AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

A Prospective Study On Adverse Drug Reactions In General Medicine Department In A Tertiary Care Teaching Hospital

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ABSTRACT

The field of patient's drug safety has been receiving great deal of attention, since adverse drug reaction has been recognized as hazards of drug therapy. Adverse drug reactions are a great cause of concern to the healthcare professionals, patients and the pharmaceutical industry. However, may times it goes undetected and ignored by the patients and healthcare professionals. Hence we took a prospective observational study to analyse the Adverse Drug reactions among all patients admitted in general medicine department in Justice KS Hegde Charitable Hospital, Mangalore. The study was carried out for a period of eight months from September 2012 to April2013. The suspected adverse drug reactions were later analysed for their causality, severity and preventability by using the different adverse drug reaction assessment scales. A total of 640 cases has been followed and 47 Adverse Drug Reactions has been reported from the 40 patients during the study period. Male predominance was noted over females in case of total number of patients. Majority Adverse Drug Reactions were in the age group 70-79(31.91%). The most common class of drugs involved in adverse drug reactions is Antibiotics (17.39%) followed by Antihypertensive 7(15.21%). The most common system involved in adverse drug reaction is Digestive system (19.36%) followed by dermatological system (13.04%). Out of the 47 adverse drug reactions reported, 53% were probable, 45% were possible and 2% were unlikely. The severity assessment done by using the Hartwig and Seigel scale indicate that majority of the ADRs were 'Mild' followed by moderate and severe respectively. The preventability assess shows that most of ADRs are Probably Preventable 28(59.57%) followed by Not preventable 16(34.04%) and definitely preventable 3(6.38%). Monitoring and reporting of adverse drug reactions in the hospital is one of the best method to identify the causality between exposure to the drug and the occurrence of adverse drug reaction. Proper education and training to the healthcare professional's towards ADR reporting will have a positive attitude towards continuous reporting and improving patient safety.

Keywords: Adverse Drug Reaction (ADR), prospective observational, Causality, Severity, Preventability, Predisposing factors.

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Received 05 November 2013, Accepted 14 November 2013

Please cite this article in press as: Shareef J. *et al.*, Identification of Bioactive Compounds from *Spirulina* by Gas Chromatography Coupled with Mass Spectrophotometer (GC-MS). American Journal of PharmTech Research 2013.

INTRODUCTION

Today, it is well known that adverse drug reactions (ADRs) constitute a major problem in society and in drug therapy, as a health care problem and as an economic burden. They are a common cause of hospitalization, especially among the elderly. In several studies, it has been shown that the frequency of patients being admitted to hospital as a direct effect of an ADR can be estimated to be 5-10%. In some studies, however, the frequency was estimated to be as high as 20% of all cases admitted to a department of internal medicine or to a geriatric clinic.[1]

Though many drugs are precisely targeted to the causes and mechanisms of diseases, and are brilliantly effective in treating them, they may also have some minor or major negative effects on other parts of the body, or may interact negatively with the systems of the particular individual or with other drugs or substances that are taken by the individual[2]. Whenever a drug is administered a risk is undertaken which may be due to the properties of the drug, patient factors and of the environment. Psychotropic drugs are plentiful in number and their use is increasing day by day. These drugs are capable of causing a number of adverse drug reactions (ADRs) some of which may be fatal[3].

ADRs associated with psychotropic drugs can lead to noncompliance, and at times discontinuation of therapy. Pharmacovigilance in psychiatry units can play a vital role in detecting ADRs and alerting physician to possibility and circumstances of such events, thereby protecting the user population from avoidable harm[4]. As far as India is concerned, ADR reporting rate observed to be very low. There might be many factors responsible for this scanty reporting such as heavy patient load on prescribers, irrational prescribing drugs are dispensed without prescription, polypharmacy, use of many alternative system of medicine, and unavailability of sufficiency trained and motivated doctors and other paramedical staff for ADR reporting[5,6].

There are many factors that can predispose to the occurrence of adverse drug reaction in a patient. Patients who have one or more of the following predisposing factors are at high risk of developing ADRs.[2]

Polypharmacy:

Patients with multiple drug therapy are more prone to develop an adverse drug reaction either due to alteration of drug effect through an interaction mechanism, or by synergistic effect.

