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EVALUATION OF THE PATTERN OF ADVERSE DRUG REACTIONS IN A TERTIARY CARE HOSPITAL OF PUNJAB

Pharmacology

Gaurav Gulrez Associate Professor, Department of Pharmacology, Christian Medical College and Hospital, Ludhiana, Punjab.

Anuradha Bhatia* Associate Professor,Department of Dermatology, Christian Medical College and Hospital, Ludhiana, Punjab. *Corresponding Author

Dinesh K. Badyal Professor & Head,Department of Pharmacology, Christian Medical College and Hospital, Ludhiana, Punjab

Himani Khatter Biostatistician, Christian Medical College and Hospital, Ludhiana, Punjab.

Masroor Aftab PG Demonstrator, Department of Pharmacology, Christian Medical College and Hospital, Ludhiana, Punjab.

ABSTRACT

Adverse Drug Reactions (ADRs) constitute an enormous burden for the society. Due to the lack of knowledge and awareness, many ADRs remain unnoticed. Identification of ADRs and their reporting pattern can provide useful information for their management. Hence, this study was planned to evaluate pattern of ADRs. A total of 300 ADRs reports were analysed. The WHO (world health organisation) scale for causality assessment was used. Evaluation of the data was done for drug groups causing ADRs, body systems affected, reporters and seriousness of reactions. In the males the overall occurrence of ADRs was more. Skin was the most commonly affected organ system. Antimicrobials were the drug group most commonly responsible for causing ADRs. Upon causality assessment, majority of the ADRs were rated as probable. Most of the reports were contributed by the clinicians.

KEYWORDS

Adverse Drug Reactions, Reporting Pattern Of Adverse Drug Reaction.

INTRODUCTION

Adverse drug reactions (ADRs) have been identified as a top safety priority because they cause morbidity, mortality leading to prolonged hospitalization and pharmacoeconomic burden. ADRs put additional financial burden on patients. Around Rs. 690 (US $15) per ADR is the attributable financial burden of drug-related problems (M. Ramesh, Pandit, & Parthasarathi, 2003; L. Rolfes, Hunsel, Taxis & Puijenbroek, 2016). Studies have indicated that ADRs occur almost daily in the patients. However, health care professionals often do not recognize, report or appropriately treat instances of drug-related harm. World Health Organization (WHO) defines, ADR, "a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function."(The safety of medicines in public, 2006). Pharmacovigilance, as defined, is the science and activities relating to the detection, assessment, understanding and prevention of adverse events or any other possible drug-related problems (The importance of pharmacovigilance, 2002). India has 10% of global intake of medicines; though contributes very less to the global ADR database. This is due to the poor reporting of ADRs in India (Bahri, 2016). In order to promote reporting of ADRs in India; Central Drugs Standard Control Organization (CDSCO) Ministry of Health and Family Welfare Government of India, initiated a nationwide Pharmacovigilance programme of India (PvPI) in 2010, coordinated by the Indian Pharmacopoeia Commission (IPC), National Coordinating Centre (NCC) Ghaziabad, executed with the help of ADR monitoring centres (AMCs). Currently, there are around 170 AMCs throughout India (Indian Pharmacopoeia Commission, 2013). The most common way through which various

