Original Research Article

Monitoring of adverse drug reactions in medicine, paediatric and surgical departments of a tertiary care hospital: a prospective observational study

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INTRODUCTION

Drugs are meant to relieve suffering but sometimes they themselves can cause adverse drug reactions ranging from minor inconvenience to serious organ dysfunction or even death. Their awareness to the medical world, public and official bodies was highlighted mainly after the Thalidomide disaster in 1961. The WHO defines ADR as “Any reaction which is noxious and unintended, and which occurs in man due to use of a drug for the prevention, treatment or diagnosis of disease or for the modification of physiological function”. WHO defines Pharmacovigilance as “The science and activities which are related to the detection, assessment, understanding and the prevention of adverse effects or any other drug related problems”. ADRs are a common cause of morbidity and place a substantial burden on limited healthcare resources. Adverse drug reactions constitute a significant economic burden for hospitals. Hospital based adverse drug reaction monitoring and reporting programmes aim to identify and quantify the risks associated with the use of drugs provided in a hospital setting. A study conducted at four hospitals in South Africa showed that 2.9% and 16% of the mortality were...
due to ADRs and ADR related complications respectively. Studies have found the overall incidence of adverse drug reactions in skin in developed countries as 1-3% and in the developing countries it is higher between 2-5%. 5-10% of hospital admissions are due to drug related problems, in which 50% are avoidable. 7 ADR reporting is crucial because two independent studies in India have concluded that some patient groups are at a particular risk of developing ADRs, for example infants, those using cardiovascular drugs and patients receiving four or more types of medication.8,9

Adverse reactions are recognized hazards of drug therapy. Early detection, evaluation and monitoring of Adverse drug reactions are essential to reduce harm to patients and thus improve public health. With the increase in the production of various pharmaceutical products, newer drugs are being introduced every year.10 Hence it has become essential to monitor the effects and adverse drug reactions pertaining to these drugs.

The present study was undertaken in order to study the adverse drug reactions in the departments of Medicine, Paediatrics and Surgery including ENT and Gynaecology as a part of the Pharmacovigilance study of East Point Medical College and Hospital. The aim was to develop an efficient ADR monitoring centre at the Hospital.

Benefits of ADR monitoring

An ADR monitoring and reporting programme can furnish following benefits:

- It caters information about quality and safety of pharmaceutical products.
- It initiates risk-management plans.
- It prevents the predictable adverse effects and helps in measuring ADR incidence.
- It instructs health care team, patients, pharmacists and nurses about adverse drug effects and creates awareness regarding ADRs.

Aims and objectives

- To study the adverse drug reactions with regard to their causality, severity, drugs causing the ADRs, clinical presentation of the ADRs.
- To study the gender wise and age wise distribution of the ADRs and the duration of exposure.

METHODS

This was a prospective, observational, descriptive study carried out at East Point Medical College and Hospital. The hospital is a 300 bedded tertiary care hospital. The study was carried out for a period of one year. All the patients who reported in the departments of Medicine, Surgery, Gynaecology of the hospital with suspected ADR during the study period were included in the study.

Table 1: WHO UMC causality assessment Scale.

| Causality term          | Assessment criteria                                                                                                                                                                                                 |
|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Certain                | • Event or laboratory test abnormality, with plausible time relationship to drug intake                                                                                |
|                        | • Cannot be explained by disease or other drugs                                                                                                                        |
|                        | • Response to withdrawal plausible (pharmacologically, pathologically)                                                                                               |
|                        | • Event definitive pharmacologically or phenomenologically (ie.an objective and specific medical disorder or a recognized pharmacologic phenomenon)                  |
|                        | • Rechallenge satisfactory, if necessary                                                                                                                              |
| Probable/Likely        | • Event or laboratory test abnormality, with reasonable time relationship to drug intake                                                                               |
|                        | • Unlikely to be attributed to disease or other drugs                                                                                                                   |
|                        | • Response to withdrawal clinically reasonable                                                                                                                          |
|                        | • Rechallenge not required                                                                                                                                             |
| Possible               | • Event or laboratory test abnormality, with reasonable time relationship to drug intake                                                                               |
|                        | • Could also be explained by disease or other drugs                                                                                                                      |
|                        | • Information on drug withdrawal may be lacking or unclear                                                                                                               |
| Unlikely               | • Event or laboratory test abnormality with a time relationship to drug intake that makes a relationship improbable (but not impossible)                                 |
| Conditional/ Unclassified | • Event or laboratory test abnormality                                                                                                                                 |
|                        | • More data for proper assessment needed or                                                                                                                             |
|                        | • Additional data under examination                                                                                                                                     |
| Unassessable/ Unclassifiable | • Report suggesting an adverse drug reaction                                                                                                           |
|                        | • Cannot be judged because information is insufficient or contradictory                                                                                            |
|                        | • Data cannot be supplemented or verified                                                                                                                                 |
The diagnosis of the adverse drug reaction was based on the history of drug exposure and clinical findings and was done by the consultant Physician or Surgeon or Gynaecologist depending on the respective department. The parameters were recorded on an ADR monitoring form which included Demographic characteristics of the patient, type of ADR, drug causing ADR, duration of exposure, causality, severity, treatment for the ADR. Causality was assessed based on the WHO Causality Assessment Scale and severity was assessed based on the Hartwig and Siegel Scale.

