e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(7); 109-113

Original Research Article

A Retrospective Cross Sectional Analysis of Drug Induced Diseases in A Tertiary Care Teaching Hospital Western Rajasthan

Rajesh Ramwani1[1], Puja Khanna Malav[2], Savita Saini[3], Chetan Prakash Suman[4], S.K. Mathur[5]

[1]Final Year Resident, Department of Pharmacology, JLN Medical College, Ajmer (Rajasthan) India
[2,3]Associate Professor, Department of Pharmacology, Government Medical College, Kota (Rajasthan) India
[4]Assistant Professor, Department of General Medicine, Government Medical College, Kota (Rajasthan) India
[5]Senior Professor, Department of Pharmacology, JLN Medical College, Ajmer (Rajasthan) India

Received: 27-04-2023 / Revised: 28-05-2023 / Accepted: 30-06-2023
Corresponding author: Dr. Chetan Prakash Suman
Conflict of interest: Nil

Abstract:

Introduction: Adverse drug reaction (ADR) has been implicated as a leading cause of considerable morbidity and mortality worldwide. The prevalence rate of ADRs has been reported to range from 0.16 to 15.7 per cent. Drug induced diseases (DIDs) are well known but least studies. Data on DIDs from India are not available. Hence, this retrospective study was conducted.

Material& Methods: The present study was conducted in the department of Pharmacology, Government Medical College Kota. It was a cross sectional retrospective observational study carried out over a period of one year from Jan 2022 to December 2022. Data were collected to evaluate the prevalence and profile of DIDs in Adverse Drug Reaction Monitoring (ADRM) Centre, working under Pharmacovigilance Programme of India (PvPI) in a tertiary care teaching hospital from north India (Government Medical College, Kota) using suspected drug reactions monitoring data collection form used under PvPI.

Results: In this study, indoor & outdoor patients' were analyzed and patient reported experience adverse drug reaction on the basis inclusion and exclusion criteria. The total number of ADR events reported during the one year study period was 1385 and out of these 546 (39.42%) were the drug induced disease rate. Among them 243(44.5%) were male and 303(55.5%) were female. The maximum number of patients were found to be in geriatric age group 301(55%); followed by adult 201 (36.8%) and paediatric population 44(8.05%). Mean duration of appearance of DIDs was 28.05±9 days.

Conclusion: Our study concluded that, the total number of reported ADR events, Drug Induce disease rate found high. The maximum number of patients was found to be in geriatric age group. In our study, Maximum ADR events were probable followed by possible according to causality WHO-UMC scale. Our findings show that DIDs are significant health problem in our country, which need more attention.

Keywords: ADR, DIDs

Introduction

Adverse drug reaction (ADR) has been involved as a leading cause of considerable morbidity and mortality worldwide. The prevalence rate of ADRs has been reported to range from 0.16 to 15.7 per cent.[1] Morbidity related to ADRs is also well known and causes a large number of hospital admissions. Further, ADR related hospitalization in emergency and intensive care units (ICU) is very high among high risk population like elderly population with multiple co-morbidities. Morbidity related to ADRs can be permanent sometimes to the extent of 20.4 per cent of admissions in ICU.[2,3] Drug induced diseases (DIDs) is the unintended effect of a drug, which results in mortality or morbidity with symptoms sufficient to prompt a patient to seek medical attention and/or require hospitalization and may persist even after the offending drug has been withdrawn. In the history of drug induced diseases, Public and professional concern about drug induced diseases first appeared in the late 19th century. In 1922, there was an enquiry into the jaundice associated with the use of SALVARSAN, an organic arsenical used in the treatment of Syphilis. In 1937 in the USA, 107 people died from taking an elixir of sulfanilamide that contained the solvent diethylene glycol. This led to the establishment of the Food and Drug Administration (FDA), which was given the task of

enquiring into the safety of new drugs before allowing them to be marketed. The major modern catastrophe that changed professional and public opinion towards medicines was the thalidomide tragedy. The thalidomide incident led to a public outcry, to the institution all round the world of drug regulatory authorities, to the development of a much more sophisticated approach to the preclinical testing and clinical evaluation of drugs before marketing, and to a greatly increased awareness of adverse effect of drugs and methods of detecting them. With the adverse reactions some drugs have been withdrawn from use or for some the label has been changed.

