

## Research Article



## Monitoring and Reporting of Adverse Drug Reactions in A South Indian Tertiary Care Hospital

Palanisamy Sharmila Nirojini\*, Raghavendra Yemineni, Rama Rao Nadenla

Department of Pharmacy Practice, Chalapathi Institute of Pharmaceutical Sciences, Lam, Guntur.

\*Corresponding author's E-mail: [niro\\_shar@yahoo.co.in](mailto:niro_shar@yahoo.co.in)

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### ABSTRACT

Globally there is growing concern about the safe use of medications in hospital settings. It is well known that adverse drug reactions (ADR) constitute a major problem in drug therapy and in our society, both as a health care problem and as an economic burden. However ADR monitoring and reporting activity is in its infancy stage in India. Hence we undertook a prospective, observational study for nine months to record and analyze adverse drug reactions among all patients admitted to the neurology department of a tertiary care hospital. A total of 295 patients, 218 men and 87 women using drugs for central nervous system related disorders were entered the study, among them 157 patients 108 men and 49 women were experienced 199 adverse drug reactions. Upon age distribution of ADRs in patients, adult patients experienced 58.58% of ADRs followed by geriatrics 41.42%. Majority of patients (68.79%) who developed an ADR were male. Central nervous system and gastrointestinal system disorders were the most common and frequent classes affected with ADRs. Headache (21.65%), sedation (11.46%), sweating (10.19%) insomnia (8.91%) and dizziness (8.91%) were the most frequent reactions. The highest rate of ADRs was recorded to be induced by anti-platelets (aspirin and clopidogrel) 45 (22.61%) and lowest rate was found with anti-manic drug like lithium carbonate 1 (0.50%). Majority of the ADRs 161 (80.90%) were scored probable, 33 (16.58%) possible, 03 (1.50%) unlikely and 2 (1%) definite, 148 (74.37%) reactions were mild 50 (25.12%) moderate and one (0.50%) were severe. Withdrawal of offending drug was necessary in 15 patients; the treatment is continued for 142 patients. This study found that much more knowledge to be needed to the healthcare professional to reduce the incidence of adverse drug reactions. By regulating the ADR reporting system in India can controls the adverse events.

**Keywords:** Adverse Drug Reactions, Neurology, Causality Assessment.

### INTRODUCTION

Adverse drug reactions have been creating headlines over the last forty years since the thalidomide tragedy. International attention to patient safety has been growing significantly since the publication of the US Institute of Medicine report "To err is human: building a safer health system".<sup>1-3</sup> Voluntary adverse drug reaction (ADR) reporting schemes have operated since the early sixties in many Western countries.<sup>4</sup> These surveillance systems enable physicians and pharmacists to report suspected ADRs and thus act as a tool to identify new ADRs and risk factors predisposing to recognized ADRs. Adverse drug reactions (ADRs) are global problems of major concern.<sup>5, 6</sup> They affect both children and adults with varying magnitudes, causing both morbidity and mortality.<sup>7</sup> In addition to the human costs, ADRs have a major impact on public health by imposing a considerable economic burden on the society and the already stretched health-care systems.<sup>8,9</sup> Post marketing surveillance of drugs is very important in analyzing and managing the risks associated with drugs once they are available for the use of the general population. Spontaneous reporting has contributed significantly to successful Pharmacovigilance. The information presented above clearly suggest a significant number of people suffering from these diseases, the number of drugs consumed per patient is relatively predictable and thus ADRs are inevitable, which needs continuous monitoring.<sup>10</sup> Drugs acting on central nervous system like

thrombolytics, antiplatelets, antiepileptics, antipsychotics, anxiolytics were prescribed with associated side effects like extrapyramidal symptoms, insomnia, sedation and even serious effects like increasing suicidal tendency and depression.<sup>11</sup> The main aim of this study was to determine the prevalence of ADRs associated with drugs prescribed in neurology and psychiatric department's hospitalized patients and to examine their prevalence rates, to study the incidence and the pattern of ADRs occurring in this hospital, to assess the causality, to identify the offending drugs, to establish a causal relationship with the suspected drug, to identify suspected ADRs and to establish their frequency of occurrence.

