



GLOBAL JOURNAL OF MEDICAL RESEARCH: B
PHARMA, DRUG DISCOVERY, TOXICOLOGY AND MEDICINE
Volume 14 Issue 4 Version 1.0 Year 2014
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

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GJMR-B Classification : NLMC Code: QV 738



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The Need of Pharmacovigilance Activities in Yemen

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Abstract- Adverse drug reactions, medication errors and other drug-related problems are the leading causes of hospitalisation and are associated with a huge economic burden and significant human suffering. This serious issue of medication therapy also contributes to morbidity and mortality. At present, the monitoring of adverse drug reactions was started in Yemen by establishing a pharmacovigilance centre in 2011. Till now there is no published information about its work, number of reports and how they process it. The country and public are facing with many safety problems related to drug smuggling, counterfeit drugs, improper and irrational use of drugs, importation of unnecessary drugs and medical errors. Therefore, it is necessary to make serious steps and active regulations in Yemen to ensure patients and public safety in relation to medicines use.

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I. INTRODUCTION

Adverse drug reactions (ADRs) represent a serious health problem.¹ ADRs account for 3.2-7% of acute hospital admissions.^{2,3} They cause morbidity, mortality, and longer duration of hospital stay⁴ and increase hospital costs.⁵ Over 770,000 people are injured or die each year due to adverse drug events.⁶ A commonly quoted meta-analysis performed in the United States indicated that ADRs were ranged between the fourth and sixth most common cause of death in 1997.⁷ The World Health Organization (WHO) defines an ADR as 'any response to a drug that is noxious and unintended, and that occurs at doses used in humans for prophylaxis, diagnosis, or therapy, excluding failure to accomplish the intended purpose'.⁸

Several previous studies have reported the incidence of ADRs. A prospective observational study from Iran identified that 11.75% of patients had experienced at least one ADR.⁹ In another study done in Iran reported about 16.8% of patients had at least one ADR, and 2.9% of ADRs were identified as lethal.¹⁰ A study in South India found that the overall incidence of ADRs was 9.8%. This included 3.4% ADR-related hospital admissions and 3.7% ADRs occurred during the hospital stay.¹¹ In Saudi Arabia, a retrospective study showed 54% of ADRs to be preventable. The prevalence per year ranged from 0.07% in 1993 to 0.003% in 1999.¹²

In Nepal, the prevalence of ADRs was 0.86%. In addition, the male to female ratio of patients experiencing ADRs was 0.85, and 10.81% of the ADRs were severe.¹³

Pharmacovigilance is defined by the WHO as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems.¹⁴ Thalidomide was the greatest tragedy of 1961 and led to the establishment of the drug regulatory mechanisms of today.¹⁵ Pharmacovigilance is an arm of patient care that aims at making the best use of drugs and medicines for the treatment or prevention of disease without undesired effects. The history of international pharmacovigilance goes back as far as forty years, when the twentieth WHO assembly adopted a resolution to start an international system of monitoring ADRs.

The evolution of pharmacovigilance in recent years and its growing importance as a science have created much interest worldwide. Pharmacovigilance is based on sound scientific principles and is integral to effective clinical practice. The national pharmacovigilance centres have exercised significant influence on drug regulatory authorities. All developed countries have established national pharmacovigilance centres affiliated to the Uppsala monitoring centre in Sweden. Several developing countries requested WHO support and advice for building their pharmacovigilance centres.

All of the information about ADRs that is collected during the marketing phase of a drug is incomplete for five reasons: first, tests in animals are insufficient to predict human safety. Secondly, the limited number of patients are involved in clinical trials and carefully selected. Third, the licensing exposure of less than 5000 human subjects to a drug allows only more common ADRs to be detectable. Fourth, at least 30000 people required treatment with a drug to avoid missing of any patient. Fifth, information about rare but serious adverse reactions, chronic toxicity, use in special groups (such as children, the elderly or pregnant women) and drug interaction are often incomplete or unavailable; thus the high benefit of post-marketing surveillance to detect common ADRs.¹⁵ There are differences between countries in the occurrence of ADRs and other drug-related problems. This may be due to differences in diseases, prescribing practices, genetics, diet, and culture. The drug manufacturing