AMCs report the occurrence of ADRs is spontaneous reporting structure which is a voluntary type of reporting. Healthcare professionals, nurses, pharmacists and patients can report. Despite of the fact that in last 5 years, NCC PvPI worked hard to enhance ADR reporting in India, currently, India contributes just 3% of the WHO global individual case safety reports (ICSRs) database (Amale et al., 2018).Spontaneous reporting structure suffers from the main problem of under-reporting which can be as high as 98% (A.P. Fletcher, 1991). The reasons for this low level of ADR reporting include lack of awareness and training. An additional factor is that the government has not made it mandatory for the health care providers to report ADRs, unlike some countries such as Spain and Sweden (Brewer & Colditz, 2015). Therefore, it is the need to identify ADRs as early as possible and to prevent them. Evaluating ADR reports are essential part of Pharmacovigilance as it helps to collates and analyze data to arrive at an inference for regulatory purposes (Y. Arimone, Bégaud, Miremont-Salamé, Fourrier-Réglat, Moore, Molimard, & Haramburu, 2005). ADR monitoring play a vital role in detecting ADRs and alerting physicians to the possibility, circumstances and consequences of such events, thereby protecting the user population from avoidable harm (S.Gupta, Nayak, Shivaranjani, & Vidyarthi, 2015). It is essential to have collection, constant surveillance and analysis of the collected ADR data for assessing the safety of drugs in a tertiary hospital and also the evaluation of the pattern of reported ADRs has an important educational and practical value. This information about the various aspects of ADRs can provide useful information to manage the ADRs. Thus, the present study was done to study the patterns of reported ADRs in tertiary care hospital.

METHODS

A total of 300 ICSRs submitted to ADR monitoring centre of the institute were evaluated. These ICSRs were of the patients visiting the outpatient and inpatient departments in the various clinical departments in the institute. ADR reports of patients of all ages and both gender, ADR reports of patients having definite history of consumption of drugs and reporting with ADRs were recruited in the study. ICSRs of patients with incomplete data were rejected.

Study procedure

To collect information on ADRs, we used ADR reporting form (version 1.2) of CDSCO, New Delhi, India (Pharmacovigilance program of India, 2010). We distributed ADR reporting form to all of the clinical departments of the institution. The health care providers were briefed about how to collect and record information on the ADR form. They submitted filled ADRs reporting forms to AMC of the institution. The available information of all the patients including relevant history, examination details, investigations and drug therapy was collected. Any untoward event was labelled as ADR as per WHO definition (Edward & Aronson, 2000). WHO causality assessment scale was used for the ADR causality assessment (Safety of medicines, 2002). After analysis, all ICSRs were entered online into vigiflow at the centre. We evaluate the data for various parameters, patient demographics, drug and reaction characteristics and outcome of the reactions. Assessment was also done for causality and seriousness. We also recorded the reasons for seriousness. The serious ADRs and drug causing these were sorted out. Data was analysed using descriptive statistics and expresses in percentages.

RESULTS

The mean age of patients reported with ADRs was 41 years. ADRs were reported more in males (55%) as compared to females (45%).

Various ADRs reported as per gender is depicted in Table 1. The commonest drug group responsible for ADRs was antimicrobials (49%) followed by analgesics and anticancer drugs (11%), drugs acting on central nervous system (CNS) (8%) and hormones (6%) drugs acting on cardiovascular system (CVS) and vitamins (3%) followed by drugs acting on gastrointestinal tract (GIT) and diagnostic dyes (1.7%), drugs used in gout (1.3%), disinfectants and muscle relaxants (0.7%), intravenous fluids (0.3 %) , drugs used in osteoarthritis and autacoids (0.3%) (Figure 1).

Table1: Characteristics of patients

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Predictors	**Frequency (Percentage)**
Age (years)	
< 20	50 (16.7)
21-40	89 (29.7)
41-60	107 (35.7)
≥ 61	54 (18.0)
Mean±S.D	41±21.05
Gender	
Male	165 (55.0)
Female	135 (45.0)
Weight Mean±S.D	57.6±21.28
Outcome	
Recovered	259 (86.3)
Recovering	11 (3.7)
Continuing	9 (3.0)
Unknown	21 (7.0)

