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Review Article

Development of Pharmacovigilance Culture

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ABSTRACT

The history of international pharmacovigilance goes back as much as fifty years, with the thalidomide tragedy in the early 1960s, in which many thousands of congenitally deformed infants were born as the result of in utero exposure to a medicine. As a result, the Sixteenth World Health Assembly in 1963 adopted a resolution (WHA 16.36) that reaffirmed the need for early action with regard to the rapid dissemination of information on adverse drug reactions. This resolution led to the creation of the WHO Pilot Research Project for International Drug Monitoring in 1968. Since its inception, the project has evolved into the WHO Program for International Drug Monitoring, which is coordinated by the Uppsala Monitoring Centre in Uppsala, Sweden, and has 118 official member states, and 29 associate member states. The last few decades have also seen a major increase in the public availability and access to medical and biopharmaceutical information in many respects pharmacovigilance. The WHO defines pharmacovigilance as "the science and activities concerned with the detection, assessment, understanding and prevention of adverse reactions to medicines". Effective Communications in pharmacovigilance is a "public health activity with profound implications that depend on the integrity and collective responsibility of all parties – consumers, health professionals, researchers, academia, media, biopharmaceutical industry, drug regulators, governments and international organisations – working together. "Together the best practices described within each of these phases of pharmacovigilance combine to form a 'Gold Standard' of a robust pharmacovigilance system.

Key words: Pharmacovigilance, Drug, safety, quality, adverse reactions, public health, patient care.

INTRODUCTION

Pharmacovigilance, usually defined with the World Health Organization (WHO) definition of "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problems," [1] it is a mandate for the pharmaceutical industry, including Market Authorisation Holders (MAHs), in most developed countries, but this is not the case for all countries. The International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) has a statement on their website regarding the importance of pharmacovigilance [2]. It should also be considered the responsibility of all governments and health care providers (HCPs) in the interest of the public's health; a clearer role for the public is being established. This special issue of the International Journal of Clinical Pharmacy looks at the current state of pharmacovigilance from different countries and provides some insight into the future. It also explores some special patient populations. Fornasiern et al. [3] presents an overview of the history of pharmacovigilance, while Baldo et al. [4] offers a guide to the terminology. The definitions of pharmacovigilance used by the authors are broad or narrow interpretations of the WHO definitions for adverse drug reactions (ADRs) and adverse drug events (ADEs). These definitions can limit pharmacovigilance programs to ADRs or broaden them to include medication errors, inappropriate use, counterfeiting, quality issues and lack of effectiveness. Causality is always an issue; Behera et al. [5] compare different methods of assessment. The European Medicines Agency (EMA) [6] working closely with WHO and the United States Food and Drug Administration (FDA), has established good pharmacovigilance practices. The range of compliance with these guidelines is very good in many developed countries but may be non-existent in the developing nations, representing a large percentage of the world's population. Eight working groups identified and discussed this and numerous other issues at a 2016 Oman meeting of the WHO Programme for International Drug Monitoring [7]. The pharmacovigilance of rare diseases is even more complicated, since the number of reports will be extremely low. Chaumais et al. [8]. Clinical pre- and post-authorization studies are the primary source of

ADRs reports early in the product life cycle. Spontaneous reports become more important in the later stages of the cycle. Concerns about the ability and responsibility to collect data on generic versions have been raised [9]. Historically, most information outside of studies has come from spontaneous reports from HCPs; although pharmacists have been reporting for years, expanding this role in many countries is critical. A drug registry is normally maintained by the reference drug MAH throughout the life cycle (from discovery to end of product life); including for biological. Registries from outside industry are also important data collection methods for information such as on drugs in pregnancy, oncology, and rare diseases. AlSaad et al. [10] explore the use of registries and other sources of real-world data on the effects of psychotropic in pregnancy. Other sources of data, including health system records, were used by Wall et al. and Gonzales [11,12]. The use of large databases such as for pharmacovigilance systems and the storage of national, regional or organizational health records is an increasing source of information. The major systems are VigiBase, the WHO Program for International Drug Monitoring; EudraVigilance, the EMA system for European Economic Area members; and FAERS/VAERS, the FDA pharmacovigilance reporting systems. Countries also have their own systems. At least 130 countries submit data to Vigibase, in an attempt to create a global system [13]. Algorithms, such as that used by Zhao et al. [14] and rule-based data mining are being used to identify ADRs in those large databases. Artificial intelligence may be able to make this process automatic. The use of social media, especially by patients, to post information on drug events is now a major source of data [15] in the second paper, presents the progress and continued needs for the developing nations. Many studies employing these databases and registries use proxies to identify ADRs; harmonization of the systems is important to avoid missing these reactions. Aquiar et al. [16]. Modig and Elmståhl [17] used a population database to identify use of non-steroidal anti-inflammatory drugs in those at risk for renal dysfunction, increased use of these sources for signalling and monitoring of ADRs is expected. Biomarkers that may eventually be included in the databases could improve identifying those at risk. Claus [18] asks whether the process is cost-effective. Future studies are needed on the use of genetic testing, big data, artificial intelligence and block chain technology to understand if they provide solutions or add more ethical and other challenges to the pharmacovigilance process. Industry and regulatory bodies are important partners, but innovation comes from the researchers and practitioners. The pharmacist is in the ideal environment to work with patients and organizations to create a better pharmacovigilance world.

