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Digitalisation of Pharmacovigilance: The Role of Artificial Intelligence and Data Analytics

Farmakovijilansın Dijitalleşmesi: Yapay Zekâ ve Veri Analitiğinin Rolü

Algül Dilara Dokumacı[1], Yusuf Karataş[1]

[1]Çukurova Üniversitesi Tıp Fakültesi Tıbbi Farmakoloji Ana Bilim Dalı, Adana, Turkey

ABSTRACT
The digital transformation of healthcare and the pharmaceutical industry is considered an important step in the field of pharmacovigilance. Standard pharmacovigilance approaches have more time and labor requirements, and it is suggested that the use of big data and artificial intelligence can improve the effectiveness of pharmacovigilance activities. Therefore, in this article we address the digitalisation of pharmacovigilance and the role of artificial intelligence and data analytics. The challenges and costs of drug discovery are discussed, highlighting the high failure rate of drug programs and the importance of the cost of bringing new drugs to market. Additionally, this article emphasizes the future possibilities for drug safety and suggests that the healthcare and pharmaceutical industries can move forward with a focus on digitalisation.
Keywords: Adverse events, pharmacovigilance, PV digital

ÖZET
Sağlık hizmetlerinin ve ilaç endüstrisinin dijital dönüşümü, farmakovijilans alanında önemli bir adım olarak kabul edilmektedir. Standart farmakovijilans yaklaşımları daha fazla zaman ve iş gücü gerektirmekte ve yapay zekâ kullanımının farmakovijilans faaliyetlerinin etkinliğini artırabileceği önerilmektedir. Bu nedenle, bu makalede farmakovijilansın dijitalleşmesi ve yapay zekâ ile veri analitiğinin rolü incelenmektedir. İlaç keşfinin zorlukları ve maliyetleri tartışılmakta, ilaç programlarının yüksek başarısızlık oranı ve yeni ilaçların piyasaya sürülme maliyetinin önemi vurgulanmaktadır. Ayrıca bu makale, ilaç güvenliği için gelecekteki olasılıkları vurgulamakta sağlık ve ilaç endüstrilerinin dijitalleşmeye odaklanarak ilerleyebileceğini önermektedir.
Anahtar kelimeler: Advers olaylar, farmakovijilans, PV dijital

Introduction

Drug discovery is indeed a challenging and costly endeavour. It is reported that, substantial risks are related to the development of a new drug with a high failure rate of 97% in drug programs[1]. Moreover, the average cost of bringing a new medicine to market is 2.8 billion dollars ($). These aspects highlight the massive financial investment required by pharmaceutical companies and significant unpredictability that arises during the drug development process[1,2]. Due to these issues, the healthcare and pharmaceutical industries are rapidly adopting digital transformation to improve drug discovery and development procedures.

Today's healthcare and drug development procedures are accelerating with the support of the digital revolution. Pharmacovigilance is the post-marketing activity of monitoring drug safety and reporting adverse drug events, and it is one of the key programs benefiting from the digital revolution. Traditional pharmacovigilance methods rely on manual data collection, classification, and analysis, which can be time-consuming and labour-intensive. Traditional pharmacovigilance processes can be implemented more efficiently and quickly by merging the use of big data and artificial intelligence. These processes can be carried out faster and more efficiently by the implementation of digitalisation. Therefore, this narrative review focuses on how pharmacovigilance is becoming digitalised, as well as the role of artificial intelligence and data analytics on digitalisation.

Digitalisation of Pharmacovigilance: Gaining a New Dimension

Pharmacovigilance is formed by combining the Greek word "pharmakon" meaning medicine and the Latin word "vigilance" meaning to be alert and vigilant[3]. In general, it is defined as the science of detection, evaluation, understanding and prevention of adverse drug events[4]. It is a process that regularly monitors, evaluates, and reports the effects, side effects and safety profiles of drugs[5]. Pharmacovigilance, an integral part of drug development and safety measures, is dedicated to the vigilant observation of adverse events (AEs) caused by specific medications. Its primary objective is to detect patterns of adverse drug reactions (ADRs) and to mitigate their impact on public safety throughout the entire drug life cycle. This multidimensional process involves diverse components, including comprehensive review of clinical trial data, literature evaluation, risk management strategies, and individual case reporting[6].

