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MONITORING AND ASSESSING ADVERSE DRUG REACTIONS AT A TERTIARY CARE TEACHING HOSPITAL, BANGALORE.

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ABSTRACT

OBJECTIVES: To determine the prevalence, nature, probability, severity and preventability of ADRs in a hospital settings. **METHODOLOGY:** A prospective, observational study was conducted in the Medicine and Pediatrics wards, between December 2013 and August 2014. All in-patients who experienced an ADR and admissions due to an adverse drug event were included in the study. Probability (Narinjo and WHO-UMC scales), severity (Hartwig et al scale) and preventability (Shumock and Thornton preventability scale) were assessed. **RESULTS:** Over the study period of 9 months, a total of 153 ADRs were reported in 94 patients in which [7(4.57%)] were ADRs induced hospital admission. ADRs were higher in patient in the age group of 61-70 years [34(22.22%)], female predominance of gastro – intestinal reactions [72(47.05%)] was observed. Therapeutic classes of drugs frequently associated with ADRs were anti-microbial agents [57(37.25%)] followed by antihypertensive agents [11(7.18%)]. The most common drugs involved in causing ADRs were ceftriaxone and tramadol. The most commonly reported ADR was vomiting [23(15.03%)]. Of the 153 ADRs, [132(86.27%)] was probable and [11(7.18%)] was possible, [15(9.8%)] of the ADRs were possible and [10(6.53%)] were certain. Majority of the ADRs were of moderate severity [145(94.77%)]. Of the 153 ADRs, [17(11.11%)] were preventable and [35(22.87%)] of the ADRs were not preventable. Majority of the ADRs [117(76.47%)] were managed without withdrawing the suspected drug. A recovery rate of (95.43%) was achieved. **Conclusion:** The importance of adverse reactions is often underestimated. They are common and can be life threatening and unnecessarily

expensive. Vigilance by clinicians in detecting, diagnosing and reporting adverse reactions is important for continued drug safety monitoring.

KEYWORDS: Adverse drug reaction, Monitoring, Hospital.

INTRODUCTION

An adverse drug reaction is any injury caused by taking a medication. ADR's may occur after a single dose or prolonged administration of a drug or results from the combination of two or more drugs. The meaning of this expression differs from the meaning of "side effects", as the last expression might also imply that the effects beneficial. Several definitions of ADR's exists; World Health Organization defines adverse drug reaction as "Any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of diseases, or for the modification of physiological functions".[1]

Patients above the age of 65 years are found to be the prime users of prescription and non-prescription medications, the use of medications among elderly as become more than double since 1990.[2] Physiological and pathological changes observed in elderly population may lead to altered pharmacokinetics of administered drugs.[3] Also, in appropriate prescription of medications due to wrong dose, incorrect frequency of administration, prescribing in effective medication, prescribing the wrong medication or duplicate therapy may lead to many unintended effects.[3,4]

ADE is an untoward medical occurrence that may occur during the treatment with medicines, but may not necessarily have a causal relationship with the treatment. Preventable ADE's are associated with substantial morbidity, increased mortality, a longer length of stay in the hospital and costs.[5,6]

OBJECTIVES

To study the extent, incidence and severity of ADRs and assess the causality, probability, severity and preventability of ADRs. To see the underlying reasons of ADRs like idiosyncrasy and to motivate the health care professional to report ADR.

METHODOLOGY

A prospective observational study was carried out at St. Philomena's hospital, Bangalore. The study was carried out for a period of 9 months from December 2013 – August 2014.

Ethical committee clearance was obtained from the Institutional Ethical committee of St. Philomena's hospital, Bangalore. The study includes all in-patients who experience an adverse drug reaction (ADR) from Medical and Pediatric departments except those patients with intentional and accidental Poisons and drug abuse.

During the study patient's data such as demographic details, past medical history, Present medical condition and Patient's known allergies were documented. Adverse drug related data such as brief description of reaction, date of onset of reaction, ADR in relation to Hospital admission and suspected drug/s, their therapeutic class, dose, route, frequency and date of starting and stopping.

RESULTS

During the 9 months study period from December 2013 to August 2014, a total of 153 ADRs were observed in 94 patients In which 7 were ADRs induced hospital admission, whereas, 146 ADRs (95.42%) occurred after hospitalization. ADRs induced hospital admission, comprising (4.57%), whereas, 146 ADRs (95.42%) occurred after hospitalization.

Demographic details of the patients suffering from ADRs were studied and it revealed that females were more susceptible to ADRs than males, with 96 females (62.74%) developing an ADR as compared to 57 males (37.25%).

Our study revealed that the incidence of ADRs was higher in patients in the age group 61-70 years. 34 patients, (22.22%) developing ADRs followed by those in the age group 51-60 years with 29(18.95%) developing ADRs.

