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Pharmacovigilance and Managing ADRS in Bangladesh: Eccentric or Non-existent?

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ABSTRACT

Bangladesh became the 120th member of the WHO's International Drug Monitoring Center (WHO-UMC). Through this membership, Bangladesh has gained international recognition and access to early worldwide information about potential safety risks. It was introduced in Bangladesh in 1999. However, due to a shortage of manpower and a lack of financial support, the program became dormant. It was revived in 2013 when the DGDA established the ADR Monitoring cell. Major advancements of the discipline of pharmacovigilance have taken place in the West, still, not much has been achieved in Bangladesh. The article highlights the various serious incidences ADRs, present health situation and broader scope of pharmacovigilance in Bangladesh.

Keywords: National Drug Policy (NDP), The Directorate General of Drug Administration (DGDA), Drug Control Ordinance, Essential Medicine List (EML), Standard Treatment Guidelines (STG)

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Purpose of the study: Discussion and projection of drug use and monitoring status in Bangladesh. The pharmacists have a vital role to play which is thoroughly discussed.

Methodology: Research conducted a year-round comprehensive literature search, which included technical newsletters, newspapers journals, and many other sources. Medicine and technical experts, pharma company representatives, hospital nurses and chemists were interviewed. Projections were based on estimates such as drug end users, providers or prescribers, general knowledge of rational use, consequence and types of different incidences of ADR and non-compliance, their managements or overlooking.

Findings: Bangladesh is a highly populated country. Economic development and academic flourishment do not represent development in health sector. Both the providers and patients are responsible for ADR incidences. Ignorance, non-compliance/non-adherence, negligence and many others are contributors for such incidences.

Research limitations: Very few articles found in matters regarding along with a very less interest paid by general people to talk about medicine use and prescription, ADRs and their management. It was very difficult to bring out facts because of the business mentality of the providers and very little patients' knowledge about health and drugs crippled the facts.

Practical Implication: The soul of this article was to detail about bizarre incidences of drug and therapeutic failure. Along with students, researchers and professionals of different background and disciplines, e.g. Pharmacists, marketers, doctors, nurses, hospital authorities, public representatives, policy makers and regulatory authorities have to acquire much from this article.

Social Implication: Rational drug use and monitoring is the soul of healthcare system in a country like Bangladesh as there is a scarcity of resources, fewer access to general people for adequate and better treatment, misbeliefs and mistrusts about physicians. The article should contribute an integrated guideline for patient compliance, demand pharmacovigilance and last but not the least a silvery lining to better treatment culture near future.

Introduction

Pharmacovigilance is a very significant and inseparable part of clinical research. Both clinical trials safety and post-marketing pharmacovigilance (popularly known as Post marketing studies or Phase IV clinical trials) are critical throughout the product life cycle. With a reasonably high number of recent high-profile drug withdrawals, both the pharmaceutical industry as well as various regulatory agencies across the globe have raised the bar. Early detection of signals from the post-marketing surveillance studies and clinical trials in early phases have now been adapted by major pharmaceutical companies in order to identify the risks associated with their medicinal product/s as early as possible. ADRs commonly reported in due to known or unknown pharmacological features, poor product quality (e.g., spurious, adulterated, misbranded, counterfeit, substandard), medication errors in prescribing, preparing, administering, or taking the medicine which requires hospitalization, causing significant disability/incapacity, sometimes life threatening and also death reported. Bangladesh is a developing country where 75% of total population lives in rural area. Subsequently they have poor healthcare access as 26% of rural professionals remain vacant and nearly 40%, absent. Although official documents indicate that 80% of the population has access to affordable essential drugs, there is plenty of evidence of a scarcity of essential drugs in government healthcare facilities. Nearly 45% rural people take medical assessment from unqualified health workers including medical assistants, mid-wives, village doctors, community health workers in comparison to that by qualified medical graduates (only 10%-20%). More than 75% women having complications

sought treatment from an unqualified provider. These are mostly because concern over medical costs, and pronounced socioeconomic disparities found for care-seeking behavior in both urban and rural Bangladesh.

