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MONITORING AND REPORTING OF ADVERSE DRUG REACTIONS WITH CARDIOVASCULAR DRUGS IN A TERTIARY CARE HOSPITAL IN SOUTH INDIA

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ABSTRACT

A prospective observational study was conducted for a period of nine months in a tertiary care hospital in South India. The aim of this study was to monitor and report cardiovascular drugs induced adverse drug reactions. A total of 227 patients, 152 men and 75 women using cardiovascular drugs entered the study; among them 115 patients 78men and 37 women were experienced 176 adverse drug reactions. Detected ADR were mostly observed in the age group of 55-65. Majority of the ADRs were observed with male 78(67.8%) compared to female 32 (32.2%). Headache (24.1%), nausea vomiting (10.7%), weakness (9.6%) and dizziness (9%) were the most frequent reactions .When analysed ADRs by Naranjo ADR probability scale, majority of the ADRs 112 (63.6%) were scored probable, 54 (30.6%) possible, 6 (3.4%) unlikely and 4 (2.2%) definite. Severity of ADRs were analysed with modified Hartwig scale 125 (71%) reactions were moderate, 49 (28%) mild and 2(1%) were severe. This study found that much more knowledge to be needed to the healthcare professionals to reduce the incidence of adverse drug reactions. By regulating the ADR reporting system in India can controls the adverse events.

Key Words:- Adverse Drug Reactions, Pharmacovigilance, Cardiovascular Drugs, Causality Assessment.

INTRODUCTION

Globally there is growing concern about the safe use of medications in hospital settings. It is well known that adverse drug reactions constitute a major problem in drug therapy and in our society, both as a health care problem and as an economic burden (Backstrom *et al*., 2007). Adverse drug reactions (ADRs) which are officially described as a response to a drug which is noxious and unintended and which occurs at doses normally used for the prophylaxis, diagnosis or therapy of disease or for the modification of physiological function. (Nebekar *et al*., 2004)A meta-analysis of the incidence of adverse drug reaction 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 (Bates *et al*., 1995). ADR are a major cause of morbidity and repeated ADRs related hospitalizations have consistently increased faster than first time ADRs (Zhang *et al*., 2007) .India has seen a rapid transition in its disease burden (number of cases/lakh) over the past couple of decades (Nutrition transition in India, 2007). This is largely because, with India's economic growth and urbanization over the past decades, a large section of the population has moved towards unhealthy lifestyles with decreasing physical activity, increasing stress levels, and increasing intake of saturated fats and tobacco. The average life span has increased due to improvements in medical care. Cardiovascular diseases (CVDs) are the largest cause of

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mortality, accounting for around half of all deaths resulting from Non communicable diseases (NCDs) (Cardiovascular Disease in India 2011). Various studies shows that cardiovascular drugs are among the most common cause of adverse events (AEs) in hospitalized patients (Levy *et al*., 1980). One study report reveals that cardiovascular drugs may cause half of all hospital admissions due to adverse drug reactions (Bond *et al*., 2006) .The information presented above clearly suggest a significant number of people suffering from these diseases, the number of drugs consumed per patient is relatively predictable and thus ADRs are inevitable, which needs continuous monitoring. ADR monitoring and reporting activity is in its infancy stage in India. Lack of well-structured and effective ADR reporting and monitoring programme is a major problem in India. Studies from various literatures revealed that review and monitoring of prescribed medicines by pharmacists may help to improve the clinical condition of the patients and may reduce the incidence of adverse events and also the cost of treatment (ASHP guidelines 1995). By understanding the responsibility of pharmacist to control AEs of cardiovascular drugs the present study was aimed to monitor, report and determine the severity and causality of ADRs occurs in cardiovascular department.

