Orginal Article

Response of Reporting Adverse Drug Reactions among Medical Practitioners

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Abstract

Adverse drug Reactions (ADRs) is a global problem of major health concern. Spontaneous reporting of ADRs is the cornerstone of pharmacovigilance. However, underreporting is a huge problem due to lack of reporting culture among medical practitioners. This observational descriptive study was done with the aim to find out the response of reporting adverse drug reactions among medical practitioners and to describe pattern of adverse drug reactions during their practice. Self administered ADR reporting form was distributed to one teaching hospital and ten (10) medical practitioners during the period of December 2009 to December 2010. Total 85 report forms were supplied and response rate was 35% (30/85). Among 30 reported cases 16 (53%) were due to antimicrobial, agents and other 14 (47%) cases were due to NSAIDs, anti psychotics, antidiabetic, antithyroidal, antiepileptics, muscle relaxants and anesthetic agents. 15 cases (50%) need hospitalization for ADRs, 04 (13%) cases suffer > 1 month and one (3%) case was fatal. 20 cases (67%) express hypersensitivity reaction of various grade and rest reports septicemia, fever, palpitation, tachycardia, dryness of mouth, abdominal pain, swelling of limb, heart burn, restlessness, anorexia, apnoea during anesthesia. All reaction is very important and successfully managed by physicians but reporting not done may be due to lack of awareness. So, steps should be taken at different levels to increase the awareness of reporting adverse drug reactions among medical practitioners and we should strengthen pharmacovigilance in our country

Keywords: Adverse drug reactions, response, medical practitioners, pharmacovigilance.

Introduction:

Efficacy and safety are the two major concerns about a drug. While efficacy of a drug can be quantified with relative ease, the same cannot be said about safety.[1] Medicines can treat or prevent illness and diseases. However, sometimes medicines can cause problems. These problems are called adverse drug reactions. Anybody can have an adverse drug reaction. However, people who take more than 3 or 4 medicines every day are more likely to have an adverse drug reaction.[2]

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Adverse drug reactions are defined as 'Any noxious unintended and undesired effects of a drug that occur at doses used for prevention, diagnosis or treatment.[3] The definition already includes all unintended reactions to a medication, However adverse drug reactions that are not fatal or life threatening and that do not lead to hospitalization or permanent disability are generally not identified or quantified to the same extent as more serious reactions.[4] This is unfortunate, since less severe adverse drug reactions may affect patient's quality of life and lead to noncompliance.

Adverse Drug Reactions (ADRs) are associated with a significant morbidity and mortality.[5, 6] The recognition and resolution of medication related problems are increasingly regarded as an important part of primary care medicine.[7] The estimated percentage of outpatient who has an ADRs each year ranges from 2.5% to 50% [7,8] and overall incidence in hospital inpatient is 10-20%.[5] Medication related problem results in an annual costs of approximately $177 billion and causes an estimated 2,18,000 deaths per year and is the third leading cause of death after heart disease and cancer in the United States.[7,9] This gave birth to the branch of pharmacovigilance. By definition, pharmacovigilance is, "The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problems.[3]

Post marketing surveillance of drugs is very important in analyzing and managing the risk associated with drugs once they are available for the use of the general population. Spontaneous reporting has contributed significantly to successful pharmacovigilance. The contribution of health professionals, in this regard, to ADRs databases is enormously significant and has encouraged ongoing ascertainment of the benefit-risk ratio of some drugs [10,11] as well as contributed to signal detection of unsuspected and unusual ADRs previously undetected during the initial evaluation of a drug.[12,13]

In spite of these benefits, under reporting remains a major drawback of spontaneous reporting.[13,14] The Uppsala Monitoring centre (UMC, WHO), Sweden is maintaining the international database of adverse drug reaction reports (currently about 6 million case reports) received from several national centres (104 member countries). However, still, it is estimated that only 6-10% of all ADRs are reported.[15,16] This high rate of under reporting can delay signal detection and consequently impact negatively on the public health.[1]

In Bangladesh under the guidance of WHO, a cell has been established in the Directorate General of Drug Administration (DGDA) in 1996. The cell is trying to introduce a systematic mechanism for ADR monitoring program in Bangladesh for collection, analysis and compilation of ADRs which will be spontaneously reported by the medical and pharmaceutical professional from all health services outlets of the country. The Ministry of Health & Family Welfare formed 10 (Ten) Members ADR Advisory Committee (ADRAC) on 6th July 1997 to evaluate, analyze and make recommendations for solving problems of medicinal hazards due to ADRs.[17]

The Directorate General of Drug Administration (DGDA) had organized ADR Monitoring Workshop meeting in the medical colleges and hospitals of the country and distributed printed ADR reporting forms to the medical practitioners for spontaneous reporting of ADR cases. But spontaneous reporting to DGDA is very little and it may be due to the absence of a vibrant ADR monitoring system and also lack of a reporting culture among physicians and health care providers.[17]

In order to improve spontaneous reporting it is necessary to increase awareness of health care professionals regarding ADR reporting and pharmacovigilance. So, this study was done with the objectives- a) to find out response of reporting ADRs among medical practitioners b) to identify common drugs causing ADRs and c) to describe the pattern of reported ADRs.

