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Original Research Paper

Pharmacology

EVALUATION OF ADVERSE DRUG REACTIONS BY COMMONLY PRESCRIBED ANTIMICROBIAL AGENTS IN TERTIARY CARE TEACHING HOSPITAL, KANPUR.

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ABSTRACT

Aim: the main aim of our study was to observe Adverse Drug Reaction(ADRs) in indoor patients of Medicine ward with prescribed antimicrobial drugs of a tertiary care hospital Kanpur. **Methods:** A retrospective, observational study was conducted on the ADRs reported in the hospital for six months on hundred patients who required antimicrobial therapy. **Results:** A total of 138 ADRs were reported , 58% were males and 42% females. 54% of the patients were in the age group of 41-60 years. Main adverse reactions were dermatological manifestations followed by that of Gastrointestinal tract. Majority (81.15 %) of the reactions were mild not requiring any pharmacological intervention. Rest were managed conservatively. No mortality were reported due to the ADR. It was further noted that 82.6% were probable and 11.59% as possible. 8 ADR reported were definite manifestations according to probability scale. **Conclusion:** the study was done to note ADR in the medicine ward and also to sensitize the prescribing doctors and health care workers on the importance of early detection, monitoring and reporting of the Adverse drug reactions.

KEYWORDS : Adverse Drug Reaction ,Antimicrobial drugs, Beta lactams.

INTRODUCTION

Adverse drug reaction (ADR) are hazardous and unpleasant reactions to drug usage in clinical practice. Aptly said they are double edged sword for the clinician. According to WHO,an ADR is defined as "any response to a drug which is noxious and unintended, and occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiologic function"(1). ADRs contribute significantly to the morbidity and mortality of patients worldwide. ADRs not only result in hospital admissions or prolonged hospitalization but also may lead to permanent disability or even death. Hence a comprehensive approach to the detection,evaluation,monitoring and reporting of the ADR is prudent. In practical manners, it can be used for pharmacotherapy,drug safety and effectiveness and being cost effective to the patient also.

In clinical practice, the most notorious class of drugs which contribute to the major burden of ADR are AMA(antimicrobial agents) or antibiotics followed by anticancer drugs. (2)The administration of an empirical antimicrobial therapy can be life-saving. Appropriate antibiotic use has been shown to enhance survival and shorten hospital-stays. (3)Regardless of the ama to be used, a risk benefit analysis should be done circumspectly to weigh the risks of toxicity and antibiotic resistance against the intended therapeutic benefit.Types of ADR can be divided into two main kinds. Predictable reactions (Type A or augmented reactions) which are related to theirpharmacological actions including side effects, secondaryeffects and toxic effects. Second type are Unpredictable reactions (type B or Bizarre reactions) which are Non-dose , non - pharmacological actions of the drugs likeallergic reactions and idiosyncrasies.(3) There are Factors that can also induce adverse Drug Reactions. These can be broadly described as Patient-related which includes age ,sex, pregnancy states ,Drug and disease related such as drug dose, frequency and length of treatment and Societal and multi-ethnic factors such as smoking and alcohol use .Further it is essential for every medical institute as well as hospital to have their own antibiotic policies and antibiogram laid down to ensure that optimal choices are made by the prescribers. (4,5) The main aim of our study was to analyze the adverse drug reactions of commonly prescribed antimicrobial agents and identify the incidence of ADR in the in-patient admissions by Medicine unit for six months at a tertiary care teaching-hospital &Research Centre, Kanpur.

MATERIAL AND METHODS

The present study was a retrospective, observational and non-interventional study conducted in association of departmentsof Pharmacology and Medicine. Data was collected from 100 admitted patients in Medicine ward in the teaching hospital and research center, Kanpur. ADRs with antibiotics prescribed were observed and noted from August 2021- February 2022. Patients of either sex and of age groups from 20- 85 years who consented formally were included in our study. Gravely sick, unconscious emergency cases,drug addicts, suicide cases, mentally challenged patients were excluded from our study.Spontaneous ADR reporting technique was used for data collection by reviewing case sheets and treatment charts and consulting the same with prescribing healthcare professionals.

Drug Causality Assessment was performed by Naranjo assessment scale(6) and WHO -UMCassessment was used for severity assessment(7).The outcome of the patients was recorded as probable, possible and definite and as mild, moderate and severe respectively. Unknown and insufficient documentations were not considered in the study(8). The present study was approved by Institutional Ethics Committee of the teaching hospital Kanpur and coordinated with AMC in Kanpur. Final permission was sought from IPC Ghaziabad UP.