Drug-induced diseases (DID) also called as iatrogenic diseases, are well known. Some of the risk factors of DIDs are multiple chronic diseases, multiple physicians, hospitalization, medical or surgical procedures, long duration of medicine use, advancing age, female sex and a particular class of drugs. Most of these DIDs are largely preventable, if strict vigilance and proper periodic clinical and diagnostic monitoring are undertaken.[4,5] In spite of being a major concern in clinical practice, the DIDs are least studied entity. In India, Sparse data available on DIDs, Hence this retrospective cross sectional study is planned to evaluate the profile of iatrogenic (Drug Induced) Diseases using suspected adverse drug reaction data collected from ADR monitoring centre under Pharmacovigilance programme of India (PvPI).

Material and Methods

The present study was conducted in the department of Pharmacology, Government Medical College Kota. It was a cross sectional retrospective observational study carried out over a period of one year from Jan 2022 to December 2022. Before initiation of the study, ethical approval was obtained from the Institutional Ethics Committee. Data were collected to evaluate the prevalence and profile of DIDs in Adverse Drug Reaction Monitoring (ADRM) Centre, working under Pharmacovigilance Programme of India (PvPI) in a tertiary care teaching hospital from north India (Government Medical College, Kota) using suspected drug reactions monitoring data collection form used under PvPI.

Information about patient, suspected ADRs in the form of DID, suspected medication, reporter, date of reaction, date of recovery and presentation of problem was recorded. Under suspected medication, name of the drug, brand and generic name of manufacturer (if known), expiry date, dose used, route, frequency and therapy dates as well as reason for prescribing suspected drug were also assessed. The information about dechallenge and re-challenge, concomitant medical treatment record, the relevant biochemical abnormality and use of any diagnostic tool was recorded separately. Other relevant history including pre-existing medical conditions like allergy, pregnancy, smoking and alcohol used and any organ dysfunction was noted.The severity and seriousness of reaction, the outcome of reaction were recorded for every suspected ADR in the form of DID as recommended under PvPI. The suspected ADRs in the form of DIDs were classified in term of causality using WHO-UMC (Uppsala Monitoring Centre) scale26. Types of reaction were classified as Type A (augmented); Type-B (bizarre), Type C (continuous use); Type D (delayed); and Type E (end of use as per recommended standard operating procedure of PvPI.

Inclusion & exclusion criteria: Any ADR in the form of DID report from OPD or inpatient of any severity, duration, and any type of reaction was included pertaining to drugs and vaccines. Any case of poisoning, medication error, over dosage, over/non-compliance, natural products/alternate medicines and unidentified drugs were excluded from the analysis. Analysis was carried out with the help of computer software Epi-info software. Data were expressed in percentage and descriptive statistics were used.

Results:

In this study, indoor & outdoor patients' were analyzed and patient reported experience adverse drug reaction on the basis inclusion and exclusion criteria. The total number of ADR events reported during the one year study period was 1385 and out of these 546 (39.42%) were the drug induced disease rate. Among them 243(44.5%) were male and 303(55.5%) were female. The maximum number of patients were found to be in geriatric age group 301(55%); followed by adult 201 (36.8%) and paediatric population 44(8.05%). Mean duration of appearance of DIDs was 28.05±9 days.(Table I)

During the study observed that, overall, 13.79, 16.11, 69.97 and 0.10 per cent DIDs were mild, moderate, severe and fatal, respectively; 18.11, 10.79 and 71.08 per cent, respectively were sub acute, acute and latent in nature. In our study, Maximum ADR events were probable (94.95%), followed by possible (5.04%) according to causality WHO-UMC scale. Overall, 95.60 per cent of DIDs recovering and 4.37 per cent continued in similar mode at the time of report collection (Table I). In present study, Acne (24%), Gastritis (13.18%), diarrhoea (11.17%), hypotension (6.04%), hepatic dysfunction (4.58%), were some of the common DIDs were reported. The list of other DIDs and the common suspected drugs are depicted in Table II a, b.