Multiple and intercurrent diseases:

Patients with multiple diseases are at an increased risk of developing an ADR due to multiple

drug use for their multiple diseases. Similarly, patients with impaired hepatic or renal status are also at high risk of developing an ADR to drugs which eliminated by these organs.

Age: Elderly and paediatric patients are more vulnerable to develop ADRs. Elderly patients are more susceptible to ADRs due to the physiological changes which accompany aging, and also because they are often taking many drugs for chronic and multiple diseases. Paediatric patients may develop serious adverse drug reaction to some drugs since all children, especially neonates, differ in their drug handling capacity compared to adults. An example of such a serious reaction is the Gray baby syndrome with chloramphenicol.[3]

Drug characteristics:

Some drug are highly toxic in nature and patients who are treated with these agents are at an increased risk of ADRs. Also with drugs which have narrow therapeutic index such as digoxin and gentamicin are more susceptible to develop ADRs.

Gender:

Women are thought to be greater risk of ADRs than men. Females appear to have 1.5 to 1.7 -fold greater risk of developing an ADR. The reasons are idiopathic but may include gender-related differences in pharmacokinetic, immunological and hormonal factors.[3]

Race and genetics:

The discipline of pharmacogenetics deals with variability in drug response that is under hereditary control Genetic variation in genes for drug-metabolizing enzymes, drug receptors and drug transporters have been associated with individual variability in the efficacy and toxicity of drug.[7]

WHO in the 1960s in the wake of 'thalidomide' disaster, is currently an integrated global effort of more than 70 countries worldwide. After the "thalidomide tragedy" many countries have established drug monitoring systems for early detection and prevention of possible drug-related morbidity and Mortality[8]. In India, ADR monitoring was started in 1982 under the chairmanship of Drugs Control General of India (DCGI). This was started as an institutional activity, where intensive monitoring of 58194 cases collected from various centers was done in 1987 under the guidance of Indian Council Of Medical Research.[5]

Adverse reactions may be prevented as never use any drug unless there is a good indication. If the patient is pregnant do not use a drug unless the need for it is imperative, Allergy and idiosyncrasy are important causes of adverse drug reactions. Ask if the patient had previous reactions[9]. Ask if the patient is already taking other drugs including self-medication drugs, health supplements, complementary and alternative therapies; interactions may occur, Age and hepatic

or renal disease may alter the metabolism or excretion of drugs, so that much smaller doses may be needed. Genetic factors may also be responsible for variations in metabolism, notably of isoniazid and the tricyclic antidepressants. Prescribe as few drugs as possible and give very clear instructions to the elderly or any patient likely to misunderstand complicated instructions. Whenever possible use a familiar drug; with a new drug, be particularly alert for adverse reactions or unexpected events. Warn the patient if serious adverse reactions are liable to occur.[10] The present study was carried out with the objectives to analyse the adverse drug reactions among patients in the general medicine department , to determine the nature and frequency of adverse drug reactions in medicine department and to assess the causality, severity and preventability of the ADRs.

MATERIALS AND METHODS

A prospective observational study was conducted after getting approval from the Institutional Ethical Committee. The study was conducted over a period of eight months (September 2012-April2013).In which In-patients admitted in General Medicine department of Justice K.S Hegde Charitable Hospital, has been included in the study. All In- patients of either sex of eighteen years and above who developed an ADR during their hospital stay were included in the study. Patient data collection form, ADR reporting form, ADR Alert cards, ADR notification form was designed as per the need of the study Patients who are admitted during the study period were reviewed by pharmacist and the patient who met the study criteria were enrolled into the study after getting the written informed consent signed. Patients case notes, medication charts, laboratory data and other relevant documents of enrolled patients was reviewed on daily basis whenever a suspected ADR has been notified in hospitalized patient during the study period, after proper discussion with respected physicians and proper literature review it will be documented in the ADR reporting form and later will be evaluated by using Causality, Severity and Preventability scales. Several measures were suggested for improving ADR reporting. These include creating awareness about ADR reporting among healthcare personnel through appropriate educational interventions through ADR information leaflets. The collected information's were analyzed by using Descriptive statistics (mean, median, frequency, percentage) independent sample T test, Mann-Whitney and Fisher's Exact test to study association and level of significance between gender, hospital stay and severity.

