Research Article

A prospective study of causality and severity assessment of adverse drug reactions of antibiotics at an Indian tertiary care teaching hospital

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ABSTRACT

Aim: The main aim of this study is to detect and evaluate the adverse drug reactions (ADRs) of antibiotics using causality and severity assessment scales. **Materials and Methods:** A prospective observational study was conducted for a period of 6 months. In this study, case reports of all the inpatients were included and outpatients were excluded. The causality assessment of reported ADR was carried out using World Health Organization Uppsala Monitoring Centre (WHO-UMC) system and Naranjo scale. Modified Hartwig-Siegel scale (MHS) was also used for the severity assessment of adverse events. **Results:** A total of 106 ADR were reported from 143 patients. Among them, 60.4% were male and 39.6% were female. Majority of the ADR were found in the age group of 46–55 years (40.6%). It was reported that azithromycin was the most frequent cause of ADR accounted for 23.6%, with vomiting, dysgeusia, erythema, and swelling. As per the WHO-UMC system, majority were observed with certain (56.6%) related adverse event and least was observed with conditional (1.9%). As per Naranjo scale, majority of the reports were comes under definite (58.5%) and least observed reports were comes under doubtful (4.7%). According to MHS scale, majority of the reports were with moderate reactions (70.8%). Severe reactions were least observed in this study. **Conclusion:** Reviewing of medication history of antibiotics plays an important role in preventing adverse effects. Hence, clinical pharmacists should take the responsibility in providing evidence-based therapeutic recommendations for better management of adverse reactions.

Keywords: Adverse drug reactions, modified Hartwig-Siegel scale, Naranjo scale, World Health Organization Uppsala Monitoring Centre

Introduction

Adverse drug reactions (ADRs) are the key reason for the flare up of morbidity, mortality, and leading cause of hospitalizations globally. The ADR is a substantially harmful and unpleasant reaction which results from the use of a drug.[1] The identification of ADR is very challengeable process, because the effect of ADR differs in different age groups and pathological conditions. Antibiotics are the most commonly prescribed drug in modern medicine which cures the disease by killing or inhibiting the growth of microorganisms.[2] However, antibiotics sometimes kill the good bacteria, which protect people from fungal infections and as a result fungal infections develop in vagina, mouth, and throat. Therefore, to improve and to safeguard the health of people, pharmacovigilance was initiated. Pharmacovigilance is the pharmacological science which promotes and ensures the drug safety by corroborating, understanding, assessing, and prevention of ADR.[3] Since, April 15, 2011, Indian pharmacopoeia commission started working as the National coordination center. At present, there are 170 ADR monitoring centers (AMCs) set up across the country in medical colleges which is approved by the Medical Council of India. AMCs are responsible for the collection of ADR as per the standard operating procedure and reporting to the net based ADR reporting software Vigiflow.[4] Nowadays, the ADRs are the main reason to develop higher health-care cost in many patients.[5] However, the benefits of the drug should surpass the risk of ADR. Hence, the main aim of this study is to detect and evaluate the ADR of antibiotics at an Indian tertiary care teaching hospital.

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Materials and Methods

A prospective observational study was conducted for a period of 6 months (November 2020–April 2021) at GSL General Hospital, Rajahmundry. A total of 106 antibiotics ADR were found among 143 patients. In this study, case reports of all the inpatients were included and outpatients were excluded. The causality assessment of reported ADR was carried out using the World Health Organization Uppsala Monitoring Centre (WHO-UMC) system and Naranjo scale. The WHO-UMC system was meant as a practical tool for the causality assessment of ADRs. The assessment criteria of various categories were certain, probable, possible, unlikely, conditional, and unclassifiable.[6] The Naranjo (or) ADR probability scale was meant to assess whether there was a causal relationship between an identified untoward clinical event and a drug. Total scores were ranging from–4 to +13. If the scores were 9–+13, the ADR was considered as definite. If the scores were 5–8, the ADR was considered as probable. If the scores were 1–4, the ADR was considered as possible. If the scores were 0—4, the ADR was considered as doubtful.[7] Modified Hartwig-Siegel scale (MHS) was meant for the severity assessment of adverse events. Depending on the severity of the suspected reaction, ADRs were categorized into seven levels. Levels 1 and 2 may come under mild category, levels 3 and 4 may come under moderate, and levels 5, 6, and 7 may come under severe category.[8]

Results

In this 6 months study, a total of 106 ADR were reported from 143 patients. Among them, 64 (60.4%) were male and 42 (39.6%) were female. Table 1 represents the age-wise categorization of patients involved in this study. About 12.2% of individuals were in the age group of 26–35 years, 27.3% were in the age group of 36–45 years, 40.6% were in the age group of 46–55 years, and 19.9% were in the age group of 56–65 years.

