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A STUDY ON ASSESSMENT, MONITORING, DOCUMENTATION AND REPORTING OF ADVERSE DRUG REACTIONS AT A MULTI-SPECIALTY ERTIARY CARE TEACHING HOSPITAL IN SOUTH INDIA

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Abstract: A prospective observational study was carried out for a period of 6 months in an inpatient and outpatient department of a south Indian hospital. In a total of 96 patients, nearly 59 percent of patients were male it indicates that the prevalence of ADRs is more in men than in women. 42.71 percent (41) ADRs were found in the age group between 41 and 60 shows that ADRs in this locality hospital is more in these age group peoples. Most of the ADRs were treated by withdrawing the offending drug (81.25%). WHO probability assessment scale shows 42.71% (41) cases were probable, of which 27.08% (26) were male and 15.63% (15) were female. 5.21% (5) ADR were unclassified or in assessable. Naranjo's causality assessment scale shows 5.21% (5) of ADRs were Definite, 90.62% (87) of ADRs were probable, and 4.17% (4) of ADRs were possible. Many of the ADRs were reported from Neurology department (40.63%), it is followed by internal medicine department (20.83%) and other departments,

Key-words- Adverse drug reactions, Naranjo's scale, Adverse reaction, Causality assessment

General, Introduction: Adverse drug reaction is a recognized hazard of the drug therapy. The pharmacist, along with the prescriber has a duty to ensure that patients are aware of the risk of side effects and a suitable course of action should they occur. With their detailed knowledge of medicine, pharmacists have the ability to relate unexpected symptoms experienced by patients to possible adverse effects of their drug therapy. The practice in clinical pharmacy also ensures that ADRs are minimized by avoiding drugs with potential side effects in susceptible patients. Thus pharmacist has a major role to play in relation to prevention, detection and reporting ADRs.[1]

WHO defines any response to a drug which is noxious, unintended and which is occur at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases ,or for the modification of physiological function.[2] Other terms that may be included such as side effects, secondary pharmacological effects, drug intolerance, idioscyncratic reactions, toxic reactions, allergic reactions or hypersensitivity reactions. ADRs as any response to a drug that is noxious, unintended and that occurs at a doses used in humans for prophylaxis, diagnosis or therapy, excluding failure to accomplish the intended purpose. [4]

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Classification of ADRs

The classification proposed by Rawlins and Thompson was used to establish the potential for predicting suspected adverse drug reactions. The reactions were defined as:- **Type A-** When they were predictable, expected due to the drug's pharmacological characteristics and **Type B-** When they were unpredictable. The algorithm of Naranjo and co-workers used to establish the causality between the drug and the suspected adverse reaction. Suspicions are then classified as definite, probable, possible or doubtful.

ADRs may also be classified by cause and severity.

Cause

- Type A: Augmented pharmacologic effects
- Type B: Bizarre effects (or idiosyncratic)
- Type C: Chronic effects
- Type D: Delayed effects

- Type E: End-of-treatment effects
- Type F: Failure of therapy

Types A and B were proposed in the 1970s[5], and the other types were proposed subsequently when the first two proved insufficient to classify ADRs[6].

Seriousness and Severity

The American Food and Drug Administration define a serious adverse event as one when the patient outcome is: Death, Life-Threatening, Hospitalization (initial or prolonged), Disability - significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities or quality of life, Congenital Anomaly or Requires Intervention to Prevent Permanent Impairment or Damage

Severity is a point on an arbitrary scale of intensity of the adverse event in question. The terms "severe" and "serious" when applied to adverse events are technically very different. They are easily confused but cannot be used interchangeably, require care in usage.

A headache is severe, if it causes intense pain. There are scales like "visual analog scale" that helps us assess the severity. A headache, on the other hand, can hardly ever be serious, unless it also satisfies the criteria for seriousness, listed above.

Overall Drug Risk

While no official scale exists yet to communicate overall drug risk, the iGuard Drug Risk Rating System is a five color rating scale similar to the Homeland Security Advisory System.[7] it classifies the drugs as Red (High Risk), Orange (Elevated Risk), Yellow (Guarded Risk), Blue (General Risk) and Green (Low Risk)

The main sources of ADR data are Spontaneous reporting by doctors, pharmacists nurses etc, ADR monitoring schemes in hospitals, Clinical trials (all phases including post marketing surveillance), Vital statistics (mortality, morbidity registers, birth registers for congenital defects) and Special studies (case control studies, cohort studies)

ADRs are an important cause of hospital admissions, resulting in a considerable use of the bed base, and a significant number of deaths. Many may be preventable through simple improvements in prescribing. We concentrate on ADRs causing hospital admissions and evaluate the burden caused by ADR occurring while patients are in hospital. The need to develop a new classification system to evaluate the patients' reports, based on different criteria, arose because of the lack of temporal data available to enable any of these standard criteria to be used[8].