Present Scenario of Bangladesh Health Sector

Misbeliefs and Superstitions in Health Seeking Behavior

Common disease of under five children are gastroenteritis, pneumonia, diarrhea, skin infection, helminthiasis, abdominal pain, dental problem & chronic suppurative otitis media (Anne et.al 2015). Among them diarrhea and pneumonia cause death of more than ten lac children every year. Majority parents seek treatment from homeopaths, PCs, retailers or non-qualified allopath. A social phobia prevents women from standard treatment interventions. Antenatal care situation is also in a worse situation. Half of the pregnant women reported one or more life threatening complicacies, among them three fourth had convulsion or bleeding, only one third of them sought treatment from qualified prescriber. The principal reason was medication cost and social disparity in both rural and urban Bangladesh (Koeing et.al 2007).

Compromised Access to Healthcare System

A wide variety of inpatient care services is available in public hospitals. On the other hand, the three-tiered PHC system (sub-district, union and village level) established to serve the population at large. However, access to this network of health care facilities is often seriously compromised. It should be noted that while basic health care service is supposed to be free in public hospitals and other facilities, patients end up bearing the costs of medicine and laboratory tests, as well as some additional unseen costs. These costs seriously restrict the access of the poor and the disadvantaged to most publicly-funded health care services. Moreover, in many public hospitals the available ambulances are either inoperative or being used by the physicians and other staff. Patients are deprived of use of ambulance services. In short, there is a gap between principle and practice in public health facilities seriously compromising the accessibility of the poor. The fact that nearly 70% of health care costs are out-of-pocket expenses borne by individuals and families also serious restricts the access of the poor to the health system undermining the principle of equity so enshrined in the country's constitution (Anwar, et.al., 2014).

Poor Access to Essential Drugs

Although official documents indicate that 80% of the population has access to affordable essential drugs, there is plenty of evidence of a scarcity of essential drugs in government healthcare facilities. One study conducted in four district hospitals and one medical college hospital showed that only eight per cent of patients received the prescribed medicines from these facilities. In another report, two major hospitals in the capital city of Dhaka were operating without essential medicines for eight consecutive weeks. There are countless such incidents relating to the supply of essential medicines in Bangladesh. In most such cases, government officials and health professionals are responsible for the shortage as they often sell government-supplied drugs to local drug stores instead of dispensing them to poor patients. The government must be cognizant of this fact, but rarely takes any action.

Substandard Quality of Available Drugs

1 in 10 medical products in developing countries is substandard or falsified (WHO, 2017). Of the 300 pharmaceutical companies in Bangladesh, only the 20 to 25 top ones produce drugs of standard quality. Reports show that numerous small companies' market substandard drugs in the country. Fake or substandard medicines, including lifesaving ones, with an estimated worth of US$ 150 million per year, are flooding the domestic market. In its annual testing in 2004, the government laboratory detected 300 counterfeit or very poor-quality drugs out of 5,000 drug samples. A recent assay involving 15

brands of ciprofloxacin showed that nearly 50% of samples contained less than the specified amounts of the active ingredient. Another report noted that approximately 70% of paracetamol tablets and 80% ampicillin capsules produced by small companies were of substandard quality. Good manufacturing practice (GMP) is a major criterion to maintain standard quality in drugs, and it was one of the principal objectives of the NDP to ensure standard manufacturing practices for drug manufacturers. But there are some 265 pharmaceutical companies in Bangladesh that do not follow or comply with GMP. It is widely alleged that adulteration flourishes in the country because of poor government vigilance and supervision over drug manufacturers and sellers. Unfortunately, a section of corrupt physicians and government officials is involved in these underhand dealings. The government states that it has limited manpower and facilities to cope with the country's fast expanding pharmaceuticals sector. In fact, the regulatory authorizes have given scant attention to quality matters in Bangladesh.

