International Journal of Pharmacy Teaching & Practices 2011, Vol.2, Issue 3, 96-101.

A Study On Adverse Drug Reactions At A Tertiary Care Teaching Hospital

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Research Article

Please cite this paper as: Sivanandy Palanisamy, Kottur SG Arul Kumaran, Aiyalu Rajasekaran. A Study On Adverse Drug Reactions At A Tertiary Care Teaching Hospital. IJPTP, 2011, 2(3),96-101.

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Abstract

Objective: The main objectives of the study were to assess the incidence and pattern of ADRs, identifying co-morbidities, past, present illness, assess causality, and offending drugs, monitoring, documenting suspected adverse drug reaction(s) and estimate the cost involved.

Methods: A prospective, spontaneous, reporting study was conducted over a period of 6 months by clinical pharmacists using various scales, namely WHO probability scale, Naranjo's scale and severity assessed by using modified Hartwig and Siegel scale. The management of reported ADRs and the outcome of the management of ADRs were determined.

Results: A total of 60 ADRs were identified out of which 34 (56.67%) were male and 26 (43.33%) were female patients. The assessment by Naranjo's scale showed that out of 60 ADR's 44 (73.33%) ADR's were possible, 16 (26.67%) were classified as probable and 0 (0.0%) were definitely related to the drug. WHO probability assessment scale revealed that out of 60 ADR's 43(71.67%) ADR's were possibly drug-related, 16 (26.67%) ADR's were probably drug-related and 1 (1.66%) ADR were identified as certain. Severity Assessment by Modified Hartwig and Siegel Scale showed that 35(58.33%) ADRs were moderate, 21(35%) ADRs were mild and 4(6.66%) ADRs were severe. No lethal effects were observed or produced.

Conclusion: Adverse drug reactions (ADRs) related hospital admissions are a significant problem in the health care system. There is a need for a greater awareness among the healthcare professionals, regarding not only the potential for adverse drug reactions but also in the prevention (or) minimization of the occurrence of ADRs.

Key words: Adverse drug reactions, spontaneous reporting, ADR management, hospital admission, preventability.

Introduction

An adverse drug reaction is an expression that describes harm associated with the use of given medications at a normal dose(s) [1]. The meaning of this expression differs from the meaning of "side effect", as this last expression might also imply that the effects can be beneficial [2]. The study of ADRs is the concern of the field known as pharmacovigilance. The occurrence of adverse drug reaction is a price that we or rather our patients have to pay for the great benefits that have been produced by modern medicine and which we anticipate will continue to be produced in the future [3]. Tracking of adverse drug reactions is now mandated by regulatory agencies. In order to identify and prevent adverse drug reactions, methods that can accurately predict those most at risk for an adverse drug reaction must be developed. Concurrent with this need, is the need to ensure that the methods developed to identify this sub-population are efficient, practical, and less expensive than current methods [4].
Adverse drug reactions may also result in diminished quality of life, increased physician visits, hospitalizations, and even death. In addition, they result in increased health care costs. The numerous medications, multiple chronic medical problems, and frequent acute illnesses experienced by the patients put them at increased risk for ADRs and makes detection more difficult. The fundamental role of the Health Care Professionals is to identify potential and actual drug related problems, resolve problems, and prevent potential drug-related problems. Health Care Professionals are encouraged to take responsibility in the development of Adverse Drug Reaction Monitoring and Reporting Programs. This should lead to a heightened awareness of ADRs, increased reporting of ADRs, and increased opportunities to review drug selection and prescribing practices affecting patient outcome [3].

Furthermore, ADRs contribute to an increased attendance at primary health care level and may complicate hospital in-patient stay in as many as 10% to 20% of patients. Moreover, ADRs may be responsible for deaths and they may possibly be the fourth commonest cause of death. They may increase the length of hospital stay and therefore increase the cost of patient care. In addition ADRs may adversely affect quality of life and may cause patients to lose confidence in Health Care Professionals [5].

Adverse drug reactions caused by immune and non-immune mechanisms are a major cause of morbidity and mortality worldwide. They are the most common iatrogenic illness, complicating 5 to 15 percent of therapeutic drug courses [6, 7].