Table 2 represents the categorization of antibiotics related to frequency of ADR. Among them, azithromycin was the most frequent cause of ADR which includes vomiting, dysgeusia, erythema, and swelling accounted for 23.6%. ADR of ceftriaxone includes constipation, bloating, indigestion, and swelling accounted for 19.9%. ADR of ampicillin includes bloating, anorexia, stomach cramps, and constipation accounted for 16.9%. Ciprofloxacin and gentamycin were the least cause of ADR, both accounted for 6.6% in this study.

Table 3 represents the categorization of ADR using WHO-UMC system, in which 56.6% of patients were observed with certain, 24.5% were observed with probable, 12.3% were observed with possible, 4.7% were observed with unlikely, 1.9% were observed with conditional, and 0% were observed with unclassifiable related adverse events.

Table 4 represents the categorization of ADR using Naranjo scale. In this study, 58.5% were observed with definite, 26.4% were observed with probable, 10.4% were observed with possible, and 4.7% were observed with doubtful related adverse events.

Table 1: Age-wise categorization of patients

Age	Frequency (%)
26–35	13 (12.2)
36–45	29 (27.3)
46–55	43 (40.6)
56–65	21 (19.9)
Total	106 (100)

Table 2: Categorization of antibiotics related to frequency of ADR

Antibiotics	ADR	Frequency of ADR	Frequency (%)
Ciprofloxacin	Constipation	5	7 (6.6)
	Pruritis	2	
Amoxicillin	Anaphylaxis	5	14 (13.2)
	Nausea	6	
	Indigestion	3	
Ampicillin	Bloating	8	18 (16.9)
	Anorexia	5	
	Stomach cramps	3	
	Constipation	2	
Azithromycin	Vomiting	4	25 (23.6)
	Dysgeusia	11	
	Erythema	8	
	Swelling	2	
Ceftriaxone	Constipation	6	21 (19.9)
	Bloating	3	
	Indigestion	8	
	Swelling	4	
Erythromycin	Flatulence	3	14 (13.2)
	Anorexia	7	
	Dysgeusia	4	
Gentamycin	Stomach cramps	4	7 (6.6)
	Indigestion	3	
Total		106	106 (100)

ADR: Adverse drug reaction

Table 3: Categorization of ADR using WHO-UMC system

WHO-UMC	Frequency (%)
Certain	60 (56.6)
Probable	26 (24.5)
Possible	13 (12.3)
Unlikely	5 (4.7)
Conditional	2 (1.9)
Unclassifiable	0 (0)
Total	106 (100)

Table 5 represents the categorization of ADR using MHS scale. Mild reactions were accounted for 28.3%. Moderate reactions were

accounted for 70.8% and severe reactions were accounted for 0.9% in this study.

Table 6 represents the categorization of ADR based on onset of time. In this study, 52.8% reactions were observed after 1 day, 27.4% were observed after 2 days, and 19.8% were observed on the same day.

Table 7 represents the categorization of ADR based on duration. About 33.1% were observed for the duration of 2 days, 27.4% were observed for the duration of 3 days, and 1.8% was observed for the duration of 6 days.

Discussion

Several studies have reported that antibiotics are the most frequent cause of ADRs. Antibiotics are considered safer, only when they are used rationally. Like all other drugs, they also have some adverse effects over and above beneficial effects.[9] Among the 143 study participants, 106 ADRs were reported in this study. Gender categorization of the study participants revealed that 64 (60.4%) were male and 42 (39.6%) were female, showing that males are more prone to get adverse effects. It was shown that majority of the ADR were observed in the age group of 46–55 years (40.6%). These findings were similar to the study conducted by Parekh *et al*.[10] The prevalence of ADR increases with age due to altered body functions that cause decreased muscle mass and increased body fat.

It was reported that azithromycin was the most frequent cause of ADR accounted for 23.6%, with vomiting, dysgeusia, erythema, and swelling. Maximum numbers of drug reactions were also observed with ceftriaxone (19.9%), with constipation, bloating, indigestion, and swelling. These findings were similar to the study conducted by Brijittsangha *et al*.[11] The risk of adverse effect increases because of high biliary concentrations of the ceftriaxone and also hypersensitivities in patients. The WHO-UMC system was used for the causality assessment of ADR. It was found that majority were observed with certain related adverse event and least was observed with conditional. No reactions were observed to be unclassifiable. In this study, Naranjo scale was also used to predict the relation between drug and the adverse event. Majority of the reports were comes under definite (58.5%) and least observed reports were come under doubtful (4.7%). Specific treatment was provided to all the patients along with the symptomatic therapy. According to MHS scale, majority of the reports were shown moderate reactions (70.8%) followed by mild reactions (28.3%). Severe reactions were least observed in this study. These findings were similar to the study conducted by Rajiv Mahajan *et al*.[12] Most of the ADR reported were of moderate level.