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processes, which in turn, influence pharmaceutical quality and composition, drug distribution and use, including indications, prescribed dose and availability as well as the use of traditional and complementary drugs (e.g., herbal remedies) are some of the other contributory factors that may pose specific toxicological problems when used alone and/or in combination with other drugs.¹⁵

Yemen is an Arab country located in the southern Arabian Peninsula. The Kingdom of Saudi Arabia, Oman, the Red Sea and the Arabian Sea border it. Yemen has a population of approximately 20 million, with more than 70% live in rural areas. The illiteracy rate is still high at about 55.7%. Yemen is a low-income country with a per capita Gross Domestic Product (GDP) of USD 659.¹⁶ The total expenditure on health is not available at the present time, but the governmental contribution is about USD 256 million a year or \$13 per capita and represents only 2% of the GDP. In general, the health services (either public or private) mainly focus major cities; though primary health centres/units and polyclinics are scattered throughout the whole country, including some rural areas. The statistical report (2003-2004) of the Ministry of Public Health & Population (MoPH) shows a total of 136 general hospitals (93 private), 470 polyclinics (341 private), 626 health centres (115 private), 2185 primary health care units, 380 maternity and child health centres, 1768 private pharmacies and a total of 4799 physicians (329 dentists and 974 specialists). In addition, there are a few non-governmental organisations (NGOs) and foreign medical missions.¹⁶

The local pharmaceutical industry is evolving gradually, covering only around 8% of the total market share. Medicines are imported via private sector agents and cover most of the country's needs.

There are critical health challenges in Yemen, including the high incidence of both communicable diseases (such as malaria, tuberculosis, schistosomiasis, sexually transmitted infections and vaccine-preventable diseases) and noncommunicable diseases (such as cardiovascular diseases, renal problems, cancer, and eye diseases). In addition, Yemen exhibits higher prevalence of lifestyle risk factors (including tobacco use, 'qat' chewing, malnutrition, injuries and accidents) and lacks the necessary sanitation (especially water sanitation).¹⁷

In Yemen, there is no systematic plan to monitor adverse drug reactions and drug-related problems. By the end of 2011 the SBDMA established a pharmacovigilance centre, till now there is no published information's about number of reports or how they process it.

This paper addressed the drug safety issues and highlights the justification of having pharmacy-vigilance activities in Yemen.

II. DRUG SAFETY PROBLEMS IN YEMEN

Drug safety issues in Yemen include many serious problems that can have detrimental effects:

a) *Smuggling of medicines*

Studies have confirmed that the proportion of drugs entering Yemeni territory via illegal channels amounts to 60% of all imported medicines. According to Supreme Board of Drug and Medical Appliances (SBDMA), a society for consumer protection that monitors the use of 192 fake medicines, 176 different drugs are smuggled into Yemen, 46 of which are fake.¹⁵ Medicines of doubtful quality, origin and expiry date are smuggled into the country through illegal channels and pose a serious threat to public health. Exposed to moisture and light during transport, their quality is also affected. Sometimes these medicines become quite popular and the demand for them increases, as in the case of phenolphthalein laxative tablets, which are illegal in Yemen but continue to be sold.¹⁸

b) *Fake drugs*

Huge amounts of fake drugs flood Yemeni markets and pose serious health threats. Many Yemeni patients have become victims of fake drugs that are not appropriate for human use. Faking of medicines generally begins with the most sought after and rare drug types and then further expanded to other therapeutic categories. Faking of medicines can only be identified by their side effects on the patients. There is no control over these drugs' safety, quality and effectiveness; SBDMA statistics indicate the presence of 46 different fake drugs on the Yemeni market.¹⁸

c) *Policies of pharmaceutical companies in developing countries*

Harmful drugs are still finding their way to developing countries. Some pharmaceutical companies market their products in developing countries, which are banned in their country of origin. These dangerous drugs generally sold without any concern for the health of the people, assisted by weak legislation and poor legal control of medicines in these countries.