RESULTS

A total of 138 ADRswere collected over a period of six months and tabulated in CDSCO form .The data was analyzed and assessment was done on Naranjo assessment scale as well as on WHO-UMC causality assessment scale. The data collected in the study period was number of ADRs reported, commonly prescribed antimicrobial groups and the casuality and severity assessment. Our study showed a male domination (58%, n=100) over females(42% n=100) who were prescribed antimicrobials.(table 1). The data collected also revealed that middle aged patients(age 41-60 years ,54 %) were

predominantly admitted in our hospital followed by geriatric group (61-80 years ,22%) and young patients (20-40 years, 20%).(table 2)It was interesting to observe signs and symptoms of rash (12.31%), pruritis (2.17 %) and inflammatory swelling or urticaria (3.62 %) and oral ulcers (2.89 %) which pointed towards ADRs involving the Skin and mucocutaneous areas.

Table 1: Gender classification

Gender	No. of patients prescribed with antimicrobial drugs(n=100)
Male	58
Female	42

Table 2 : Age groups in patients

Age group (in years)	No. of Patients
20-40	20
41 – 60	54
61-80	22
.> 80	4

Our study also exhibited the next most affected organ due to the ADR of antibiotics was GIT with marked symptoms of and loss of appetite (10.86 %), constipation (7.24%), nausea/vomiting (8.69 %), metallic taste(6.52 %), abdominal pain (5.79 %) and changed stool color (2.89 %) . In the same settingcough and dyspnoea (5.07 % and 3.62 %) appeared in the respiratory system as ADRs of admitted patients .Few patients also reported throat pain (5.07 %) and tinnitus (2.17 %) referring to ENT system involvement. Headache (5.79 %) body-ache (3.62) and joint pains (1.44 %) were suggestive of involvement of musculoskeletal system due to antimicrobial drug therapy.(Table 3)

Table 3: ADRs observed in patients

ADR reported as	No of ADR reported(n=138)	Percentage(%)
Abdominal pain	8	5.79
Headache	8	5.79
Rash	17	12.31
Dysponea	5	3.62
Pruritis	3	2.17
Cough	7	5.07
Changed Color of stool Loss of appetite Body ache Throat pain Tinnitus Joint pain	4 15 5 7 3 2	2.89 10.86 3.62 5.07 2.17 1.44
Diarrhoea	14	10.14
Oral ulcers	4	2.89
Constipation	10	7.24
Nausea /Vomiting	12	8.69
Metallic taste	9	6.52
Inflammatory swelling /urticaria	5	3.62

All the ADRs collected where assessed for their severity. According to Hartwig's assessment scale8), it was found that most of the ADR were of Mild type (n=112, 81.15 %) followed by Moderate type (n=16 , 11.59) and Severe type (n=10, 7.24%). (Table 4). In continuation, causality assessment was also carried out by using WHO causality assessment scale.(9) 114 ADRs (82.6%) fell in the category of "probable" .16 ADRs (11.59%) were "possible" category of the scale. ADRs (5.79 %) were "definite" in our study. (Table 5)In our study period of six months, 100 in patients were also recorded for the use of Antimicrobial classes.Out of all the prescriptions and treatment charts in the ward, fifteen most frequently used Antimicrobial drugs were chosen.Beta-lactamantibioticsgroup (Pipracillin/tazobactum,Ceftrioxone, Amoxicillin /clavulanic acid and cefixime) was most widely used for patient care. Second to it was fluoroquinolones (levofloxacin,ofloxacin and moxifloxacin) and lincosamides (clindamycin). Following it were nitroimidazoles (metronidazole), aminoglycosides (amikacin, gentamycin, kanamycin), macrolides (azithromycin) and urinary antiseptics (nitrofurantoin). (Table 6)

Table 4: Hartwig's Severity Assessment of ADRs

Grade of Severity	Number of ADR (%)
Mild	112 (81.15)
Moderate	16 (11.59)
Severe	10 (7.24)

Table 5:WHO Causality assessment of ADRs

Seriousness	Number of ADR (%)
Definite (>/= 9)	8 (5.79)
Probable(5-8)	114 (82.6)
Possible(1-4)	16 (11.59)

Table 6: Therapeutic Group of Antimicrobials frequently used in patients

Drug group	Drug names	Percentage receivingdrug)
Fluroquinolones	Levofloxacin Ofloxacin Moxifloxacin	59 45 15
Macrolides Lincosamides	Azithromycin Clindamycin	30 60
Aminoglycosides	Amikacin Gentamycin Streptomycin Kanamycin	20 14 42 16
Beta lactam	Pipracillin/tazobactum Ceftrioxone Amoxicillin /clavulanic acid Cefexime	80 36 70 18
Others	Metronidazole Nitrofurantoin	73 54