In the United States, more than 100,000 deaths are attributed annually to serious adverse drug reactions [8]. Three to 6 percent of all hospital admissions are because of adverse drug reactions, and 6 to 15 percent of hospitalized patients (2.2 million persons in the United States in 1994) experience a serious adverse drug reaction [6-9]. Epidemiologic data support the existence of specific factors that increase the risk of general adverse drug reactions, such as female gender [10] or infection with human immunodeficiency virus (HIV) [11] or herpes [12]. Factors associated with an increased risk for hypersensitivity drug reactions include asthma [13], systemic lupus erythematosus [14], or use of beta blockers [13]. Although atopic patients do not have a higher rate of sensitization to drugs, they are at increased risk for serious allergic reactions [15].

The Naranjo's causality algorithm [16] is widely used to determine the likelihood of whether an ADR was actually due to the drug identified by the clinical event monitor, rather than the result of other factors. The Naranjo algorithm is used to compute a weighted score based on answers to a short standardized questionnaire that correlates with causality probability. Similar to other clinical event monitor studies, computer alert signals with a score of ≥1 on the Naranjo's scale, indicating a possible ADR, were classified as true positives [17].

Causality assessment is the method by which the extent of relationship between a drug and a suspected reaction is established. Currently wide variety of causality assessment scales exists, to attribute clinical events to drugs in individual patients or in case reports, each with their own advantages and limitations. These scales includes WHO probability scale, Naranjo's scale, Karch & Lasagna scale, Spanish quantitative imputation scale, Kramer's scale, Jones scale, European ABO system and Bayesian system. The Naranjo's scale and the WHO scale of assessment are the most commonly used scales [18].

Methods Of Detecting An ADR [19]

The first step in the detection of ADRs is collection of data. The data to be collected include patient's demographic data; presenting complaints; past medication history; drug therapy details including over-the-counter drugs, current medications and medication on admission; and lab data such as hematological, liver and renal function tests. Details of the suspected adverse drug reaction such as time of onset and duration of reaction, nature and severity of reaction, details of the suspected drug including dose, frequency, time of administration, duration of treatment, plasma concentration of drug, previous report on reported reaction, data on any other causes including risk factors and predisposing factors are useful.

Every healthcare practitioner should see it as a part if his/her professional duty to report any suspicion of a drug unexpectedly causing a risk situation for a patient under his/her cares. Pharmacovigilance should however not be limited to the reporting of classical adverse effects. It should also be concerned with identification of product defects, unexpected insufficient therapeutic effects, intoxications and misuse-abuse situations.

- Pre-marketing studies
- Post marketing studies

Pre-Marketing Studies

It involves two types pre-clinical studies and clinical studies. In pre-clinical studies the safety of new medicines is tested in animal models. A great deal of risk information may be obtained from such tests, for example the level of acute toxicity, which organs will be affected in case of toxicity and dose dependency of such tissue injuries. Specific animal tests for carcinogenicity, teratogenicity and mutagenicity are also available. However, animals can only serve as approximate models for humans. If animal tests do not reveal particularly worrying results, safety tests proceed onto testing in humans in clinical trail programmes. In clinical studies, the clinical trials are carried out in three different phases prior to the submission of a marketing authorization application, with a stepwise increase in the number of individuals being exposed.

Post-Marketing Surveillance

It involves case reports, cohort studies, case control studies, prescription event monitoring and spontaneous reporting system. The most sensitive, powerful and cost-effective system for identification of unknown drug-related risks is spontaneous adverse reaction reporting.

Management Of An ADR

First and foremost step is withdrawal of suspected drug(s), if the reaction is likely to be dose related, dose reduction should be considered and treatment for suspected reaction may be symptomatic or specific. While managing an ADR, always have a clear therapeutic objective in mind, do not treat for longer than is necessary, review the patient regularly and look for ways to simplify management.

Role Of Pharmacist In ADR [3, 20]

The pharmacist's role is to promote the development, maintenance, and ongoing evaluation of a program to reduce the risk of ADRs through detecting, reporting and

assessing any suspected ADR. Investigate every suspected ADR for its nature, probability, and severity, Develop risk reduction strategies as part of an ongoing program, Enlist the continued support of other health professionals in this program, Provide information to other health care professionals to better identify ADRs, e.g., list of common ADRs by therapeutic category. Report serious or unusual ADRs through the FDA's MedWatch program; disseminate information about previously unreported ADRs.

