Global Pharmacovigilance, challenges, and future considerations: West globe and East globe

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ARTICLE INFO

Keywords: pharmacovigilance, safety, west globe, east globe

Introduction: Pharmacovigilance (PV) plays a consequential role in the drug regulatory system and is a constantly evolving multifaceted field. In the process of carrying out its effective management, the PV system does undergo a lot of challenges on a global pitch. PV system is well developed in the western globe (United States, United Kingdom, Germany) while the east globe (e.g.: India) is still in the evolving stage.

Methods: Major discrepancies include different regulatory authorities for each nation with different forms for ADR reporting and also different timelines.

Results: To mention a few; there is a regulatory gap because of the continuously evolving regulations and business processes, it is difficult to comply with the diverse regulations effectively; gross underreporting in the east as compared to the west; increased concern about the safety and potential toxicity of traditional Chinese herbs in the east; self-medication; linguistic barrier, etc. Steps like harmonization of regulation by drafting guidelines that are uniform globally; leveraging digital technologies to optimize ADR reporting; meticulous and timely reporting; inclusion of PV in the curriculum etc. can be employed.

Conclusions: While PV has witnessed substantial development over the years, areas of discrepancies need to be identified to build a seamless PV system. Need for an effective revolutionary roadmap to tackle all the hindrances to fortify its harmonious functioning.

An official publication of Global Pharmacovigilance Society.

Introduction

Pharmacovigilance (PV) plays a consequential role in the drug regulatory system and is a constantly evolving multifaceted field. The World Health Organisation (WHO) defines PV as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems." It helps in identifying adverse drug reactions (ADR) thus improving patient care and safety and also encouraging safe, rational, and effective use of medicines from both therapeutic and economic frames of reference (Fernandes et al., 2018).

There are mainly 4 cornerstones involved in the PV system which have been proved effective in safeguarding public health. They are
- Collection of ADR through various sources
- Analysis and understanding of the data and information
- Communication with all stakeholders
- Regulatory action for public health protection.
In the process of carrying out the effective management of these cornerstones, the PV system does undergo a lot of challenges on a global pitch.

**PV in the West Globe**

PV in the western globe particularly United States (US) and Europe which are the first and second-largest pharmaceutical markets in the world respectively are well developed because of their well-established regulatory bodies which have laid out clear PV functioning and reporting requirements. On the other hand, in the east globe particularly Asia which is the third-largest pharmaceutical market in the world (Japan, China, India) national regulators, as well as their respective regulations, are still evolving (Biswas P, 2013).

The major differences between PV regulations in the West and East globe are given below in Table 1 (Jose et al., 2019; Hans and Gupta, 2018; Hori et al., 2011).

### Table 1: Comparison of PV Systems

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>United States</th>
<th>Europe</th>
<th>Japan</th>
<th>China</th>
<th>India</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Regulatory authority</td>
<td>FDA</td>
<td>EMA</td>
<td>PMDA and MHLW</td>
<td>CNDA and MOH</td>
</tr>
<tr>
<td>2</td>
<td>PV authority</td>
<td>CDER/CBER</td>
<td>EVDAS</td>
<td>PMDA</td>
<td>CNDA</td>
</tr>
<tr>
<td>3</td>
<td>Guidelines followed</td>
<td>GVP and Pharmacoepidemiologic assessment</td>
<td>GVP</td>
<td>ICH-E2A</td>
<td>ICH-2EA</td>
</tr>
<tr>
<td>4</td>
<td>Online ADR reporting software</td>
<td>MedWatch</td>
<td>Eudravigilance</td>
<td>PMDA database</td>
<td>Chinese ADR database</td>
</tr>
<tr>
<td>5</td>
<td>PV database</td>
<td>FAERS Sentinel system</td>
<td>EVDAS, EVWEB</td>
<td>JADER database</td>
<td>CADRMS</td>
</tr>
<tr>
<td>6</td>
<td>ADR form types</td>
<td>3 forms: a)3500 b)3500A c)3500B</td>
<td>Yellow card ADR form</td>
<td>Online spontaneous reporting system</td>
<td>Online spontaneous reporting system</td>
</tr>
<tr>
<td>7</td>
<td>PSUR timeline</td>
<td>15-day alert reports, quarterly for the first 3 years and annually thereafter</td>
<td>First two years-every 6 months, once a year for two consecutive years once in 3 years thereafter</td>
<td>Every 6 months for the first two years and annually later</td>
<td>Annually for the first 5 years then every 5 years</td>
</tr>
</tbody>
</table>