It was also found that 52.8% of reactions were observed after 1 day of administration of the drug followed by 27.4% after 2 days of administration of the drug. Very few were observed on the same day. The duration of the ADR was observed from 1 to 6 days. Majority were cured within 2 days (33.1%) and 3 days (27.4%) in this study.

Table 4: Categorization of ADR using Naranjo scale

Naranjo	Frequency (%)
Definite	62 (58.5)
Probable	28 (26.4)
Possible	11 (10.4)
Doubtful	5 (4.7)
Total	106 (100)

Table 5: Categorization of ADR using MHS scale

MHS	Frequency (%)
Mild	30 (28.3)
Moderate	75 (70.8)
Severe	1 (0.9)
Total	106 (100)

Table 6: Categorization of ADR based on onset of time

Onset (day)	Frequency (%)
Same	21 (19.8)
After 1	56 (52.8)
After 2	29 (27.4)
Total	106 (100)

Table 7: Categorization of ADR based on duration

Duration (day)	Frequency (%)
1	13 (12.2)
2	35 (33.1)
3	29 (27.4)
4	14 (13.3)
5	13 (12.2)
6	2 (1.8)
Total	106 (100)

Conclusion

Reviewing of medication history of antibiotics plays an important role in preventing adverse effects. Clinical pharmacists should take the responsibility in providing evidence-based therapeutic recommendations for better management of adverse reactions.

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References

1. Shenoy ES, Macy E, Rowe T, Blumenthal KG. Evaluation and management of penicillin allergy: A review. JAMA 2019;321:188-99.
2. Kotha P, Vasabhakthula NV, Undurthi C. A study on the effect of exacerbations on the quality of life of patients with chronic obstructive pulmonary disease. World J Curr Med Pharm Res 2020;2:319-21.
3. Kumar AP, Bhoopathi D, Sunkara H. An overview of various scales used

in causality assessment of adverse drug reaction. Int J Pharm Pharm Sci 2017;12:1-5.

4. Jones BM, Avramovski N, Maria A, Crosby J. Clinical and economic outcomes of penicillin skin testing as an antimicrobial stewardship initiative in a community health system. Open Forum Infect Dis 2019;6:1-9.
5. Bhattacharjee P, Vats S, Das L, Ghosh R, Bhattacharjee S. Pattern of adverse drug reactions of antimicrobial agents in a tertiary care teaching hospital of Tripura: A prospective study. Int J Contemp Med Res 2019;6:G6-10.
6. Arulappan AL, Danial M, Sulaiman SA. Evaluation of reported adverse drug reactions in antibiotic usage: A retrospective study from a tertiary care hospital, Malaysia. Front Pharmacol 2018;9:809.
7. Gatti M, Raschi E, De Ponti F. Relationship between adverse drug reactions to antibacterial agents and the Klebsiella pneumoniae carbapenemase-producing (KPC) Klebsiella pneumoniae outbreak: Insight from a pharmacovigilance study. BMC Pharmacol Toxicol 2019;20:65.
8. Neelotpol S, Marzia A, Mimmi SF, Albee H. Knowledge and attitude about pharmacovigilance: A cross-sectional study involving pharmacy students of selected universities in Bangladesh. J Pharmacovigil 2020;8:289.
9. Hodkinson A, Tyler N, Ashcroft DM, Keers RN, Khan K, Phipps D, *et al*. Preventable medication harm across health care settings: A systematic review and meta-analysis. BMC Med 2020;18:313.
10. Parekh N, Ali K, Davies JG, Stevenson JM, Banya W, Nyangoma S, *et al*. Medication-related harm in older adults following hospital discharge: Development and validation of a prediction tool. BMJ Qual Saf 2020;29:142-53.
11. Jourdan A, Sangha B, Kim E, Nawaz S, Malik V, Vij R, *et al*. Antibiotic hypersensitivity and adverse reactions: Management and implications in clinical practice. Allergy Asthma Clin Immunol 2020;16:6.
12. Mahajan R. Inclusion of medical colleges as adverse drug reaction monitoring centers under pharmacovigilance programme of India: Missing the targets. Int J Appl Basic Med Res 2017;7:217.