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Review Article

Safety Monitoring of Medicines: The Available Mechanism in Yemen

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ABSTRACT

Adverse drug reactions (ADRs) are considered among important causes of morbidity and mortality. In order to minimize the harmful effects of medicines, countries have developed their own pharmacovigilance mechanisms. Yemen is a developing country located in Southern West of Asia which launched its own national pharmacovigilance program. The current pharmacovigilance program started with a limited activities implemented over a restricted area of the country and received only limited ADR reports. Though the program is successful to a certain extend, still there is a scope for improvement. This review addressed the drug regulation in Yemen, including the implementations and limitations of these regulation, highlighting the need for pharmacovigilance and go throughout the different stages of pharmacovigilance activities in Yemen and, finally suggesting measures and steps to foster pharmacovigilance activities to achieve the desired health care outcomes in Yemen.

Keywords: Adverse drug reactions, Drug safety, Pharmacovigilance, Yemen

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INTRODUCTION:

Adverse drug reactions (ADRs) represent a serious health problem [1]. Statistical evidence continues to mount that ADRs are common, yet often preventable cause of illness, disability and even death. ADRs are responsible for a significant number of hospital admissions ranging from 0.3% to 11% [2]. Over 770,000 people are estimated to be injured or die annually from adverse drug events [3]. A commonly quoted meta-analyses performed in the United States ranked ADRs at the 4th and 6th most common cause of death in 1997 [4]. In UK, a study had reported the occurrence of ADRs among 6.5 per cent of all hospitalized patient. Regrettably, among those patient, about 80 per cent the incidents of ADR were the leading cause for hospital admission. A similar percentage (4%) had been also reported in UK by another study in which excluded drug overdose from ADRs and reported annual cost to the NHS of £466 million. An alarming statistical finding of the later study demonstrated that over 2 per cent of those patients who were admitted to hospital with an ADR died. This would make the overall fatality rate from ADRs within the population 0.15 per cent [5]. 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 [6]. Developing countries probably had registered a higher trend. For instance, a prospective study from Iran reported 11.75% of the patients had had experienced at least one ADR in 2008 [7]. While, in an Iranian study in 1999 reported approximately 16.8% of the patients had at least one ADR whereas 2.9% of the ADRs were classified as lethal [8]. A remarkable

reduction in ADRs rates probably reflecting the improvement of ADRs preventive measures. Another study conducted in India, reported an overall incidence of 9.8%. In the latter study, 3.4% of ADRs as a cause of admission, and 3.7% ADRs occurred during the hospital stay [9]. A similar study was conducted in Riyadh, Saudi Arabia reported 54% of the ADRs to be preventable [10]. While, in Nepal, the prevalence of ADRs was 0.86% and tendency of severe ADRs to affect females more likely than mal. [11]

Hence, in order to prevent harm effect to patients from both, clinically prescribed or over-the-counter dispensed medications, there is a need to monitor ADRs by effective system able to; detect early ADR, obtain much more knowledge to ensure safety of drugs and to assess the harm, benefits and risk of available drugs [12]. Pharmacovigilance is emerged in the last few decades as evolving science and activities dealing with detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems'. Recently, its scope has been spread to cover herbals, traditional and complementary medicines, blood products, biologicals, medical devices, vaccines [2]. Nonetheless, there are a number of issues could be tackled by the strategic activities of pharmacovigilance – not exclusively – non-evidence based drug prescriptions, medications used with low level of evidence and misuse of medicines, food and chemicals.

The Need for indigenous pharmacovigilance programs in every country:

Beginning of any pharmacovigilance program, developer must take in account all the factors that will shape the program activities such as disease registry, health practices and rules at the area of concern, inhabitants culture, and the quality of pharmaceutical processed and how the medications made available and distributed to final destinations and outlets. Therefore, it is not surprising to find a pharmacovigilance programs varies from region to region within a country [12].

Data derived within a country or region may have greater relevance and educational value which probably would encourage national regulatory body towards proper decision-making. Nonetheless, applying information obtained another country (e.g. the country of origin of the drug) might not be relevant as well as cannot be applied to other parts of the world where all previously mentioned factors and circumstances might differ [6]. Again, we would like to stress on drug monitoring a tremendous value detecting ADRs and specifically in relation to counterfeit and substandard quality products. ADR monitoring is to assure that patients obtain safe and efficacious products.