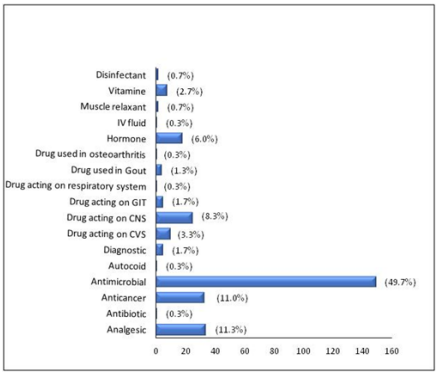

Figure 1: Distribution of ADR's according to drug group involved

The most of the ADRs with a single drug were attributed to Amoxicillin/Clavulanate potassium (n=16; 5%), followed by Ceftriaxone (n=7; 2.3%), Cisplatin, vancomycin, pipracillin/ tazobactum (n=6; 2 %). Figure 2 depicts the distribution of ADRs according to body system involved. Skin was the most commonly affected organ system (51%) followed by systemic reactions involving whole body (15%), GIT (12%), CVS (6%), CNS (5%).Most of the ADRs related to skin were erythematous rash type reactions.

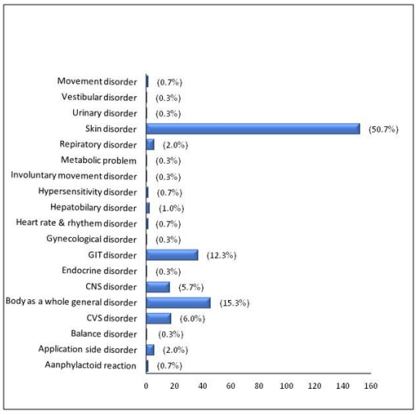

Figure 2: Distribution of ADR's according to system involved

Almost all of the reports were contributed by clinicians (94%). Contribution of nursing staffs in reporting the ADRs was very less (9%) and negligibly contributed by the pharmacists and the dentists. Causality assessment as per WHO scale is depicted in Figure 3. The causality of most ADRs was "probable/likely in nature" with majority of the drugs (83.7%) followed by possible in 14.7% reports.

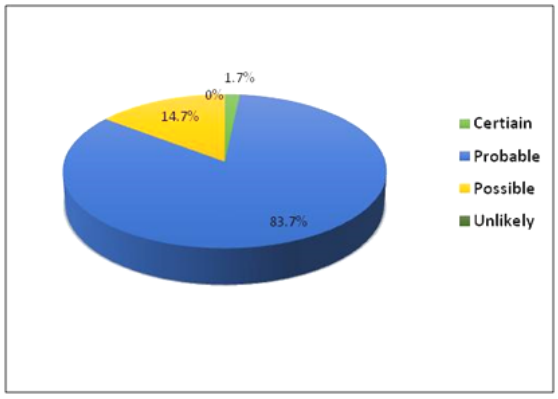

Figure 3: Causality assessment of ADRs according to WHO causality assessment scale

Few of the ADRs were serious (15%). The major cause for seriousness was prolongation of hospitalization (65%). Anaphylaxis was reported in one report with Imipenem. Steven Johnsons Syndrome was reported in 3 reports with Amoxycillin, Phenytoin, and Allopurinol. Fixed drug eruption was reported in 14 reports in total with Norfloxacin, Ibuprofen, Cotrimoxazole, Everolimus, Ofloxacin, Ciprofloxacin/ tinidazole, Ciprofloxacin, Amoxicillin, Paracetamol, Ornidazole and Allopurinol. QT prolongation was reported with Arsenic and Azithromycin. Epidermal necrolysis was reported with Allopurinol. Sub acute intestinal obstruction was reported with Clozapine. One patient developed seizures with administration of Imipenem. Hypertension, breathing difficulty (ST depression on ECG) was observed with Paclitaxel. Decrease in haemoglobin with Interferone was reported in one patient. Most of the patients recovered (86.3%) after ADR occurrence, figure 4.

