Original Research Article

A retrospective analysis of adverse drug reaction reported in a tertiary care hospital

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INTRODUCTION

Adverse drug reaction (ADR) as defined by WHO are "any noxious, unintended, undesired effect that occurs at dosage used in human for prophylaxis, diagnosis and therapy." There is need to strengthen the ADR reporting system in India because of underreporting of ADR (<1%) as compared to other countries. This may be due to multiple factor including lack of awareness among health care professionals and poor post marketing surveillance by pharmacists.

ADR reporting is an important component of monitoring and evaluation activity in hospital. In November 2004 CDSCO, ministry of health and family welfare government of India launched the National Pharmacovigilance programme (NPP) which was converted to Pharmacovigilance Programme of India (PvPI) in 2010 to monitor the ADRs that include government or private sector. The PvPI aims at safe use of medicine. Thus, it is important to have ADR data of all the drugs, so that necessary measures can be taken in this regard. The present study was planned to analyse ADRs reported in tertiary care hospital.

The objective of the study was to retrospectively analyse ADRs reported to Pharmacovigilance centre in a tertiary care hospital. Analysis was done to find out the incidence and causality of reported ADR.

METHODS

This was a retrospective study. The analysis of ADR reported at Pharmacovigilance centre in tertiary care hospital during last one and half year (from 1-1-2014 to 30-4-2015) was done. The clearance from institutional

ABSTRACT

Background: The adverse drug reactions (ADRs) reported to pharmacovigilance centre in tertiary care hospital was analysed to find out the incidence and causality.

Methods: This was a retrospective study to analyse the ADR reported at pharmacovigilance centre after ethical clearance from Institutional Ethic Committee (IEC). ADR data were analysed and ADRs were categorized as department-wise, system affected and causative drug. The causality of each ADR was assessed by WHO-UMC scale.

Results: The majority of patients who had suffered from ADRs were between 19-64 years of age (94.2%) and male patients (58.6%) were affected more than female (41.4%). Pulmonary medicine department has reported highest number of ADR followed by dermatology department. Skin (46.5%) was most affected system followed by gastrointestinal (30.45%), CNS (21.26%), respiratory (9.0%) and remaining systems. Rifampicin (13.79%) shows the largest numbers of ADR followed by zidovudine (13.21%), nevirapine (12.64%) and diclofenac sodium (8.0%). The maximum ADRs reported were probable (94.8%) followed by possible (5.2%).

Conclusions: In conclusion, the skin was most affected system followed by gastrointestinal, central nervous and respiratory system. Rifampicin has caused maximum ADRs followed by zidovudine, nevirapine and diclofenac sodium. The causality analyses showed that majority of ADRs were probable (94.8%) while remaining falls in possible (5.2%) category.

Keywords: Adverse drug reaction, Pharmacovigilance, UMC scale
ethical committee was taken before the commencement of study. Confidentiality was maintained at all the level.

Completed ADR reporting forms submitted to ADR monitoring centre were analysed. The details filled up in the form were checked for mandatory parameters including patient’s detail, type of ADR, drugs causing ADR, etc.

ADRs were analysed and results were categorized as follows:

- Demographic details
- Department-wise
- System affected
- Causative drug
- Causality of ADRs

WHO-UMC scale adopted by PvPI was used for causality assessment.

Results were presented in tabular form, Pie chart and bar diagram.

RESULTS

A total of 174 ADRs were detected, documented and reported during the last one and half year.

The majority of patients who had suffered from ADRs were between 19-64 yrs. of age (94.2%) of total ADRs followed by 0-18 yrs. (5.2%). There was only 0.6% of reporting in the age group more than 65 yrs. The studies also revealed male patient (58.6%) were affected more than female (41.4%) (Table 1).

| Gender       | Total no. 174 | Percentage |
|--------------|---------------|------------|
| Male         | 102           | 58.6       |
| Female       | 52            | 41.4       |

The analysis showed that Pulmonary medicine department reported highest number of ADRs (31.6%) followed by dermatology department (24.1%). The least number of reporting were from surgery department (0.6 %) (Table 2).

| Age distribution | No. of ADR | Percentage |
|------------------|------------|------------|
| 0-18 yrs         | 9          | 5.2        |
| 19-64 yrs        | 164        | 94.2       |
| 65 yrs and above | 1          | 0.6        |