Materials and Methods:

It was an observational descriptive study conducted during the period of December 2009 to December 2010. Reporting forms (as it was supplied by DGDA)[17] were distributed to ten medical practitioners in their private chambers and in one teaching hospital. Form was supplied during their consultation time and requested to fill up when they found any case of ADRs. Follow up was done after every two weeks whether any case was reported or not. The respective physician was contacted over telephone before collection the form. Total 20 forms were given to a teaching hospital and 65 forms were given to 10 medical practitioners of medicine, orthopaedics, paediatrics, psychiatrists, endocrinologists, dermatologists in their private chambers of Dhaka.

A presumptive diagnosis of ADRs was made on the basis of recent ingestion of drugs and classical presentation. In case of more than one drug close temporal relationship between ingestion and development of symptoms was identified. Types of reaction were categorized according to sign symptoms and system involved. Descriptive analysis was done with percentage of occurrence and express by table according to response rate, causative drugs, reaction type, action taken and outcome.

Results:

Response rate: Total 85 reporting form was supplied to one teaching hospital (20) and 10 private chambers (65). Among them 11 out of 20 was returned from the teaching hospitals and 19 out of 65 was returned from 10 medical practitioners. Total response rate was 35% (30/85), whereas from teaching hospital it was 55% (11/20) and 29% (19/65) from ten private chambers.

Table-1: Response rate of reporting ADRs

Location	No. of Reports collected/received	Percentage
Teaching hospitals	11/20	55%
Private Chambers	19/65	29%
Total	30/85	35%

Treatment of reaction, Outcome and patients suffering after ADRs: 15 patients (50%) need hospitalization for ADRs out of 30. After ADRs 22 out of 30 recovered (73%), 23% i.e 7 out of 30 not yet recovered and one case was fatal (3%). Considering patients suffering 5 out of 30 i.e 17% suffered > 1 week, one (3%) out of 30 suffered > 3 weeks, 4 patients out of 30 i.e. 13% were suffered > 1 month.

Table-2: Treatment of reactions, Outcome and patients suffering due to ADRs

Features	Parameter	No. of cases	Percentage
Treatment	Hospitalization and treatment given	15	50%
	Not hospitalized, conservative treatment	13	43%
	Spontaneously resolved	02	7%
Outcome	Recovered	22	73%
	Not yet recovered	07	23%
	Fatal	01	03%
Patients suffering	Suffer > 1 week	05	17%
	Suffer > 3 week	01	03%
	Suffer > 1 month	04	13%

Descriptions of ADRs: In most cases the ADRs was hypersensitivity reaction (20/30) i.e.67%. Various form of hypersensitivity reaction includes- rash, itching, erythematous lesion, urticaria, swelling of face or leg, blister, high fever, headache, swelling of whole body, septicemia, pancreatitis, arrhythmia, Stevenson Johnson syndrome etc. Other form of reaction were 33% which includes- GIT disturbances, loss of appetite, dryness of mouth, palpitation, restlessness, high fever, heart burn, vomiting, apnoea after anesthetic drugs.

Table-3: Description of reactions

Description of reaction	No. of cases	Percentage
Hypersensitivity reactions-(rash, erythematous lesion, urticaria, swelling of face, blister)	20	66.66%
Others- GIT disturbances, swelling of limbs, loss of appetite, high fever, septicemia, headache, dryness of mouth, palpitation, restlessness and apnea after administration of drugs	10	33.33%

Responsible drugs caused ADRs: 20 categories of drugs were identified as causative agents for ADRs. Among them 16 cases (53%) were due to antimicrobials and other 14 cases (47%) were due to NSAIDs, antipsychotics, antidiabetics, anti epileptics, antithyroidal agents and anesthetic agents. The antimicrobials that causes ADRs were ciprofloxacin(08), levofloxacin(03), ceftriaxone(01), cephradine(01), cefixime(01), clindamycin(01), sodium stibogluconate(01). NSAIDs are etoricoxib(02), nambuten, aceclofenac, dexibuprofen, naproxen. Other agents are glibenclamide, quetiapine, carbamazepine, sodium valproate, carbimazole, zoledronic acid, tolperisone, halothane, atropine Note: Now it is Directorate General of Drug Administation (DGDA) so it should used instead of DGDA.