Unstructured Framework of Drug Prescription

In reality, there is no mechanism or legislation exists in the country for assessing the competence of prescribing medical practioners. No legal action is taken against them even if a serious mistake leads to a fatal outcome. The relatives of the victim accept it as fate, and no complaint is lodged. A medical practioner can prescribe anything from vitamins to vincristine, for anything from the common cold to cancer. Inappropriate prescriptions are readily available due to poor consulting period (a mean of only 54 seconds!) of doctors in Bangladesh. It is estimated that more than half of medicines are inappropriately prescribed, dispensed or sold. Moreover, polypharmacy is very common among the rural medical practioners with antibiotics and vitamins prescribed widely. The prescription procedure of antibiotics in Bangladesh is less than ideal as prior identification of the pathogens and its sensitivity to the drug is rarely determined before the drug is prescribed. The situation is very alarming in the rural areas. For example, one survey conducted among rural medical practitioners with an average of 11 years' experience showed 60% of antibiotics prescriptions written based on the symptoms alone. All antimicrobial agents were prescribed mainly on the patient's complaints, and all available antibiotics were prescribed in inappropriate doses and duration as has been showed in another similar survey. Children are mostly affected by inappropriate antibiotics prescribing in Bangladesh. In a study it was showed 26% of purchased drugs were antibiotics for children aged 0-4 year(s) and 48% of antibiotics were purchased in quantities of less than a single day's dose. Pneumonia and diarrhea are the two most common infectious diseases among children in Bangladesh with the annual deaths of about 230,000 children due to diarrhea. But the percentages of appropriate antimicrobial treatment of pneumonia, and diarrhea were 57.1% and 67.8% respectively as shown in one study. Misuse of drugs in the treatment of acute diarrhea among under-five children is highly prevalent and WHO-recommended treatments were seen in only 26.7% of cases and metronidazole was prescribed in all 38.6% cases. Multiple and inappropriate antimicrobial drugs is the most common treatment errors in dysentery with failure to recommend use of oral rehydration solution. Over-statements and misinformation are very common in Bangladesh, which greatly influences doctors' prescribing behaviors. Currently, drug companies are the only organizations in Bangladesh to provide information to health personnel and the information supplied is often not consonant with recommendations from public health bodies. Along with bribe in the form of cash, a large number of doctors accept various gifts including free air ticket for foreign trips, computers, mobile phones, air conditioners, table lights, telephones, towels, calendars, paperweights, pens and what not. Ultimate result is

prescriptions of inappropriate or unnecessary and expensive medicines.

Irrational Patterns of Drug Use: To ensure rational and appropriate use of drugs in Bangladesh was another prime concern of the NDP. But there has been no drug use study in the country. Clinically inappropriate and inefficient use of medicines is a serious problem. More than half the medicines in Bangladesh are inappropriately prescribed, dispensed or sold. Despite legal prohibitions, numerous drugs with similar or no significant benefits are available in the market. As a specific example, there are seven members of the angiotensin-converting enzyme (ACE) inhibitors available in the country. The efficacies and chemical structures of these molecules are more or less similar, but their price vary significantly. The drug policy clearly prohibits the production of multi-ingredient preparations of vitamins and minerals with the exception of B-complex vitamins. But a mixture of 32 vitamins and minerals including selenium, vanadium, molybdenum, tin and many other unnecessary ingredients has been marketed in the country for a few years, violating the principles of the NDP. The need for these trace elements in Bangladesh is not established whereas nutritional deficiencies are mainly related to vitamins A and B-complex, iron, calcium, iodine and zinc. Irrational prescription and use of antibiotics are rampant throughout the country, with an estimated half of all antibiotics being sold without prescriptions. Self-medication is widespread, and all types of medicines can be purchased without a prescription. There were about 1,10,000 illegal and unlicensed drug stores operating in the country reported back in 2010. It is alleged that both legal and illegal drug dealers are engaged in selling fake, smuggled and adulterated medicines in the country (Mohammad et.al 2008).

Misuse of OTC Drugs: In real sense, there is no 'prescription only drug' in Bangladesh at present. One can get any drugs from anywhere. Only need is money; no prescription indeed. Over the counter (OTC) drugs have emerged recently as drugs of serious misuse across Bangladesh, and other neighboring countries. One report estimates that there are four million drug misusers in the South Asian region, with Bangladesh accounting for nearly 500,000. Self-medications in a population with low literacy level like Bangladesh are very challenging, which poses risks such as incorrect diagnosis, absence of knowledge of alternative treatments, irrational use of drugs and neglecting side effects and drug interactions. Study showed that around 30- 40% of disadvantaged population including the women, elderly, ethnic minorities, poor / ultra-poor undertake self-medications for managing illness.