RESULTS AND DISCUSSION

Medicines are used to treat diseases as they have ability to modify the physiological processes in

the body and often carry risk of unwanted effects known as adverse drug reactions. No drug is absolutely safe, even when prescribed in therapeutic doses.Many studies have revealed that the ADRs are the fifth leading cause of mortality in USA. ADRs not only cause the morbidity and mortality but also increase the overall cost of healthcare.[6]

1.Demographics

Of the total 640 cases followed in the general medicine wards during the study period, a total of 57 adverse drug reactions were reported but only 47 were accepted and remaining 10 were not accepted due to lack of information and some reactions were not categorized as adverse drug reactions. Out of 47 Adverse Drug Reaction occurred in 40 cases, 26 were males (65. 0%)n=65 and 14 were females (35.89%) n=35.89. which is given in (Table 1), shows that males were predominant than females. The study results was similar to the study of Shadi Baniasadi et al[8]; and Palanisamy S et al[15];

Table 1 Gender wise distribution of study populations

Male	Female
26	**14**
65%	**35.89%**

2.Age wise distribution

In case of age wise distribution, incidence of ADR among 11 patients in the age group (70-79) was found to be higher followed by 10 patients in age group (60-69), 9 patients in age group (50-59), 5 patients in age group (20-29), 3 patients in age group (30-39) and 2 patients in age group (40-49). Since most of the ADR occurred in age group between (70-79), study shows that Geriatric patients are more prone to ADR. This may be due to the fact that elderly were receiving multiple drug therapy and also presented with co-morbidities such as diabetes, hypertension and other cardiovascular diseases.The study results was similar to the study conducted by Jimmy Jose and Padma G.M. Rao[6] and Emily R. Hajjar et al[16];

Table2: Age wise distribution of study populations

Age wise distribution	Number	Percentage
20-29	5	12.5
30-39	3	7.5
40-49	2	5
50-59	9	22.5
60-69	10	25
70-79	11	27.5

3.Duration of Hospital stay

Duration of hospital stay also is a factor for occurrence of ADR, here in this study results obtained were patients which got ADR on more than seven days of hospital stay are significantly

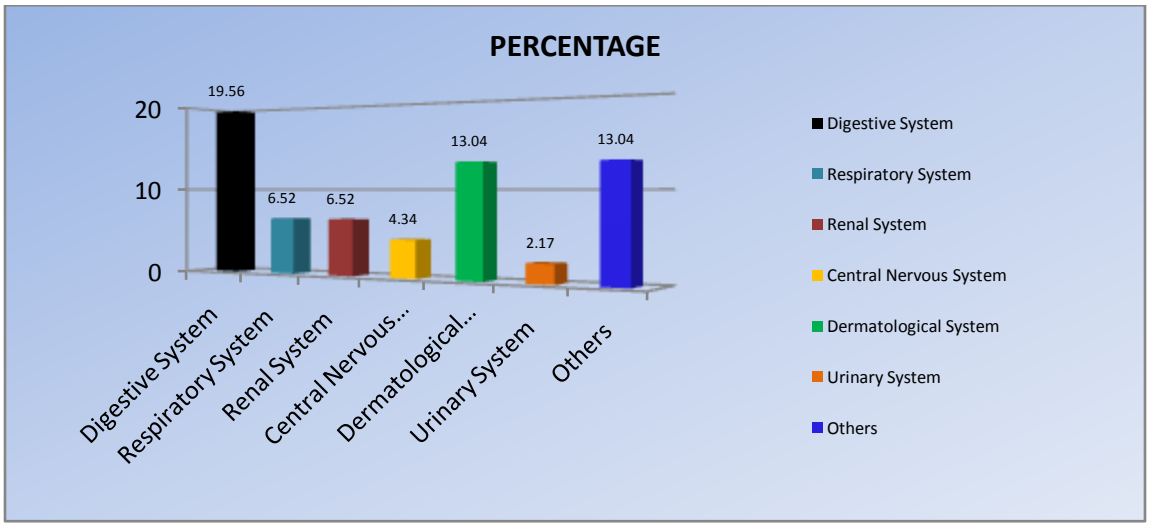
higher about 33(82.85%), followed by less than seven days of hospital stay of 5(12.5%), seven days of hospital of 2(5%) so the chance for development of ADRs may be increased with prolonged hospital stay which shows similarity with the study conducted by Tumwikirize WA et al[14];

