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Review Article

Pharmacovigilance in India and five ASEAN countries (Malaysia, Singapore, Thailand, Indonesia, Philippines): A comparison study

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ABSTRACT

The World Health Organization (WHO) defines PV as the science and activities related to the detection, assessment, understanding, and prevention of adverse effects or any other possible drug-related problems (WHO 2004). In 1968, during the 16th World Assembly the 16.36 resolution called for "a systematic collection of information on serious adverse drug reactions during the development and particularly after medicines have been made available for public use". This led to the formation of the WHO Programme for International Drug Monitoring (PIDM) in 1968. PV systems should include all entities and resources that protect the public from medicines-related harm (adverse reactions, poor product quality, medication errors, and therapeutic ineffectiveness), whether in personal healthcare or public health services. The PV system safeguards the public through efficient and timely identification, collection, and assessment of medicine-related adverse events and by communicating risks and benefits. The WHO has provided technical and normative leadership on PV since the development of the first voluntary notification scheme in 1961. As of January 2016, 123 countries have joined the WHO PIDM, and in addition 28 associate members are awaiting full membership. WHO has defined norms and guidelines for PV and has allowed information sharing among the participant countries. Another WHO PV-related activity is the work of the Council for International Organizations of Medical Sciences (CIOMS) which was established jointly by WHO and UNESCO in 1949. Starting with the publication of the Suspect Adverse Reaction Report Form (CIOMS Form I) by the CIOMS working group II, other CIOMS publications have greatly shaped the direction of PV. CIOMS publications have also greatly influenced the development of International Conference on Harmonization of Technical requirements for Registration of Pharmaceuticals for Human Use (ICH) E2A-E2F guidelines in drug safety. The standards for the electronic transmission of regulatory information regarding the individual case safety report (ICSR) has been changing over the last decade. The ICH adopted the E2B (R2) in February 2001 and the E2B (R3) in 2005, is being developed as the proposed harmonized international standards for health products safety reporting. These ICH guidelines have facilitated the adoption of harmonized standards for PV activities. This study contributes to filling the gap in the understanding of the PV systems capacity in Indian and five ASEAN countries namely Malaysia, Singapore, Thailand, Indonesia, and Philippines.

1. Introduction

Pharmacovigilance system in India was launched in 1986 with a formal adverse drug reaction (ADR) monitoring system. India joined the WHO Programme for International Drug Monitoring in the year 1998. Malaysia established its own Pharmacovigilance system in the year 1987 and became a member of the WHO Program for International Drug Monitoring in 1990. The Malaysian Adverse Drug Reaction Adverse Committee (MADRAC)

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oversees the Pharmacovigilance program since its inception. The Adverse Drug Reaction Monitoring Unit (ADRMU) in Singapore was established in 1993. The unit has joined the WHO in the year 1994. The Thai National ADR Monitoring Center was set up in 1983 as a part of Thai Food and Drug Administration, Ministry of Public Health. In Indonesia the initiation of PV activities started first between 1975 and 1978 as a pilot project involving six public hospitals. Subsequently in 1980, the national program on monitoring of ADRs through voluntary reporting by HCPs started. In 1990, the National Agency of Drug and Food Control (NADFC) joined the WHO Program for International Drug Monitoring. The ADR reporting system in the Philippines was established in August 1994 and was recognized as a national center member of the WHO International Drug Monitoring, Uppsala in February 1995.

2. Materials and Methods

The method involved the review of research articles, review articles and other materials from the common internet sources. Various journals Articles and reports were thoroughly searched for analysis of Pharmacovigilance system in India and five other ASEAN countries (Malaysia, Singapore, Thailand, Indonesia, Philippines). The comparison study would help us to analyses the positive and negative aspect of Pharmacovigilance system these countries.

3. PV System in India and ASEAN Nations

3.1. PV System in India

National Programme of Pharmacovigilance was launched in 2005 and was renamed as the Pharmacovigilance Programme of India (PvPI) in 2010. The PvPI works to safeguard the health of the Indian population by ensuring that the benefit of medicines outweighs the risks associated with their use. The culture of reporting of ADRs has achieved remarkable success, with 250 PvPI-established adverse drug monitoring centers all over India and provision of training to healthcare professionals.[1] Currently, almost hundred thousand case reports are submitted to NCC-PvPI each year through its 250 ADR Monitoring Centers (AMCs) located across India, and India is the one of the top contributor countries under WHO-Uppsala Monitoring Centre since 2012 and start issuing drug safety alerts from March 2016.[2,3] The ADRs collected by the ADR monitoring Centres and MAHs are communicated to NCC-PvPI in the form of Individual Case Safety Report (ICSR). The annual database accounts 64, 441 ICSRs for the period APR-2018 to MAR-2019. Reporting patterns are on the increase every year and have shot up in recent years.[4]

3.2. PV System in Malaysia

The number of ADR reports received from HCPs by MADRAC reached 5850 in 2009. However, according to WHO guidelines for the optimal national PV center, this number of ICSR is considered low. The Malaysian PV reporting system, like most others countries around the world, suffers from underreporting of ADRs by HCPs.[2] All ADR associated with the use of CAM (Complementary and alternative medicine) products (including health supplements) submitted to the Malaysian Centre for ADR Monitoring, National Pharmaceutical Regulatory Agency over a 15-year period were reviewed and analyzed. From a total number of 74 997 ICSR reports in the database, 930 involved CAM products.[5] Malaysia started consumer reporting to improve compliance level from recent times.[6] Various guidance documents are being prepared with the aim of developing a uniform framework towards assuring patient safety while expediting the availability of biosimilar products.[7] Pharmacy student of several Malaysian universities confirmed that they had taken courses on the concept of pharmacovigilance during their current pharmacy curriculum.[8]