The causality assessment of the adverse drug reactions was done using this scale.\(^{13}\)

**Severity assessment by the modified hartwig and Siegel Severity Assessment Scale\(^{14}\)**

Severity of the adverse drug reactions was assessed using the Modified Hartwig and Siegel Severity Assessment Scale. The severity is broadly categorized into “mild”, “moderate” and “severe” for each ADR. The suspected ADR is mild when “an ADR occurs but requires no change in treatment with the suspected drug, or the ADR requires that treatment with suspected drug be held, discontinued, or otherwise changed. No antidote or other treatment was required. The suspected ADR is “moderate” when the ADR requires treatment with the suspected drug be held, discontinued or otherwise changed and or an antidote or other treatment was required. No increase in length of stay (LOS) or any level 3 ADR that increases LOS by atleast one day or the ADR was the reason for the admission.

**RESULTS**

**Figure 1: Age wise distribution of patients.**

In the present study, there were various types of adverse drug reactions which were due to various drugs. The results were calculated in the form of percentages. A total of 33 adverse drug reactions were reported during the period of the study. The maximum number of cases of adverse drug reactions were seen in the age group of 21-30 years (30.3%) followed by 11-20 years (15.1%) followed by 51-60 years (12.1%) and less than 10 years (12.1%). There were only two cases seen above the age of seventy years (6.1%).

The number of adverse drug reactions were more in females than in males. Out of thirty-three cases, 11 cases (33.33%) of ADRs were seen in males and 22 cases (66.66%) were seen in females. There was a female preponderance (Figure 2).

**Figure 2: Gender wise distribution of ADRs.**

The maximum number of ADRs were reported from the department of Medicine (33.3%) followed by Surgery (27.3%) and followed by Paediatrics (18.2%). Few cases were reported from Gynaecology (12.1%), ENT (6.1%) and Ophthalmology (3%) departments also (Figure 3).

**Figure 3: Department wise distribution of ADRs.**

Drug rash was the commonest clinical presentation seen in 9 cases (27.2%). The other cases seen were Steven Johnson syndrome 1 (3%), Anaphylaxis 1 (3%), Oculogyric crisis 1 (3%), fever with chills 2 (6%), pruritis2 (6%), rash with pruritis 2 (6%), periorbital edema 4 (12%), FDE2 (6%), local swellings 2 (6%), oesophagitis 2 (6%), chills 1 (3%), vomiting 1 (3%) and edema in skin 1 (3%), swelling of lips 1 (3%) and swelling of ear lobe 1 (3%) (Figure 4).

Antibiotics caused the largest number of ADRs (30.3%), followed by intravenous fluids (12.1%), analgesics (9.1%),...
vaccines (9.1%), anaesthetics (6.1%), Vitamin (3%), Iron (3%) anti-psychotic (3%), Phenytoin Sodium (3%) and Metformin (3%), Hydroxychloroquine (3%), Metronidazole (3%), Acetylcysteine (3%), Atorvastatin (3%), Anti-snake venom (3%), Ondansetron (3%) (Figure 5).

**Severity**

The severity of the ADRs was classified according to the Hartwig and Siegel Severity Scale. An equal number of ADRs could be classified as Moderate (42.4%) and Mild (42.4%). Severe cases accounted for a lesser number (12.1%) (Table 3).

**DISCUSSION**

The maximum number of cases of adverse drug reactions were seen in the age group of 21-30 years (30.3%) followed by 11-20 years (15.1%) followed by 51-60 years (12.1%) and less than 10 years (12.1%). There were only two cases seen above the age of seventy years (6.1%). In a study conducted in Brazil the maximum number of ADRs were seen in the adult age group as compared to children. The findings in another study conducted in central India also matches with our study in that cutaneous adverse drug reactions were maximum in the 21-30 years age group.

Even in the study conducted on adverse effects of antimicrobials the highest number of ADRs were found in the adult age group (63.1%). There was a female preponderance. This matches with other studies carried out in South India.

The maximum number of cases were reported from the department of Medicine (33.33%) whereas from Surgery (27.3%), and ENT (6.1%). This may be due to under-reporting of cases and or lack of awareness that the ADRs have to be reported. The most common ADR was skin rash. This is in accordance with another study conducted in central India in 2014. There were two Serious adverse events, one being Steven Johnson Syndrome due to Phenytoin Sodium and Linezolid and the other Anaphylaxis due to N-Acetylcysteine. Oculogyric crisis caused by Ondansetron is a rare adverse effect and requires a special mention. In this study antibiotics were the group contributing to maximum number of ADRs (30.3%). This finding is similar to other studies conducted. Among the antibiotics Intravenous Ceftriaxone was the most common offending agent. There were reactions caused by intravenous fluids such as Normal saline. Another special mention needs to be made about a skin rash occurring due to vitamin B complex capsules given orally. Most of the adverse drug reactions fell in the probable (63.6%) category with regard to Causality assessment according to the WHO-UMC Causality Assessment criteria as was seen in the study carried out in Thrissur on adverse drug reactions to psychotropic drugs and the study on antimicrobials. The reason for this is that rechallenge is not ethical. The majority of the ADRs were either mild or...
moderate in severity (42.4%) each category while severe reactions were very few (12.1%). The moderate ADRs had to be treated appropriately.

CONCLUSION

All physicians need to be aware of that ADRs may occur with as simple a drug as a vitamin tablet and hence exercise precaution while prescribing drugs. ADRs that occurred in this hospital are comparable to other studies, with differences in some aspects. Antibiotics were the most common group of drug causing ADRs and this included Ceftriaxone and Linezolid. Intravenous fluids such as Normal saline and Dextrose can also lead to ADRs. Results of our study emphasize the need of reporting ADRs in a hospital in order to assess the benefit-risk ratio of drugs and improve health care.

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