Updates on pharmacovigilance process

Machine learning and Artificial intelligence in PV

Use of technology on scale may enable the pharmacovigilance industry to increase operational efficiency and the consistency of data quality when processing ICSRs. An interviewee stated "Aside from the obvious case volume challenges, I think one of the main challenges is separating the needles from the haystack. Making sense of the huge amount of information we currently have and the enormous amount of untapped information in registries, social media, Excel sheets, literature out there. But also going even further, linking other data sources to this data to make even more sense of it and start looking for relationships other than drug–drug interactions or drug–adverse event relationships. Maybe even moving into predictive models." ML has the potential to enhance and increase the efficiency of DS professionals' work by augmenting decision-making processes when viewing machine predictions in 496 K. Danysz et al [19]. machine-readable documents. This could allow DS experts to focus on other aspects of pharmacovigilance.

New Core Competencies.

As AI is introduced to pharmacovigilance, these core competencies are not considered all-inclusive for the field of computer science but serve as an indication of what skills a DS professional should acquire to work with AI in pharmacovigilance. Given the principles set out by King's model [20] of the DS/pharmacovigilance professional core competencies and skill sets, a DS professional should be able to understand and interact with the safety database they are using. AI in pharmacovigilance is a novel concept and would require more effort and time to be invested in training personnel.

Social networking sites and their relevance to pharmacovigilance

Social networking sites (SNS) and applications allow for the exchange of user-generated content where by people talk/ communicate, share information, network and participate in community activities. The motivation to connect

and learn about one another has given rise to niche SNS. Recent years have seen the emergence and proliferation of SNS dedicated to healthcare communities (usually consisting of health professionals and/or consumers/patients), which have become particularly popular among patients, with the most common intended use being self-care [21], i.e. social media serving as a platform that allows patients to exchange information about their health condition with others who are battling with the same health issues, and receive peer-to-peer support (online patients communities)[22,23]. Social support is deemed extremely beneficial in combating health concerns like depression and mental illness [24, 25].

Specialised healthcare social networks and forums can include

Generic health-centred SNS (generic networking sites on general health topics and disease support, usual requiring user profiles), such as Patients Like Me (www.patientslikeme.com), DailyStrength(www.dailystrength.org),MedHelp(www.medhelp.org),WebMD (https://exchanges.webmd.com/), and Cure Together(http://curetogether.com/), where users discuss their health related experiences, including use of prescription drugs, side-effects and treatments–Medicine focused sharing platforms (patient forums), like Ask a Patient(http://www.askapatient. com) and Medications.com (http://www.medications. com/), which allow patients to share and compare medication experiences. Disease specific online health forums focused on specific diseases, e.g. the Talk Stroke forum (https://www.stroke.org.uk/forum) for stroke survivors and caregivers hosted by UK's Stroke Association [26], Australia's ReachOut.com (https://au.reachout.com/forums) forum for mental health support, etc.

Health search logs

Health information seeking represents a purposeful and goal-oriented activity that according to Niederdeppe et al [27] describes active efforts to obtain specific information in response to a relevant event, outside of the normal patterns of exposure to mediated and interpersonal sources that constitute mere information scanning. Tapping on back-office social data, several scholars have demonstrated how search logs can be used to detect new ADRs. White et al. [29] demonstrated that anonymised signals on drug interactions can be mined from search logs, using a 2011-reported adverse event (hyperglycaemia) due to a previously unknown interaction between the drugs paroxetine, an anti-depressant, and pravastatin, a cholesterol lowering drug. By mining search queries on Google, Bing and Yahoo Search from 2010, White et al. [28] found that people who searched for both drugs were also more likely to search for terms related to the adverse event than those who searched for only one of the drugs. Search information was provided to the researchers anonymously by users who agreed to share their search history. The study was carried out after the ADR had been identified, and using this approach for the identification/detection of unknown ADRs will remain a challenge. Similarly, Chokor et al. [29]

Conclusion

As outlined in objectives, the present paper makes a number of contributions to the area of pharmacovigilance and particularly to its social data applications and also recent developments of pharmacovigilance in machine learning and artificial intelligence and development of pharmacovigilance culture how it's used to be and how it has changed the safety of the patients and gained insights of the developments.

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