

Original Research Article

Burden of drug induced allergic reactions: a 3-year experience in a tertiary care hospital

Shatavisa Mukherjee*, Santanu Kumar Tripathi

Department of Clinical and Experimental Pharmacology, School of Tropical Medicine, Kolkata, West Bengal, India

Received: 10 November 2020

Revised: 09 December 2020

Accepted: 10 December 2020

*Correspondence:

Shatavisa Mukherjee,

E-mail: shatavisa100@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: DIARs includes a wide spectrum of immunologically-mediated hypersensitivity reactions with varied mechanisms and clinical manifestations. Besides affecting a patient's quality of life, it may also lead to increased treatment cost and length of hospitalization. The present study aims to provide an overview of drug induced allergic reactions experienced in a tertiary care set-up.

Methods: A prospective observational outcome research was conducted over a 3-year period on patients encountering drug induced allergic reactions, who has been analysed for their spectrum of presentation, clinical outcomes (including severity, management and outcome of reaction), economic outcomes (including cost of treatment) and humanistic outcomes (including assessment of quality of life).

Results: Drug induced allergic reactions accounts for 2.71% of total hospitalization in this study period. While majority reactions were moderate in severity grading, most were preventable. Direct cost of treating such preventable reactions were much higher along with increased indirect cost (due to prolonged hospitalization) adding to economic burden. Quality of life in patients encountering such reactions was also compromised as assessed using EQ-VAS.

Conclusions: Prompt identification, consultation, cessation of culprit drug, management and patient counselling can act as strategies to minimize the burden of these reactions on society and healthcare system at large.

Keywords: Cost, Drug induced allergic reactions, EQ-VAS, Outcomes

INTRODUCTION

Adverse drug reactions (ADRs) remain as a significant concern for increase of morbidity and mortality worldwide related to medicine use. Studies across the world has reported the global ADR incidence rate to range from 5 to 30%.¹ Drug induced allergic reactions (DIARs) accounts for approximately 5-10% of all suspected ADRs. It encompasses a spectrum of immunologically-mediated hypersensitivity reactions with varying mechanisms and clinical presentations. DIARs occurs in 1% to 2% of all admissions and 3% to 5% of hospitalized patients.² Risk factors for drug allergy include age, gender, genetic polymorphisms, viral infections and drug-related factors. Drug-induced allergic

reactions can affect numerous organ systems and manifest in a variety of reactions, including various drug-induced allergic syndromes, and many drug-induced allergic reactions can have multiple mechanistic pathways. Given the variance of symptoms and clinical presentations associated with DIARs, identification and diagnosis pose a significant challenge. Thus, suspicion of DIAR should immediately follow consultation with allergist for further management. DIARs, besides affecting a patient's quality of life, may also lead to prolonged hospitalization, increased cost of treatment and even mortality.³

The present study thus aimed to provide an overview of DIARs experienced in a tertiary care set-up in Eastern India.

METHODS

A prospective, observational, outcome research was carried out over a period of 3-years on inpatients, those admitted with ADRs and those encountering ADRs during their tenure of hospitalization. Patients experiencing DIARs was considered as a subset population. The study site was a 150 bedded tertiary care government hospital admitting patients over 12 years of age. The resident doctors, nurses and pharmacists on duty were priorly informed about the study objectives and were requested to report cases due to suspected DIARs on a pre-structured case notification form. Decision of the treating physician regarding the diagnosis was considered final. All such patients were also independently reviewed twice a day to determine if any cases had not been reported to the investigator by the on-duty personnel. Each DIAR cases were analyzed and details of demographic characteristics, diagnosis, type of DIARs, past medical history, drugs, other alternative therapy history, and personal history were collected. Spectrum of clinical presentation, clinical outcomes (including severity, management and outcome of reaction), economic outcomes (including cost of treating the DIAR) and humanistic outcomes (including quality of life) were assessed. The causality assessment of ADRs was done by the Naranjo ADR Probability Scale.⁴ DIARs were also evaluated and assessed in terms of preventability using the criteria of Schumock and Thornton's scale, and the severity will be evaluated by Hartwig and Seigel's severity assessment scale.^{5,6} Patients were followed until four months post hospital discharge for evaluation of reaction outcome and quality of life indices.