Table 3: **Duration of hospital stay of the study populations**

Duration of Hospital stay	Total Numbers	Percentage
Less than seven days	5	12.5
Seven days	2	5
More than seven days	33	82.5

4.Adverse Drug Reactions under system vice classification

Adverse Drug Reactions under system vice classifications, major system involved is digestive system of (19.56%), followed by dermatology of (13.04%), Respiratory of (6.52%), Renal of (6.52%), CNS of (4.34%), Urinary system of (2.17%), metabolic and endocrinologic factors consist of 17(36.17%).



Figures 1: includes different systems & its percentage.

5.Common classes of drugs causing Adverse Drug Reactions

Reported ADRs are classified under different classification of drugs In which 8 ADRs fall under Antibiotics, 7 ADRs in Antihypertensive & Anti diabetics, 4 in Diuretics and NSAID's and 2 reports in immunosuppressant. Antibiotics are major drugs causing ADRs in our study followed by Antihypertensive and Anti diabetics drugs. This may be due to more use of antibiotics for treating the suspected infections in the hospitals. This study shows similarity with the study made by Sriram et al[5]; and A Harugeri et al[13] which has shown that antibiotics were found to be the most common class of drug causing adverse drug reactions.

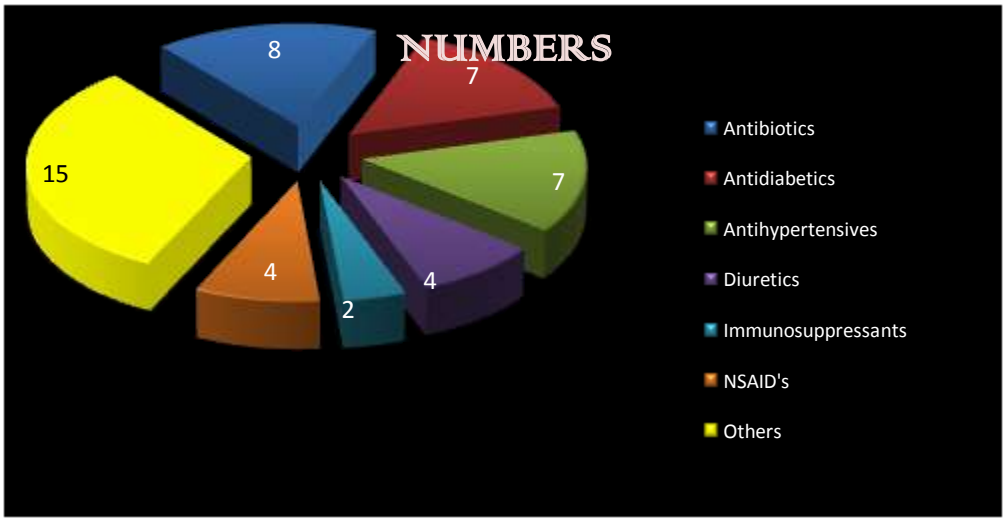


Figure 2:Includes Number of ADRs with different classification of drugs

6. **Results of Causality assessment done from the study using Naranjo's Scale and WHO scale**

Up on Causality assessment scales, majority of report were rated as probable 25(53.19%), followed by possible 21(44.68%), and unlikely 1(2.12%) in Naranjo's scale and in W.H.O scale there are certain ADRs 25(53.19%), unassessable ADRs of 15(31.91%), probable ADRs of 5(10.63%), conditional and possible ADRs of 1(2.12%). Similar findings were noted from other studies also, most of the reported adverse drug reactions were belonged to the category of probable (70%) followed by possible (30%) of cases[17].