Educate staff (physician, nurses, etc.) and encourage compliance with the ADR reporting program. The objectives were to study the pattern of ADRs occurring in this hospital, to identify the co-morbidities, past and present illness, to assess causality, and to identify the offending drugs, monitoring and documenting the suspected adverse drug reaction(s), to estimate the cost involved in the treatment of adverse drug reaction(s) and reporting of the suspected ADRs to the concerned department and to the ADR monitoring authorities.

Methodology

The prospective, spontaneous, reporting study was conducted at KMCH Hospital, Coimbatore, Tamilnadu, a 700 bedded multi-disciplinary super-specialty hospital in South India, over a period of 6 months between July 2010 and December 2010. All department of the hospital were included in this study, which has enormous potential of the adverse drug reactions, human ethical committee clearance was obtained. Inpatients, those who were exposed to any adverse drug reactions in the hospital and those who were admitted for the treatment of adverse drug reaction (ie. reason for admission was ADRs) were included in the study. Patients presenting difficulties in communication and accidental or intentional poisoning due to drugs were excluded from the study.

Causality Assessment

A separate data entry format was specially designed for the study. The drug chart, ADRs algorithm and causality assessment scale were also included in the data entry format. The patients and offending drugs were identified through routine ward rounds, prescription monitoring and reports from the health care professionals (nurses, doctors etc). Data were collected from patient's case sheet and transferred to data entry format for evaluation. The collected data's were analyzed by using Naranjo's causality assessment scale, WHO probability assessment scales, Hartwig and Siegel severity assessment scale.

The collected data were further analyzed for its appropriateness and suitability and the interpretation was made for the collected data. The suspected ADRs were reported to the regional pharmacovigilance centre and to the peripheral centre.

Results and Discussion:

In the study population 60 ADRs were identified, out of which 34 (56.67%) were found in male and 26 (43.33%) were found in female patients. Out of 60 suspected ADRs, 58 (96.67%) ADRs were reported from in-patient department and 2 (3.33%) ADRs were reported from out-patient departments. Age was found to be important criteria, patients in the age group between 41 and 60 years experienced 32 (53.33%) ADRs, followed by 14 (23.33%) ADRs in the age group between 21 and 40, 10 (16.66%) ADRs in the age group between 61 and 80 years. In our study out of 60 patients, 36 patients (60.0%) required hospital admission due to an ADR's while 24 (40.0 %) patients were affected by ADR after hospital admission.

Causality Assessment by Naranjo's Scale

Causality assessment was done by using both naranjo's and WHO scale. The assessment by naranjo's scale showed that out of 60 ADR's 44 (73.33%) ADR's were possible, 16 (26.67%) ADR's were classified as probable and none of the ADR was definitely related to the drug (Figure 1).

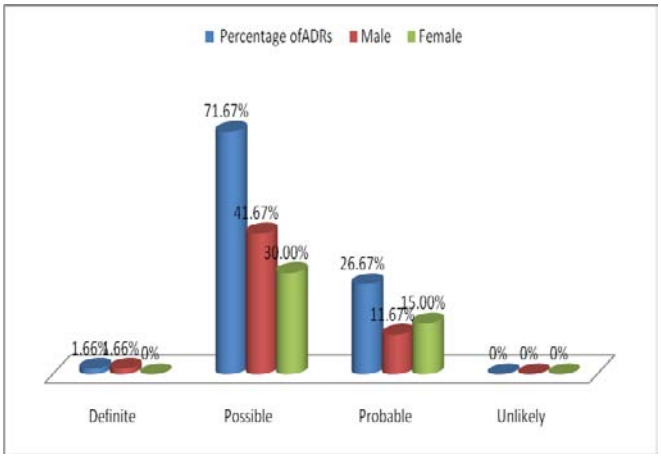

Figure 1. Naranjo's causality assessment of ADRs

WHO Probability Assessment Scale

The assessment done by using WHO scale showed that out of 60 ADR's 43(71.67%) ADR's were possibly drug-related, 16 (26.67%) ADR's were probably drug-related and 1 (1.66%) ADR was identified as certain. Preventability assessment showed that 54 (90.0%) ADR were probably preventable and 06 (10.0%) were non-preventable (Table 1).