### MATERIALS AND METHODS

The prospective observational study was conducted for a period of nine months in the neurology department in a tertiary care hospital in South India. This study was approved by the institutional human ethical committee. All patients either sex visited in the neurology departments during the study period were evaluated for drugs induced adverse reactions; patients developed with ADR during hospital stay or hospitalized due to ADR were included in the study. Patient previously used or newly started on drugs prescribed for central nervous system related problem were monitored and followed for detecting and recording of ADRs. Adverse drug reactions were detected by daily interviewing patients, consulting with physicians and reviewing patient charts. World



health organization (WHO) definition for ADR was adopted. If a sign or symptoms suspected to be induced by drugs was found and the ADR notification form was filled. Patient demographics were recorded. The time of onset and duration of the reaction, suspected drug, outcome and actions taken for managing the adverse reaction were recorded. Causality and severity assessments were performed by using Naranjo's ADR probability scale and modified Hartwig scale respectively.<sup>12, 13</sup>

## RESULTS

A total of 295 patients, 218 men and 87 women using drugs for central nervous system related disorders were entered the study, among them 157 patients 108 men and 49 women were experienced 199 adverse drug reactions (Table 1). Upon age distribution of ADRs in patients, adult patients experienced 58.58% of ADRs followed by geriatrics 41.42% (Table 2). Majority of patients (68.79%) who developed an ADR were male. One thirty two patient experienced atleast one ADR, there were 25 patients who developed more than one ADR, two ADRs in 22 patients (14.01%), more than two ADRs in 3 patients (1.91%) (Table 4), maximum of three reactions were observed with single patient and maximum of four drugs were suspected for the reactions. A total of 157 hospitalized patients experienced an ADR; only ten patients were admitted in the hospital due to ADR. Central nervous system and gastrointestinal system disorders were the most common and frequent classes affected with ADRs. In Table 6, Headache (21.65%), sedation (11.46%), sweating (10.19%) insomnia (8.91%) and dizziness (8.91%) were the most frequent reactions. Skin rashes (7.64%), muscle pain (7%) somnolence (5.73%) fatigue (3.82%) also occurred frequently. Rhabdomyolysis (0.63%) observed with a patient due to statins. Hypothyroidism occurs with lithium carbonate prescribed for severe headache due to neurons degeneration. The highest rate of ADRs was recorded to be induced by anti-platelets (aspirin and clopidogrel) 45 (22.61%) and lowest rate was found with anti-manic drug like lithium carbonate 1 (0.50%).

**Table 1:** Gender distribution of patients (n=157)

Gender	Number of patients and percentage (n=157)
Male	108 (68.79%)
Female	49 (31.21%)

**Table 2:** Age wise distribution of patients

Age	No. of patients	Percentage
18-29	12	7.64%
30-49	36	22.92%
50-59	44	28.02%
60 above	65	41.42%

**Table 3:** Number of medication caused ADRs

Number of medications	Number of patients and percentage (n=157)
Single drug	74 (47.13%)
2 drugs	27 (17.19%)
3 drugs	38 (24.20%)
4 drugs	18 (11.46%)

**Table 4:** Number of reactions per patient

Number of reaction /patients	Number of patients and percentage (n=157)
One	132 (84.07%)
Two	22 (14.01%)
More than two	3 (1.91%)

**Table 5:** Systems associated with adverse drug reactions

System affected	Number of ADRs (n=199)	Percentage of ADRs
Central nervous	74	37.18%
Gastrointestinal	28	14.07%
Musculoskeletal	12	06.03%
Dermatology	12	06.03%
Cardiovascular	02	1.00%
Metabolic changes	02	1.00%
Endocrine	01	0.50%

**Table 6:** Reported Adverse Drug Reactions

Suspected adverse drug reactions	NO. of ADRs (n=199)	Percentage of ADRs
Headache	34	21.65%
Sedation	18	11.46%
Sweating	16	10.19%
Insomnia	14	8.91%
Dizziness	14	8.91%
Skin rashes	12	7.64%
Abdominal pain	11	7.00%
Muscle Pain	11	7.00%
Somnolence	09	5.73%
Cough	08	5.09%
Vomiting	06	3.82%
Fatigue	06	3.82%
Decreased Co-Ordination	04	2.54%
Nervousness	04	2.54%
Weakness	04	2.54%
Diarrhoea	04	2.54%
Constipation	04	2.54%
Dry mouth	03	1.91%
Slurred speech	02	1.27%
Loss of appetite	02	1.27%
Ataxia	02	1.27%
Weight gain	02	0.63%
Urinary retention	01	0.63%
Tachycardia	01	0.63%
Rhabdomyolysis	01	0.63%
Apnoea	01	0.63%
Dysarthria	01	0.63%
Mental confusion	01	0.63%
GI ulcer	01	0.63%
Hypothyroidism	01	0.63%
Peripheral ademia	01	0.63%



**Table 7:** Management of ADR

Treatment	No. of ADRs	Percentage of ADRs
Withdrawing offending drug	15	7.53%
Systemic treatment for ADR	22	11.05%
Substituted another drug	32	16.08%
Reduced the dose	57	28.64%
Continue same	72	36.18%
Change in route of administration	1	0.50%

**Table 8:** ADR Distribution according to the Naranjo's Algorithm Probability scale

Naranjo's scale	No. of	Percentage
Probable	161	80.90%
Possible	33	16.58%
Unlikely	03	1.50%
Definite	02	1.00%