For cost evaluation, direct and indirect cost-generating components were taken into consideration. Direct expenditures due to hospital admission were cost of the drugs and consumables, cost of hospital stay (which includes diet for the patient), investigations and interventions. Indirect cost calculation included the cost of travel, food and stay for the caregiver(s) and loss of wages due to loss of productivity for both patient and caregiver(s). For the cost of travel, one to and fro visit was included. A sensitivity analysis was conducted including the maximum, minimum and average expenditure per day per person for food, travel and wages. Expenditure on food for caregiver(s) were calculated. Where not reported, expenditure was assumed as average cost of one meal, INR 25 to INR 100 with an average of INR 50. For calculation of travel expenses, auto rickshaw fares for all local patients and the ordinary bus and local train fare for all patients living further away were used as minimum. Loss of productivity was calculated on the basis of a minimum wages model in India. Total economic burden was calculated by adding these direct and indirect costs. Humanistic outcomes were adjudged in terms of health-related quality of life in patients encountering ADR(s) using Euro QoL visual analogue scale (EQ-VAS).⁷

RESULTS

Out of 8315 admissions in the index period, 226 cases of DIARs were recorded, thus accounting for 2.71% of total hospitalization. Out of total 226 DIARs noted, 89 were encountered by patients hospitalized for other causes, while rest were admitted with DIARs itself. Female preponderance was noted to be higher than males striking the male: female ratio as 1:1.5. The age range varied from 17 to 74 years.

Spectrum of clinical presentation was assessed. Type IV reaction accounted for maximum presentations (n=103 cases), including skin rashes. 72 DIAR cases belonged to type I immune reaction including urticaria, angioedema, bronchospasm. Type III reactions include 38 cases ranging from vasculitis, fever, rash. Only 13 cases of type II reactions were noted which included anemia, thrombocytopenia etc.

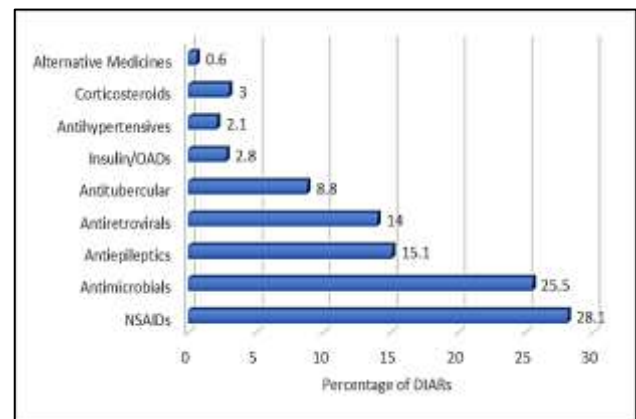


Figure 1: Drugs in Suspicion.

Probing the drugs in suspicion, it was observed that non-steroidal anti-inflammatory drugs (NSAIDs) accounted for maximum DIARs followed by antimicrobials, antiepileptics, antiretrovirals, antitubercular, anti-diabetic, antihypertensives and others.

Mean length of hospital stay was increased in cases with DIARs i.e. 10.33 ± 7.39 days (2-33 days) [expressed as Mean \pm SD (range)]. This was in contrast with mean length of hospital stay of non-DIAR hospitalized cases, where the figure was 7.28 ± 5.71 days (2-26 days).

Causality assessment using Naranjo's algorithm conferred 67.25% DIARs were 'probable', 19.91% DIARs were 'possible' and 12.83% DIARs were 'definite'. Severity assessment was done using Hartwig Seigel Severity Assessment Scale. Majority of the DIARs i.e. 65% were found to be of "moderate" grade (N=147), while 22% were "severe" (N=49) and rest "mild". Preventability assessment using Schumock Thornton preventability scale conferred around 71% of DIARs (n=160) to be preventable in nature.

Of 226 DIAR cases, 61 were benefitted with only drug discontinuation, 11 required desensitization while 154 required pharmacological management. Pharmacological management mainly included use of antihistamines, corticosteroids, immunoglobulins, immunosuppressants and IV fluids.

Table 1: Management of DIARs.

| Management approach | Frequency |
|----------------------------|-----------|
| Drug discontinuation | 61 |
| Desensitization | 11 |
| Pharmacological management | 154 |
| Antihistamines | 138 |
| Corticosteroids | 110 |
| Immunoglobulins | 83 |
| IV fluids | 72 |

As in for the outcome of DIARs, 5 cases were fatal, while rest recovered. Assessing the cost quotient, the cost of treating severe DIARs were significantly high as compared to mild ones. Mean cost of therapy was significantly dependent on the length of hospital stay of the affected.

Table 2: Cost of Treating DIARs.

| | | Mild DIARs | Moderate DIARs | Severe DIARs |
|-----------------------------|-----------------|------------|----------------|--------------|
| Average direct cost (INR) | Drugs | 973.61 | 2247.55 | 6783.51 |
| | Investigations | 509.12 | 981.22 | 2179.10 |
| | Consumables | 672.19 | 1582.90 | 2071.92 |
| Average indirect cost (INR) | Cost of food | 1003.47 | 1384.55 | 1575.00 |
| | Travel expenses | 1071.13 | 1377.61 | 1565.37 |
| | Loss of wages | 1265.00 | 2072.45 | 4755.31 |
| Total treatment cost | | 5494.52 | 9646.28 | 18930.21 |

DIARs were assessed for their impact on quality of life (QoL) using EQ-VAS instrument. On a 100-point scale, patients admitted with DIARs showed diminished QoL at baseline, as compared to those encountering DIAR during their hospital stay. For both groups the QoL indices increased over the time period.