Inferior Domestic Drug Dissemination: Bangladesh's drug distribution marketplace is composed of small independent pharmacies. Although there are approximately 200,000 private pharmacies in Bangladesh, the government lists officially only 76,000 pharmacies. The rest are illegal, without a license or a licensed pharmacist on staff. Pharmacists have varying education levels and many lacks adequate training. For example, a visit to four pharmacies in Dhaka and ten pharmacies in the bordering Gazipur, Narayanganj, Keranigonj and Manikgonj Districts revealed that each had one professional pharmacist, who had four years of coursework; while the two medium-sized pharmacies visited had one person with a year's training and several untrained coworkers, all of whom were working as pharmacists. Rural pharmacies may have pharmacists with high school education and approximately two weeks training. A significant number of drug consumers obtain drugs without a prescription. When consumers lack a prescription, they will usually either ask a pharmacist for a specific drug or describe their ailment to a pharmacist who diagnoses the problem and recommends a drug on the spot. Popular products include a variety of antibiotics, painkillers, and gastric remedies. Consumers purchase one to ten tablets or

capsules at a time. The quantity of drugs purchased often depends more on the consumer's finances of than on the required dose of medicine (Janet et.al 2008).

Major Reasons of ADRs in Bangladesh

1. Self-medication
2. Poly pharmacy
3. Aggressive promotion and push sell of drug products
4. Unethical practice of healthcare providers
5. Irrational use of antibiotics, steroids and other drugs
6. Registration of more combination products where alternative options are there
7. Distribution/purchase of medicine from any unauthorized source
8. Improper storage and distribution of drugs. (Nusrat et.al 2017)

A Few Therapeutic Non-Compliance Reports in Different HCEs

a) Patients with Rheumatic Heart Disease: Therapeutic compliance among patients with rheumatic heart disease in NCCRH, Dhaka, Bangladesh reveals compliance in 50% patients which was less than level determined by an aboriginal community in Harrington, Australia (Kakon et.al 2018).
b) Compliance to Anti-hypertensive Medications: A WHO multicenter shows around 50% Indian and Bangladeshi elderly suffers from hypertension, among 50% of them are aware of disease and only 10% are compliant. In the year 2007 a study done in Rajshahi, Bangladesh revealed that 85% of the hypertensive patients either do not checkup regularly or non-adherent to their antihypertensive medications (Hussain et.al 2011).
c) Type 2 Diabetes Mellitus Patients' Compliance: A study in BIRDEM, Dhaka found that among
the diagnosed Type 2 people insulin intake was high in urban area due to cost and availability of the drug in local market and also nearly 25% respondents was found took herbal medications for controlling diabetics which is lower in cost (Salma et.al 2015).
d) Cost of non-compliance among diabetes patients: In this cross-sectional study of patients with diabetes clinics in Mirzapur, Bangladesh shows dim vision or blindness nearly70 %, poor wound healing and dizziness nearly 30% and sexual dysfunction in nearly 15% of men (Lana et.al 2015).
e) Antibiotic Resistance: A recent study shows that half of the antibiotics are sold without prescription, people prefer self-medication rather than visiting a doctor. Rural people do not always do what the prescribers advise them to do. Financial ability was not the sole cause. Antibiotic resistance found due to inappropriate prescription, poor consulting period and expense behind drugs (Kumar et.al 2014).

Why Vigilance is a Crying Need for Bangladesh?

Bangladesh needs a system with autonomous expertise to ensure that safety information on all available drugs is adequately collected, impartially appreciated and made available to all. Advancement in medication observing and conveying data about the safety and viability of prescriptions can make pharmacovigilance system more effective. Health care provider and the public in the core debate about the risks and benefits of medicines. Also, the choice of treatment is also mentioned in this case. Bangladesh is an underdeveloped country. According to the DGDA, we are now exporting wide range of products to more than 130 countries of the world. It includes all major therapeutic class & dosage forms along with high-tech products like inhalers, nasal sprays, suppositories, IV fluids and injectables etc. On the other hand, a major

portion of the people of Bangladesh are unconscious about the health and the drug they intake during diseases. They have limited ideas about their health and medicines. The quest for gaining from different orders about how

pharmacovigilance techniques can be improved, close by boundless expert, official and public collaboration. The following incidences clearly demands multi-dimensional vigilance:

a) *Diethylene Glycol Tragedy*: Diethylene glycol is a highly toxic organic solvent that causes acute renal failure and death when ingested. It gets importance because of some recent incidence. In 2009, 26 children died due to formulation alteration in case of paracetamol syrup, where propylene glycol was replaced by diethylene glycol as a solvent. Health officials in the country said that so far 26 children aged between 11 months and three years have died after taking paracetamol (acetaminophen) syrup contaminated with diethylene glycol that was manufactured by local drug producer Rid Pharmaceutical Co (Arrest warrants issued after DEG kills 26 infants in Bangladesh). The trade name of the drug was Temset (paracetamol suspension). In addition, three hundred thirty-nine (339) deaths attributed to paracetamol syrup contaminated with diethylene glycol in 1990-1992. This incidence shows that, the formulation alteration by harmful chemical can pose a serious threat to health care system.
b) *Substandard Vitamin A Tragedy*: The Government of People's Republic of Bangladesh conducts National vitamin A plus campaign every year. In 2013 due to ingestion of substandard vitamin A capsule many children became sick, and online reports talked about some patients experiencing vomiting sensation and feeling unwell. Children were reported sick at Chittagong, Cox's Bazaar and Lakhimpur among other places. Rumors of death were also reported with one report claiming a child had died from administration of Vitamin A capsule which were supplied by Indian source, Olive healthcare (Nusrat et.al 2017).
c) *Most Pharma Companies Tempt Doctors With 'Gifts':* With a view to popularizing their brands, most of the pharmaceutical companies in the country allegedly practice unethical drug promotion alluring doctors with free samples and gifts to prescribe their medicines. To stop such unethical promotion of drugs, there was no effective implementation of the Drugs (Control) Ordinance, 1982 that regulates manufacture, import, distribution and sale of drugs in Bangladesh. The Drug Administration, which regulates manufacture, import and quality control of drugs in the country, is also inactive to put a stop to such unethical practices. Pharmaceutical companies practice drug promotion to boost sales and earn more profit, although it is clearly unethical, as stated by secretary general of Bangladesh Medical Association (BMA). According to Chairman of the Eye Department at Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladeshi pharmaceutical companies produce standard medicines but all companies cannot produce quality products. According to the industry reports, the pharmaceutical companies allocate huge sums in their annual budget for gifts to be distributed among the medical practitioners. A number of representatives of pharmaceutical companies, both local and multinational, said they often bribe doctors to promote their particular drugs. A former medical representative of a pharmaceutical company, said the pharmaceutical companies offer attractive gifts to the doctor on various occasions. "The pharmaceutical companies offer doctors many things - from pens to cash money - as part of their promotional activities. Sometimes they even undertake decoration of the doctors and also offer sarees for doctors' wives," he said. Narrating his own experience, He said that during his service as a medical representative, he offered crystal flower vase to a doctor to prescribe his company's drugs. Instantly, the doctor prescribed the tablet for a patient without trying to know its quality. Many companies

give Tk 5,000-10,000 to popular and familiar doctors per month in rural areas to promote their drugs. This rate is reportedly higher in urban areas. Bangladesh Legal Aid and Services Trust (BLAST) Deputy Director, who is working for strengthening the government regulatory bodies like Drug Administration, suggested the government to recruit more manpower in the Drug Administration to make it more effective as well as to follow 'Code of Pharmaceutical Marketing' to check such unethical practice to save the lives of people (Unb Dhaka, 2011).

d) *Shameless Unethical Drug Promotion And Their Consequences*: Doctors are writing more prescriptions for Nitazoxanide instead of Metronidazole for amoebiasis and diarrheas; Azithromycin for diarrhea, typhoid and PID. Other misused drugs are caffeine with paracetamol, Diclofenacs, Statins, Irrational vitamin preparations with all sorts of mineral which cannot be detected in Government Drug Laboratory; Benzodiazepines, sex hormones, steroids, Terbinafine, Butenafine, Crotamiton etc. Promoting Directly to Consumers through daily newspaper with separate advertising sheet on Dukoral (a Swedish company, Crucell product) for prevention of diarrhea and cholera tactfully using name of WHO and ICDDR, B. Aggressive and unethical promotion increases irrational prescriptions leading to multiplication of profit of the companies. Counterfeit version of costly drugs surfacing in progressive order. More spurious and substandard drugs freely moving into the market (Development dialogue 1995:1).

