Do current pharmacovigilance systems enable early public protection?

Editorial Article

Semra ŞARDAŞ*

Istinye University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Istanbul, Türkiye

Regional Pharmacovigilance (PV) systems, coordinated by regulatory authorities, collect and analyze safety data, primarily through spontaneous reporting (SRS) remains a cornerstone of PV. However, underreporting, delays, and limited real-time analysis restrict their public health impact. Adverse drug reactions (ADRs) significantly impact healthcare systems, leading to increased hospitalization rates and costs.

Drug toxicity determination is a main step in drug design and involves identifying the adverse events (AEs) of chemicals on humans, plants, animals, and the environment. Pre-clinical evaluations are a necessity for preventing toxic drugs from reaching clinical trials. Despite this, high toxicity is still a major contributor to drug failure accounting for two-thirds of post-market drug withdrawals and for one-fifth of failures during clinical trials. Thus, accurate toxicity estimates are necessary for ensuring drug safety, and can help reduce the cost and development time of bringing new drugs to market.

Animal studies have historically been the most conventional approach taken to assess toxicity. However, these studies are constrained by cost, time, and ethical considerations. Numerous computational, in silico, approaches have demonstrated utility in estimating the toxicity of drug candidates. These approaches predict toxicity by evaluating various features of the drug and include target-based predictions and Quantitative Structure- Activity Relationships (QSAR).

With the growing adoption of Artificial Intelligence (AI) in healthcare, machine learning models offer promising solutions for ADR prediction. While drug ap-

* Corresponding author: Sema ŞARDAŞ
E-mail: semra.sardas@istinye.edu.tr
ORCID: 0000-0001-5456-8636

proval requires rigorous clinical testing, many adverse reactions only become apparent after widespread public use.

When we look at the global PV practices that emphasizes mandatory reporting by manufacturers and healthcare institutions in Europe, the European Medicines Agency (EMA) and EudraVigilance which is the EU's central database for adverse event reporting facilitates early detection of safety signals across EU member states. The PV Risk Assessment Committee (PRAC) plays a key role in assessing and managing risks. In the United States Food and Drug Administration (FDA) collects ADRs through MedWatch and the FDA Adverse Event Reporting System (FAERS). Japan's Pharmaceuticals and Medical Devices Agency (PMDA) operates a robust PV framework, which includes reexamination and reevaluation of drugs based on post-marketing data.

WHO and the Uppsala Monitoring Centre (UMC) manages VigiBase, the global database of individual case safety reports (ICSRs). It promotes harmonization of safety data and collaborates with more than 130 countries to enhance global PV practices.

The question is; Do Current Systems Enable Early Public Protection?

While existing systems provide a vital safety net, they often fail to ensure early intervention for several reasons;(i) Underreporting: It is estimated that less than 10% of all ADRs are reported. (ii) Latency: Signal detection and regulatory action can take months or even years. (iii) Bias and Incompleteness: Many reports lack crucial information, and rare or long-term side effects are easily missed. (iv) Public Communication Gaps: Safety updates may not effectively reach or influence public behavior. Consequently, while global PV systems are essential, they do not consistently enable the public to take early preventive measures before facing adverse effects.

AI can significantly improve PV. For example, by incorporating the present large datasets rapidly to AI and detect complex tools for active surveillance. Such contributions would not only reduce health risks but also place AI-driven PV innovation for early signal detection and patient risk profiling. By the help of this Predictive Modeling, AI systems can forecast which patient populations are at higher risk of specific ADRs for early signal detection and patient risk profiling. Privacy and Consent in using real-world data for PV must respect patient confidentiality

In conclusion PV systems around the world have made remarkable progress in identifying and managing drug-related risks. However, to empower the public and minimize harm proactively, these systems must evolve beyond traditional

spontaneous reporting. AI offers promising tools to enhance real-time monitoring, predictive risk assessment, and effective communication by developing ethical and transparent AI solutions that protect public health and align with global PV regulations. Since, PV is essential to post-marketing surveillance of pharmaceuticals, ensuring that the benefits of medicines outweigh their risks (AI) will improve signal detection, enhance real-time surveillance, and support risk minimization by presenting opportunities and challenges for public health which is yet unclear. Therefore, AI can have an emerging role of in PV for adverse drug reaction prediction.

REFERENCES

Raies AB, Bajic VB. *In silico* toxicology: computational methods for the prediction of chemical toxicity. WIREs Comput Mol Sci, 2016;6(2):147-172. Doi: 10.1002/wcms.1240

Onakpoya IJ, Heneghan CJ, Aronson JK. Worldwide withdrawal of medicinal products because of adverse drug reactions: a systematic review and analysis. Crit Rev Toxicol, 2016;46(6):477-489. Doi: 10.3109/10408444.2016.1149452

Segall MD, Barber C. Addressing toxicity risk when designing and selecting compounds in early drug discovery. Drug Discov Today, 2014;19(5):688-693. Doi: 10.1016/j.drudis.2014.01.006

Anna OB, Alexandre Y, Nicholas PT. Artificial intelligence for drug toxicity and safety. Trends Pharmacol Sci, 2019;40(9):624-635. Doi: 10.1016/j.tips.2019.07.005