Table 1: Profile Of Drug-Induced Diseases (DIDS)

Study Parameter Variables
Total number of ADRs & events reported 1346
Total number of drug-induced diseases (DID) & detection rate 546 (39.42%)
Mean duration of appearance of DID in days (Mean± SD) 28.05 ± 9 days
Sex distribution- male Vs female ratio 243 (44.5%) Vs 303 (55.5)
Age-wise classification-adult, geriatric & paediatric (%) 201(36.81%), 301(55%), 44(8.05%),
OPD Vs In ward (%) 454(83.15%) Vs 92 (16.84%)
Urban Vs rural (%) 367 (67.21%) Vs 179 (32.7%)
Single disease Vs >1 co-morbid conditions (%) 78% Vs 22%
Route of drug administration- Oral/iv/im/sc (%) 85.15/10.95/2.15/1.72 (%)
Severity – mild/moderate/severe/fatal (%) 13.79/16.11/69.97/0.10 (%)
Mode of onset DID – sub acute/acute/latent(%) 18.11/10.79/71.08 (%)
Type of reactions - A,B,C,D,E & unclassified (%) 99/0/1/0/0 (%)
Causality as per WHO - UMC scale – 0/94.95/5.04/0/0 (%)
certain/probable/possible/unlikely/unclassified/unassessible (%)
Outcome of the DIDs - recovered/recovering/continuing (%) 0/95.60/4.37 (%)
Management of DIDs - intervention required vs non-intervention 100 Vs 0
Required (%)

Table 2 A: Commonly suspected drug causing Drug-Induced Diseases (DIDs)

System	Drugs Induced Disease	No. of event (%)	Commonly Suspected drugs
Skin	Acne	133 (24)	Betamethasone, Clobetasol
252 (46.15%)	Itching	35 (6.4)	Steroid, Peracetamol, doxycycline, ketoconazole, topical homeopathic/ ayurvedic
	Dermatitis	23 (4.21)	B. Tex Lotion, Valproic Acid, Diclofenac Gel
	Fixed drug eruption	16(2.92)	Paracetamol, Diclofenac
	Erythematous skin rashes	31 (5.7)	Steroids, Imatinib, Paracetamol, Phenytoin, Ketoconazol, Fluconazol
	lipodystrophy	6 (1.09)	Insulin, ART
	Toxic epidermal necrolysis	6 (1.09)	Cefixime, Amoxycillin
	Lichenoid drug eruption	2 (0.37)	Phenytoin
GIT	Gastritis	72 (13.18)	ATT, Diclofenac, NSAIDs
152(27.83%)	Diarrhoea	61(11.17)	Imatinib, ,Methotrexate, Amoxicillin
	Upper GI Bleed	9(1.64)	Ibuprofen, Diclofenac, NSAIDs
	Vomiting	6(1.09)	Resperidone, Cycloserine
	Mucositis	2(0.37)	Cytarabine, Methotrexate
	Abdominal Pain	1(0.18)	l- asparaginase
	Dryness of mouth	1(0.18)	Clonazepam
CVS	Hypotension	33(6.04)	Frusemide, CCBs Plus ACEIs, Ceftriaxone
60 (10.99%)	Hypertension	18 (3.29)	Prednisolone, Theophylline
	Bradycardia	4(0.73)	Atenolol, Metoprolol, Diltiazem
	Shock	2 (0.37)	Radiacontras agent, NSAIDs
	Arrythmia	3 (0.55)	Digoxin, Bupivacaine, Verapamil
Hepatic Dysfunction	Deranged LFT	25(4.58)	ATT, ART
Renal Dysfunction	Deranged RFT	12 (2.19)	Cefriaxone, ATT

GIT-Gastrointestinal System, CVS- Cardiovascular system, CNS- Central Nervous system, ATT- Anti tubercular treatment, ART- Anti retroviral treatment, NSAIDS- Non steroidal anti-inflammatory drugs, FDC- Fixed dose combination

Table 2 B. Commonly suspected drug causing Drug-Induced Diseases (DIDs)