e) *Hospitals Found Selling Counterfeit Drugs, Keeping Expired Reagents*: A mobile court of the Rapid Action Battalion or RAB has fined the Apollo Hospitals in Dhaka for selling in their pharmacy 30 types of counterfeit drugs and keeping expired reagents in its laboratory (bdnews24 October 10, 2018). A similar report was found with United Hospital, Gulshan 2, they were for use of expired reagent, selling unapproved drugs (DhakaTribune 2018). Seven employees including two fake doctors of Crescent Hospital, a private hospital in Dhaka's Mohammadpur, were sentenced to different jail terms today on charges of providing wrong treatment. The hospital was fined Tk 10 lakh also due to charging high fees from patients and providing fake medical reports (Star online March 28, 2018). Privately run clinics and diagnostic centers in Chittagong are rife with anomalies owing to a lack of proper monitoring. These clinics and centers often produce erroneous diagnostic reports that often lead the patients to serious health risks. A recent mobile court drive of the Chittagong district administration revealed that a reputed private clinic of the port city was running its operating theatre with expired medicine and reagents. Moreover, the assistant radiologist of the private clinic did not have any professional experience or academic qualifications. It has been alleged that most of the diagnostic centers are poorly equipped and lack modern laboratory facilities to conduct pathological tests (Anwar, 2018). Technicians in these substandard private diagnostic centers often don't possess the required qualifications to perform the tests properly, which can result in incomplete or inaccurate test results being filed. Consequently, patients lose their confidence in the test results provided by the sub-standard diagnostic centers. Seeing no other option, many resorts to going abroad and paying huge sums of money, which causes a loss for the Bangladesh economy (DhakaTribune October 10, 2018). During a visit to the Bangladesh Medical Association building market, EM Surgicals was found to be storing antibiotic disks for diagnostic tests in a refrigerator set to 11^0C, beyond the recommended temperature range in which such a product can be stored. This

essentially means that the diagnostic tests done with these disks may not be accurate. Several shops of the same market were found selling expired insulin and reagents, namely Lotus Surgical, Midland, SA Surgical, Medifair, Bhuiya Surgicals, EM Surgicals and Atlanta Medica. A RAB unit raided two pharmaceutical distributors in Shyamoli on November 1 last year and found them selling large quantities of expired drugs and diagnostic reagents. None of the drugs or reagents were stored at their proper temperatures, thus effectively denaturing them; the warehouses kept no record of where and when they were manufactured (Zyma, 2017).

f) *High Court bans 34 pharmaceutical companies from producing medicines*

High court justices came after hearing of a rule issued earlier on a petition filed by the Human Rights and Peace for Bangladesh (HRPB) to stop production and marketing of substandard medicines. The order asked the Bangladesh drug regulatory authority to regularly monitor whether these companies continued to produce and market medicines and file a report to the High Court after every four months. HRPB counsel Manzill Murshid said that the government has already cancelled the license of 7-8 of these 34 companies (bdnews24). The High Court has constituted a five-member committee to examine fresh application by those companies who have not had their license cancelled, if they agreed to abide by existing drug regulatory parameters. The committee consists of a representative each from World Health Organisation, Bangladesh Drug Regulatory Authority, Dhaka University's Pharmacy department and the Health Ministry. Twenty companies banned from producing all medicines namely Exim Pharmaceuticals, Avert Pharma Ltd, Bikalpa Pharmaceuticals Ltd, Dolphin Pharmaceuticals Ltd, Drugland Ltd, Globe Laboratories Pvt Ltd, Jolpa Laboratories Ltd, Kafma Pharmaceuticals Ltd, Medico Pharmaceuticals Ltd, National Drug Pharma Ltd, North Bengal Pharmaceuticals Ltd, Rimo Chemicals Ltd, Rid Pharmaceuticals Ltd, Skylab Pharmaceuticals Ltd, Spark Pharmaceuticals Ltd, Star Pharmaceuticals Ltd, Shunipun Pharmaceuticals Ltd, Today Pharmaceuticals Ltd, Tropical Pharmaceuticals Ltd and Universal Pharmaceuticals Ltd. Fourteen companies banned from producing antibiotics Ad-dwin Pharmaceutical Ltd, Alkad Laboratories Ltd, Belsen Pharmaceuticals Ltd, Bengal Drugs and Chemicals (Pharma) Ltd, Bristol Pharma Ltd, Crystal Pharmaceuticals Ltd, Indo-Bangla Pharmaceuticals Ltd, Millat Pharmaceuticals Ltd, MST Pharma and Healthcare Ltd, Orbit Pharmaceuticals Ltd, Pharmic Laboratories ltd, Phoenix Chemical Laboratory Ltd, Rasa Pharmaceuticals Ltd and Save Pharmaceuticals Ltd (The Daily Star February 14, 2017, The Daily Sun 13th February, 2017, NEWAGE Bangladesh, Feb 14,2017).

