Review

Current status, and future prospects of pharmaco-epidemiology and post-marketing surveillance in Saudi Arabia: A review of literature

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A B S T R A C T

Background: Pharmacoepidemiology is the concept used for evaluating the impact of drugs among a large number of people in the post-marketing phase. The use of this concept makes it increasingly necessary to detect the recurrence of drug-related anomalies that mostly occur through health care professionals or patients themselves. Pharmacoepidemiology is important since it helps to provide the right balance of benefits versus risks of the drug products while remaining an excellent tool to prepare the risk/benefit balance profile.

Aim: The objective of this study is to review and explore the current status and future prospects of pharmacoepidemiology and post-marketing surveillance in Saudi Arabia.

Methods: A literature review has been conducted using keywords such as pharmacoepidemiology; ‘post-marketing’; ‘surveillance’; ‘Saudi Arabia’; ‘ADRs’; and ‘pharmacovigilance’. The study refines its focus on 13 pharmacoepidemiology and post-marketing surveillance research studies conducted in Saudi Arabia using the databases; Embase, PubMed, EBSCOhost, MEDLINE, and AMED.

Results: Pharmacoepidemiology and post-marketing surveillance creates a body of research in Saudi Arabia, but within a restricted scope. The studies that were reviewed assessed the challenge from various perspectives. Lack of knowledge, post-marketing surveillance, ADR reporting, and increased use of generic products were reported.

Conclusion: The current level of research may be widened and increased through improving the process of ADRs reporting system. More research needs to be conducted based on nation-wide observational studies. Collaboration among medical professionals, academics and industries should continue to establish a more efficient and consistent post-marketing surveillance system.

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1. Introduction

Pharmacoepidemiology is the concept used for evaluating the impact of drugs among large number of people in the post-marketing phase. Similar to other common problems with the epidemiology of diseases, it remains a significant issue of concern to health authorities, specifically within the area of Saudi Arabia. Saudi Arabia itself spans a large geographical area with an estimated population of 315 million. Drug development remains a major concern that health services have encountered in Saudi Arabia in the last four decades (Al-Jazairi et al., 2011).

A question remains as to whether the pharmacoepidemiology in Saudi Arabia is capable of preventing adverse drug events (ADEs). This makes it increasingly important to detect the recurrence of drug-related anomalies that mostly occur through health care professionals or patients themselves. Pharmacoepidemiology forms a part of the health economics used for analyzing the efficient use of pharmaceuticals. Pharmacoeconomic researches are important since they assist in the measurement of the use and clinical outcomes of the pharmaceutical products and services in a country. Such evaluation is significant as it can rectify the system and allocation of healthcare resources in a more efficient manner (Al-Jazairi et al., 2011).

Public-sector providers are integral to the healthcare industry in Saudi Arabia since they dominate the market. Accordingly, the Ministry of Health (MOH) is primarily responsible for healthcare spending. Approximately 75% of the total healthcare spending in Saudi Arabia is made by the government (Al-Jazairi et al., 2011). At the same time, however, the pharmaceutical market heavily relies upon imports; most importantly the high-tech patented drugs. The Saudi Food and Drug Authority (FDA) regulates the marketing of drugs and does not allow sales of any pharmaceutical product that does not conform to the country’s licensing requirements. Moreover, a strict price control policy prevails aimed to limit both the private and public spending on the generic, branded, and over-the-counter (OTC) pharmaceuticals. Until the Saudi FDA was established in 2003, MOH remained the responsible authority to register all the pharmaceutical companies. In July 2009, the Saudi FDA became the responsible authority for adopting this function. It now provides licensing for these products.

The post-marketing surveillance of medical products can best be achieved through collaboration between the patients, the healthcare providers, and the regulatory bodies. Saudi Arabia became a member of the WHO pharmacovigilance program after the FDA was established in 2009. The center formed an integral part of the Saudi FDA associated with the WHO Uppsala Monitoring Center to provide local data on the Adverse Drug Reporting (ADR). The study of pharmacoepidemiology is important in health care since it helps provide the correct balance of benefits versus risks of the drugs products while remaining an excellent tool to prepare the risk/benefit balance profile. Pharmacoepidemiology research will help analyze the ADRs in Saudi Arabia and the way these can be prevented. The aim of this study is to review and explore current status and future prospects of pharmacoepidemiology and post-marketing surveillance in Saudi Arabia.

