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Pattern of spontaneously reported adverse drug reactions in ANIIMS Port Blair

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Abstract

Background: The data pertaining to Adverse drug reactions is very limited especially in India. Adverse drug reactions are known to cause mortality and increased morbidity and hence increase the burden of disease. Therefore this study was done over a period of 18 months to assess the causality of adverse drug reactions, nature of their seriousness and to know if they could have been prevented or not.

Materials & Methods: A number of spontaneous reports of ADR's were included in the study over a period of 18 months from June 2015 to December 2016 reported from different clinical Departments of ANIIMS, Port Blair. The World Health Organization (WHO) definition of an ADR and its seriousness was adopted. The organ system involvement was labeled by WHO-ADR terminology. ADRs were analyzed for causality by Naranjo's algorithm.

Results: A Total of 200 reactions were reported in this time period, and out of these, most common Adverse drug reactions were Hypersensitivity reactions accounting for more than half of cases ie 54 %. A look at the causative agents revealed antimicrobials as the commonest agents causing these ADR's 48%, followed by drugs affecting GIT 20%, then autacoids 10%. Of these, about two-thirds of the reactions i.e. almost 65% were classified as probable and one-tenth were classified as preventable. Serious ADRs were 0.25 per 1000 patients.

Conclusion: Most of the ADR's were caused by Antimicrobial Agents, and further large sample size studies are needed to confirm the association of particular Drugs with the ADR's.

Keywords: Pharmacovigilance, Adverse drug reaction monitoring, Serious ADR's, Causative Agents..

1. Introduction

Adverse drug reactions (ADRs) are a major part of healthcare system as they are leading to prolongation of hospitalization, rising economic burden, and mortality.[1,2] Women, elderly, polypharmacy and the evolution of new drugs are important risk factors for ADRs.[3] Other important factors for their occurrence are race, pregnancy, breastfeeding, alcohol intake, and state of liver and kidney functions.[4] Antimicrobial agents followed by analgesic agents are most frequently ADRs encountering class of Drugs. However, patterns of ADR's and causative drugs may vary because of different prescribing habits, emergence of newer drugs and referral bias.[5,6] Most of these ADRs can be prevented and it may substantially decrease the overall cost of Healthcare system.[7]

It is because of the spontaneous reporting system that many drugs are withdrawn from the market for the safety concerns.[8] India does not have its own database of Adverse Drug Reactions. Therefore this study was conducted to analyze the causative agents responsible for ADRs, its seriousness and other clinical patterns in a tertiary care teaching hospital like ANIIMS Port Blair.

2. Materials & Methods

This study was conducted over a period of 18 Months from June 2015 to December 2016 after prior

approval from the institutional ethics committee. Suspected ADR reporting form of Central Drug Standard Control Organization (CDSCO) India was used in this study for the reporting of ADRs. Monthly analysis of reported ADRs was done and results were compiled accordingly.

2.1 Inclusion Criteria

All suspected reactions following justifying the WHO's definition of ADR were included in the study.

2.2 Exclusion Criteria

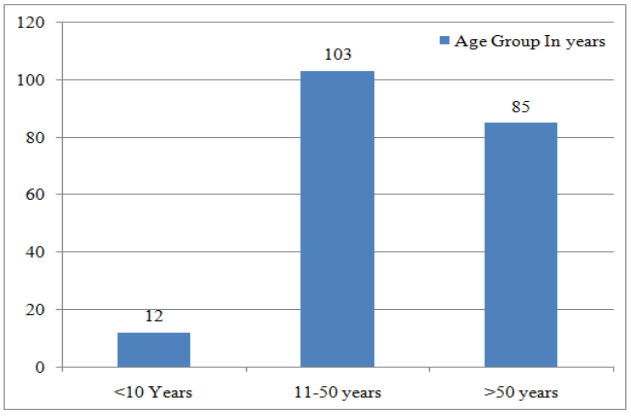
1. Cases of drug poisoning
2. Medication errors
3. Unestablished causality
4. ADR forms with insufficient information were excluded

Data thus collected was extracted in Excel sheet using a structured format. The age group, gender, diagnosis, drugs, organ system involved, types, onset of reactions, outcome, causality, seriousness, were presented in proportions and statistical analysis was done. Coding of the suspected drugs was done as per WHO-anatomical therapeutic chemical classification.[9] The organ system involvement for ADR was labelled per WHO-ADR terminology.[10] ADRs were classified in to three categories for the onset of reactions: acute those occurring within 1 hr of administration of suspected drugs, subacute those occurring within 1-24 hrs of administration of suspected drugs and latent those developed after 2 days of administration of suspected drugs. ADRs were also categorized into two types - augmented (A) and bizarre (B) as per Rawlins and Thompson classification.[11]

3. Results and Observations

During the study period, a total of 212 ADRs were reported. Of 212 reactions, 12 reactions were excluded for the doubtful causality by Naranjo's algorithm. A total of 200 Adverse Drug Reactions were included in the study. A total of 40 ADRs (20%) were reported as serious adverse drug reactions.