Pharmacovigilance Studies in Bangladesh

Finally, as part of the agreed-upon Risk Evaluation and Mitigation Strategies (REMS), the manufacturer commits to report to the FDA with regard to the various elements of the risk mitigation program. This may include specific data elements regarding the particular risk under management (i.e. number of adverse events, pregnancies, etc.) measuring the effectiveness in achieving the goal of continued benefit from the drug with minimization of the risk. The manufacturer-conducted REMS assessment may also include surveys of prescribers and patients, to understand knowledge, attitude, and behaviors (KAB) related to the understanding of the risks to the therapy, with the ultimate goal being to determine the effectiveness of the REMS plan in aggregate. Depending upon the results of these evaluations, the manufacturer may seek to modify the REMS to improve its effectiveness and acceptability in the marketplace over time (Muntasir et.al 2013).

Role of Pharmacist in the Management of ADRs

A pharmacist plays a pivotal role in the identification, detection, prevention, and management of drug-drug interactions, drug-food interactions and ADRs. Pharmacist can carry out such activities in inpatient setting, while taking part in viewing charts during ward rounds, and during medication management while dealing with prescriptions. Since pharmacists have a vast knowledge on drugs and therapeutics, their ability to discover and deal with ADRs is quite important. Keeping in view the reporting of ADRs, according to a study carried out by Sriram et al on the prevalence of ADRs, a pharmacist's participation enhances reporting rate with higher caliber. The intervention of pharmacists by organizing lectures and group discussions thus providing information about the importance, seriousness, preventability and necessity of reporting shows heightened improvement of knowledge, attitude and perception about ADRs. All health professionals play their respective roles in balancing between benefits and risks of medication when it is introduced in the market. However, the expertise of a pharmacist about a drug, especially if newly marketed, play a more important role in ADRs reporting to the authorities which helps in either withdrawing the product from the market or cause labelling changes. Pharmacists working in community pharmacy have an added advantage of detecting and reporting ADRs while dealing with on the counter prescriptions and herbal products. In a community pharmacy, a pharmacist may not have direct and definite patient list but the patients coming to the same pharmacy to refill their prescription gives the pharmacist an opportunity to detect a possible ADR that the patient might be experiencing and can help in the management and the reporting of the said ADR.

Role of pharmacist in Pharmacovigilance

The pharmacist could be a coordinator between different members of healthcare team and the patients, to ensure both vigilance and compliance. Thus, involvement of pharmacists in health management system is becoming very crucial day by day. Pharmacists are involved in providing health care facilities as well as suggesting medical staff on proper selection of drugs. They also plan, monitor and evaluate drug programs to improve health and reduce health inequalities. Hospital pharmacists ensure that medicines are managed safely and effectively so that they are appropriate for the age, sex, body weight and clinical status of the patient. Community pharmacists on the other hand come in direct contact with the public and they not only dispense medications but also counsels' patients regarding general health topics such as diet, exercise, stress management, over-the-counter medications etc. Some community pharmacists also provide specialized services to help patients with diabetes, asthma, smoking cessation, drug addiction, and patients with high blood pressure. Pharmacists can prevent drug interaction, counsel patient regarding the disease and medication e.g. providing information, advice and assistance about medication and therapy due to their access of interpersonal communication. Thus, pharmacists can play a key role in preventing drug abuse by providing clear information about the adverse effects of medications.

ADR Reporting System in Bangladesh

It is important to recognize the adverse drug reaction first and according to the identification or observation action is taken. ADRs mostly act through similar patho-physical pathways for different diseases, distinguishing them is difficult, even impossible sometimes. However, the following step-wise approach may be helpful in assessing possible drug-related ADRs (Bangladesh National Formulary, 2015)

1. Ensuring that the medicine prescribed is the medicine received and actually taken by the patient at the dose advised.

2. Verification of the fact that, the onset of the suspected ADR was after the drug was taken,

not before. A careful observation of the patient feedback is desired.