2. Methods

Methodological differences play an important role in epidemiological studies across the field of pharmacology (Jensen & Stovner, 2008). The current study follows a qualitative research design in conducting a literature review of the primary studies published in the selected area of research. An electronic search was conducted to identify articles in Embase, PubMed, EBSCOhost, MEDLINE, and AMED. The following keywords were searched: ‘pharmacoepidemiology’, ‘post-marketing’, ‘surveillance’, ‘Saudi Arabia’, ‘ADRs’, and ‘pharmacovigilance’. The factors which have been applied for research influence the interpretation of results and therefore the study outcomes (Al-Homrany, & Irshaid, 2007).

The literature search was conducted through a combination of these keywords in order to retrieve 39 peer-reviewed articles. The search was limited to articles specifically focused on pharmacoepidemiology in Saudi Arabia and excluded any other country. This methodology forms a qualitative review study precisely focused on pharmacoepidemiology in Saudi Arabia. Approximately 13 studies related to the pharmacoepidemiology and pharmacovigilance challenges in Saudi Arabia met the inclusion criteria. The search included pharmacovigilance for the hospitals, communities, over-the-counter-drugs, and by the regulatory bodies. Keywords: Pharmacoepidemiology; ‘Post-marketing’; ‘Surveillance’; ‘Saudi Arabia’; ‘ADRs’; and ‘Pharmacovigilance’ in Saudi Arabia

3. Results

A number of potential studies were selected to address the aim of the paper. The studies selected provided an overview of the current status of pharmacoepidemiology and pharmacovigilance in Saudi Arabia; however, the relevant studies conducted are quite limited in their scope. There has been only limited evidence present regarding the research status of pharmacoepidemiology in Saudi Arabia. Alshammari et al. (2015) stated that pharmacovigilance forms a well-established topic among various nations, but it remains a new concept in Saudi Arabia. Saudi Arabian contributors consider it a collective effort that is made by various stakeholders to promote the effective and safe use of medicines among the population. The author has highlighted the need of extending research on pharmacovigilance which has not yet
reached the expected level of attention in Saudi Arabia, in particular by the authorization holders and the healthcare professionals.

3.1. Pharmacoepidemiological studies

Self-Medication has been the major threat identified in the region of Saudi Arabia in regards to pharmacoepidemiology. A qualitative review by Khalifeh et al. (2016) provides evidence regarding the prevalence of self-medication in the Middle East including Saudi Arabia. The study identifies weaknesses in the enforcement of regulations in Saudi Arabia, a finding which explains why the majority of prescription medications are purchased as self-medication. This indicates a potential abuse of medications in Saudi Arabia. Medications, abused as self-medication in Saudi Arabia, include the codeine-containing products, the anabolic steroids, decongestants, psychoactive-prescription only medicines, sedative antihistamines, and laxatives. The study further highlights the paucity and inadequacy of research in the field, since the available research rarely reports post-marketing surveillance, especially with regards to self-abuse.

Another systematic review conducted by Limaye et al. (2017) has also identified self-medication as a great public threat in Saudi Arabia that evades regulatory mechanisms. There have been no established standards in Saudi Arabia that may assess self-medication. The author reported that there have been various academic investigations regarding self-medication practices in Saudi Arabia, although most of these are meta-analysis and comparative studies. These studies, however, lack pertinent adequacy regarding the status of post-marketing surveillance.

Al-Jazaieri et al. (2008) has highlighted generic substitution of drugs as a common practice globally, which has given rise to safety suspicions. The author reports of an increased local product circulation in the pharmacology market of Saudi Arabia, which is alarming. This has given rise to concerns regarding the switching from name brands to generics. Synthesis of data suggests that bioequivalence testing must form an essential part of post-marketing surveillance, and that the providers must routinely consider the generics for innovative products. It is difficult to ensure the safe switching for critical dose drugs, narrow therapeutics, and highly variable drugs. Additionally, the use of drugs in Saudi Arabia is inadequately supported with special precautions, mainly in the field of post-marketing surveillance. It is highly advisable to perform a switch process to reduce the healthcare costs in the country while also strengthening the post-marketing surveillance program. It is advisable for Saudi Arabia to implement strengthened post-marketing surveillance initiatives especially for the highly variable drugs prescribed and those with a narrower therapeutic index.