On analysis of system affected the skin was most commonly affected (46.5%) followed by gastrointestinal (GI) tract (30.45%), CNS (21.26%) and respiratory system (9.19%). The involvement of genitourinary and haemopoietic systems was (1.72 % each). The endocrine system (thyroid) was affected in (0.57%) of patients (Table 3).

| Departments        | No. of ADR (n=174) | Percentage |
|--------------------|--------------------|------------|
| TB and Chest       | 55                 | 31.6       |
| Dermatology        | 42                 | 24.1       |
| ART center         | 36                 | 20.7       |
| Psychiatric        | 17                 | 9.8        |
| Medicine           | 11                 | 6.3        |
| Obs. and Gynec.    | 5                  | 2.9        |
| Pediatric          | 5                  | 2.9        |
| Orthopedic         | 2                  | 1.1        |
| Surgery            | 1                  | 0.6        |

The details of ADR related to each system are mentioned in Table 4.

| Systems            | No. of Patient (Total=174) | % of patients |
|--------------------|----------------------------|---------------|
| Skin               | 81                         | 46.55         |
| GIT                | 53                         | 30.45         |
| CNS                | 37                         | 21.26         |
| Respiratory System | 16                         | 9.19          |
| Genitourinary      | 3                          | 1.72          |
| Anemia             | 3                          | 1.72          |
| Endocrine          | 1                          | 0.57          |

In our study the rifampicin shows the largest number of ADRs (13.79%) of total followed by zidovudine (13.21%) then nevirapine (12.64%). Diclofenac sodium also shows significant no. of ADR (8.0%) (Table 5).

The maximum ADRs reported were probable (94.8%). This was followed by possible (5.2%). No ADR was reported from any other category of WHO-UMC scale (Table 6).5

DISCUSSION

In this study, the Patient suffering from ADRs were between 19-64 years of age in which males (58.6%) were more affected than females (41.4%). In contrast to A. P Gor’s study which showed that the sex of the patients did not affect the incidence rate of ADR, our study showed a higher prevalence among males.5

Patidar et al observed that the occurrence of ADRs was (45.94%) in men and (54.05%) in women.6 Other studies by Sriram et al, Richa, VR Tandon et al reported that males have greater risk of ADR than females.12,13 There are various factors like age of patients, gender, number of drug taken, duration of hospital admission, genetic factors, ethnicity, dietary, and environmental factors affecting the ADR incidence.
Table 4: Clinical feature wise ADR reports.