Table 3: Quality of life index (using EQ-VAS score).

| | EQ-VAS score | | |
|---|--------------|----------|----------|
| | Baseline | 2 months | 4 months |
| Admitted with DIARs | 34.69±2.03 | 76±4.37 | 82±2.97 |
| Encountering DIARs during hospital stay | 46.44±3.11 | 83±3.92 | 85±3.22 |

DISCUSSION

DIARs, a subset of ADR family, accounts for a substantial proportion of in-patient hospitalizations, leading to increased clinical and economic burden. Alongside, DIARs can also lead to diminished quality of life owing to the added physical agony and anxiety due to the ongoing therapy. Drug allergic reactions have been reported to most every medication, with certain drugs having increased propensity for some specific type of reactions. Though cutaneous manifestations are the most common presentation for DIARs, many also present with non-cutaneous physical findings, which are generally nonspecific posing difficulty in diagnosis and management decisions. The present study tried to assess outcomes of DIARs.

Our study witnessed 2.71% of total hospitalizations accounting for DIARs, of which 1.64% accounts for DIAR related hospitalization while rest were encountered by in-patients admitted for other causes. Incidence of DIAR was found more in females in comparison to males in our study. This was in line with the global reported literature.⁸ An increased length of hospital stay was noted in cases with DIARs in contrast to those without.

The most important and effective therapeutic measure in managing DIARs is the cessation of the offending drug, if possible. However, the clinical consequence of the drug stoppage should be closely monitored and also alternative drugs with unrelated chemical structures should be substituted as and if available. While, in majority of the patients the symptoms gradually resolve in weeks, some need additional intervention for its further management. Additional therapy for drug hypersensitivity reactions is largely supportive and symptomatic. Systemic corticosteroids may speed recovery in severe cases of drug hypersensitivity. Topical corticosteroids and oral antihistamines may improve dermatologic symptoms. In our study, 26.99% patients were benefitted with only drug stoppage, while 68.14% required further pharmacological management with drugs like antihistamines, corticosteroids, immunoglobulins, immunosuppressants and IV fluids. For around 11 cases, offending drug deemed essential and no alternatives existed, hence desensitization was attempted.

Assessing the economic constraints, direct cost of treating DIARs largely varied with severity of DIAR. With severe DIARs, the length of hospital stays also increased, thereby increasing the total cost burden. With 71% of the DIARs assessed as preventable, it was found that direct cost of treating such preventable reactions were much higher along with increased indirect cost (due to prolonged hospitalization) adding to economic burden. This is in contrast to non-preventable ADRs and was found in line with previous established literature.¹⁹ Quality of life in patients encountering such reactions was also compromised as assessed using EQ-VAS. On a 100-point scale, patients admitted with DIARs showed

diminished QoL. Factors responsible for such observation can be anxiety over disease status, economic constraints faced etc.

Our study has its strength in being a prospective comprehensive study of a long duration in a tertiary set-up. Assessing economic impact of DIARs in countries like ours, where healthcare cost is everyday increasing, is of prime importance which was dealt in our study.

However, a single center experience cannot generalize the data, but can provide an estimate of the situation. Moreover in government hospitals, hospital stay is free of cost. Hence the computed burden estimation may not be in agreement with other private, corporate hospitals.

CONCLUSION

Prompt identification, consultation, cessation of culprit drug, management and patient counselling can act as strategies to minimize the burden of these reactions on society and healthcare ecosystem at large.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Coleman JJ, Pontefract SK. Adverse drug reactions. Clin Med. 2016;16(5):481-5.
2. Warrington R, Silviu-Dan F, Wong T. Drug allergy. Allerg Asthma Clin Immunol. 2018;14(2):60.
3. Schnyder B, Pichler WJ. Mechanisms of drug-induced allergy. Mayo Clin Proc. 2009;84(3):268-72.
4. Naranjo CA, Busto U, Sellers EM. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30(2):239-45.
5. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm. 1992;27(6):538.
6. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm. 1992;49(9):2229-32.
7. Feng Y, Parkin D, Devlin NJ. Assessing the performance of the EQ-VAS in the NHS PROMs programme. Qual Life Res. 2014;23(3):977-89.
8. Jensen-Jarolim E, Untertsmayr E. Gender-medicine aspects in allergology. Allergy. 2008;63(5):610-5
9. Bates DW, Spell N, Cullen DJ, Burdick E, Laird N, Petersen LA, et al. The costs of adverse drug events in hospitalized patients. Adverse Drug Events Prevention Study Group. JAMA. 1997;277:307-11.

Cite this article as: Mukherjee S, Tripathi SK. Burden of drug induced allergic reactions: a 3-year experience in a tertiary care hospital. Int J Res Med Sci 2021;9:200-3.