

Original Article

**DRUG UTILIZATION BASED ADRS MONITORING OF ANTIHYPERTENSIVE AGENTS
PRESCRIBED IN AL-QUWAYYAH GENERAL HOSPITAL, SAUDI ARABIA**

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ABSTRACT

Objective: To monitor drug utilization based adverse drug reactions (ADRs) of antihypertensive agents prescribed in Al-Quwayyah general hospital, Saudi Arabia.

Methods: An open, non-comparative, observational study was conducted on hypertensive patients attending the medicine outpatient department of Al-Quwayyah general hospital, Al-Quwayyah, Saudi Arabia. Data were collected by conducting patient interviews. Data were captured for adverse drug reaction monitoring based on Narinjo scale and WHO format.

Results: 25 ADRs were observed out of 212 hypertensive patients. Incidence was found to be higher in patients more than 40 y age, and females experienced more ADRs (n = 16, 7.54%) than males, 9 (4.62%). Combination therapy was associated with more number of ADRs (64.0%) as against monotherapy (36.0%). Calcium channel blockers were found to be the most frequently associated drugs with ADRs (n = 8), followed by diuretics (n = 6), and β -blockers (n = 5). Among individual drugs, amlodipine was found to be the commonest drug associated with ADRs (n = 8), followed by torasemide (n = 4). ADRs associated with the central nervous system was found to be the most frequent (48.0%) followed by musculoskeletal complaints (20.0%) and respiratory system disorders (16.0%).

Conclusion: ADRs were experienced by taking the antihypertensive drugs prescribed in Al-Quwayyah general hospital, Saudi Arabia. The findings would be useful for physicians in rational prescribing. Calcium channel blockers were found to be the most frequently associated drugs with ADRs.

Keywords: Adverse drug reactions (ADRs), World health organization (WHO), Drug utilization, Antihypertensive drugs

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INTRODUCTION

Hypertension is the most common cardiovascular disease and it has been defined arbitrarily as a systolic blood pressure greater than 140 mm Hg or a diastolic pressure greater than 90 mm Hg [1]. The world health organization (WHO) has estimated one in every eight death globally due to hypertension. It's an increase in hypertension approximately 1/4 of the Saudi Arabia population and has become an important health problem affecting a large number of Saudi people [2].

In 90-95% of cases of hypertension, there is no underlying medical illness to cause an increase in B. P. This is termed essential hypertension. The etiology of essential hypertension tends to run in families, with hypertension being twice as common in families who have a hypertensive patient [3].

Improvement in patient's awareness, compliance and physicians adherence to treatment guidelines of various pharmacological approach exist for the control blood pressure [4]. It's a global challenge to control hypertension, requires mutual co-operation among multiple constituencies, including patients, health-care professionals, industry, media, health-care educators, health planners and governments. The health-care team needs to take action locally with patients to manage blood pressure treatments [5].

Adverse drug events (ADEs) are described as any unwanted events resulting from therapy; it may be physical, physiological, mental and loss of function of any organ [6]. As per WHO ADR is "A response to a drug that is untoward and unintended events occur at doses level normally used in human for the prophylaxis, diagnosis, treatment of disease and for modification of physiological function"[7]. Hospital Pharmacists of an American Society defined that a countable ADR is any unpredicted, unintended, undesired or unexcessive response to a drug, that requires discontinuation, changing, modifying the dose of a drug, necessary to get hospitalized, prolonged to stay in touch with healthcare facility, supportive treatment required, complicate

the diagnosis, badly affects prognosis or results in temporary or permanent harm, disability or death [8]. Food Drug and Administration defines a severe adverse reaction as one in which the patient may be dying, or life-threatening consequences, hospitalization, disabilities, congenital abnormalities or need intervention to progress permanent impairment or damage [9].

ADRs cause many leading morbidity and mortality, Monitoring are more important in case of chronic disease as hypertension. Hypertension is an asymptomatic disorder and requires long-term therapy predisposing to ADEs [10]. The use of antihypertensive drugs related to the development of ADRs to about 1/4th of the patients in the OPD of cardiovascular unit [11]. With an impairment of the quality of life and an increase in healthcare costs, monitoring of ADRs through pharmacovigilance is useful to improve the safety of each patient [12]. The objective of present study was to focus on ADRs of antihypertensive drugs in the outpatients attending the OPD, Department of Medicine in general hospital Al-Quwayyah, Saudi Arabia.

MATERIALS AND METHODS

Methodology

Study design: Prospective, observational analysis of Adverse drugs reactions Patterns in patients with established hypertension. All the observations were recorded in special designed documentation form.

Study site: The Study was carried out in the OPD of cardiovascular diseases in the college of Applied medical science Al-Quwayyah General Hospital, Al-Quwayyah, Saudi Arabia.