System	Drugs Induced Disease	No. of event (%)	Commonly Suspected drugs
CNS	Anxiety	13 (2.38)	Theophylline, FDC(Paracetamo plus Acelofenac plus Chlorzoxazone)
(5.49%)	Peripheral neuropathy	8 (1.47)	ATT, ART
	Seizures	4 (0.73)	Tramadol, Diphenhydramine, Isoniazid
	Giddiness, Headach	3 (0.55)	Minoxidil Lotion
	Cognitive decline	2 (0.37)	Barbiturates, Presdnisolone
Metabolic	Diabetes	4 (0.73)	Presnisolone, Deflazacort
6 (1.09%)	Obesity	1 (0.18)	Olanzapine
	Dyslipidemia	1 (0.18)	Quetiapine
Blood	Anaemia	5 (0.92)	ART Plus Tirofiban
8 (1.47%)	Thrombocytopenia	2 (0.37)	Enoxaparin
	Bone Marrow Suppression	1 (0.18)	Fluorouracil
Chest	Asthma	1 (0.18)	NSAIDs, Paracetamol
3 (0.55%)	Tuberculosis (TB)	2 (0.37)	Prednisolone, Methotrexate plus Sulfasalazine plus Leflunomide
Gynaecological	Menstrual Dysfunction	6 (1.09)	Aspirin, Naproxen, Misoprostol, Prednisolone
Musculoskeletal 3 (0.55%)	Osteoporosis	2 (0.37)	Heparin, Glucocorticoids
	myalgia	1 (0.18)	Atorvastatin
Miscellaneous	Secondary Infection	9 (1.64)	

Discussion

The safe use of medicine is an important criterion that any regulatory authority within a given Country has to ensure in order to protect the public health. Iatrogenic disease (Drug Induced diseases) significant health problem concern for patients, health care professionals and health administrators. The present study was indicating drug induces diseases (DIDs) in indoor and outdoor patient in tertiary care teaching hospital.

In current study, the total number of ADR events reported 1385 and out of these 546 (39.42%) were the drug induced disease rate. The present study result were comparable with other study atiqi R et al.,[6] there incidences of DIDs 33.9 percent. In our study, female predominated than male and these results were in accordance with study of Zopf Y et al.[7] Geriatric population (55%) accounted for maximum DIDs cases. Similar finding were observed in study done by permpongkosol et al, where geriatric patients were shown to encounter more DIDs.[4] Mean duration of drug induced diseases in current study was 28.05±9 days. On the basis of severity scale, maximum DIDs cases were found severe in our study. The total ADR events were reported in this study type A reaction. These results were accordance with other study Ahern F et al.[5] In this study, the clearly indicated that most of the drug induced disease have been prevented if strict vigilance, proper periodic clinical and diagnostic monitoring were undertaken.In current study, most common suspected drug and group of drugs that caused DIDs Acne, gastritis, diarrhoea, hypotension, hepatic dysfunction due to steroids, NSAIDs, Beta lactam antibiotics, antihypertensive drugs and antitubercular drugs treatment (ATT) respectively. Similar findings were observed in studies done bt Atiqi R et al[6] and Brvar M et al.[8] In contrast to our study, phlebitis at the injection site has been reported as most frequently occurring iatrogenic events in another study.[9]

Majority of DIDs events were found in skin and subcutaneous tissue disorder (46%) followed by gastrointestinal system (27.83%), cardiovascular system (10.99%) as a most common DIDs in our study. This results were accordance with other study Theissard F et al.[10] Peripheral neuropathy, hepatitis were most prevalent DIDs with the use of Antitubercular therapy and HAART(Highly active anti-retroviral therapy treatment in this study. Similar to other study Anwikar SR et al.[11] Another study Tariq et al[12] also accordance with our study, In this study conclude that anti tubercular treatment (ATT) induced hepatic dysfunction and renal dysfunction most common DIDs. In contrast to our study, Another study where antidepressants were shown to be associated with causing hepatotoxicity. Paroxetin, fluoxetin, citalopram and mirtazapin were associated with reversible liver injury.[13]

In present study, Hypotension, hypertension, bradycardia and arrhythmia most common cardiovascular events were reported. Other study Common cardiovascular adverse drug events reported were drug-induced arrhythmias, blood pressure abnormalities and heart failure.[14] Drug

induced haemolytic anaemia has been commonly reported with cefotetan, ceftriaxone and piperacillin few studies.[15,16] However, ART and tirofiban most commonly offending agents to cause anaemia in our study. The major limitation of the present study is that it does not represent the true prevalence of the problem due to voluntary/spontaneous nature of ADR reporting.

