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Research Article

Drug Reactions

Adverse Drug Reactions Monitoring in Inpatients department of tertiary care Teaching Hospital

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Introduction and Objectives: The aim of study was to detect, document and to do causality analysis of ADRs in In-patients of tertiary care teaching hospital. **Method:** It is a prospective observational study being conducted in a tertiary care hospital of central India. In addition to spontaneous voluntary reporting system, an active search was also used to collect ADRs. The data collected was recorded on standard ADR reporting forms. Each reported form was then assessed for its causality and severity as per the standard criteria. **Results:** A total of 171 ADRs in 126 patients were detected. Out of which 66.1% ADRs occurred in males and 33.9% ADRs in females. Majority of the ADRs were related to the gastro-intestinal system (50.29%), with vomiting and nausea being the most common. Maximum number of ADRs were due to Antitubercular drugs (58.48%). The causality assessment as per Naranjo's scale showed that out of 171 ADRs, 98.83% were probable and 1.16% were possibly due to drug use. According to the WHO probability assessment scale, 66.66% were in possible and 33.33% ADRs were in probable categories respectively. Severity assessment by modified Hartwig and Siegel scale showed that 74.27% ADRs were mild and 25.73% were moderate. **Conclusion:** Considering the magnitude of ADRs related problems, there is a need for greater awareness among health care professionals to detect and report them. These ADRs if recognised in time and managed properly can prevent treatment interruption

Keywords: Adverse drug reactions, WHO, Naranjo scale, ADR

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Introduction

Adverse Drug Reactions (ADRs) are of great concern to the general public, the pharmaceutical industry, the regulatory authorities and the medical professionals. According to WHO an ADR is as "any response to a drug which is noxious and unintended, and which occurs at doses normally used in men for prophylaxis, diagnosis or therapy of a diseases or for the modification of physiological functions"[1].

Adverse Drug Reactions (ADRs) are common occurrence in hospital settings and more so in community and is attributed to the severity and complexity of disease process, use of multiple drugs, drug introduction.

In simple terms ADRs can be defined as any undesirable effect of drug beyond its intended therapeutic effect when used for clinical purposes. ADRs are not only increase the morbidity, mortality but also contribute to the total health care costs to a great extent and adversely affect patient's quality of life.

Adverse drug reactions constitute a significant medical and national health problem. According to US Food and Drug Administration we need ADR monitoring because Over 2 million serious ADRs reported yearly

- 100000 death yearly
- ADRs are 4th leading cause of death ahead of pulmonary disease, diabetes, AIDS, pneumonia, accidents and automobile deaths
- Ambulatory patients ADR rate- unknown
- Nursing Home Patient ADR rate-350000 yearly [2- 4]
- Costs associated with ADRs €136 billion yearly
- Mean length of hospital stay, cost and mortality for ADR patient are double that for control patients [5- 7]
- New drugs safety profile is limited because most drugs approved by FDA with average of 1500 patient exposures so rare ADRs are hidden.
- For drugs with rare toxicity ,more than 100000 patients must be exposed to generate a signals i.e. after drug is marketed [8]

Unexpected adverse drug reactions had caused the Withdrawal of 24 drugs from the United states and United kingdom markets from 1964 to 1983 [9].

An increasing awareness of morbidity and mortality associated with idiosyncratic adverse drug reactions has stimulated interest in methods of improving initial detection of putative ADRs and subsequent confirmation [10].

The growing number of newly approved drugs and their increased potency, coupled with the complex treatment modalities, have contributed to the increased risk of adverse drug reactions (ADRs) in ambulatory care setting [11].

The introduction of newer bio-molecules has dramatically changed the ability of clinicians to alter the course of human disease. However the benefits of these agents have not come without cost. One of the major costs of widespread use of new therapies is adverse drug reactions, which represents a major clinical problems [3].

Our institute C R Gardi Hospital is tertiary care teaching hospital attached with R D Gardi medical college Ujjain, MP was chosen to be a peripheral pharmacovigilance centre under this programme till 2008. Presently our institute is a ADR monitoring centre and become a part of pharmacovigi-lance programme of India.

The present study was conducted with a view to evaluate the incidence and spectrum of ADRs in hospitalized patients. It was designed and crafted to create awareness among prescribing physicians to improve knowledge and motivation of pharmacovigilance and thereby to encourage and promote better reporting of ADRs.

The present study is carried to detect adverse drug reactions (ADRs) in In-Patients of C R Gardi Hospital, R.D. Gardi Medical College, Ujjain.

Materials & Methods

After the approval by institutional ethics committee this study was carried out in 600 bedded private tertiary care teaching hospital.

The duration of study was 18 months from April 2011 to Sep. 2012. It is a prospective observational study and was conducted on in-patients of all department who experienced an adverse drug reactions
to medicine use.

Study Criteria

Inclusions: Patients who had any ADRs, of either sex and of any age, reported to treating physician.

Exclusions: The Adverse drug reactions that results due to

- Medication errors
- Over prescribing
- Excess consumption
- The use of alternative systems of medicine like Ayurveda, Homeopathy, Unani etc.