Table 1. WHO probability assessment of ADRs (n=60)

S.No	Type of Reaction	No. of ADRs (%)	Sex Distribution (%)	
			Male	Female
1	Certain	1(1.66%)	1(1.66%)	0(0%)
2	Possible	43(71.67%)	25(41.67%)	18(30.0%)
3	Probable/ likely	16(26.67%)	7(11.67%)	9(15.0%)

Severity Assessment by Modified HARTWIG and SIEGEL Scale

The severity assessment showed that 35(58.33%) ADRs were moderate, 21(35%) ADRs were mild and 4(6.66%) ADRs were severe. No lethal effects were observed or produced (Table 2).

Table 2. Severity of reported ADRs by Modified Hartwig and Siegel scale (n=60)

S.No	Severity of ADRs	No. of ADRs (%)	Sex Distribution (%)	
			Male	Female
1	Mild	21(35%)	13(21.66%)	8(13.33%)
2	Moderate	35(58.33%)	21(35%)	14(23.33%)
3	Severe	4(6.66%)	1(1.66%)	3(5.0%)

ADR's affecting the gastrointestinal system were high 15 (25.0%), while ADR's affecting other systems were as follows dermatology 14 (23.33%), CNS 14 (23.33%), renal system 10 (16.66%), immune system 4 (6.66%) and followed by respiratory system was 3 (5.0%) (Figure 2). The most commonly identified adverse drug reaction was skin rash in 18(30.0%) cases followed by nausea and vomiting in 7(11.66%) cases, headache in 4(4.66%) cases and hyperglycemia in 3(5.0%) cases etc (Table 3).

In our study, ADR's were most commonly associated with antibiotics in 13 (21.67%) patients and NSAIDs in 9 (15.0%) patients while other drugs classes were associated such as antileprotic and sulpha drugs 6(10.0%), cardiovascular drugs 5(8.33%), antidiabetics 5 (8.33%) and corticosteroids 4 (6.66%) etc (Table 4). In 47 (78.33%) cases, the drug was withdrawn and dose was altered in 13 (21.66%) patients. Adverse reactions were encountered and the final outcome was measured, in this about 46 (76.67%) patients recovered, while in 14 (23.33%) cases the symptoms were alleviated. No fatalities were reported. Specific treatment was given to 55(91.67%) patients and symptomatic treatment was given to 4(6.67%) patients. There was no change in the treatment observed in one patient.

Table 3. Type of reactions observed from reported ADRs (n=60)

S.No	Type of reactions	No. of ADRs (%)
1.	Skin rashes	18(30.0%)
2.	Nausea and Vomiting	7(11.66%)
3.	Headache	4(4.66%)
4.	Hyperglycemia	3(5.0%)
5.	Hypoglycemia	3(5.0%)
6.	Postural Hypotension	3(5.0%)
7.	Oral candidacies	3(5.0%)
8.	Constipation	3(5.0%)
9.	Hyperkalemia	2(3.33%)
10.	Gastric irritation	2(3.33%)
11.	Elevated blood pressure	2(3.33%)
12.	Diarrhorea	2(3.33%)
13.	Dysuria	1(1.66%)
14.	Drycough	1(1.66%)
15.	Hematuria	1(1.66%)
16.	Skin peeling	1(1.66%)
17.	Arthritis	1(1.66%)
18.	Aphasia	1(1.66%)
19.	Steroid induced adrenal insufficiency	1(1.66%)
20.	Cushing syndrome	1(1.66%)

The total cost involved for the treatment of ADR's was found to be USD 414.250 with an average of USD 6.90. It indicates that the health care cost was increased due to ADR, because this ADR's treatment cost was an additional cost incurred by the patients in addition to the normal treatment cost. Pharmacovigilance may be enforced in the country for better and safe use of any drug.