Thus, there might be many other confounding factors which affected the final outcome of the present study data. Such DIDs studies conducted across the country in future. These studies provide information to clinicians and policy regulators about adverse drugs events which can be largely prevented in the interest of patient safety.

Conclusion

Our study concluded that, the total number of reported ADR events, Drug Induce disease rate found high. The maximum number of patients was found to be in geriatric age group. In our study, Maximum ADR events were probable followed by possible according to causality WHO-UMC scale.

In present study, Acne, Gastritis, diarrhoea, hypotension, hepatic dysfunction were some of the common DIDs were reported. The results of this study will be useful in future for making and improving standard treatment guidelines. It also promotes the rational prescription and rational use of medicines. Our findings show that DIDs are significant health problem in our country, which need more attention.

References

1. Kongkaew C, Noyce PR, Asheroft DM. Hospital admission associated with adverse drug reaction: a systematic review of prospective observational studies. Ann Pharmacother 2008; 42 : 1017-25.
2. De Paepe P, Petrovic M, Outtier L, Van Maele G, Buylaert W. Drug interactions and adverse drug reactions in the older patients admitted to the emergency department. Acta Clin Belg 2013; 68: 15-21.
3. Pérez Menéndez-Conde C, Bermejo Vicedo T, Delgado Silveira E, Carretero Accame E. Adverse drug reactions which provoke hospital admission. Farm Hosp 2011; 35 : 236-43.
4. Permpongkosol S. Iatrogenic disease in the elderly: risk factors, consequences, and prevention. Clin Interv Aging 2011; 6 : 77-82.
5. Ahern F, Sahm LJ, Lynch D, McCarthy S. Determining the frequency and preventability of adverse drug reaction-related admissions to an Irish University Hospital: a cross-sectional study. Emerg Med J 2014; 31 : 24-9.
6. Atiqi R, van Bommel E, Cleophas TJ, Zwinderman AH. Prevalence of iatrogenic admissions to the Departments of Medicine/Cardiology/ Pulmonology in a 1,250 bed general hospital. Int J Clin Pharmacol Ther 2010; 48 : 517-24.
7. Zopf Y, Rabe C, Neubert A, Hahn EG, Dormann H. Risk factors associated with adverse drug reactions following hospital admission: a prospective analysis of 907 patients in two German university hospitals. Drug Saf 2008; 31 : 789- 98.
8. Brvar M, Fokter N, Bunc M, Mozina M. The frequency of adverse drug reaction related admissions according to method of detection, admission urgency and medical department specialty. BMC Clin Pharmacol 2009; 9 : 8.
9. de la Sierra A, Cardellach F, Cobo E, Bové A, Roigé M, Santos MJ, et al. Iatrogenic illness in a department of general internal medicine: a prospective study. Mt Sinai J Med 1989; 56 : 267-71
10. Thiessard F, Roux E, Miremont-Salamé G, Fourrier-Réglat A, Haramburu F, Tubert-Bitter P, et al. Trends in spontaneous adverse drug reaction reports to the French pharmacovigilance system (1986-2001). Drug Saf 2005; 28 : 731-40.
11. Anwikar SR, Bandekar MS, Smrati B, Pazare AP, Tatke PA, Kshirsagar NA. HAART induced adverse drug reactions: a retrospective analysis at a tertiary referral health care center in India. Int J Risk Saf Med 2011; 23 : 163-9.
12. Tariq S, Khan TS, Malik S, Anwar MS, Rashid A. Frequency of anti-tuberculous therapy-induced hepatotoxicity in patients and their outcome. J Ayub Med Coll Abbottabad 2009; 21 : 50-52.
13. Park SH, Ishino R. Liver injury associated with antidepressants. Curr Drug Saf 2013; 8: 207-23.
14. Kennelly C, Esaian D. Drug-induced cardiovascular adverse events in the intensive care unit. Crit Care Nurs Q 2013; 36: 323-34.
15. Garratty G. Drug-induced immune hemolytic anemia. Hematol Am Soc Hematol Educ Program 2009; 1 : 73 9.
16. Garratty G. Immune hemolytic anemia associated with drug therapy. Blood Rev 2010; 24:143-50.