Data Collection & Analysis: Formal permission from medical superintendent and head of respective department were obtained prior to initiation of study. Patients admitted in wards and intensive care units of the hospital were screened for any suspected ADRs. ADRs were collected by using spontaneous reporting technique. Information regarding ADRs was collected with the help of treating physician and other health care professionals. All relevant information recorded in ADR reporting form obtained from CDSCO website.

- All relevant data including age, sex, all drugs the patient received prior to onset of reaction, their respective dosages, route of administration with frequency, date of onset of reaction, suspected drug causing ADRs were recorded. Confirmation of drug responsible for ADRs was done by subsidence of reaction on withdrawing the drug if possible.
- Cases were further analyzed for types of ADRs, drug classes associated with ADRs, and their causality and severity assessment.

Results

In present study total of 171 ADRs were collected from 126 patients because some patients must have more than one ADRs. In which there were 82 male patients which have 113 ADRs and 44 female patients which have 58 ADRs.

Table No 1: Age & Sex Wise Distribution of ADRs

Age group	No. Of Patients		No. Of ADRs	%
	Male	Female		
Paediatrics/Children	07	07	17	9.94
Adult (18 – 59 years)	57	33	128	74.85
Geriatrics (60 years & above)	18	04	26	15.2
Total	82	44	171	100

Maximum number of ADRs were observed in Adult age group (74.85%) followed by geriatrics (15.2%) and paediatrics (9.94%) population.

Table No 2: Onset of ADRs

Time Duration	No. Of ADRs	%
Immediate	16	9.36
< 1 week	89	52.05
1week – 1 month	29	16.96
>1 month	37	21.64

Maximum No of ADRs (52.05%) were seen in 1st week of treatment.

Immediate onset of ADRs (9.36%) were mostly hypersensitivity reaction.

Table No 3: Organ Systems Affected Due To ADRs

System	No. Of ADRs	%
Gastrointestinal System	86	50.29
Cutaneous	24	14.03
Immunological	18	10.52
Central Nervous System	08	4.68
Hepatobiliary system	05	2.92
Musculoskeletal System	03	1.75
Others	27	15.79
Total	171	100

We observed a predominance of Gastro-intestinal system related ADRs (50.29%).

Cutaneous (14.03%) is most common system involved next to Gastro-intestinal system.

Table No 4: Most Common ADRs

Organ system	ADRs	Number	%
Gastrointestinal System	Nausea- Vomiting	48	28.1
	Epigastric Pain	33	19.3
	Jaundice	05	2.92
Cutaneous	Rashes	13	7.6
	Itching	07	4.1
Immunological	Hypersensitivity Reaction	18	10.53
Central Nervous System	Vertigo	4	2.34
	Convulsion	1	0.58
Others	Restlessness or Ghabrahat	17	9.94

In Gastrointestinal system Nausea &Vomiting & Epigastric pain were most common ADRs observed.

Rashes and Itching were commonly seen adverse events.

Table No 5: Pharmacological Classes of the Drugs Implicated To Cause ADRs

Pharmacological Classes of the drug	No. of Patients	No. of ADRs	%
Antitubercular drugs	63	100	58.48
Antimicrobial drugs	31	31	18.12
NSAIDS	11	14	8.19
Miscellaneous Drugs	22	26	15.16
Total	126	171	100

Maximum number of ADRs occurs due to Antitubercular drugs (57.89%) followed by Antimicrobial (18.12%) and NSAIDs (8.19%).

Table No 6: Most Common Drugs Causing ADRs with ATC code

ATC class	Drug class	Drugs	ATC code25	No. Of ADRs	%
J04	Ant tubercular	Isoniazide+Rifampicin+Pyrazinamide+Ethambutol	J04AM06	100	58.45
J01	Antibacterial for systemic use	Ceftriaxone	J01DD04	8	4.68
J01	Antibacterial for systemic use	Ofloxacin	J01MA01	4	2.34
J01	Antibacterial for systemic use	Piperacillin+tazobactam	J01CR05	4	2.34
J01	Antibacterial for systemic use	Cefoperazone,Combinations	J01DD62	4	2.34
M01	Anti-inflammatory and Ant rheumaticProducts	Diclofenac	M01AB04	6	3.51
M01	Anti-inflammatory and Ant rheumaticProducts	Ibuprofen, Combinations	M01AE51	8	4.68

Antitubercular are responsible for maximum No. of ADRs (58.45%). In Antibacterials Ceftriaxone, Ofloxacin, Piperacillin+tazobactam and Cefoperazone are most commonly involved in Adverse Events. In Anti-inflammatory agents Diclofenac and Ibuprofen, combination causes maximum no of ADRs.

Table No 7: Management of ADRs

Management	No of ADRs	%
Withdrawal	55	32.16
Symptomatic	62	36.25
No Treatment	54	31.59

In 67.84% patients suspected drugs was continued .Withdrawal of suspected drugs were required in 32.16% ADRs and Symptomatic treatment is given in 36.25% ADRs.