3. Determination of the time interval between the beginning of drug treatment and the onset of the event.

4. Evaluation of the suspected ADR after discontinuing the drugs or reducing the dose and monitoring the patient's status.

5. Analysis of the alternative causes (other than the drug) that could on their own has caused the reaction.

6. Usages of relevant up-to-date literature and personal experience as a health professional on drugs and their ADRs and verify if there are previous conclusive reports on this reaction.

7. Reporting any suspected ADR to the person nominated (if any) for ADR reporting in the hospital or directly to the ADR Cell of the Directorate General of Drugs Administration (Nusrat et.al 2017).

How to report ADRs?

1. Patient should immediately report any type of adverse drug reaction due to the use of any medication to their primary doctor and help the doctor fill out the special ADR form.

2. Doctor, nurses, pharmacist and health workers can fill out the ADR form in PDF format and send it back to the DGDA.

3. Government/Private Hospitals/Clinics: Every hospitals and clinics must decide for itself how the reporting system should be operated and by whom. Generally, the physicians themselves act as reporters, completing the reporting form, keeping a record and sending them to the ADRM Cell, Directorate General of Drug Administration, Aushad Bhavan, Mohakhali, Dhaka-1212, Bangladesh. The hospital pharmacy in-charge may also report ADR by completion of the form after reporting physician consultation. He should report:

1. Apparent ADRs previously unknown to the reporter

2. Serious ADRs

3. All suspected ADRs to new drugs

4. Cases of suspected dependence

Challenges of Pharmacovigilance

- ✓ Several reports of irrational prescribing reported despite presence of growing body of knowledge on rational use interventions
- ✓ Along with knowledge multifaceted and complex solutions required to bring changes in behavior.
- ✓ Many new drugs and second-line drugs are very expensive and accordingly unaffordable for many governments and consumers.
- ✓ It's very difficult for DTC to run with traditional medical and pharmacy training where little emphasis is given to public health, managing drug, patient care and prescribing skills.
- ✓ Influence of pharmaceutical representatives, who always pushing doctors with bribe. Doctors merely stick to the principles of rational prescribing.
- ✓ It's the end users taking decision about medicine, provider, source and quantity.
- ✓ There's always a fund crisis for drug information and education to general people.
- ✓ Lack of independent drug information and advice. Worldwide, patient compliance is close to 50%. Part of the problem is that self-medication is widespread.
- ✓ Drug purchase in certain areas are handled by private sector but prescription and medicine purchase are combined. Commercialism and patient pressure lead to over treatment and misuse of antimicrobials.

Recommendations

- Building and maintaining a robust pharmacovigilance system
- Making pharmacovigilance reporting mandatory and introducing pharmacovigilance inspections
- High-level discussions with various stakeholders i.e., Ministry of Health, Pharmacy Council, Nursing Council, Dental Council, Pharmaceutical Companies and their associations, Consumer Associations,

nongovernmental organizations (NGOs) working in this.

- Creating a clinical trial and post marketing database for SAEs and ADRs for signal detection and access to all relevant data from various stakeholders
- List all new drugs / indications by maintaining a standard database for every pharmaceutical company
- Education and training of medical students, pharmacists and nurses in the area of pharmacovigilance.
- Collaborating with pharmacovigilance organizations in enhancing drug safety
- Building a network of pharmacovigilance and pharmaco-epidemiologists in Bangladesh
- Interaction with the IT sector in building a robust pharmacovigilance system for Bangladesh

Conclusion

Being drug expert and mentor of safe and effective drug use, pharmacists have important role play in detection, report, monitoring along with prevent ADRs. The lack of apprehension still exists among pharmacists who are confined to transition from product oriented to patient oriented. The gap can be minimized through continued professional development programs as well as reinforcing knowledge base in undergraduate level. An empowerment and engagement of community pharmacists to patient record check and electronic reporting may also reduce ADR related events. Without adequately identifying and fulfilling training needs of pharmacists and other health care professionals, the efficiency of national pharmacovigilance systems is unlikely to improve, which may compromise patient safety.

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