Our study revealed that the most common drugs involved in causing ADR related hospitalization were metronidazole, ceftriaxone and tramadol. The ADRs are vomiting caused by Metronidazole, Ciprofloxacin, and Tramadol. Ceftriaxone, amoxicillin caused Diarrhoea.

The most common anti-microbial class associated with ADR was cephalosporin [24(42.10%)] followed by nitro-imidazole [20(35.08%)]. Metronidazole (n=12) was the most common drug to cause ADRs followed by ceftriaxone (n=12), Amoxicillin (n=7), clindamycin (n=5), cefuroxime (n=4), levofloxacin (n=3), cefaperazone (2), ciprofloxacin (n=1), Ofloxacin (n=1), Meropenem (n=1) and Ampicillin (n=1).

The most commonly implicated antihypertensive drug was angiotensin receptor blockers [8(32%)] followed by calcium channel blocker, mainly amlodipine (n=8) followed by furosemide (n=5), losartan (n=5), Olmeseratan (n=3), Metoprolol (n=3) and Verapamil (n=1).

Table 1: Clinical Presentation of ADRs

System	ADR	No. of cases	Percentage%
Gastrointestinal tract	Vomiting Diarrhoea Nausea Abdominal discomfort Constipation Gastritis Bad taste & dry tongue Throat irritation	23 15 10 6 12 1 4 1	47.05
Dermatologic	Itching Rashes	6 6	7.84%
Neurologic	Insomnia Headache Giddiness Drowsiness Dizziness Shivering	5 7 5 3 3 1	15.68%
Endocrine	Hypoglycaemia Menstrual ir-regulation	3 1	2.61%
Hematologic	Anaemia	2	1.30%
Cardiovascular	Tachycardia Hypotension Hypertension	2 4 1	4.57%
Respiratory	Cough	14	9.15%
Renal	Dysuria	3	1.96%

Table 2: Therapeutic drug classes implicated in ADRs

Therapeutic Class	Number of ADRs	Percentage %
Antimicrobials	57	37.25
Analgesics	11	7.18
Anti-psychotics	1	0.65
Steroids	1	0.65
Antidiabetic Agents	8	5.22
NSAIDs	8	5.22
Anti-hypertensive	25	16.33
Anti-convulsant	6	3.92
Anticoagulant	1	0/65
Anti-depressant	1	0.65
Anti-platelet	1	0.65
Anti-histamine	1	0.65
Anti-emetic	6	3.92
Folic acid Supplement	4	2.61

Cardiovascular agent	4	2.61
Anti-asthmatic	3	1.96
Anti-muscarinic	4	2.61
Laxatives	3	1.96
Anti-cancer	1	0.65
Oral contraceptives	1	0.65
Anti-inflammatory bowel disease	2	1.30
Steroid	1	0.65

Table 3: Rawlins and Thompson's Classification of ADRs

Reaction Type	Number of ADRs	Percentage (%)
Type A	142	92.81%
Type B	11	7.18%

Table 4: Causality Assessment of ADRs using Naranjo's Scale

Score	Total Number of ADRs	Percentage (%)
Definite	10	6.53
Probable	132	86.27
Possible	11	7.18
Doubtful	0	0

Table 5: Causality Assessment of ADRs using WHO-UMC Scale

Score	Total Number of ADRs	Percentage (%)
Certain	10	6.53
Probable	128	83.66
Possible	15	9.80
Unlikely	0	0
Unconditional	0	0
Unassessable	0	0

Table 6: Severity assessment of ADRs using Hartwig scale

Severity	Number of ADRs	Percentage (%)
Mild	7	4.57
Moderate	145	94.77
Severe	1	0.65

Table 7: Preventability of ADRs using Shumock and Thornton's Scale

Score	Number of ADRs	Percentage (%)
Definitely Preventable	17	11.11
Probably Preventable	101	66.01
Not Preventable	35	22.87

Table 8: Management of ADRs

Fate of suspected drug	Number of cases	Percentage (%)
Drug Withdrawn	17	11.11
No change (continue same drug)	117	76.47

Alternate drug	14	9.15
Dose altered	5	3.26

Table 9: Outcome of ADR

Outcome	Number of cases	Percentage (%)
Recovered	146	95.43
Not Recovered	7	4.57

DISCUSSION

During the course of treatment or after, some drugs prescribed to patients produce certain effects other than those desired or expected. These adverse effects cause concern both to the physician and the patient, adding to the spiraling costs of medical treatment, morbidity and mortality. They rank between the fourth and sixth leading cause of death.[5]

A prospective observational study was carried out at St. Philomena's Hospital which was carried out for a period of 9 months from December 2013 to August 2014.