One expert noted that the goal of the multinational companies that have planted their roots in developing countries is to achieve the highest level of profit regardless of humanitarian considerations. Pharmaceutical companies are not alone in using developing countries in this manner; contaminated food and radioactive waste were also shipped to developing countries for disposal.²⁰

Ten thousand companies produce drugs in the world, but 90% of the drug trade is controlled by 100 companies, of which only 25 multinational companies account for 60% of international sales.²⁰ Forty-five percent of the poorest nations of the world are still

entirely dependent on imported medicines. The third world produces only 10% of all medicines.²⁰

d) The lack of an active national drug policy

The primary goal of any policy is to ensure the availability of safe and effective, and quality medicines to meet the healthcare needs of the country.

Drug policy is an integral part of any comprehensive policy for health care. The formation of any national drug policy should take into account the health situation in the country, the medical care system, education and training of health care workers, possibilities for research and local production of medicines.²¹

The demand for medicines, distribution systems, possibilities for the evaluation and control of drugs, and international policies for pharmaceutical products are some of the other factors that should be considered at the time of formation of National Drug Policy. The need for a national drug policy and national system to monitor drug production and the presence of good governance to regulate matters relating to the implementation of drug control are some of the essential components of a robust functioning healthcare system.²¹

e) The lack of legislation

Till to date there is no legislation and regulation governing distribution and importation of drugs. There are no laws for the selection, registration, marketing and testing of medicines as well as no checks and balances to control importers and stop smuggling.

f) Weakness of local industry

The national pharmaceutical industry in Yemen is still emerging. It is still far short of the demand for domestic consumption. The eight existing local factories meet only 8.5% of the actual need in Yemen. They are unable to compete with world-famous brand names, and some of their products have lost credibility with Yemeni consumers. In addition, the local companies manufacture only medicines that will result in a quick profit and even unable to manufacture some life-saving drugs, worth mentioning are the therapeutic categories related to tuberculosis and cancer.

g) Registration of medicines without scientific criteria

The process of evaluation and registration of drugs should be based on the established requirements of quality, safety, efficacy, necessity and cost of drugs. The standards applied to the selection of the drugs should meet the following parameters:

1. Drugs must be selected based on scientific documentation.
2. The ratio between toxicity and effectiveness of a drug must be balanced by the severity of the disease.
3. The benefits of new drugs must be weighed against the availability of better therapeutic drugs in the market.

4. Combinations of drugs must be avoided unless and until it is clear that the compound has the advantages of both constituent drugs.
5. Definite medical need for new drug products should exist, and there should be medical justification of this need.
6. Drugs must be granted approval for a specific term (e.g., five years).
7. Price of drugs should be acceptable.²¹

h) Importation of unnecessary medicines

The private sector benefits from importing unsafe, nonessential and unnecessary medicines, merchandised by different means. World Bank study indicated that 41% of medicines imported in Yemen are unnecessary.¹⁸ The importation of such medicines from abroad exacerbates Yemen's imbalance in payments. Yemen officially imports 13,000 products that cost around 50 million Yemeni riyal every year.¹⁹

i) Uncontrolled medicine distribution

The aim of planned medicine distribution is to meet public health needs. Distribution of medicines through agents and pharmacies should take into consideration the population density, the distance and transport requirements.

Governmental medicines generally distribute via central stores to government clinics without the consideration of real need. The conditions in which these drugs are stored leave them susceptible to the sun, the rain, and theft.

There is no control over the private sector, which distributes medicines through pharmacies far more efficiently than public-sector distribution. The private sector nurtures financial gains and sometimes distributes dangerous medicines.

j) Improper prescription of drugs by physicians

Some physicians prescribe medicines to patients unnecessarily. Others prescribe the wrong medicine or one that is not consistent with the diagnosis. At other times, unsafe medicines are being prescribed for minor cases; either in response to the patient's desire or because the physician believes that more intensive treatment is better. Some physicians even prescribe medicines without a diagnosis when their clinics are crowded.

k) Improper dispensing by pharmacists or salespeople

Some pharmacists dispense drugs incorrectly. They aim to sell medicines for profit without adherence to the basic standards of humanity and ethics of the profession of pharmacy. For example, they may switch the medicine prescribed by a physician with a similar drug available in the pharmacy. The pharmacist does not explain the indications, contraindications or side effects of the drug to the patient. Pharmacists sell prescription drugs, including sedative and antibiotics, without a prescription. Many workers in the pharmacies

do not have a higher education. They often lack adequate scientific understanding, and some of them know only the names and locations of the medicines on the shelves of the pharmacy.