Duration of study: The study was carried out during the period of December 2011 to May 2012 (6 mo).

Subject demographics: Study was conducted on 212 eligible patients at Al-Quwayyah General Hospital who were willing to participate. Patients (n=25) presenting with ADR were observed for

changes in physical and biochemical parameters based on pathological lab reports.

Material used: Adverse Drug Reaction Monitoring form, Naranjo's probability scale and WHO form.

Inclusion criteria: All hypertensive patients irrespective of age and sex visiting Medicine OPD in General Hospital were included in the study Patients treated with at least one antihypertensive agent.

Exclusion criteria

- Patients who were not treated with antihypertensive agents
- Drug addicts
- All the mentally retarded and unconscious patients

Sources of data

- Physician prescribing records.
- Patient's medication profile

Data collection

Information on age, gender, drugs prescribed and ADR information were recorded on special design form in Medicine OPD by conducting a patient interview after their informed consent was obtained. All the data were kept confidential.

Sample collection

The hypertensive patients presenting with ADRs were called to the pathology sample collection centre and their fasting venous blood sample (5 ml) was collected by a trained laboratory technician to established ADRs.

RESULTS

Gender distribution of the subjects

During the study period, a total of 212 hypertensive patients visited Al-Quwayyah general hospital. Among the 212 hypertensive patients, 115 (54.2%) were males and 97 (45.8%) were females indicating that hypertension is slightly more prevalent in the female gender.

Monitoring of ADRs

Gender distribution of ADRs in hypertensive patients

A total of 25 ADRs were observed in 212 hypertensive patients in which 115 male and 97 female were taken for study. In which it was found that females experienced more ADRs (n=16) than males (n=9).

Distribution of ADRs among various age groups

The most vulnerable age group was 41-50 y with respect to ADRs (n=8) followed by 71-80 y (n=5), 51-60 y and 61-70 (n=4 each), 31-40 y and 21-30 y (n=2 each).

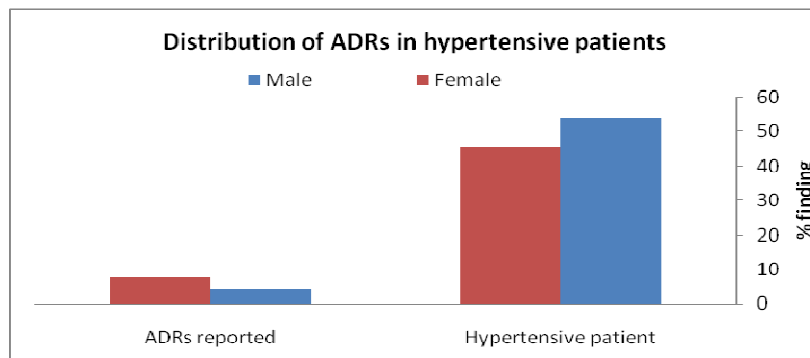


Fig. 1: Gender wise distribution of ADRs

ADRs in mono vs. combination therapy

Combination therapy was associated with more number of ADRs (64.0%) as against monotherapy (36.0%).

ADRs and therapeutic class of suspected medication

The details of ADRs associated with the antihypertensive medicines observed in our study are shown in table Calcium channel blocker was found to be the commonest therapeutic class associated with

ADRs (n=8), followed by diuretics (n=6), β-blockers (n=5), ACE inhibitors (n=2) and Angiotensin receptor blockers (n=4).

Classification of ADRs on the basis of severity

The ADRs observed in our study mostly in the class of mild (n = 15, 60%), which were well tolerated by the patients for example, Nausea, headache, dizziness etc. followed by moderate (n = 10, 40%) as for example sleeping disturbances, depression etc. None of the ADRs was categorized as severe.