Causality

- Naranjo's scale

	Numbers	Percentage
Possible	21	44.68
Probable	25	53.19
Unlikely	1	2.12

- WHO scale

	Numbers	Percentage
Certain	25	53.19
Unassessable	15	31.91
Probable	5	10.63
Conditional	1	212
Possible	1	2.12

7. **Assesses data for the Severity scales of ADRs using Hartwig et al; scale**

Data which are assessed for the Severity scales of ADRs using Hartwig et al; scale, Mild ADRs are of 29(61.63%), which Mild Level 1 consist of 5(10.53%) and Mild Level 2 of 24(51.06%), in Moderate ADRs of 16(34.03%), in which Moderate Level 3 consist of of 7(14.89%), Moderate

level 4a of 1(2.12%) and Moderate Level of 4b of 8(17.02%) were the study results are similar to the study conducted by Mrugank B.P[12].

Severity

	Numbers	Percentage
Mild Level 1	5	10.63
Mild Level 2	24	51.0
Moderate Level 3	7	14.89
Moderate Level 4(a)	1	2.12
Moderate Level 4(b)	8	17.02
Severe Level 5	2	4.25
Severe Level 6	0	0
Severe Level 7	0	0

8. **Assessment for Preventability using Schumock & Thornton scale**

Assessment for Preventablity ADR done using Schumock & Thornton scale has shown that probably preventable ADRs are most common than definitely and not preventable ADRs. Probably Preventable ADRs consist of 28(59.57%), not preventable of 16(34.04%) and definitely preventable of 3(6.38%) which does not show similarity to the study done by Asawari L Raut et al.[11]

Preventability

	Number	**Percentage**
Definitely Preventable	3	6.38
Probably Preventable	28	59.57
Not Preventable	16	34.04

9. **Assessment for predisposing factors**

The most common Predisposing factors associated were Age 14(29.78%) followed by Multiple Drug Therapy 13(27.65%), Inter current Diseases 11(23.40%), Gender 7(14.89%), and other factors 2(4.25%).

Predisposing factors

	Number	**Percentage**
Age	14	29.78
Gender	7	14.89
Intercurrent Illness	11	23.40
Multiple Drug Therapy	13	27.65
Other	2	4.25

10. **Results for the statistical analysis which done through independent sample T- test, Mann-Whitney test and Fisher's exact't' test**

In case of statistical analysis which done through Mann-Whitey Test a difference is found out in medium duration of hospital stay at 5% level of significance, its Pvalue=0.015. In Fisher's Exact T Test P Value is found to be (p=0.008) and there is a difference in proportion of results obtain

through W.H.O & Naranjo's scale at 5% level of significance An another Fisher's Exact T Test were done between Gender and W.H.O scale in that there is no assossiation between Gender and severity measured by W.H.O scale, Fisher's Exact T Test P value= 0.422, Another statistical analysis was done against Gender and Naranjo's scale and result was found as there is no association between Gender ad severity.

Independent Sample t-test

	Mean	Standard Deviation	P value
Male	53.90	15.103	0.091
Female	62.75	19.413	

Mann- Whitney test

	Median	IQR	P value
Male	11	9.21	0.015
Female	8	7.13	

Fisher's Exact t test P value

Naranjo	WHO					Total
	Certain	Probable	Possible	Unassessable	Conditional	
Probable	18	3	0	3	1	25
Possible	7	2	1	11	0	21
Unlikely	0	0	0	1	0	1

Fisher's Exact t test P value

Gender	WHO					Fisher's Exact test P value
	Certain	Probable	Possible	Unassessable	Conditional	
Male	15	3	0	12	1	0.422
Female	10	2	1	3	0	

		Naranjo's Probable	Possible	Unlikely
Gender	Male	16	14	1
	Female	9	7	0

CONCLUSION

Adverse drug reactions are a significant cause of morbidity and mortality and can contribute to significant healthcare cost. Poly pharmacy, intercurrent illness and longer hospital stay will play a major role in occurrence of serious and multiple adverse drug reactions. Developing an ongoing adverse drug reaction reporting system with continuous motivation and creating awareness among the healthcare professionals for reporting suspecting adverse drug reactions will help to continue reporting and improving the patient safety.

ACKNOWLEDGEMENT

Authors are thankful to NGSM Institute of Pharmaceutical Sciences for providing necessary

support to the study. Secondly we express special thanks and gratitude to Department of General Medicine, Justice K. S. Hegde charitable Hospital, Mangalore for permitting to conduct the study in the hospital.

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