The main Aim and Objectives of the study were to determine the prevalence of hospital admissions associated with ADRs and examine to differences in prevalence rates, to study the incidence and the pattern of ADRs occurring in this hospital, to assess causality, and identify the offending drugs, to establish a causal relationship with the suspected drug(s), to identify suspected ADRs and establish their frequency of development and to educate health care professionals and patients about drug effects and increasing their level of awareness regarding ADRs.

Methodology

The prospective observational study was carried out for 6 month, in inpatients and outpatients department. Patients of both sex and of any age, who were developed with ADR were included. Allergic reactions due to pollens, dust, and insects are excluded from the study, reaction due to drug only were included.

Method:

All the necessary and relevant data were collected from patients case notes, treatment charts, laboratory reports, ADRs notification forms, patients interview and reporters interview. ADRs alert form was framed and implemented in each and every ward of the hospital. The prescriber noted in the ADR alert form if they found any ADR in their routine ward rounds. Nurses also encouraged to note the ADR if any.

The noted ADRs were assessed by using Naranjo's causality assessment scale, new algorithm to identify the causality of ADR and WHO causality assessment scale. The noted ADRs were into definite, probable, possible and unlikely.

The patients were classified or categorized according to their demographics, diseases status, and the disease severity. The collected ADRs data were reported to the peripheral center in the locality.

This study considered hospitalized patients at five inpatient internal medicine units in a multi-specialty hospital located in south India. The patients are enrolled after a written informed consent as per prescribed proforma. The ADRs are recorded in the specified proforma designed by the National Pharmacovigilance Programme for this purpose. Laboratory investigations are done in appropriate cases. Dechallenge and rechallenge are done if possible.

Patients are intensively monitored in order to identify suspected ADRs during hospitalization. The types of reactions are classified and a causal relationship is established using an algorithm. This method is chosen based on the study by Berry and co-workers[8].

In the present study, the reports of ADRs in the inpatients are evaluated. The incidence and pattern of ADRs are evaluated. Further, the individual ADR reports are assessed to find out whether the ADR is the reason for the present admission of the patient to the hospital. All reported ADRs are evaluated for the following parameters using appropriate scale.

1) Causality(Naranjo'salgorithm) [8]

2) Severity (Hartwig *et al* scale)[9]

Causality assessment is done using the Naranjo's Scale. This scale evaluates the degree of association of an adverse effect with the suspected drug and involves a set of questionnaires, which are ascribed a certain score (ranging from -1 to +2). Total score for a particular drug-ADR combination is calculated and the association is termed - highly probable, probable, possible or doubtful-depending on the score.

For the study purpose, the following documents are used. Suspected ADR notification form, ADR reporting and documentation form, ADR alert card, Thank you card, Causality assessment scale (Naranjo's scale), Severity assessment and Preventability assessment scale (Hartwig *et al.* scale).

The methods used to detect ADRs are also likely to explain much of the variation in the reported ADR prevalence rates. A number of drugs in combination are used and ADRs are often multiple. Clinical studies to elicit the toxicodynamics of these ADRs and safety *vs* risk issues could be beneficial in devising strategies for the rational use of drug in different diseases.

Data collection

Patient's data collection using a specific data collection sheet to be designed for this investigation. Information on drugs used immediately before hospitalization and symptoms present upon patient admission to be collected in an attempt to identify suspected adverse reactions that started previous to hospitalization.

In order to identify and monitor the ADRs during hospitalization, the medical prescriptions and intercurrences to be recorded throughout the entire follow-up period, and the information has to be transferred to the data collection sheet. Patients will be followed during the entire hospitalization period. However, data collection may be interrupted for analysis purposes if a patient is transferred to other units that are not included in this study.

Statistical analysis

Statistical analysis is performed and the results are presented either as medians and interquartile ranges or percentage frequencies and 95% confidence intervals, as appropriate. A P value < 0.05 is regarded as being significant.

Results and Discussion

The total number of patients had developed ADRs in the study was 96 out of this 56 (58.33%) patients were male and 40 were female (41.67%). It shows that the prevalence of ADRs in this locality were more in male than in female.

Among the total ADRs, 81(84.37%) ADRs were reported from the inpatients department, in which 49 (60.49%) were male patients and 32 (39.51%) were female patients. Out-patient department reported 15 (15.63%) ADRs, among this 7(46.67%) were male patients and 8 (53.33%) were female patients.