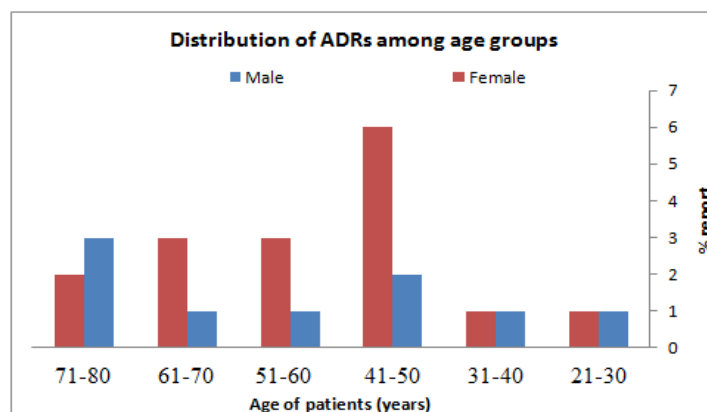


Fig. 2: ADRs distribution in various age groups

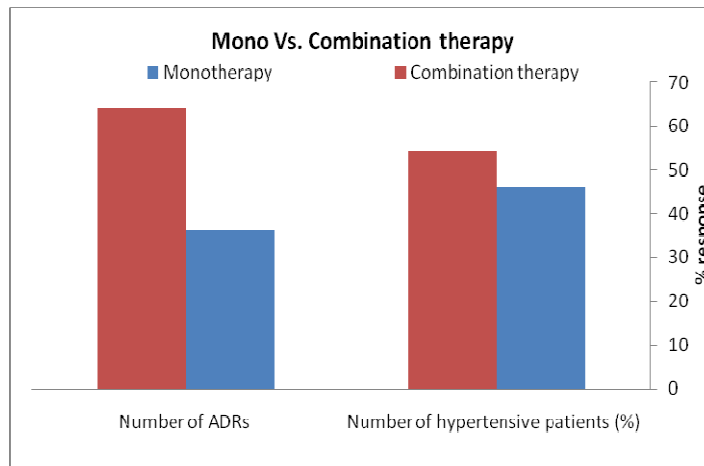


Fig. 3: Distribution of ADRs among different antihypertensive patient

Table 1: Types of ADRs shown by different antihypertensive medicine

Suspected drugs	ADRs experienced	No. of ADRs (%)	Interventions
Calcium channel blockers			
Amlodipine	Ankle edema	02	Dechallenge
	Abdominal pain	02	Symptomatic treatment
	Sedation	02	Symptomatic treatment
	Pedal edema	01	Symptomatic treatment
	Back pain	01	Symptomatic treatment
Total		08 (32.0 %)	
Diuretics			
Torasemide	Fatigue	01	Symptomatic treatment
	Visual impairment	01	Dechallenge
	Dizziness	02	No change in treatment
Total		04 (16.0%)	
Amiloride	Dizziness	01	No change in treatment
	Loss of appetite	01	Symptomatic treatment
Total		02 (8.0%)	
Grand total			
		06 (24.00%)	
Beta-blockers			
Atenolol	Bradycardia	02	No change in treatment
Metoprolol	Headache	01	No change in treatment
Propranolol	Insomnia	01	Dechallenge
	Depression	01	
Grand total		05 (20.0%)	
ACE inhibitors			
Ramipril	Dry cough	02	Dechallenge
Total		02 (8.0 %)	
Angiotensine receptor blockers			
Telmisartan	Dizziness	01	Dechallenge
Losartan	Dizziness	02	No change in treatment
Olmesartan	Dizziness	01	No change in treatment
Grand total		04 (16.0 %)	

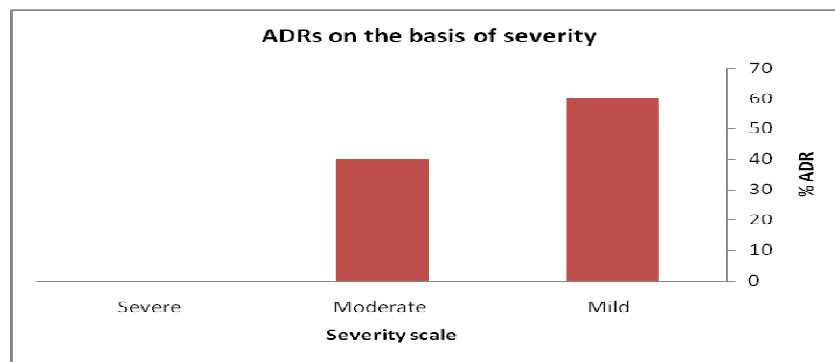


Fig. 4: Severity of ADRs

Organs/systems affected due to medicines

ADRs associated with CNS (n = 12, 48%) were found in majority of patients e. g. dizziness, headache, depression etc. followed by

musculoskeletal (n = 5, 20%) problems example back pain, fatigue. Similarly respiratory related complaint like cough (n=4, 16%), gastrointestinal disorders (n = 3, 12%) abdominal pain, anorexia and ophthalmic dry eye symptoms (n=1, 4%).