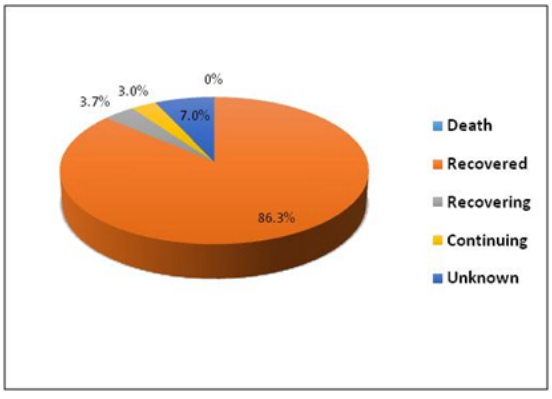

Figure 4: Outcome of adverse drug reaction

DISCUSSION

In our study we collected ICSRs of 300 patients. ADRs were reported more in males as compared to females, which is in accordance with some of the earlier conducted studies (P. Subish., Mishra, & Shankar, 2008; R. Rajesh, & Patil, 2017). Antimicrobials were the most common drug group involved in ADRs in present study, in accordance with earlier conducted studies (R. Arulmani, Rajendran & Suresh, 2008). The common antimicrobials which were associated with ADRs belonged to penicillins and cephalosporins. This trend is same as from earlier reports. In other studies also skin was reported to be the common organ system affected, as skin is the largest organ of the body R. Rajesh et al. (2017). Serious ADRs observed in our study are lesser than other studies S. Gupta et al. (2015). An ADR is said to be serious when it leads to death, congenital anomaly, disability, are life threatening, needs intervention to prevent permanent disability and prolongation of hospitalization. In our study most of the serious ADRs were due to the prolongation of hospitalization. Anaphylaxis was reported in one report with Imipenem. Steven Johnsons Syndrome was

reported in 3 reports with Amoxicillin, Phenytoin, and Allopurinol. The above mentioned antimicrobial drugs and other drugs are very commonly used by the health care professionals; therefore the clinicians should be very careful in observing these serious ADRs. In present study with most of the ADRs causality assessment shows the relatedness, "probable", in accordance with earlier conducted studies R. Rajesh et al. (2017). In present study most of the ADRs were reported by clinicians'. Very few nursing staffs reported the ADRs and negligible number of the pharmacist and dentists reported the ADRs. There is a need of educational intervention to enhance the ADR reporting by the nurses and also among dentists and pharmacists. All health care professionals must report ADRs as part of their professional responsibility. In present study, the suspected drugs were discontinued in most of the patients. These findings are similar with the earlier conducted studies (J. Jose, & Rao, 2006; A. Gupta, Kaur, Shukla, & Chhabra, 2017). Most of the patients recovered fully after discontinuing the suspected drug. Thus highlighting the proper management of ADRs. The most important and basic principle which should be followed while managing the patients of ADR is to discontinue the suspected drug and substitute with another drug if it is required.

In India ADR monitoring and reporting is in its infancy and needs rigorous attitude of ADR monitoring centres towards sensitizing the health care professionals' to highlight the importance and moral responsibility to report ADRs. This study is a step towards enhancing a culture of ADR reporting. This study exposed health care providers to the methodology of ADR monitoring and they got familiar with the importance and methodology of ADR monitoring in the institution.

CONCLUSION

The pattern of ADRs reported in our hospital is comparable with the results of studies conducted in other tertiary hospitals. Antibiotics comprise the major drug family associated with ADRs so, should be rationally prescribed. Information obtained from the present study may be useful for identifying and minimizing preventable ADRs, and may enhance the ability of prescribers to manage ADRs more effectively and to facilitate the development of a hospital Pharmaco vigilance service. At present, contribution of India to the global ADR database is very less (3%) hence is necessary to conduct continuous ADR-related educational programs, training programs, seminars and workshops on Pharmacovigilance on regular basis for all health care professionals. Other than the physicians, nurses, pharmacists, dentists, patients and the general public must also be made aware to report ADRs to detect the full spectrum of complications from pharmaceuti cal treatment.

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