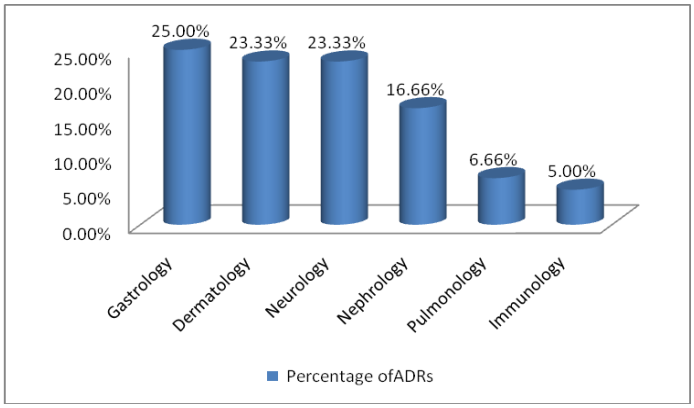

Figure 2. Department wise classifications of reported ADRs

Our ability to anticipate and present such ADR's can be facilitated by the establishment of standardized approaches and active reporting of suspected ADR's by all healthcare professionals including, clinical pharmacists. It is important to remember non- serious ADR's, for example constipation from using opioids, can have a significant impact on quality of life of the patient's.

Table 4. Classification of drugs associated with ADRs (n=60)

S.No	Type or class of drug. n (%)	Name of the drug	No. of ADRs (%)
1.	Antibiotics 13 (21.67%)	Amoxycillin Ciprofloxacin Moxifloxacin Cloxacillin Ofloxacin Doxicyclin	5(8.33%) 2(3.33%) 2(3.33%) 2(3.33%) 1(1.66%) 1(1.66%)
2.	NSAIDs 9 (15.0%)	Naproxan Paracetamol Diclofenac sodium Aspirin	3(5.0%) 3(5.0%) 2(3.33%) 1(1.66%)
3.	Antileprotic and Sulpha drugs 6(10.0%)	Dapsone Sulphonamide	3(5.0%) 3(5.0%)
4.	Cardiovascular Drugs 5(8.33%)	Carvedilol Amlodipine	3(5.0%) 2(3.33%)
5.	Antidiabetics 5(8.33%)	Glipizide Gliclazide Metformin	3(5.0%) 1(1.66%) 1(1.66%)
6.	Corticosteroids 4(6.66%)	Dexamethasone Hydrocotisone	2(3.33%) 2(3.33%)
7.	Anticonvulsant 3(5.0%)	Carbamazepine Phenytoin	2(3.33%) 1(1.66%)
8.	Antimalarial drugs 3(5.0%)	Chloroquine	3(5.0%)
9.	Antiemetic drugs 3(5.0%)	Ondansetron	3(5.0%)
10.	Opiod analgesic 2(3.33%)	Tramadol	2(3.33%)
11.	Antibacterial 2(3.33%)	Penicillin	2(3.33%)
12.	Lipid lowering agent 1(1.66%)	Atorvastatin	1(1.66%)
13.	Diuretics 1(1.66%)	Losartan potassium	1(1.66%)
14.	Anticoagulants 1(1.66%)	Clopidogrel	1(1.66%)
15.	Antiparkinson drugs 1(1.66%)	Cabergoline	1(1.66%)
16.	Neuroprotective 1(1.66%)	Methyl cobalamine,, pyridoxine and folic acid	1(1.66%)

Conclusion

In India there are very few active ADRs monitoring centers and a lot of effort is required to collect ADR data which may generate from safety surveillance of billions of therapeutically active substances either alone or in combinations.

Most medicines will only have been tested for short-term safety and efficacy on a limited number of carefully selected individuals. Therefore, it is important to monitor the use of medicines for their ongoing effectiveness and safety. Pharmacists have an important responsibility in monitoring the ongoing safety of medicines and able to provide a patient's complete medication history.

The incidence of adverse drug events is not directly proportional to the number of drugs being taken but increases remarkably as number of drugs rises. Poly-pharmacy needs to be discouraged for a good number of ADRs results from drug-drug interactions.

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AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

PEER REVIEW

Not commissioned; externally peer reviewed

CONFLICTS OF INTEREST

The authors declare that they have no competing interests