Drug regulation in Yemen:

In general, medicine regulations and legislations aims to ensure the quality, safety, efficacy of medicines and accuracy of medicine information. It is developed, implemented, monitored and re-enforced by Medicine Regulatory Authority (MRA). The government of Yemen granted the power of responsibility to the MRA. MRA currently, is responsible for registration of medicines; importation, distribution and sales of medicines; medicine promotion; licensing of pharmaceutical establishments, their staff and performance; pharmaceutical quality assurance; commitment to Good Manufacturing Practice (GMP) and regulation enforcement. The SBDMA is the main MRA in the country. It has a semi-autonomous agency and concerned mainly with authorizing marketing, importing and manufacturing control; providing licenses for medicines, medicine producers and wholesalers; controlling the medicine market and controlling the quality and pharmacovigilance of the imported medicines and medical appliances [13]. In the last five years, medicines regulatory system has been placed under proper assessment. The SBDMA receives funding governmental budget and retains its revenues from regulatory activities as well. However, the apparent limitation of MRA was the inability to distribute a list of the registered products, updating the names of the products on a regular basis in order to provide a reliable source about the authorized products which have been officially available in the country. The profile further revealed that unused guide being published for the registered pharmaceuticals. Unfortunately, this guide had not been updated for more than a decade. Another limitation, is registration and authorization which are paramount for the public feel 'safe' about using the medicines that are suitable to their health and needs, but the seemingly lackadaisical attitude of the authority regarding marketed medicines and pharmaceuticals update have created loopholes in Yemen healthcare system. Similarly, even though legal provisions

were existed to allow the appointment of government pharmaceutical inspector's role to check premises in which pharmaceutical activities are performed. Surprisingly, local manufacturers, private wholesalers and retail distributors were claimed that inspection visits were irregular, infrequent, and an emerging issue of concern appeared on the surface, which is the contradiction between the responsibilities of the MRA and those accountable for the pharmaceutical affairs in the MOPHP [13].

Current pharmacovigilance program in Yemen

At present, the monitoring of adverse drug reactions was launched in Yemen by establishing a pharmacovigilance centre in 2011. Currently, there is no published information about its activities, number of reports it received and clear guideline to deal with incidents and process reported documents. The country and public are encountered 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 clear regulations in Yemen to ensure patients and public safety in relation to medicines use.

Academics from Faculty of Pharmacy in Aden University decided recently accompanied with appointed representatives of SBDMA in Aden to initiate a pharmacovigilance program in Yemen, to activate the pharmacovigilance centre of SBDMA to cover the whole country and to establish plan to implement the basic steps for the establishing pharmacovigilance program according to Uppsala Monitoring Centre (UMC) guidelines.

Activities began towards the end of 2014 by reviving of the center, designing a website and reporting forms for HCP and consumer, with aim to raise the awareness among HCP and consumers. There were many articles in Yemeni journals were published as well as many posters were distributed in hospitals to achieve the desired objective. A number of educational interventions were conducted among HCP in hospitals and teaching pharmacovigilance for pharmacy students in Aden University and conducting research activities in pharmacovigilance. Dr Alshakka has studied the current practices of pharmacovigilance when he surveyed for CPDs in Aden [14]. The report showed a poor KAP towards ADR reporting and pharmacovigilance. Participants have insufficient knowledge about pharmacovigilance practices, operation, purpose and the usefulness of pharmacovigilance. The results of the study emphasized the importance of continuing efforts to promote ADRs reporting program to ensure patient and public safety in relation to medicine use. Education and training of health professionals and public will be important in increasing and maintaining ADR reporting. In another paper, Alshakka et al found that a relatively good level of pharmacovigilance knowledge has been encountered among physicians and nurses. Nurses had had more positive perception towards pharmacovigilance compared to physicians who demonstrated more valued consumer reporting [15].

The National Center, followed up drugs after marketing, assess the quality of pharmaceuticals, disclosure of side

effects, and evaluate and develop solutions leading to prevent these incidents, and receive communications on this matter, as well as the follow-up news from international bodies and organizations to take appropriate decisions about the safety of pharmaceuticals trade.

The objectives of the Yemeni pharmacovigilance center:

1. Detect, early, of the symptoms of drug side effects.
2. Discover the increased frequency of the known side effects of some medications
3. Identify the risk factors and symptoms of potential mechanical side.
4. Assure quality control of medicines.
5. Prevent damage resulting from the use of medicines.
6. Gather information and opinions regarding the safety of medicines and participating transparency and clarity in the program.
7. Support and encourage the legalization of the use of medicines to reach the best ways to treat patients and improve public health.
8. Carry education and communication on a global level with regard to the safety, efficacy and quality of pharmaceuticals used in the treatment.