### The Challenges

Table 2: Challenges in PV systems in West and East Globe

<table>
<thead>
<tr>
<th>West Globe</th>
<th>East Globe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory gap because of the continuously evolving regulations and business processes, it is difficult to</td>
<td>Gross underreporting due to lack of awareness among HCP and consumers, excess workload lack of medical</td>
</tr>
</tbody>
</table>
comply with the diverse regulations effectively (Beninger P, 2018). Encouraging collaboration of PV centers with public health authorities to ensure ADR reporting is done at the right time and does not hinder access to essential medicines. (Dal Pan et al., 2014).

System integration by maintaining high levels of data quality and privacy (Dal Pan et al., 2014). Lack of resources (people, time, money) in comparison with the growing proportion of available data.

Self-medication: In the current era of the internet where everything is available on the internet, over-the-counter drug consumption has increased significantly creating a new challenge for PV (Fernandes et al., 2018).

Social media: Difficult to interpret layperson terminologies i.e. inability to identify the patient reporter which raises ethical concerns and regulatory issues (Sloane et al., 2015).

Discussion

Comparing the specific components of the PV system namely PV regulation, regulatory authority, and processes across the west and east globe (US, UK, India, China, Japan) shows many areas of dissonance. Major discrepancies include different regulatory authorities for each agency with different forms for AR reporting and also different timelines. Being the largest pharmaceutical market, there is disharmony in many areas which need to be assessed and worked upon to bring a robust and compendious PV system ensuring international harmonization. The deficiencies that our study identified confront low- and middle-income countries which are less of a constraint in developed countries. A strong PV system is a crucial part of the overall medicines regulatory system which indicates the rigor and competence of the regulatory bodies in fulfilling their responsibilities for oversight of producers and markets (Hans and Gupta, 2018). Understanding what is a safety concern versus a crisis and what is required for reporting safety information between industry and regulators would help in minimizing miscommunications and help in maintaining greater worldwide drug safety and utilization. The WHO, The ICH of Technical Requirements for Registration of Pharmaceuticals for Human Use, and the CIOMS and their efforts toward harmonization of pharmaceutical regulation specific to PV and towards safer medicines are of great importance. They have made great strides toward coalescing PV practices globally but a level of complete harmonization of the adverse event reporting systems and risk management strategies does not yet exist (Andrews et al., 2006).

Future considerations

While PV has witnessed substantial development over the years, areas of discrepancies need to be identified to build a seamless PV system with sustained efforts. This is a collaborative venture which requires the teamwork of HCP, patients, and stakeholders to build an efficient and stringent PV setup.

The following considerations can be employed going forward-

- Harmonization of PV legislation-Drafting of guidelines for ADR reporting which are uniform globally.
- Adopting ‘Generic ADR form’ worldwide mandatorily for reporting of any/all ADRs (Singh et al., 2012).
- Shifting from Big data to Smart data- This will strengthen PV network and improve operating PV
capabilities and collaborative working in terms of coordination, communication, evaluation, and assessment of ADR reporting, signal management, and quality assurance management thus causing standardization of PV processes (Dal Pan et al., 2014).

- Volume to Value-Leveraging digital technologies like machine learning, natural language processing (NLP), robotic process automation, application programming interface (API) to optimize reporting of adverse events.
- Expand the involvement of regulators and manufacturers with professional and academic institutions, patient-based organizations, financial institutions, and IT sectors.
- Building up of the foundation with EU2P model (European training program in pharmacovigilance and pharmacoepidemiology) which will help stakeholders in collaborating with academic institutions thus helping present PV professionals and new ones expand their skills. Introducing such programs in other regions/countries will help broaden the horizon of existing PV (Fernandes et al., 2018).
- Mandatory inclusion of PV course in the undergraduate curriculum.
- Training of the health personnel.
- Increase the number of ADR monitoring centers (AMC) where reporting centers are not available (Fernandes et al., 2018).

Conclusions
PV is the most proficient tool to safeguard public health. By combined efforts and a streamlined approach, and effective revolutionary roadmap can be crafted to tackle all the hindrances to fortify its harmonious functioning. As Wallace and Evans have rightly said PV should operate in a culture of scientific development. This requires the right balance of inputs from various disciplines, a stronger academic base, and greater availability of basic training and resource which is dedicated to scientific strategy.

Conflict of Interest
No conflict of interest

References