| System            | ADR                                                                 | Drug                                                                 | No. of patient |
|-------------------|----------------------------------------------------------------------|----------------------------------------------------------------------|----------------|
| Skin              | Multiple Scaly Plaque like lesion                                    | Losartan, Atenolol                                                   | 2              |
|                   | Angioedema                                                           | Iron Sucrose, Diclofenac Sodium, Ibuprofen, Ceftriaxone, Artether, Amoxicillin + Clavulanic acid | 11             |
|                   | Hyperpigmented patches                                              | Cotrimoxazole                                                        | 1              |
|                   | Multiple Erythromatous Maculopapular Rash                            | Nevirapine, Cotrimoxazole, Cefoperazone, Azithromycin, Ibuprofen, Phenyo tin Sodium, Multivitamin Tablets Isoniazid, Isoniazid+ Rifampicin, Diclofenac Sodium + Paracetamol, Zidovudine | 43             |
|                   | Exfoliative Dermatitis                                              | Zidovudine+ Lamivudine+Nevirapine                                    | 10             |
|                   | Urticaria (itching)                                                 | Dilofenac Sodium, Amoxicillin, Navirapine, Abacavir, Topiramate       | 13             |
|                   | Steven Johnson Syndrome (Cutaneous ulceration Epidermal Necrosis)    | Lamotrigine                                                          | 1              |
| GIT               | Gastritis ((Gastric Intolerance, Vomiting Nausea, Abdominal Pain and Decrease appetite) | Zidovudine, Nevirapine, Lorazepam, Capreomycin, Levofloxacin, Pyrizinamide | 52             |
|                   | Jaundice                                                            | AKT (Cat. I)                                                         | 1              |
|                   | Excessive Sedation (Drowsiness)                                     | Mirtazepine, Olanzepine                                              | 6              |
|                   | Chills and Rigor                                                    | Chloramphenicol                                                      | 2              |
| CNS               | Peripheral Neuropathy (Tingling Numbness)                            | Stavudine, Stavudine +Nevirapine + Lamivudine, Stavudine +Nevirapine + Lamivudine + Zidovudine | 5              |
|                   | Dizziness                                                           | Pregabaline, Phenytoin Sodium, Mirtazepine                           | 4              |
|                   | Restlessness (Anxiety)                                              | Pregabaline, Desvenlafaxine, Quetiapine                             | 4              |
|                   | Headache                                                            | Desvenlafaxine, Etiozolam, Azithromycin                             | 5              |
|                   | Tonic Posturing                                                     | Amoxicillin + Clavulanic acid                                       | 1              |
|                   | Insomnia induced psychosis                                           | Isoniazid                                                            | 1              |
|                   | Decrease Hearing                                                    | Capreomycin                                                          | 1              |
|                   | Tonic Convulsion                                                    | Tetanus                                                              | 1              |
|                   | Fever                                                               | Rifampicin, AKT, Abacavir, Nevirapine, Isoniazid                      | 7              |
| Respiratory       | Dry Cough (Throat pain, Hemoptosis)                                  | Rifampicin, Isoniazid, Nimesulide                                    | 4              |
|                   | Angioedema                                                          | Iron Sucrose, Diclofenac sodium, Ibuprofen, Ceftriaxone, Artether, Amoxicillin + Clavulanic acid | 11             |
| Endocrine         | Hypothyroidism                                                      | AKT (Cat. IV)                                                       | 1              |
| Genitourinary     | Candidiasis. Paracystitis, cystitis                                  | Rifampicin, Tenovir Pyrizinamide                                     | 3              |
| Misc              | Anaemia                                                             | Ziduvadine                                                           | 3              |

The present study revealed a predominance of adult over paediatric populations. Most of the patients (94.1%) were between 19-64 years of age group. The reason for the high morbidity in adult population may be because of multi drug therapy or other disease like hypertension, diabetes, asthma or other chronic diseases. Our finding similar with the finding of Patidar et al, Murphy et al. The most common category associated with ADRs was skin (46.55%). This finding is consistent with the study by Coelho et al, Fredy et al, Rajesh et al, but it differs from reports of Suh et al where gastrointestinal manifestations had the highest rate, which was second highest in our study (30.45%). Srim et al, Rajesh et al, Murphy et al, Gor AP, Desai SV, Brennan TA, Leape LL et al, Fredy et al, Leone et al, reported that other antibiotics are the most common classes causing ADRs but in our study patients on anti-tubercular drugs had maximum ADRs. The most common drug causing ADR is rifampicin (13.79%). It is because of anti-tubercular drug used for long duration (minimum 6 months) as compare to other antibiotics, followed by zidovudine (13.21%) and nevirapine (12.64%).
Table 5: Drug wise ADR.

