

Spontaneous Adverse Drug Reaction Monitoring in A Tertiary Care Hospital in Northern India

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Abstract

The present study was conducted to evaluate the spontaneous ADR monitoring in a tertiary care hospital. A total of 150 ADRs reports were collected. The WHO definition of an ADR was adopted. Evaluation of the data was done for various parameters which included types, severity and seriousness of reactions. Naranjo score was used for causality assessment. Overall occurrence of ADRs was more in males. Type A reactions (77%) accounted for majority of the reports. Gastrointestinal system (33%) was the most commonly affected organ system. Antibiotics (32%) were the drug class most commonly involved in ADRs. The suspected drug was withdrawn for the management of the ADR in the majority (82%) of the reports. Upon causality assessment, majority of the ADRs were rated as possible (64%). Mild and moderate reactions accounted for 23 and 65% of ADRs, respectively. The pattern of ADRs reported in our hospital is comparable with the results of studies conducted in hospital set up elsewhere, although there are few differences. Our evaluations revealed opportunities for interventions especially for the preventable ADRs to ensure safer drug use.

Key Words

ADR Monitoring, Tertiary Care Hospital, Northern India

Introduction

This is a well-known fact that drugs prescribed for diseases may themselves be the cause of adverse reactions, ranging from mere inconvenience to permanent disability and disease. During the last decade it has been demonstrated by a number of studies that morbidity and mortality due to adverse drug reactions (ADRs) is one of the major health problems which is beginning to be recognized by health professionals and the public. It has been estimated that such ADRs are the 4th to 6th largest cause for mortality in the USA (1,2). The incidence of ADR varies with studies ranging from as low as 0.15% to as high as 30% (1,3-6). The reporting of ADRs in India is less than 1% as compared to world average of 5% (5). Rising costs of patient care, increasing awareness of patients towards the untoward effects of drugs and the rise in the frequency of cases of litigation against doctors and hospitals have made clinicians, hospital administrators and health care planners aware of the necessity of closely monitoring adverse drug reactions (7). ADR monitoring plays a major role in pharmacotherapy decision making, be it individual, regional, national or international. ADR monitoring is to help ensure that patients obtain safe and efficacious

products. The results of ADR monitoring have also a very important educational value. The Government of India in due recognition of this fact has established National Pharmacovigilance Program in November 2004. However, the program was not very effective and hence a new program Pharmacovigilance program of India (PvPI) was launched in 2010. The immediate aim of this is to foster the culture of ADR notification by health care workers in India. Subsequently, it seeks to generate broad based ADR data on the Indian population and share with WHO database(8). However, ADR monitoring is still in its infancy in India and there exists very limited knowledge about this discipline in health care providers. Health care providers are in the best position to report on suspected ADRs observed in their every day patient care. All healthcare providers should report ADRs as part of their professional responsibility, even if they are doubtful about the precise relationship with the given medication. Due to huge population and unorganized health sector ADR monitoring has not received the importance relegated to it in India. While major advancements in the discipline of ADR monitoring have taken place in the Western countries, not much has been achieved in India. The

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few studies conducted in India do provide an estimate of ADRs. However the data is very limited and ADR reporting can vary widely in different regions (3-6,9). Hence, we designed this study to collect ADRs in a tertiary care hospital.

Material and Methods

This prospective study recorded 150 ADRs of patients visiting the outpatient departments or admitted in the various departments of the institute. The study was approved by Institute ethics committee. Patients of both sexes having definite history of consumption of drugs and reporting with adverse drug events were included in the study. The ADRs were reported as per the list of "What to be reported" by World Health Organisation (WHO). The new drugs were drugs which were less than five years older in marketing (7).

The ADR form of Central Drug Standards Control Organization (CDSCO), New Delhi, India was used to collect information on ADRs (8). The form was distributed to all the departments. The health care providers were told how to collect and record information on the form. The investigators, who were medical doctors, called whenever an ADR was reported by any department. The investigator also went to all departments regularly to observe the ADRs and collect data.

Information on all the patients including relevant history, examination details, investigations and drug therapy was collected and recorded in the proforma by visiting them daily till they were discharged from the hospital. When any other relevant information was required, the treating physicians were also contacted. Any untoward event was labeled as ADE as per WHO definition.(10)

Naranjo score was used for the ADR causality assessment.(11) The Naranjo algorithm can be used to assess the likelihood that a change in clinical status is the result of an ADR rather than the result of other factors such as progression of disease. After analysis all the forms were submitted to the regional centre at New Delhi to contribute to the National database of ADRs.

ADRs were divided into two categories; ADRs due to new drugs and ADRs due to existing drugs. This was done to know the differences in the ADRs to existing drugs and new drugs. ADRs were classified according to their type and severity also (12,13). The severity of each reported ADR was assessed using the criterion developed by Hartwig *et al.*(13) Severe reactions were differentiated from serious reactions (14). Evaluation of the data was done for various parameters which included patient demographics, drug and reaction characteristics and outcome of the reactions. Assessment was also done for causality, severity and predisposing factors. The data was presented as percentages and proportions. The report

was shared with all departments.