l) Improper consumption

The increased demand for and widespread use of drugs (13,000 drugs are already registered) are very serious problems in Yemen. The widening network of drug distribution, pharmacies, and wholesale distributors and the increasing number of smuggled drugs add to the problem. Yemen imports medicines from 117 companies of 54 different countries.¹⁹ All of this has led to a pharmaceutical consumption crisis with the following adverse consequences:

First, the irrational use of medicines, improper self-medication or the overuse of medicines prescribed by doctors as some doctors prescribe more than seven medicines in one prescription. Secondly, the adverse effects of these drugs are a major concern. The government is unable to test the quality and efficacy of these drugs due to the huge quantity of medicines coming from labs where the production of these medicines was not appropriately monitored. In addition, some doctors fail to prescribe proper medicines due to the marketing of one drug under multiple names and confusion over overlapping benefits of multiple medications.

m) Improper use of medicines by patients

The majority of patients do not follow the treatment prescribed by their doctors. Around 50% of patients do not use their medicines in the proper way. The patients' level of commitment to treatment decreases with the passage of time or after the disappearance of symptoms. In addition, sometimes the patient cannot buy the full course or the real medication prescribed, but they buy other medicines in the prescription, with the intention of treating the symptoms of the disease rather than the disease itself.

The high illiteracy rate of the Yemeni population makes it impossible for most people to read the instructions that come with their medicines. Thus, there is no awareness about indications, contraindications, side effects and expiry date.

n) Improper self-medication

Some patients treat themselves or their relatives without consulting a medical doctor. This can lead to adverse consequences for the health of Yemen's citizens as those who self-medicate are likely to be unaware of how to do so properly.

o) Lack of quality monitoring after marketing

The Yemeni medical authorities do not monitor the quality of medicines after marketing. Many ineffective drugs of poor quality are available in the market. Improper storage in most pharmacies can be detrimental to drug quality and effectiveness.

p) Lack of monitoring of ADRs

Monitoring and control of the harmful effects of drugs are one of the key components of any national drug policy. The prerequisites for monitoring of ADRs are:

- Measures to obtain information on medicines.
- Development of measures to take appropriate action on medicines causing adverse reactions in a timely manner.

First, doctors and pharmacists should report ADRs and notify health authorities and stakeholders. When a severe ADR is reported, scientific studies are advised to be conducted by medical and pharmacological researchers. Second, a number of measures can be taken following notification of an ADR:

- Withdrawal of the drug from the market.
- Banning of selling and importing.
- Cancellation of registration. Destruction of existing stocks of the drug. Warning doctors, pharmacists and consumers.

q) Unethical promotion of medicines

Unethical promotion of medicines is norm of pharmaceutical companies. The representatives of these companies do not explain the risks that may arise from the use of their medications. Some companies promote their drugs only by distributing gifts and samples and thus create a real demand for ineffective or harmful medicines.

r) No oversight of medical prescriptions

A medical prescription is a legal document and must have accurate information, transparent with the seal of physician, including his/her name, telephone number, and license number. Doctors should be encouraged to write prescriptions using generic names.

s) Medical errors

The incidence of medical errors has increased in Yemeni hospitals due to ignorance or incompetence of medical staff. Many patients suffered due to medical and prescription errors, leading to morbidity and mortality. One must recognise that some complications that occur in the course of treatment cannot be avoided or predicted. The majority of medical errors do not result in legal action, and there is no strict oversight of the work of doctors and nurses by the medical authorities.

III. CONCLUSIONS

ADR-related monitoring and pharmacovigilance activities are still very poor in a country like Yemen, where drug safety problems are rampant. Pharmacovigilance might play an essential role in preventing and overcoming such problems. Yemen must institute a 'Pharmacovigilance Program' and set up Pharmacovigilance Centres in association with regulatory bodies such as SBDMA and medical and pharmacy schools

An awareness programme for local pharmaceutical companies, medical professionals and patients

to inform them about the detection and reporting of ADRs must be designed.

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