3.3. PV System in Singapore

The Health Sciences Authority (HSA) has also appointed a Pharmacovigilance Advisory Committee (PVAC), which comprises experts in the fields of medicine, pharmacy, pharmacology, and forensic sciences for proper implementation of PV system in Singapore. Their main roles is to assess the impact of major drug safety issues and give advice on the appropriate regulatory actions to be taken to enhance drug safety. The spontaneous adverse event (AE) reports submitted by HCPs and companies remain a critical information source for pharmacovigilance surveillance system. In Singapore, the Health Sciences Authority (HSA) is responsible for the management of the spontaneous reporting system (SRS).[9] One of the important decision making example in recent time is to make HLA-B*1502 testing the standard of care prior to first use of CBZ (carbamazepine) in Asians and to subsidize the genotyping test at public hospitals.[10] Expert configured natural language processing (NLP) framework in Hospital discharge summaries which offers a potentially resource of adverse event to evaluate drug safety in real-world practice.[11] Major positive attributes of the Risk management programs include active involvement of independent expert clinical advisory committees in identifying and evaluating risks through the assessment of reports of serious and unusual reactions, and regular communications about risks from HSA to HCPs by means of bulletins.[12]

3.4. PV System in Thailand

Initially, 18 regional centers were set up until 1992. However, in 1997, the regional centers were expanded to cover all the health products, and currently there are 23 centers in Thailand. However, in 2010, the focus changed from hospital-based ADR monitoring to community-based ADR monitoring. The vigilance system in Thailand started in 1983 with focus on drugs, known as "Pharmacoviglance System", and was later expanded to include other health products (e.g. herbal medicines, vaccines, and medical devices) and became "Health Product Vigilance System" in 2008. The national center's name was then changed to Health Product Vigilance Center. Reporting of ADRs is a national program and all hospitals send reports of ADRs to this center. The center receives thousands of ADRs annually from various hospitals in Thailand. The reports received at Health Product Vigilance Centre (HPVC) grew steadily from a few hundred in the beginning to 50,000 reports per year nowadays. The adverse events were reported mainly from governmental hospitals.[13] Research showed outpatients reported a high proportion of potential ADRs with high confidence and accuracy in Thailand.[14] Survey conducted involving rural communities showed nearly half of community living experienced ADRs, and has implications for other rural elderly persons of low education.[15] Thai National Pharmacovigilance Center (NPVC) has been operational since 1983, but its performance has never been formally audited. The risk communication function was evaluated to be unsatisfactory in one of the studies recently.[16]

3.5. PV System in Indonesia

In 2004, the PV unit was established under the Directorate of Distribution Control of Therapeutic and Household Healthcare Products. From the year 2008 to 2011, strengthening PV framework was happened, making it mandatory for the pharmaceutical industry to perform PV system. However, the agenda from the year 2012 to 2014 is to strengthen the risk management program, linking National Regulatory Authority (NRA) with public health program, development of dedicated website for PV activities including e-ADR reporting, collaborating with stakeholders (e.g. HCPs, pharmaceutical companies) to promote PV activities. The PV system in Indonesia consists of voluntary reporting through HCPs in hospitals and public health centers, general and private practices, through pharmacists in pharmacy. Mandatory reporting through Marketing Authorization Holders (MAH) was done through spontaneous ICSR by submitting Council for International Organizations of Medical Sciences (CIOMS) form.[2]

3.6. PV System in Philippines

The PV system in the Philippines developed with the intention of promoting safer medicines and rational drug use. It is well known that in the Philippines, there is an increased level of traditional medicines use. As with several ASEAN countries, the culture of reporting ADRs is low, and this is perhaps in part because the AEs are unrecognized, sometimes the AE is misinterpreted as part of the healing action, and practitioners of these remedies are unlikely to report them. People who resort to herbal medicines are usually from the poor segment of the population and are likely to believe in unscientific claims and unlikely to report them.[17] Recently Reporting of ADRs via texting was initiated with an existing ADR paper-based system.[18]

4. Conclusion

Strengthening the regulatory and PV system of the studied countries is a global imperative for improving outcomes in treatment and for patient safety. There is a strong and urgent need to strengthen medicine safety systems both within and outside of countries in the ASEAN region. Developing and developed countries are both suppliers and recipients of global medical product supply chain. Public health programs, global health initiatives, and entire health systems rely on safe, effective, and good quality medicines. However, fully functional regulatory systems are not yet in place in many ASEAN countries. This review calls for concrete efforts to build regional and global coalition in a consolidated manner to improve the systems and capacities required to assure patient safety and to improve health outcomes in ASEAN region.

5. Abbreviations

PV - Pharmacovigilance, WHO - World Health Organization, ASEAN - Association of Southeast Asian Nations, ICH - International Conference on Harmonization of Technical requirements for Registration of Pharmaceuticals for Human Use, CIOMS - Council for International Organizations of Medical Sciences, ADR - Adverse Drug Reaction, PvPI - Pharmacovigilance Programme of India, MADRAC - Malaysian Adverse Drug Reactions Advisory Committee, HAS - Health Sciences Authority, HPVC - Health Product Vigilance Centre, NADFC - National Agency of Drug and Food Control, ICSR - Individual case safety reports.

6. Conflicts of Interest

All contributing authors declare no conflicts of interest.

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