Figure 1: Distribution of patients based on age group



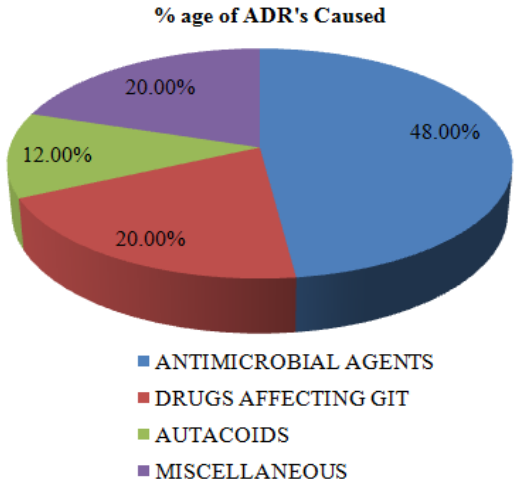
The above table shows the distribution of patients having ADR's based on their age group as 12 patients(6%) out of 200 were in the age group of less than 10 years, maximum number of patients were in the age group of 11-50 years i.e. 103 patients(52%), and 85 patients (42%) in the age group of >50 years.

Also the female patients (56%) had higher adverse reactions than males (46%). The Male: Female ratio was 1:1.2.

Table 1: Distribution of patients based on type of ADR'S

System	Adverse drug reactions	No. of patients (%)
GIT Disorders	Diarrhoea (38), oral ulcer (10), nausea & vomiting (12), constipation (5)	32.5%
Skin Disorders	Maculopapular rash (22), Fixed drug eruptions (8), contact dermatitis (3), acneform eruption (2), photosensitivity (1)	18.0%
Anaphylatic/ Hypersensitivity	Immediate hypersensitivity (14), anaphylaxis (8)	11.0%
Respiratory Disorders	Cough with expectoration (10), dyspnoea(2)	6.0%
CNS Disorders	Extrapyramidal symptoms (6), giddiness (2), sedation (2), insomnia (1)	5.5%
Reproductive System	Menstrual irregularities(8)	4.0%
Miscellaneous	Weight gain(15), Hearing loss(11), itching (7), decreased vision(6), Generalised pain abdomen (7)	23.0%

Figure 2: Distribution of patients based on group of drugs causing ADR'S



The above pie chart explains the Percentage of ADR's caused by certain group of drugs and this includes Antimicrobial agents as the forerunner with 48% of ADR's and includes Ceftriaxone (20 patients), Ciprofloxacin (17 patients), metronidazole (13patients), beta lactams (12 patients).

Table 2: Outcome of the adverse drug reactions

After dechallenge was done/stopping the drug	% of patients (Total= 200)
1. Improved	180 (90%)
2. Not improved	20 (10%)
Final Outcome	
1. Fatality	0%
2. Recovered	160 (80%)
3. Recovering	20 (10%)
4. Unknown/Lost Follow Up	20 (10%)

The above table describes the Outcome of the reactions suffered by the patients. Out of 200 adverse drug reactions, the withdrawal of suspected drugs i.e. dechallenge was performed in 200 (100%) ADR's. A total 180 (90%) reactions showed improvement after dechallenge and 20 patients (10%) showed no improvement.

Table 3: List of suspected drugs which caused these ADR'S

Class of drugs which caused ADR'S	% of patients
Antimicrobial Agents	**96(48%)**
β-lactam antibiotics	30(15%)
Fluroquinolones	22(11%)
Antitubercular drugs	18(9%)
Nitroimidazoles	14(7%)
Other antibiotics	12(6%)
Drugs affecting GIT	**40(20%)**
Anti-Ulcer Agents	24(12%)
Anti-diarrhoeal Agents	12(6%)
Autacoids	**20(10%)**
NSAIDS	**18(9%)**
I.V fluids & Miscellaneous	**26(13%)**

4. Discussion

This study showed high incidence of ADRs in females as the ratio of male: female was 1:1.2. Female gender is considered important risk factors for ADRs.[3,4] some of the studies done in india also showed the higher incidence of ADR's in female population.[12,13,16]

The incidence of ADR's was highest in 11-50 years age group patients in this study which is similar to the result shown by the studies of Venkatesan *et al*[14], Rajkannan *et al*[15] and Rao *et al*[16] This study showed the most common reaction as hypersensitivity reaction with use of antimicrobial agents which is similar with many epidemiological studies.[7,13,15,16] and second most common reactions as Gastrointestinal reactions which is similar to some other studies done.[12,14-16]

5. Conclusion

This study concludes that patients of 11-50 years age group and females experienced more ADRs. The commonly observed ADRs were hypersensitivity reactions and that caused due to drugs affecting gastro-intestinal system. Central and peripheral nervous system disorders and body as a whole - general disorder were associated with serious reactions. The commonly implicated pharmacology groups were β-lactams and fluoroquinolones, followed by autacoids and NSAIDS. Anaphylactic reactions with use of antimicrobials were also noted. The possibility of underreporting due to spontaneous nature of the study is not ruled out. One important factor is physicians' lack of interest for reporting and documentation of well-established drug-ADR pair. There should also be active involvement of private hospitals/ practitioners to have more data about the newer drugs. The reporting of ADR's should be made mandatory and this should be applicable to private hospitals and other levels of health care systems.

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Conflicts of Interest- None

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