MATERIAL AND METHODS

The prospective observational study was conducted for a period of nine months in the cardiovascular department in a tertiary care hospital in South India. This study was approved by the institutional human ethical committee. All patients either sex visited in the cardiovascular department during the study period were evaluated for cardiovascular drugs induced adverse reactions, patients developed with ADR during hospital stay or hospitalized due to ADR were included in the study. Patient previously used or newly started on cardiovascular drugs were monitored and followed for detecting and recording of ADRs. Adverse drug reactions were detected by daily interviewing patients, consulting with physicians and reviewing patient charts. World health organization (WHO) definition of an ADR was adopted. If a sign or symptoms suspected to be induced by cardiovascular drug was found and the ADR notification form was filled. Patient demographics were recorded. The time of onset and duration of the reaction, suspected drug, outcome and actions taken for managing the adverse reaction were recorded. Causality and severity assessments were performed by using Naranjo's ADR probability scale and modified Hartwig scale respectively (Naranjo *et al*., 1981; Hartwig *et al*., 1992).

Table 1. Demographic characteristics of study patients

Demographic characteristics	Number of patients and percentage (n=115)
Sex	
Male	78 (67.8)
Female	37(32.2)
Number of medications	
Single drug	22 (19.6)
2 drugs	17 (14.5)
3 drugs	18 (15.5)
4 drugs	26 (22.5)
More than 5 drugs	32 (27.9)
Number of reaction /patients	
One	78 (67.8)
Two	27 (23.4)
More than two	10 (8.8)

Table 2. Systems associated with adverse drug reactions

System affected	Number of ADRs (n=176)	Percentage of ADRs
Central nervous	74	42
Gastrointestinal	37	21
Musculoskeletal	20	11.3
Dermatology	18	10.2
Respiratory	07	8.5
Cardiovascular	06	4.5
Minerals and fluid balance	04	2.2

Table 3. Reported adverse drug reactions in cardiac department

Suspected adverse drug reactions	Number of ADRs (n=176)	Percentage of ADRs
Headache	43	24.1
Nausea and vomiting	19	10.7
Weakness	17	9.6
Dizziness	16	9.0
Fatigue	14	7.9
Dry cough	7	3.9
Dyspnoea	6	3.4
Constipation	6	3.4
Fainting	5	2.8
Epigastric pain	5	2.8
Itching	4	2.2
Rashes	4	2.2
Hypotension	4	2.2
Insomnia	4	2.2
Myalgia	3	1.7
Sore throat	3	1.7
Diarrhoea	3	1.7
Wheezing	2	1.1
Hyper uraemia	2	1.1
Palpitation	2	1.1
Sweating	2	1.1
Vertigo	2	1.1
GI bleeding	1	0.5
Haematuria	1	0.5
Hypokalaemia	1	0.5

Table 4. Classes of drug commonly implicated in adverse drug reactions

Category of drug	Number of ADRs (n=176)	Percentage of ADRs
Anti-platelets	40	22.7
Calcium channel blockers	34	19.3
ACE Inhibitors	29	16.4
Nitrates	27	15.3
Statins	18	10.2
Cardiac glycosides	15	8.5
Diuretics	08	4.5
Beta blockers	05	2.8

RESULTS

A total of 227 patients, 152men and 75women using cardiovascular drugs entered the study, among them 115 patients 78men and 37 women were experienced 176 adverse drug reactions. Twenty two patient experienced atleast one ADR. There were 93 patients who developed more than one ADR. Two ADRs in 17 patients (14.5%). Three ADRs in 18patients (15.5%) four ADRS in 26 patients (22.5%) and five more than five ADRs in 32 patients (27.9%) was reported (Table 1). Maximum of three reactions were observed with single patient and maximum of five drugs were suspected for the reactions. Detected ADR were mostly observed in the age group of 55-65. A total of 107 hospitalized patients experienced an ADR; only 8 patients were admitted in the hospital due to ADR. Majority of the ADRs were observed with male 78(67.8%) compared to female 32 (32.2%). Central nervous system and gastrointestinal system disorders were the most common and frequent classes affected with ADRs (Table 2). Headache (24.1%), nausea vomiting (10.7%), weakness (9.6%) and dizziness (9%) were the