Balkhi et al. (2017) conducted a retrospective cross-sectional study to investigate prevalence of polypharmacy among adult patients in a tertiary hospital setting in Saudi Arabia. The major objective was to determine patients’ characteristics that associated them with polypharmacy. The study derived data from electronic health records for a period of 6 months (i.e. January–June, 2016) in an outpatient setting. The study used descriptive statistics for analyzing the study sample. It used a multivariable logistic regression model for examining the associations between different polypharmacy related variables. The study found polypharmacy as highly prevalent among adult patients, especially those above 60 years. Polypharmacy is dangerous and may potentially impact the overall drug therapy process. It is found to form a major risk factor for developing undesirable adverse drug events especially among patients with chronic health conditions.

Aljhadey et al. (2015a) conducted a cross-sectional survey in Riyadh, Saudi Arabia and examined the community pharmacies across five areas including West, East, North, South, and Middle Riyadh. Consumers were randomly approached to participate in the study for buying cosmetic and medicinal equipment. The study determined the prevalence of self-medication in Riyadh and also assessed the attitudes, knowledge, and perceptions of consumers towards self-medication. The most common reasons for using medications without a prescription included considering the minor symptoms not sufficient to visit a doctor, time-saving, and the perception of minor illnesses whose treatments were already known. Lack and/or limited knowledge of consumers along with negative perceptions are the major reasons in Saudi Arabia for prevalence of self-medication among individuals. More than 68% of participants were unaware as to whether the medicine bought was a prescription only or over the counter.

3.2. Pharmacovigilance studies

Aljhadey et al. (2015) and Shankar & Jha (2015) have identified the challenges that Saudi Arabia face in regards to pharmacovigilance and have also made recommendations regarding how the procedures can be improved. The study has qualitatively analyzed the issue from the perspective of healthcare practitioners in Saudi Arabia. The studies incorporated views from pharmacists, physicians, and academicians. Major challenges identified regarding post-marketing drug surveillance were the ADR complexities and the paucity of the ADR reporting forms. The SFDA strive to improve the processes, but receive little or no feedback regarding ADR, a factor which makes the process of post-marketing surveillance weaker.

The authors have further reported lack of decision making among the local authorities regarding withdrawal of drugs from the market as well as a lack of information on pharmacovigilance. Hospitals in Saudi Arabia also fail to follow a systematic method of ADR reporting, which is the cause for many of them to go unnoticed. There prevails a significant lack of collaboration between the hospitals and regulatory bodies. The other challenges that the pharmaceutical industry in Saudi Arabia faced regarding post-marketing surveillance included lack of drug manufacturers and a system of pharmacovigilance that is less attentive. In the view of the authors, strong regulatory requirements and improved communication may help improve the transmission of data and might also establish the basis of a unified ADRs reporting system.

Mahmoud et al. (2014) assessed the knowledge of community pharmacists in Saudi Arabia, regarding their behavior and experiences towards ADR reporting, through conducting a cross-sectional study. The study specifically focused on community pharmacists in Riyadh. The study reports that pharmacists in Saudi Arabia have poor knowledge regarding reporting of the ADRs. The authors identified a direct need for implementing design interventional programs for pharmacovigilance authorities in order to increase awareness and knowledge regarding reporting of the ADRs. ADRs have been identified as a major cause of morbidity and mortality in various countries (Patel et al., 2007). Absence of post-marketing surveillance in regards to ADRs suggests the higher risks that Saudi Arabia has been facing regarding the use of pharmaceutical products once they have been released into the market. However, the initiative taken by SFDA is worth noting; it has established a National Pharmacovigilance Center. The center makes available online reporting forms and papers that encourage the ADR reporting by the public health professionals. Nevertheless, this needs further development and consideration.