In our study, 94(62.74%) ADRs were observed with females and 57 (36.25%) with males. The numbers of ADRs were high among the females than the males. These gender based differences observed were consistent with the observations of the various investigators like Agouzal et al[6], Jha et al[7] and Kelly.[8] The reason for the high incidence of ADR in females would be due to the differences in perception of ADRs, pharmacology of ADRs, differences in kinetic such as volume of distribution, polypharmacy and hormonal differences.

Incidence of ADRs was higher with age group between 61-70, this account about (22.22%) of the total patients recruited and (18.95%) observed with the age 51-60. Our study results were consistent with the results of Jha et al[8] ADRs are logically considered to be more frequent in the elderly due to polypharmacy, poor compliance, concurrent medical illness and alterations in pharmacokinetic and pharmacodynamic parameters.

Out of 153 ADRs reported 7 (4.57%) were the reason behind hospitalization. Whereas 146(95.42%) ADRs occurred during the hospital stay. Our study showed that the number of ADR induced hospital admissions were low compared to the reported incidence in the literatures, such as Bates.[9] The incidence rates of ADR induced hospitalizations in their study was 16.1%.

It was observed that several organ systems were affected by medications. However in our study, the highest frequency of ADRs occurred in gastrointestinal system 72(47.05%) manifesting as diarrhoea, vomiting, abdominal pain, constipation and gastritis. The second most commonly affected organ system was neurological system 24(15.68%) of the total cases. The results were comparable with the study conducted by Meena Shrivastav et al.[10]

The most common class of drugs that exhibited adverse reaction was antibiotics 57(37.25%) followed by antihypertensive 25(16.33%). The reports were consistent with the study conducted by Sharma H et al[11] and Agouzal et al.[6] In a study conducted by Sharma et al and Agouzal et al, antimicrobials were the second most cause of ADRs while antihypertensive and anti-inflammatory drugs topped the list.

Among Antibiotics, ceftriaxone 24(42.10%) and Metronidazole 20(35.08%) were the most common drugs implicated in causing ADRs which was consistent with the reports of Uday Kumar.[12]

The most commonly reported ADRs were vomiting 23(14.64%) followed by nausea 15(9.80%) and cough 14(9.15).

Causality assessment was performed by using WHO and Naranjo scale. The assessment by WHO scale revealed that 128(83.66%) of the reactions were probably drug related, 15(9.8%) of the reactions were possible drug related, whereas 10(6.53%) of the reactions were classified as certainly drug related. Assessment by Naranjo scale showed that 132(86.27%) of the reactions were probably drug related whereas 11(7.18%) of the reactions were possibly related to the drug. These findings were similar with the reports of Jose J, Rao PG.[13]

Severity of the suspected ADRs was assessed using modified Hartwig and Seigel scale, which revealed that 1(0.65%) of the reactions were severe 145 (94.77%) of the reactions were moderate and 7(4.57%) of the reactions were mild in severity. These data were comparable with the review conducted by Dilip C which reported that the Majority of the reactions were moderate 25(56.818%).[14]

Preventability of the suspected ADRs were assessed using Modified Schumock and Thornton scale, revealed that 17(11.11%) of the reactions were definitely preventable while

101(66.01%) were probably preventable and 35(22.87%) were not preventable which is in concurrence with the study carried out by Thomas et al.[17]

Rawlins and Thompson criteria were used to classify the ADRs and the observed ADRs were classified as Type A and Type B. Our study showed that majority of the ADRs was of Type A 142(92.81%). The predominance of Type A reactions has been reported in the study carried out by Jose J, Rao PG[13], Type A reactions represented 72.5% of all ADRs leading to hospital admissions.

In our study, the management of ADRs was such that in most of the cases the suspected drug was continued 117(76.47%), whereas in 17(11.11%) of the cases the suspected drug was discontinued and in 5(3.26%) of the cases an alternate dose was given.

CONCLUSION

In our study, it was found that, a large number of ADRs were type A, some were severe and life threatening and occurred during hospital stay hospitalization. Most of the ADRs were because of commonly used drugs like anti-microbials and a large percentage of them were probably/definitely preventable. This indicates that ADRs are a non-negligible burden on patients and the healthcare system.

The importance of adverse drug reactions is often underestimated. They are common and can be life threatening and unnecessarily expensive. Vigilance by clinicians in detecting, diagnosing and reporting adverse reactions is important for continued drug safety monitoring. Measures to improve detection and reporting of ADRs, by all healthcare professionals should be undertaken to enhance our understanding of the nature and impact of ADRs. With this information, our management of ADRs might be improved and more importantly, ADRs might be prevented by implementing strategies to target specific drugs that are commonly suspected.

Suggestions for improvement in ADR reporting and monitoring:

1. Each hospital should build local 'Pharmacovigilance unit' for disbursement and collection of ADR reporting forms.
2. Pharmacovigilance workshops for health care professionals should be initiated.
3. Positively changing the mind-set, so that ADR reporting becomes an accepted and understood routine.

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