Results

The mean age was of patients reported with ADRs was 31 ± 1.48 (mean \pm SE) years. More ADRs were reported with the existing drugs (70%) as compared to new drugs. ADRs were reported more in males (62%) as compared to females. ADRs with existing drugs were also reported more in males (65%). *Table 1* shows the various ADRs reported system wise. Gastrointestinal system was the most commonly affected organ system with ADRs (33%) followed by skin and CNS (23% each). The commonest drug group responsible for ADRs was antimicrobials (32%) followed by antiepileptics in our study (*Table 1*).

Severe ADRs were 12% and serious ADRs were 10%. Most of the ADRs were moderate in severity (*Fig 1*). This trend was seen with new as well as existing drugs. Severe ADRs were less with new drugs (1%). Most of the ADRs were not serious (90%). Type A reactions (77%) accounted for majority of the reports. The onset of ADRs was on an average after 8 days of therapy. *Figure 2* shows relatedness of ADRs with drugs. The causality of most ADRs was "possible in nature" with all drugs (64%). With new drugs most ADRs were classified as "probable" or "possible" in nature. Naranjo score shows correlation with relatedness of ADRs with drugs (*Fig 3*). The relatedness was definite in more in cases with new drugs (4%) as compared to cases with existing drugs (3%). Doubtful relatedness was least (3%) with ADRs of new drugs as compared to existing drugs (17%). In our study, the drugs suspected to be causing ADR were discontinued in 82% patients. No patient died as a sequel of ADR. All the patients except one (94.44%) recovered fully after discontinuing the offending drug. The only patient who developed Steven-Johnson syndrome recovered and discharged later on.

Discussion

A number of reports of these unwanted and untoward reactions have appeared in literature (9). These publicized cases constitute merely the tip of an iceberg, a great many go unrecognized. Every one of us has to collaborate, to make the iceberg as small as possible, simultaneously keeping in mind that the iceberg will not melt completely by itself. We collected ADR reports of 150 patients in this study. The age group affected was similar with new drugs as well as existing drugs.

Most of the ADRs were reported with the use of existing drugs (70%). This may be because of the fact, that overall prescribing is more for existing drugs as compared to new drugs in the tertiary care hospital. This is one of the important factors to decrease the exposure of patients to new drugs until and unless they are

Fig 1. Severity and Seriousness of Reported ADRs (n=150)

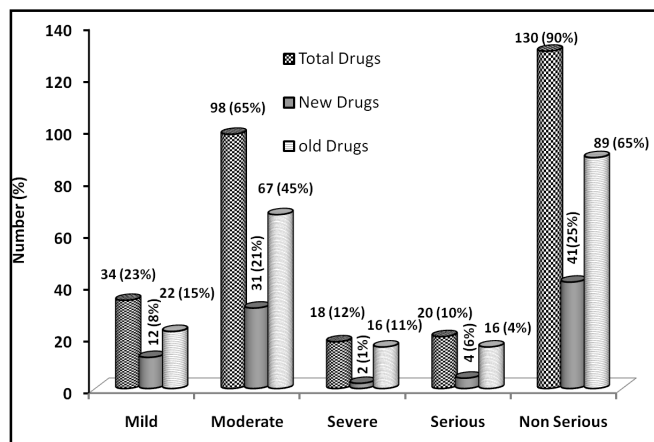


Fig 2. Relatedness of Reported ADRs Drugs (N=150)

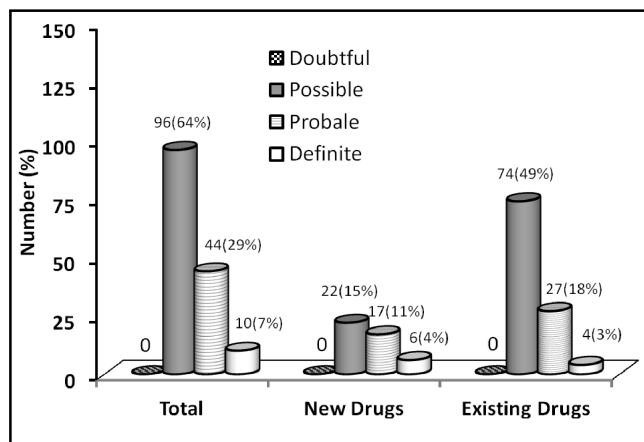


Table 1. Systems Affected by ADRs and Drugs Associated with ADRs

Systems	CNS	CVS	GIT	Lungs	Skin	Urinary	Muscular	Eye	Ear
Number	34	14	50	6	34	2	6	2	2
Percentage	23	9	33	4	23	1	4	1	1

Drugs	Antimicrobials	Antiepileptics	Steroids	Drugs in APD	NSAIDs	Antihypertensives	Antihistamines	Iron
Number	48	20	4	12	12	4	4	4
Percentage	32	13	3	8	8	3	3	3