Aljhadey et al. (2012) raised concern regarding pediatric safety of the H1N1 safety vaccine in Saudi Arabia. The study aimed to investigate the safety Pandemrix® in Saudi Arabia and the associated adverse reactions among caregivers. Children aged 6–18 were included in the study. The risk of influenza reduced among vaccinated children as compared to unvaccinated. Children with H1N1 vaccine did not show a risk of emergency room visits and hospital
ization. The study identified the need of proactive pharmacovigilance as important for assessing the safety of vaccines with other medications. The results indicate that it remains increasingly desirable to collect information for adverse reactions since it may benefit both the developed and developing countries.

Aljadhey et al. (2016) conducted a prospective cohort study for determining the incidence of adverse drug events (ADEs) for assessing preventability and severity in four Saudi hospitals. Pharmacists and independent clinicians participated in the study to identify Adverse Drug Events (ADEs), medication errors, and the potential ADEs; all of these were used to determine their severity and preventability. The study found ADEs common in Saudi hospitals and particularly in the ICUs resulted in significant mortality and morbidity. The root causes of ADEs in Saudi Arabia are unknown and form a potential area for prospective research. Such studies will help improve the development of interventions and testing to minimize the harmful impacts of medications.

Aljadhey et al. (2013) conducted a prospective cohort study to determine the incidence of ADEs, and the assessment of their severity and preventability. The study was conducted in a 900-bed tertiary academic hospital. The number of potential ADEs was reported as 13.8% per 100 admissions. The study reported 8.5% ADEs in a Saudi Hospital per 100 admissions. ADEs occurring in the ordering stage are preventable; therefore, the ordering stage must be kept as a target for reducing ADEs. The study provided baseline knowledge for future medication in Saudi Arabia and development of safety interventions. The quality of care can be improved when the administrators and healthcare professionals are able to prevent medication errors as a priority. The suggested solutions for preventing medication errors include automatic and information technology, initiation of medication safety programs and involvement of pharmacists in the medication monitoring procedures.

4. Discussion

Results suggest that Saudi Arabia has very well-established national policies for pharmaceuticals and also has an established drug regulatory framework. However, the reporting and surveillance system is found to be quite weak. The industry mainly relies upon the international market although Saudi Arabia constitutes the largest nation in the Middle East and the African (MEA) region. One particular drawback is the increased reliance on medicines influenced by the original and patented pharmaceuticals (Babar et al., 2007). The concept of pharmacoepidemiology and post-marketing surveillance has also extended the scope for the role of pharmacists and pharmacologists. Traditionally, they have only been required to prepare and dispense the drugs prescribed by the physicians. Currently, they must take into account the different aspects of patient care. The results cited, either directly or indirectly, indicate the lack of ADR reporting, although reporting the ADRs remains the key to post-marketing surveillance. The role of pharmacists has not been widely documented in Saudi Arabia, which restricts their performance for reporting ADR and pharmacovigilance. Dissemination of knowledge regarding pharmacovigilance has been found to be very low. As a result, the SFDA and MOH are not able to take into account various ADRs, and therefore the drugs responsible for causing them remain live in the market. Results retrieved regarding lack of ADRs can be verified in light of the researches by Oreagba et al (2011) and Abdel-Latif & Abdel-wahab (2015).

It can be concluded that self-medication is very common in Saudi Arabia and the responsible authorities need to focus upon improving awareness of consumers regarding self-medication to properly use medications. Easy access to the community pharmacy has been one reason identified for self-medication (Saeed et al., 2014). Increased buying power and easier access to OTC products have enabled patients get OTC medication without prescription. According to Aljadhey et al. (2015), the sources of information regarding self-medication and abuse of generic drugs are also less adequate. A need has been identified for community pharmacists to take initiative for the active counseling of consumers and for taking a cautious approach in dispensing medications.

Al-Badr et al. (2014) conducted a study to identify drug-related interactions (DDIs) among inpatients in an internal medicine ward in Saudi Arabia. This constituted an exploratory study that assessed patients in the public hospital in Al Ahsa. The study considered sociodemographic aspects of patients and conducted a descriptive exploratory review. Key findings suggested higher occurrences of DDIs in the setting. Some of the factors identified which can be associated with the occurrence of DDIs include number of drugs, lack of clinical trials, and the comorbid medical conditions. It is evident that the scenario of pharmacoepidemiology research in Saudi Arabia is somewhat similar to other countries in terms of low awareness regarding ADR reporting programs and the poor rates of reporting. According to Mahmoud et al. (2014), the ADRs reporting rates are as low as 13.2% in Saudi Arabia. This appears to be mainly because of the lack of knowledge, low awareness, and unavailability of the ADR reporting forms.