Table No 8: Causality Assessment of the ADRs by WHO Probability Scale

Causality category	No of ADRs	%
Certain	0	0
Probable/Likely	57	33.33%
Possible	114	66.66%
Unlikely	0	0
Conditional/Unclassified	0	0
Unassessible/Unclassifiable	0	0

The causality of suspected drug was assessed using WHO scale of ADR causality assessment. The assessment revealed 66.67 % ADRs were Possible and 33.33 % ADRs were Probable.

Table No 9: Severity Assessment of ADRs by Modified Hartwig and Siegel Scale

Category	No of ADRs	%
Mild	127	74.27
Moderate	44	25.73
Severe	0	0

Severity assessment was done by Modified Hartwig and Siegel Scale Majority of ADRs reported were Mild (74.27%) followed by Moderate (25.73%), No Severe ADRs were reported.

Discussions

Since we could not eliminate all the adverse effects of drugs it is necessary to evaluate pattern of adverse reactions. There is a special need for systemic collection of information on ADRs in India due to wide variation in genetic, nutritional, environmental and disease patterns. Therefore, better approaches must be devised for reporting assessment and management of individuals who present with drug induced disease.

Total number of patients admitted in C.R. Gardi hospital during the study period is very high as it is a 600 bedded tertiary care teaching hospital but ADRs detected and reported are very less only 171 ADRs were recognised in 18 months of durations. This may be because of under reporting by clinicians as many physicians are unaware of their clinical importance. Similar under reporting of ADRs was explained in the studies carried out by Smith et al [12], Christopher et al [13], and Dhasmana et al [14]. The reasons for under reporting by the clinicians/other health care professionals should be investigated and problems should be resolved to optimize the process of reporting. There should

Be programs for motivating health care professionals for continuous reporting of ADRs.

Most of the literature says that the female gender is the one of the predisposing factors for ADRs and also, studies conducted by Daphne et al [15] and Arulmani et al [16] showed that the female gender is at a high risk of developing ADRs but this findings does not correlate with our results which states that the ADRs in the In-patients were more documented in males (66.1%) which is consistent with the reports by Gupta et al. [17] and Sriram et al [18]. This can be explained on the basis of sex ratio which also does not seem to be a major determinant.

Age, as a predisposing factor, play an important role in the occurrence of ADRs. In this concern paediatrics and geriatrics are more prone to ADRs when compared to adults. In our study we saw adult populations experiencing maximum number of ADRs (74.85%) when compared to geriatrics (15.2%) and paediatrics populations (9.94%). This is in acceptance with results put forward by Pandit et al. [19] This may be due to reasons that the group of population that visiting the hospital is comprised mostly of adults.

Organ system most commonly affected in our study were gastrointestinal system in 50.29%, cutaneous (skin and appendages) in 14.03%, Immunological in 10.52 % followed by central nervous system (central and peripheral nervous system) in 4.68%.

The results were comparable with an international study conducted by Suh et al.[20] and a national study by Sriram et al [18] which revealed that the system most badly affected was and gastrointestinal the dermatological system. But there might be variation due to geographical area, pattern of disease in that area, rescription pattern of physician, knowledge of physician and so on.

These factors could further explain the occurrence of ADRs over that area. The classes of drugs that were most commonly implicated for causing ADRs during our study were Antiubercular (58.48%) followed by Antimicrobials (18.12%) and NSAIDs (8.19%).

Maximum numbers of ADRs due to Antituberculars because of use of combination of drugs for prolong time which is also reported by Dhingra et al [21]. Suh et al [20] and Murphy et al [22] demonstrated

The antimicrobials were the most commonly implicated drug class to cause Cutaneous ADRs. The results were also comparable with other studies like one done by Classen et al [21] which indicated that NSAIDs have caused extensive damage to human health.

Causality assessment was done by using WHO scale showed that 66.66% ADRs were possibly drug related whereas 33.33% ADRs were classified as probably related to drugs. The results matches with Davies et al [23] and Sriram et al [18]

Severity of suspected ADRs assessed using Modified Hartwig and Siegel Scale revealed that 74.27% of suspected ADRs were mild 24.73% of ADRs were moderate and No severe ADRs were detected. Our results shows some deflection with the results of Shuster [24] and Sriram et al [18] where large numbers of ADRs categorized as moderate in category and there was also some percentage of severe ADRs. The difference might be due to pattern of ADR reported.

Thus with this discussion we came to the conclusion that ADRs reporting should be encouraged to its fullest extent as despite its introduction since 1986 we observed that underreporting, reluctance of physicians and staff members to report ADRs and the basic difficulties in reporting of ADRs still exists, so promotion of Pharmacovigilance activity in terms to report ADRs should be emphasized to create a greater impact over the population and safety of the drugs, and hence this study was an attempt to generate more systemic knowledge about ADRs to drugs with the ultimate aim of doing something good for human being and the society.

Conclusion

This study strongly suggests that there is greater need for streamlining of hospital based ADR reporting and monitoring system to create awareness and to promote the reporting of ADR among health care professionals of the country. Measure to improve detection and reporting of ADR by all health care professionals should be undertaken, to ensure patients safety.

Thus the study was performed with the ultimate aim of generation of information about ADRs due to drugs in in-patients and to add knowledge about the safety of medicines and recognition and revention of ADRs.

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