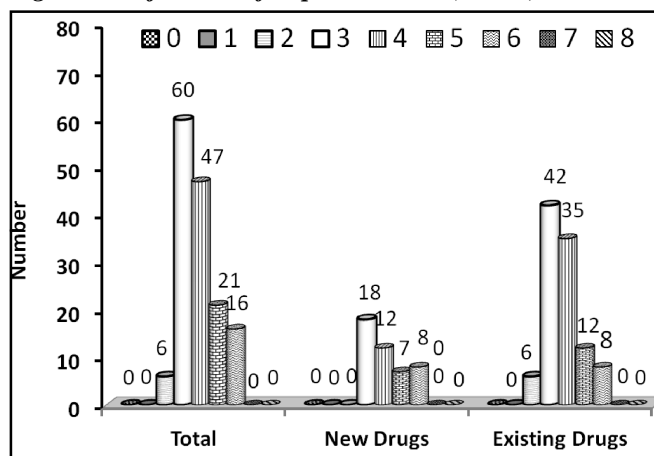
CNS-Central nervous system; CVS-Cardiovascular; GIT-Gastrointestinal; APD-Acid peptic disease

absolutely necessary. Hence, in a tertiary care hospital usually existing standard drugs are prescribed after due consideration of the disorder. This fact is further strengthened by the occurrence of only 1% of severe ADRs with new drugs as compared to 11% with existing drugs. Most of the earlier studies have reported the combined occurrence of ADRs to new and old drugs (3-6). ADRs were reported more in males (62%) as compared to females in our study. ADRs with existing drugs were also reported more in males (65%). Few earlier studies have shown no difference in genders for occurrence of ADRs, however few studies reported higher reports of ADRs in males and females respectively (4,15,16). ADR related to gastrointestinal tract (GIT) were most frequent followed by skin and cardiovascular system. As most of the drugs are taken by oral route, GIT was reported to be the common organ system affected in other studies also (3,4,17). Skin and CNS is also reported to be involved in majority of the ADRs (3,4,16). Skin is the largest organ of body and hence most ADRs can represent here. In our study antimicrobials was the most common drug group involved in ADRs (3%). In most of the earlier studies also antimicrobials were reported to be the commonest drug group involved in ADRs (3,15,16). Most of the ADRs were mild to moderate in severity (88%). This is in accordance with

earlier studies (3,16). Severe ADRs were 12%. Serious ADRs were 10%, indicating that all severe ADRs are not serious ADRs. It is important for healthcare professionals to differentiate severe from serious ADRs. This incidence of serious ADRs is in agreement with most of the studies, but much less than another study (52%) (4,5). Type A reactions (77%) accounted for majority of the reports. Since type A reactions are an extension of the active pharmacologic properties of the drug, they are preventable. They are also called predictable or anticipated events (12). Two more studies from India reported most of the ADRs as of type B or H (5,16).

The causality assessment shows that the relatedness was 'probable to possible' with most of the ADRs. Earlier studies also show similar trend in relatedness (3,5,15,16). The main reason for this trend was polypharmacy in these cases (84%). Definite relatedness was quite less (7%). In these days it is not ethical to rechallenge the patient with the same causative drug, hence the Naranjo score infrequently goes to definite side. Due to causality assessment, ADRs have today assumed a differential diagnostic role in clinical medicine. The relatedness was definite in more in cases with new drugs (4%) as compared to cases with existing drugs (3%). Doubtful relatedness was least (3%) with ADRs of new drugs as

Fig 3. Naranjo Score of Reported ADRs (n=150)



compared to existing drugs (17%). While managing the patients of ADR, the first principle which is followed is to discontinue the suspected offending drug and replace the same by another drug if required. In our study, the drugs suspected to be causing ADR were discontinued in 82% patients at the discretion of the treating physician. These findings are in accordance with earlier studies.[3,16] It was noteworthy that no patient died as a sequel of ADR. All the patients except one (94.44%) recovered fully after discontinuing the offending drug. The only patient who developed Steven Johnson syndrome recovered later on. This fact highlights the proper management of ADRs in a tertiary care hospital. The reporting of ADRs in this study added to the national database. The study also exposed physicians to the methodology of ADR monitoring. Medicine has changed, more so in the past three or four decades. The present day doctor has at his disposal a large number of potent drugs and hence it is very probable that these drugs can cause undesirable reactions/actions which have to be considered. In fact, these undesirable actions/reactions play a very important role in clinical practice today. We expect that after this study the physicians got familiar with the importance and methodology of ADR monitoring in our institution. In future they will report ADRs to regional centre. Overall, the study is a step towards fostering a culture of ADR reporting in the institute by letting them see the process when they were involved in the study. The limitations of the study may include less number of reports to generalize.

Conclusion

The pattern of ADRs reported in our hospital is comparable with the results of studies conducted in hospital set up elsewhere. Our evaluations revealed opportunities for interventions especially for the preventable ADRs to ensure safer drug use.

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