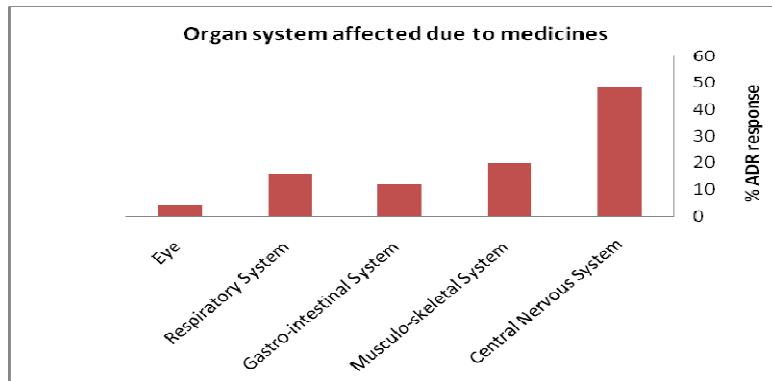


Fig. 5: Organs system affects due to medicines

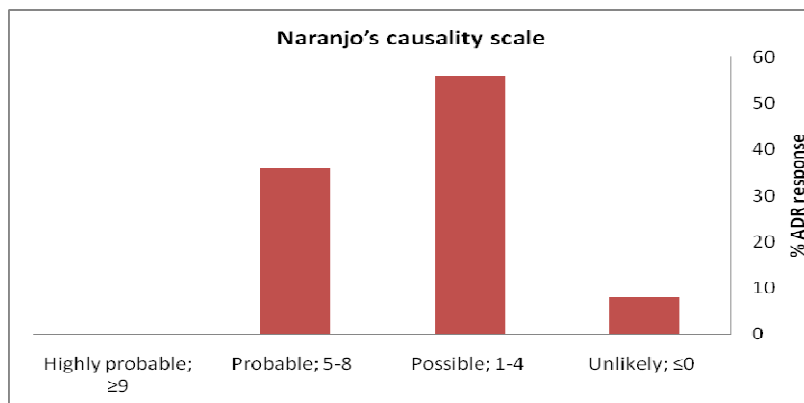


Fig. 6: Classification of ADRs on the basis of Naranjo's causality scale

Classification of ADRs on the basis of naranjo's causality scale

More than half (56%) of the reported ADRs were classified as possible, 36% as probable and 8 % as unlikely on Naranjo's probability scale.

DISCUSSION

The details of our study indicated that female-dominated over males which were similarly reported in [13]. This might be because of sedentary lifestyle which makes them more susceptible to the pharmacological adverse effects of dosages forms and increases the chance of ADRs. The older patients experienced more adverse drug reaction i.e., more than 40 years with compare to younger ones i.e., less than 40 years. The root cause behind this is compromised organ functioning, depressed of basal metabolic rate, simultaneous other disease conditions and multiple drug therapy might be the main cause of ADRs, as there is need to opt multiple drug therapy, ultimately result of that higher incidence of ADRs in older patients reported [14].

ADRs showed more in case of the multiple therapies as compared to monotherapy. Several observational studies on risk factors for ADRs had shown that patients on multiple therapies were more predisposed to develop ADRs as compared to patients on monotherapy observed [15]. Multiple drug therapy increases the probability of ADRs because drug-drug interactions.

Among individual Calcium channel blockers were showed the major ADRs. Amlodipine drug was found to be the frequent drug associated with ADRs [16, 17]. The most common ADRs with amlodipine were:

abdominal pain, ankle edema, sedation, pedal edema, and back pain. Edema has been reported as the most common problem with amlodipine [18]. Torasemide used as a diuretic was associated with fatigue, visual impairment and dizziness types of the ADRs. Dizziness and headache reported as common side effects with diuretics. These side effects may be related to the fluid retention or electrolytes imbalance caused by these drugs. Ramipril showed a dry cough most often ADRs in our study. This is in co-relation of earlier study is that almost majority of patients experienced dry cough on using ACE inhibitors the same finding was observed by [19].

The ADRs showed on different types organ/system of the body were evaluated and observed that symptoms reported by the patients who experienced ADRs. According to our study, the most prevalence systems associated with ADRs were the central nervous system (CNS) followed by musculoskeletal system. The similar finding was reported by [20].

CONCLUSION

Present study was designed and conducted in Saudi government hospital to monitor ADRs of antihypertensive medicines. The study finding showed that male was more prone to hypertension compared to female in mid-age group whereas females' patients were found more prone to ADRs in the age group of 40 y. The combination therapy showed more ADRs cases compare to monotherapy treatment scheme. The maximum ADRs observed with calcium channel blockers, followed by diuretics, β-blockers, angiotensin receptor blockers and ACE inhibitors. Amlodipine was showed to be the commonest drug associated ADRs. In most of the

ADRs cases observed in this study were mild and well tolerated by the patients. The main limitation of the present study was the limited sampled size and short duration study. It's our recommendation that more exhaustive study of special groups like pregnant women and paediatrics need to be included in the further study.

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AUTHORS CONTRIBUTIONS

All the author have contributed equally

CONFLICT OF INTERESTS

Declared none

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