DISCUSSION :

The first antimicrobial agent was discovered four decades ago which was a milestone in clinical practice. Subsequently there have been major developments for better and more potent antimicrobial drugs. These powerful and prevailing "new drugs" in the market have shown to be lifesaving and in most cases the only therapy available for severe infections. These are a class of drugs which are responsible to reduce the infection worldwide. The infections which show delayed response to one antibiotic can be dealt with provided alternative, in most cases. Consequently, they are also the class of drugs implicated to have higher incidence of ADRs in tertiary care. To minimize that, one must optimize drug usage by establishing strategies to reduce or prevent the occurrence of ADR. Such approaches improve quality of life and diminish health costs.

We observed a male predominance for ADRs with the antibiotic usage. It may be due to greater male patient admission during the study period. Our study is comparable with another similar study conducted by Dhar et al.(2) On the contrary, there was a higher percentage of female patients who reported the ADRs in the studies conducted by Khan et al.(10)and Alam et al.(11). Gupta et al. (12) also noted the same prevalence in gender classification. Our observation on age wise distribution of patients concluded that majority of them were in the middle age of 41-60 years. This observation was alike to the study done by Jose et al.(13) and Suthar et al (14) .It may be credited to the pharmaco-kinetic and pharmaco-dynamic alterations associated with age. It was also seen that the incidence of ADR reporting was higher in

adults (including geriatric age group) due to underlying comorbid conditions.(11). On the other hand, study done by Gupta et al.(12) showed that the young patients (age 21-30 years) were more involved with the ADR than older adults. It can be due to demographic variation and patient difference in that part of South India.

The most affected organ system takenby the ADRs in our hospital was skin. There are well-established ADR profiles of maculopapular or vesico-bullous rashes with the use of drugs like beta lactams and fluoroquinolones. Studies by Liang et al.(15) and Alam MS et al.(11)described itching and purpureal rashes with the use of fluoroquinolones. The extensive usage of aforesaid drug groups resulted in higher skin-relatedADR.C R Jayanthi et al.(16) reported these as Cutaneous Adverse Drug Reaction(CARD), Cefixime and Ciprofloxacin being the common offenders. Cephalosporins are likewise major contributor of ADRs in dermatological category.The difference in the study settings, the patient population studied and the drug preparations available in the hospital , all contributed to the difference and variations of the ADRs amongst various studies available.

In the current study, we deduced that most of our data on ADR were of "mild" type (81.15%) and were managed conservatively. 11.59 % of the data indicated that they were "moderate" type trailed by "severe" type (7.24%). Our study re-established the data published by C R Jayanthi et al.(16) The incidence of finding "severe" ADR in the range of 7.24 % in our study is in concordance with the author who also showed a higher incidence. Raja S et al.(17) substantiated a lower incidence of "severe" type of ADR.

Conferring the WHO Causality assessment scale, 82.60 % of ADR were "probable". 11.59 % ADR were "possible" and 5.79 % was "certain" in nature. It is in consonance with the study carried out by Khan et al.(10) who concluded that 55% of the ADRs were probable followed by 42.5 % as possible ADR. The majority of ADR reported by Alam MS et al.(11) were of "probable" nature. The above said was also verified by the study conducted by C R Jayanthi et al.(16) who interpreted that the majority of ADRs were of probable(72%) nature followed by possible(22%) ones. One similar study was also conducted by Gupta et al.(12) in southern part in India citing the same results.

Our study has few limitations. Firstly, we excluded the paedriatic population and considered only the young(>20) and adults (including geriatric patients). AndSpontaneous reporting of the ADRs and retrospective study doesn't eliminate under reporting. Further, more studies involving larger study groups which include paediatric patients also, may be prudent for appropriate drug therapy of diseases.

SUMMARY AND CONCLUSION

Increasing number of new drugs especially antibiotics entering the market marks for a more judicious drug use in all types of population. Cautious use of these life saving drugs pivots around to minimize ADR and maximize the benefits. Every clinician and healthcare worker should be encouraged to recognize and report any ADRencountered .

ADR monitoring is a remittent and constant process needing active participation by all to impart better patient care. Majorly the ADR are preventable by early detection and management .Beta lactams and fluoroquinolones were the significant groups to cause ADR .There were a few severecases, but no death was reported .

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