Table-4: Responsible drugs identified for ADRs

Groups	Agents	No. of cases	Percentage
Antibiotics		16	53%
	Ciprofloxacin	08	
	Levofloxacin	03	
	Ceftriaxone	01	
	Cefradine	01	
	Cefixime	01	
	Na Stiboguconate	01	
	Clindamycin	01	
NSAIDs		06	20%
	Nambuten (injection)	01	
	Etoricoxib (tablet)	02	
	Aceclofenac	01	
	Dex Ibuprofen	01	
	Naproxen	01	
Others		08	27%
	Glibenclamide	01	
	Carbimazole	01	
	Quetiapine	01	
	Zoledrenic acid	01	
	Carbamazepine	01	
	Na Valproate	01	
	Tolperisone	01	
	Halothane/Atropine	01	

Discussion:

The present study was done with the aim to find out the response of reporting ADRs and to describe the pattern of ADRs during the period of December 2009 to December 2010 in one teaching hospital and 10 private chambers. Response of reporting ADRs from private chambers were very poor (29%) whereas response from teaching hospital was more (55%). Poor response from physician was also observed by others.[18,19] Many factors may be associated with underreporting of ADRs among health professionals. These factors have been broadly classified as personal and professional characteristics of health careers and their knowledge and attitude to report. Inman (1996)[20] has summarized these factors as the 'seven deadly

sins'. His descriptions of the 'sins' include: attitude relating to professional activities (financial incentives, legal aspects) and problems associated with ADRs related knowledge and attitudes (complacency, diffidence, indifference, ignorance) and excuses made by professionals (lethargy i.e disinterestedness in reporting or lack of time to find a report card and other excuses).[20]

Lopez and Ganzalez[14] in their review of determinants of ADRs under reporting from the global perspective, have shown that three of the seven sins proposed by Inman that are associated with professional activity (financial incentives, fear and ambition to publish) seems to contribute less significantly to underreporting.[14] Insecurity (the belief that it is heavily impossible to determine whether or not a medicine is responsible for a particular ADR) is another factor associated with under reporting but was not proposed by Inman as stated by Gupta and Udupa.[1]

In order to improve the reporting rate it is important to improve the knowledge, attitude and practice (KAP) of the health care professionals regarding ADR reporting and pharmacovigilance.[1] The best time to do it is probably during the undergraduate and postgraduate education of the doctors and it should be included in assessment of student so that they must learn ADRs reporting importance. In our context, we must take into account that the lack of awareness of health professionals concerning their responsibility in the ADR reports results underreporting.

Antimicrobial agents (53%) were the most common suspected drugs causing ADRs in our study. Second most causative agent was NSAIDs and remaining ADRs were due to antipsychotics, antiepileptics, antidiabetics, antithyroidal, muscle relaxants and anesthetics. Our observation correspond with the findings of others.[18,19,21] Where as Aspinall et al[9] found cardiovascular drugs and antidiabetic agents are the major causes of ADRs. In this study ADRs due to antimicrobials are may be due to availability of drugs without prescription. In Bangladesh the local pharmacy shop dispenses antimicrobials without prescriptions to patients and this may lead to more occurrences of ADRs due to antimicrobials.

In was found that the system most frequently involved are dermatological and reaction type was hypersensitivity (67%) reactions of various grade followed by system involved are cardiovascular,

gastrointestinal, CNS, respiratory system, immune system. Same observations were made by Palaian et al[19] and Agouzal et al.[18] The skin and mucous membrane were the most common sites for initial presentation of many ADRs. In general it is easy to identify a cutaneous ADRs and patients can be educated by physician/pharmacist regarding common early symptoms (erythematous rash, edema, urticaria, mucosal erosions, itching, burning of skin) especially during the initial stage of therapy.[19]

However ADRs also contributed to significant economic loss (as patients need hospitalization for ADRs) and impairment of quality of life of patients. Among 30 cases 15 of them required hospitalization and medical treatment and 14 of them need medical treatment though not hospitalized and one case was fatal. In all cases suspected drugs were withdrawn and ADRS was efficiently managed by the physicians. 50% of cases required hospitalization and required medical treatment in managing the ADRs, thus it can be said that it is an economic burden to the patient experiencing the ADRs in addition to the suffering and impairment of quality of life.

There is no definitely known way to prevent development of ADRs due to medicines (as we know that any one can develop ADRs) but to reduce incidence we can take steps like-indiscriminate use of drugs should be prohibited, culprit drug should be distinguished from others as early as possible by determining the timing of administration and onset of drug reaction.[21]

Due to lack of reporting the real picture of ADRs is difficult to estimate. ADR monitoring cell of drug administration should be more active in this regard. We should strengthen the program of pharmacobigilance to ensure the safe use of medicines in the community.

Recommendation:

It is the preliminary study which tried to evaluate the response of reporting of ADRs among medical practitioners and pattern of ADRs reported. In order to improve self/spontaneous reporting Directorate

Limitations:

Our study conducted only among 10 medical

practitioners and in one teaching hospital. From this study it can not be shown the whole picture of ADRs in our country. Similar studies covering more physician and hospitals and longer period of time are requred to validate our findings.

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