Lack of knowledge can be verified by the study conducted by Jose et al. (2014). The results of this study, however, are contrary in the sense that pharmacists acquire an acceptable level of knowledge of the overall subject but are not specifically oriented towards ADR and DDIs reporting. An increase in educational programs is essentially required to increase awareness among pharmacists and other stakeholders to improve the processes of ADR reporting as well as to assure their active participation in the pharmacovigilance program. Results suggested the need of ADR reporting; the SFDA requires a multidisciplinary approach and must involve pharmacists as the major role players in it.

This review underpins several limitations. There has been a large body of evidence available on pharmacoepidemiology and post-marketing surveillance in Saudi Arabia. However, this study does not include all the papers relevant to the subject, which raises the possibility of selection bias. The paper may also have inadvertently incorporated publication bias since the study reviewed only articles available on the aforementioned databases and ignored the others, as well as unpublished research that might be worth considering.

The study followed a simple objective, i.e. to conduct a literature review, and it does not include any advocating comments regarding certain interventions that are applied in the Western world and other regions. This can be covered in future research. The major strength of this study is the consistency it shows throughout the research findings and the widespread recommendations it draws in support of pharmacoepidemiology and post-marketing surveillance in Saudi Arabia. Though the study utilizes peer-reviewed articles, it did not implement any specific searching criteria to establish quality of the cited studies. Notwithstanding, this did not fall within the objective of the current study. There have been extensive accounts of literature present on information technology and informatics regarding the significance and repercussions of pharmacoepidemiology and post-marketing surveillance in Saudi Arabia. These may be researched in greater depth and detail to precisely point out the specific challenges and issues.

5. Conclusion

Pharmacoepidemiology is integral to establish drug safety in any country. It constitutes a fundamental forum which may
exchange, communicate and disseminate information to the respective authorities. These results have been evaluated from different research papers that provide insights on the status of pharmacoepidemiology and post-marketing surveillance research in Saudi Arabia. It is evident that the concept has only been recently developed and is in its initial phases. Though the initiatives indicate potential, they require further development and establishment to reach their farther ends. The study incorporated peer-reviewed articles from recognizable databases and synthesized data to comment on the current research status of pharmacoepidemiology and post-marketing surveillance, and ultimately the pharmacovigilance in Saudi Arabia. As such, there has been a limited quantity of data available regarding the research conducted on pharmacoepidemiology and post-marketing surveillance in Saudi Arabia. This matter has been discussed from various perspectives and has been assumed as a challenge for the pharmaceutical industry. The current level of research may be widened through improving the process of a ADRs reporting system. Further research should be conducted on a larger scale nation-wide level. Precise statistics are required to elaborate the current status of research conducted on the subjects included in this study; this would indicate the right dimension for researchers to disseminate relevant information that may guide future success.

5.1. Future recommendation

Saudi Arabia must focus on developing the role of SFDA. It appears that the ADR reporting forms are integral to improving post-marketing surveillance and pharmacoepidemiology of drugs. Therefore, it is recommended that the state should focus on improving this aspect through implementing strengthened interventions. Moreover, the regulatory bodies, pharmaceutical industries, and hospitals must pay deliberate attention to raising awareness regarding the need of ADRs reporting. The four important sectors which may individually be developed include hospitals, regulatory bodies, academic bodies, and pharmaceutical companies. The aspect of pharmacovigilance is only weakly developed with processes that are less disseminated or not very feasible. There is a need to promptly identify any adverse reaction and to invoke its subsequent withdrawal from the market. Pharmacovigilance can be improved through increasing clinical trials for post-marketing surveillance of drugs, and the respective authorities must not merely rely upon the non-clinical or experimental methods for studying safety and efficacy of drugs once they are marketed. It is further recommended that all the regulatory authorities must show deliberate interest in exploring rare and non-listed ADRs, especially for newly launched medications. This shall encourage the implementation of pharmacovigilance for the pharmaceutical companies and may further improve the process of the reporting system. The result would be a follow-up of the newly launched products to report upon the impact of pharmacoepidemiology.

Conflict of interest

None.

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