42.71 percent (41) ADRs were found in the age group between 41 and 60, followed by 33.33 percent (32) in the age group of above 60. The percentage of patients with ADRs less than 40 age groups was 23.96 (23).

Number of patients developed ADRs before the hospital admission ie reason for admission is ADRs was found to be 7 (7.29%). 89 (92.71%) patients were developed ADRs during their hospital stay.

Out of 96 ADRs reported, 78 (81.25%) patients were treated by withdrawal of the offending drug. 4 (4.17%) patients were treated by dose alteration, 14 (14.58%) patients had no change in the treatment. Mostly the prescriber preferred symptomatic treatment for about 70% of the patients with ADRs.

Naranjo's causality assessment of ADRs

Among the 96 reported ADRs, 5.21% (5) of ADRs were Definite of which 4.17% (4) were male and 1.04% (1) was female patients. 90.62% (87) of ADRs were probable, of which 71.87% (69) were male and 18.75% (18) were female. 4.17% (4) of ADRs were possible, of which 3.13% (3) were male and 1.04% (1) was female. No ADRs was found in unlikely class.

WHO probability assessment of reported ADRs

The reported ADRS were assessed by using WHO probability assessment scale. Among the 96 reported ADRs 52.08% (50) were certain, of which 33.33% (32) were male and 18.75% (18) were female. 42.71% (41) cases were probable, of which 27.08% (26) were male and 15.63% (15) were female. 5.21% (5) ADR were unclassified or in assessable.

Neurology department reported many number of ADRs (39) (40.63%) followed by internal medicine department (20) (20.83%), pulmonology department (19) (19.79%), cardiology department (8) (8.33%), oncology department (7) (7.30%), nephrology department (2) (2.08%), obstetrics and gynecology department (1) (1.04%). (Table 1)

Majority of the ADRs produced skin reactions, which is followed by diarrhea, insomnia, headache, weight gain, postural hypotension, bleeding, Cushing syndrome, liver enzyme elevation, and pedal edema, dryness of mouth, renal failure, hypoglycemia, erythema multiform and hepatitis. (Table 2)

Drugs associated with ADRs

It was suspected that neurology drugs caused highest ADRs 36 (37.5%), followed by antibiotics 19 (19.79%). Of which amoxicillin was the most offending drug. Phenytoin is the neuro drug which produced 12 (12.50%) ADRs and it is followed by thalidomide 7 (7.29%) and pentoxifylline 3 (3.13%). Among the antibiotics amoxicillin produced 8 (8.33%) ADRs followed by ceftriaxone and clindamycin 5 (5.20%). NSAIDs produced 10(10.42%) ADRS and it is followed by antitubercular drugs 6 (6.25%).

Conclusion

Adverse drug reactions are an inevitable risk factors associated with the use of modern medicines. However, careful attention to dosage, age, and renal function can minimize the risk of developing ADRs in many patients. Our study shows most of the developed ADRs during hospital stays were managed by withdrawing the offending drug and symptomatic treatment. In this pharmacist, physician, nurses, patients and patient's volunteers must help in reporting ADRs. If this culture is adopted and practiced well, we can minimize ADRs and also provide a good quality of life to the patients.

Table 1. Distribution of ADRs in various departments

S. No	Name of the Department	Number of patients (Percent)
1	Neurology	39 (40.63%)
2	Internal Medicine	20 (20.83%)
3	Pulmonology	19 (19.79%)
4	Cardiology	8 (8.33%)
5	Oncology	7 (7.30%)
6	Nephrology	2 (2.08%)
7	Obstetrics And Gynecology	1 (1.04%)
	Total	96 (100%)

Table 2. Distribution of types ADRs

S. No	Name of the Reaction	Number of patients (Percent)
1	Skin Reactions	20 (20.83)
2	Diarrhea	14 (14.58)
3	Insomnia	11 (11.46)
4	Headache	10 (10.42)
5	Weight Gain	9 (9.37)
6	Postural Hypotension	7 (7.30)
7	Bleeding	5 (5.20)
8	Cushing Syndrome	4 (4.17)
9	Liver Enzyme Elevation	4 (4.17)
10	Pedal Edema	3 (3.13)
11	Dryness of mouth	3 (3.13)
12	Renal Failure	2 (2.08)
13	Hypoglycemia	2 (2.08)
14	Erythema Multiform	1 (1.04)
15	Hepatitis	1 (1.04)
	Total	96 (100)

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