| Name of Drug                        | Frequency of ADR | ADR reported                                                                 |
|-------------------------------------|------------------|------------------------------------------------------------------------------|
| **Antitubercular drugs**            |                  |                                                                              |
| AKT                                 | 10               | Gastritis, vomiting nausea anorexia                                           |
| Rifampicin + Isoniazid              | 3                | Gastritis, vomiting, abdominal pain                                           |
| Rifampicin                          | 24               | Gastritis, vomiting, abdominal pain dry cough and fever                       |
| Isoniazid                           | 9                | Maculopapular rashes with fever, chills, psychosis insomnia weakness          |
| Pyrazinamide                        | 4                | Cystitis, weight loss, dyspnoea, anorexia                                     |
| **Antiviral drugs**                 |                  |                                                                              |
| Nevirapine                          | 22               | Multiple erythromatous patch, maculopapular rashes with fever, erythromatus maculopapular lesions, nausea vomiting abdominal pain |
| Zidovudine                          | 23               | Exfoliative dermatitis, anaemia, serosis, fixed drug eruptions, acute gastritis, severe vomiting abdominal pain |
| Acyclovir                           | 1                | Skin rash and fever                                                           |
| Abacavir                            | 1                | Fever and itching                                                             |
| Tenofovir                           | 1                | Paracystitis                                                                  |
| stavudine + lamivudine              | 4                | Tingling Numbness and Peripheral Neuritis                                      |
| stavudine + lamivudine + nevirapine | 1                | Tingling Numbness and Peripheral Neuritis                                      |
| **Antibacterial Agents**            |                  |                                                                              |
| Co-trimoxazole                      | 3                | Hyperpigmented patches, erythromatous Patch                                   |
| Chloramphenicol                     | 2                | Chills and rigor                                                               |
| Azithromycin                        | 8                | Gastritis, Headache, abdominal pain, Erythromatus maculopapular rashes        |
| Ceftriaxone                         | 1                | Angioedema                                                                    |
| Capreomycin                         | 2                | Decese hearing, vomiting                                                      |
| Levofloxacin                        | 1                | Chest pain, Decrease appetite                                                 |
| Amoxicillin + Clavulanic acid       | 4                | Skin lesion, Angioedema and Tonic posture                                      |
| Cefoperazone + Sulbactam            | 1                | Erythromatous patch, Rashes                                                  |
| **Antimalarial drugs**              |                  |                                                                              |
| Artemether                          | 1                | Angioedema                                                                    |
| **Antihypertensive drugs**          |                  |                                                                              |
| Losartan                            | 1                | Multiple Scaly Plaque like lesion                                             |
| Atenolol                            | 1                | Multiple Scaly Plaque like lesion                                             |
| **Analgesic drugs**                 |                  |                                                                              |
| Ibuprofen                           | 2                | Maculopapular rashes, angioedema and urticaria                                |
| Diclofenac Sodium                   | 13               | Urticaria, angioedema - itching, tingling, numbness, maculopapular rashes and tightening in chest |
| Nimesulide                          | 1                | Burning micturition, throat pain and Steven Johnson syndrome.                 |
| Diclofenac Sodium                   | 1                | Maculopapular rashes                                                         |
| **Antidepressant and antipsychotic drugs** |               |                                                                              |
| Mirtazapine                         | 3                | Excessive sedation, vertigo and confusion                                      |
| Desvenlafaxine                      | 2                | Headache, anxiety and restlessness                                            |
| Olanzapine                          | 4                | Drowsiness and weight gain                                                    |
| Quetiapine                          | 1                | Anxiety, Restlessness                                                         |
| Etizolam                            | 1                | Severe Headache                                                               |
| Lorazepam                           | 1                | Nusea, Vomiting and Dizziness                                                 |
| **Anticonvulsant drugs**            |                  |                                                                              |
| Divaproex Sodium                    | 3                | Gastric intolerance, vomiting, abdominal fullness, giddiness and restlessness |
| Lamotrigine                         | 1                | Steven Johnson syndrome and cutaneous ulceration                              |
| Pregabalin                          | 1                | Dizziness, restlessness                                                       |
| Topiramate                          | 1                | Generalized itching                                                          |
| Phenytoin Sodium                    | 6                | Erythromatous maculopapular rashes                                            |
| **Miscellaneous drugs**             |                  |                                                                              |
| Iron Sucrose                        | 2                | Angioedema                                                                    |
| Multivitamins                       | 1                | Rashes, abdominal pain                                                        |
| Tetanus Vaccine                     | 1                | Tonic convulsion                                                              |
This study also shows significant level of ADR by diclofenac sodium (8%) similar to Shrivastava MP et al.14

Table 6: Causality of reported ADR (total 174).

| UMC-Scale                  | No. of reports | % of reports |
|----------------------------|----------------|--------------|
| Certain                    | 0              | 0            |
| Probable/likely            | 165            | 94.8         |
| Possible                   | 9              | 5.2          |
| Unlikely                   | 0              | 0            |
| Conditional/Unclassified   | 0              | 0            |
| Unassessable/Unclassifiable| 0              | 0            |

In our study, maximum ADRs reported were probable (94.8%) followed by possible (5.2%). No other ADR reported in other category of WHO-UMC System. Definite is least due to rechallenge is not possible. In contrast Sriram et al study showed that 42% were possible and 23% were probable.12

CONCLUSION

In conclusion, the skin was most affected system followed by gastrointestinal, central nervous and respiratory system. Rifampicin has caused maximum ADRs followed by zidovudine, nevirapine and diclofenac sodium. The causality analyses showed that majority of ADRs were probable (94.8%) while remaining falls in possible (5.2%) category.

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