most frequent reactions. Dry cough (7%), dyspnoea (7%) and constipation (7%) also occurred frequently. Electrolyte imbalance also observed significantly (Table 3). The highest rate of ADRs was recorded to be induced by anti-platelets (aspirin and clopidogrel) 40 (22.7%) and lowest rate was found with beta blockers 5 (2.8%) (Table 4). When analysed ADRs by Naranjo ADR probability scale, majority of the ADRs 112 (63.6%) were scored probable, 54 (30.6%) possible, 6 (3.4%) unlikely and 4 (2.2%) definite. Severity of ADRs were analysed with modified Hartwig scale 125 (71%) reactions were moderate, 49 (28%) mild and 2(1%) were severe. Moderate reactions were commonly observed with female, mild and severe ADRs were more common in male. Withdrawal of offending drug was necessary in 43 patients, the treatment is continued 78patients. Dose was altered in 15 cases and 40 suspected drugs were replaced with other agents. Of the total of 176 ADRs most (80%) were non-preventable; whereas (16%) were probably preventable and only 4% were definitely preventable.

DISCUSSION

In this study most of the patients between age of 55-65 were experienced more number of ADR, this result was similar to that of study conducted by Mandavi et al. The incidences of adverse drug reactions were found to be more in male when compared to the female. Recent study shows that the same results, (Singhal Rohit *et al*., 2011) however there is a controversy in the literature on this result (Varun *et al*., 2012). In this study 78 patients (67.8%) developed at least one ADR. The rate is higher than the rate of previous studies reported 15.3% (Davidson *et al*., 1988), 20.3% (Gholami *et al*., 2008) 58.1% (Mandavi *et al*., 2011) Detected ADR were mostly observed in the age group of 55-65. Some studies have shown that ADR is increasing with increasing age; this may be due to polypharmacy. There is a controversy with the previous literature that the female are more prone for ADR, in our study male are more prone to ADR. Central nervous system and gastrointestinal system disorders were the most common and frequent classes affected with ADRs. The same result was observed with study conducted by Gholami K et al. Headache, nausea vomiting, weakness and dizziness were the most frequent reactions, nitrates are more common to produce headache due to dilatation of cerebral blood vessels. Anti-platelets like aspirin and clopidogrel were produced highest rate of ADR. Next to that of anti-platelets, calcium channel blocker had many ADR in our study. Also, flushing, dizziness and peripheral oedema have been mentioned as common complaints with CCBs in a review (Gholami *et al*., 2008).This finding is consistent with many other studies (Ferrari *et al*., 2006; Basak *et al*., 2004) wherein it was reported calcium channel blockers, nitrated and ACE inhibitors as the most commonly associated drug classes in causing ADRs. In our study many of the patients were experienced dry cough. This is consistent with the previous study, on that 44% patient experiencing with ACE inhibitors induced dry cough. (Ferrari *et al*., 2006; Aqil *et al*., 2006) Dizziness and headache have been reported as common side effects associated with diuretics it may be due electrolyte imbalance. Our finding may be due to the fact that in the present population, these classes of drugs are widely prescribed in Indian population. When analysed ADRs by Naranjo ADR probability scale, majority of the ADRs 112 (63.6%) were scored probable, 54 (30.6%) possible, 6 (3.4%) unlikely and 4 (2.2%) definite. This is consistent with other studies probable ADRs are more (Woo *et al*., 1995) Severity of ADRs were analysed with modified Hartwig scale 125 (71%) reactions were moderate, 49 (28%) mild and 2(1%) were severe. Moderate reactions were commonly observed with female, mild and severe ADRs were more common in male. Withdrawal of offending drug was necessary in 43 patients, the treatment is continued 72 patients, Dose was altered in 15 case, 7 patients treat with alternate drugs and 40 patients went through symptomatic treatment and the remaining ten cases the treatment was continued without any change. Of the total of 176 ADRs most (80%) were non-preventable.

CONCLUSION

Monitoring adverse drug reactions in patients using cardiovascular drugs in a matter of importance since this class of medicine is usually used by elderly patients with critical conditions and underlying diseases. The literature shows that cardiovascular drugs induced adverse events are more, due to using of more than one drug for cardiovascular problems. Our study shows that many of the adverse drug reactions can be managed by withdrawal of offending drugs and by providing symptomatic treatment. Even though the pharmacovigilance programme started in our country still the health care professional are unaware about monitoring and reporting of adverse drug reactions. By providing proper training and by regulating the current system of monitoring and reporting of ADR can reduce the incidence of ADR induced hospitalization or length of hospitalization and cost of treatment.

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