The activities of the National Center:

1. Follow-up drugs after marketing.
2. Follow-up reports of the quality of pharmaceuticals and forwarded to the relevant departments.
3. Detect side effects, and evaluate and develop leading solutions to prevent or reduce their occurrence.
4. Receive communications relating to the safety and quality of medicines.
5. Create a database for dealing with approaching relevant in order to be used to communicate with them when needed.
6. Follow-up news from international bodies and organizations.
7. Carry appropriate recommendations about the safety of pharmaceuticals traded, through the decisions of the team pharmacovigilance consultant.
8. Communicate with relevant parties such as agents, pharmaceutical companies and health professionals to follow up the implementation of the requirements of the National Center and to make sure of that.
9. Preparation of annual reports on all activities of the National Center.
10. Preparation and follow-up training programs to carry out the National Center for vigilance and medication safety.

Taking in account, the fact that the public is not fully aware of the risks of medicines and the possibility of their misuse and abuse, the government of Yemen has decided to dispense drugs only by prescriptions except some medicines which can be dispensed without prescriptions namely over-the counter (OTC) medicines. However, The MOPHP and the Supreme Board of Drugs and Medical Appliances (SPDMA) showed incompetence to regulate, control, and monitor the prescriptions. Generally, people in Yemen may not have been very well informed about the potential effects of drugs and dispensing medication without a valid prescription is common practice in this country. All medicines including prescribing-only medicines (POM) such as antibiotics, antipsychotic,

cardiovascular drugs could be obtained without a prescription from pharmacies. Pharmacies are mostly run by pharmacy technicians and untrained dispensers, probably due to the availability of few qualified pharmacists in service. Thus, we cannot expect that the pharmacy staff would comprehend the detailed impact of a drug they are selling to customers. The tragedy situation when those dispensers are misinterpreted as 'physicians' for the customers, as they involved in many times in diagnosis, prescribing and dispensing medicines for various health complications and diseases, despite their ill knowledge and against authority rules. This repeated professional misconduct must be rectified. Rational use of medicines aims to improve the use of medicines by health providers, individuals and community through rational prescribing, dispensing and appropriate use of individuals and community.

Therefore, it is necessary to implement strategies to ensure patients and public safety in relations to medicines use. In developing countries generally there is a limited coverage and under-reporting of ADRs.

The effectiveness of pharmacovigilance activities in a country is directly dependent on the active participation of health professionals, patients and consumers. The more information about ADRs collected will definitely lead to more useful outcomes as national database. Therefore, all should be briefed regarding the ADRs reporting system and encouraged to report ADRs even suspected ones.

Strength and weakness of the current pharmacovigilance program in Yemen:

The strengths of the program are that it is well linked with the SBDMA. The major weaknesses of the program are poor awareness among health professionals about pharmacovigilance, difficulty of signal generation because unavailability of national computerized database on drug prescribed; poor coordination to involve pharmaceutical industries on drug safety issues; lack of information generation on genetic effects and social practices and drug interaction associated with drug use ; and also there are only a few reports about traditional and herbal drugs which were widely used.

Another major limitation of the program is under reporting. The reasons for underreporting being uncertainty of types of reaction to report, lack of awareness about the existence, function and purpose of national ADR reporting. There is also no official reports system for consumers which limit the reporting occurring at the consumer level. Finally, no involvement of nursing staff in the ADR monitoring program.

Strategies to uplift the current pharmacovigilance program:

Several strategies can be taken to uplift the current pharmacovigilance program in Yemen. Some of the proposed strategies are mentioned below.

Awareness program for the healthcare professionals: more awareness programs must be conducted regularly for the healthcare professionals emphasizing the importance and functioning of the national pharmacovigilance program.

Teaching pharmacovigilance: Pharmacovigilance should be taught to undergraduate Medical, Nursing, Pharmacy curricula and other healthcare related to ensure a well prepared graduates in future practice. Pharmacovigilance modules should be incorporated in the rational use of medicines (RUM). The Uppsala Monitoring Centre (UMC), the international collaborating centre for ADR monitoring, has suggested a number of basic components of a pharmacovigilance course for pharmacologists and other healthcare personnel.¹⁶ In Yemen, at the time being, there is a very limited educational program for the undergraduate students in the area of pharmacovigilance.

Consumer reporting: Strategies should be taken to involve the consumers in the ADR reporting program. At present the involvement of consumers in the pharmacovigilance program is very limited.

Conclusion

Though there is a national pharmacovigilance program in Yemen, there are a few limitations with the existing program. The SBDMA in the past has taken several initiatives to promote the concept in the country. In spite of these interventions under reporting is still a major concern. Strategies needs to be taken to improve the ADR reporting culture among various healthcare professionals involved in medication use. Pharmacovigilance as science must embedded in curricula to inculcate proper the healthcare practice to students and importantly to establish consumer reporting program in the country.

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