**Table 9:** Severity of ADRs According to Modified Hartwing and Siegel Scale

Severity of ADRs	No. of ADRs (n=199)	Percentage of ADRs
Mild	148	74.37%
Moderate	50	25.12%
Severe	01	0.50%

When analyses ADRs by Naranjo ADR probability scale, majority of the ADRs 161 (80.90%) were scored probable, 33 (16.58%) possible, 03 (1.50%) unlikely and 2 (1%) definite (Table 8). Severity of ADRs were analyzed with modified Hartwig scale 148 (74.37%) reactions were mild 50 (25.12%) moderate and one (0.50%) were severe (Table 9). Moderate reactions were commonly observed with female, mild and severe ADRs were more common in male. Withdrawal of offending drug was necessary in 15 patients, the treatment is continued for 142 patients. The identified Dose was altered in 27 cases and 32 suspected drugs were replaced with other agents in 32 cases, 22 cases were continued with the same drugs, and one reaction was managed by changing its route of administration (Table 8). Of the total of 199 ADRs most (80%) were non-preventable; whereas (12%) were probably preventable and only 8% were definitely preventable.

## DISCUSSION

In our study we enrolled 295 patients admitted in the neurology and psychiatric department. Among them 157 patients 108 men and 49 women where experienced at least one adverse drug reaction. Only 18(11.5%) (ADRs were the sole cause of hospital admission, while the remaining 139 (88.5%) ADRs occurred during the hospital stay. Our study found high numbers of ADRs were occurred during hospital stay. Our figure is higher than

the study conducted by Sharon John et al (62.73%). Demographic details of the patients, Adult patients experienced 58.58% of ADRs followed by geriatrics 41.42%. Many of the drugs used for psychological and neurological problem were induced adverse drug reaction to the adult patients when compared to that of older patients. Same result was observed with Meyer, he reported antipsychotic drugs induced adverse drug reactions were lower than that seen in younger adult. Male (68.79%) predominance was noted over female (31.21%), which was similar to the findings Piparva et al.<sup>14</sup> Several other studies have found that ADRs are more common in females than in males. We observed a predominance of central nervous system 74 (37.18%) followed by gastrointestinal system 28 (14.07%) this is in concurrence with the study conducted by Padmaja et al<sup>15</sup> and Piparva et al. this may be the selection of department, because CNS acting drugs mostly induced CNS related side effects. There were seven different classes of drugs acting on central nervous system cause 199 ADRS. It was observed that anti-platelet drugs cause higher percentage 45(22.61%) followed by antidepressants 34 (17.08%), which is similar to the findings of Sharmila et al.<sup>16</sup> lowest rate was found with lithium carbonate used in bipolar disorder induced severe headache. Headache 34 (21.65%), sedation 18 (11.46%), sweating 16 (10.19%), insomnia 14 (8.91%), dizziness 14 (8.91%) are common adverse effects observed with these classes of drugs our result is consistent with the review Padmaja et al. Sever adverse drugs reactions were also observed significantly like rhabdomyolysis 1 (0.63%) and hypothyroidism 1 (0.63%) due to statins and lithium respectively. The suspected adverse drug reactions were assessed for its causality by Naranjo's algorithm probability scale.

It was observed that majority of the reports were rate as probable 163 (80.90%), possible 33 (16.58%), unlikely 03 (1.50 %) and definite 02 (1%). Probable reactions were more in our study, which his consistent with Sharon John et al.,<sup>17</sup> and Sharmila et al., regarding severity of drugs majority of our patients had mild reactions 148 (74.37%), 25.12% had moderate to severe reactions only one reactions is fatal. Various other studies have showed an incidence of ADR 5.3% in Bates et al.,<sup>8</sup> and 15.8% in Davies et al.<sup>19</sup> 7.53% ADRs were managed by withdrawing the offending drug, 11.05% ADR had to be treated with another drug adding to the cost of therapy and prolonging hospitalization. Cassen et al.,<sup>20</sup> have proved in a study that attributable lengths of stay and costs of hospitalization. A study conducted by Bates et al have estimated the annual cost to treat drug induced adverse events for a 700 bed teaching hospital is 5.6 million dollars. 28.64 % ADRS were managed by reducing the dose of drug and 36.18% reactions were not treated by any of the above method, may the reason many of the reported adverse drugs reactions were mild reactions it can be tolerable.

**CONCLUSION**

By our study we concluded that the incidence of adverse drug reactions in neurology department is more. The literatures also support our study on this aspect, due to using of more than one drug. So early identification and management of ADRs are essential to avoid Special attention should be taken to the patients who are in polypharmacy. Drug withdrawal or dose reduction is usually the first step to be employed for the management of ADRs. Even though the Pharmacovigilance programme started and running in our country still the healthcare professional are unaware about the monitoring and reporting of ADRs. By regulating the current system of Pharmacovigilance can reduce the incidence of ADR and adverse drug reactions induced hospitalization.

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