angiotensin II receptor blockers.

Since antihypertensives are widely used in large number of population, monitoring their adverse drug reactions (Pharmacovigilance) in such patients is essential. Moreover, this class of drug is widely used by the elderly patients with critical conditions and underlying diseases. ADRs of these drugs mostly occur on initiation of the treatment, therefore monitoring of the patient during first few days of initiating the therapy could help in preventing the ADRs. This study also gives the demographic distribution of the prevalence of ADRs amongst different age groups. Differentiation of the frequency and the type of ADRs can be made according to several criteria like gender, severity of ADR and various classes of drugs used. The data presented can be used to create awareness of the ADRs observed in the antihypertensive class of medication. It can help in devising therapeutically safer and a rational therapy for hypertension using different classes of antihypertensive drugs.

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References

1. Kearny PM, Whelton M, Reynolds K.(2005) Global Burden of hypertension analysis of worldwide data, *Lancet* 365 (9455): 217-223.
2. Das SK, Sanyal K, Basu A. (2005) Study of Urban Community in India: growing trend of high prevelence of hypertension in a developing country. *Int. J. Med. Sci.* 2(2): 70-8.
3. Ministry of Health and family Welfare, Government of India and World Health Organization, National Cardiovascular Disease Database, 2005.
4. Rang HP, Dale MM, Ritter JM, Moore PK. (2007) 'Pharmacology', Churchill Livingstone, Elsevier Science Limited, 6th ed. 311-314,751-764.
5. CMP Medica. Current Index of Medical Specialties. CMP Medica India Private Limited 2008.
6. Bates DW, Cullen DJ, Laird N. (1998) Incidence of Incidence of Adverse Drug Reactions in Hospitalized Patients. A Meta – analysis of Prospective Studies. *JAMA* 279: 1200-5.
7. Patel H, Bell D, Molokhia M. (2007) Trends in Hospital Admissions for adverse drug reactions in England: analysis of national hospital statistics 1998 – 2005. *BioMed Central Clinical Pharmacol* [10.1186/1472-6904-7-9] 7:9.
8. Ministry of Health and Family Welfare, Central Drug Standard Control Organization (CDSCO) – Suspected ADR reporting Form. Government of India, 2009.
9. WHO Collaborating Centre for international drug monitoring, the Uppsala Monitoring Centre. Adverse Drug Reaction Terminology, 1996.
10. Kubota K, Kubota N, Pearce GL, Inman WHW. (1996) ACE Inhibitors induced cough, an adverse drug reaction unrecognized for several years: studies in Prescription-Event Monitoring. *Eur J of Clin Pharmacol*. 49: 431-437.
11. Mancia G, Grassi G. (1998) Antihypertensive Treatment: past, present and future. *J Hypertens* 16: S1-S7.
12. Tiwari H, Kumar A, Kulkarni SK. (2004) Prescription monitoring of antihypertensive drug utilization at the Panjab University Health Centre in India. *Singapore Med J*. 45 (3): 117