Pharmacovigilance depends on the active reporting of ADRs by healthcare professionals, patients, and caregivers, drawing insights from various sources like clinical trials, real-world evidence, and patient support groups. It is worth noting that ADRs account for nearly 7% of all hospital admissions in the United States, underscoring the critical significance of pharmacovigilance in maintaining a safer and healthier healthcare environment[7]. ADRs are recognized as a significant public health concern, as they contribute to a rise in severe health issues and hospitalization rates. Studies indicate that ADRs account for around 6.5% of all hospital admissions, and approximately 15% of these adverse events occur among hospitalized patients[8].

The ever-changing pharmaceutical landscape is witnessing a surge in the number of novel drugs and therapeutics introduced to the market each year, presenting both opportunities and challenges. As the industry continues to innovate and advance, ensuring drug safety has become a paramount concern, especially when it comes to monitoring and addressing AEs. This crucial aspect of drug safety is known as pharmacovigilance, and it plays a pivotal role in safeguarding public health[9].

The data on adverse event reports collected and stored by the FDA Adverse Event Reporting System (FDA-FAERS) is mentioned in Figure 1. According to the data, there is a general increase in adverse events reported through FDA-FAERS from 1994 to 2022[10]. These observed increases indicate that drug and product safety need to be better understood and corrected.

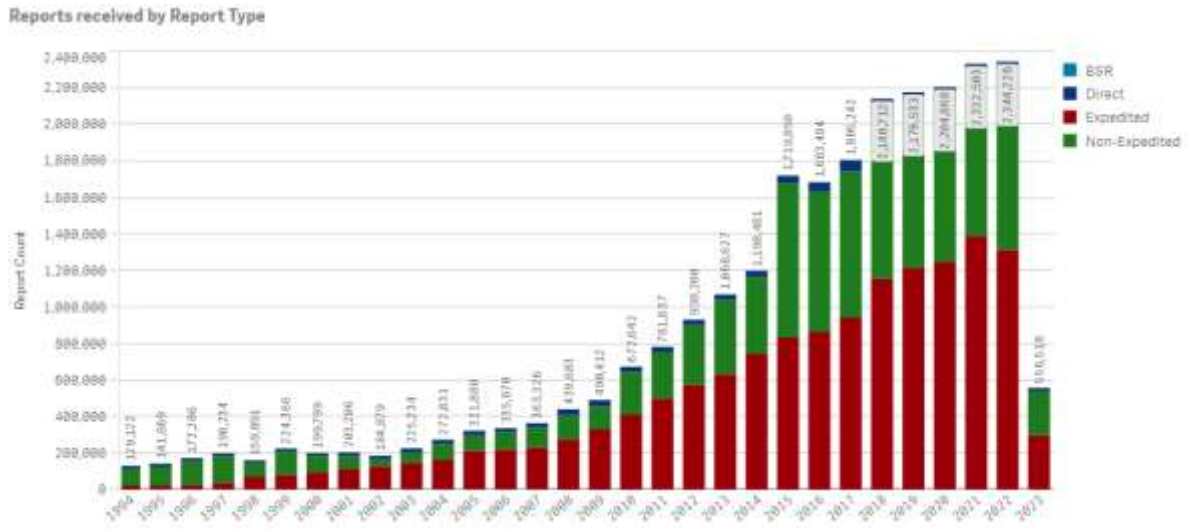

Figure 1. FDA Adverse Event Reporting System, 1994-2023.

The increasing number of adverse event reports over the years based on FAERS data further emphasizes the importance of digitalisation of pharmacovigilance. Thanks to the technological opportunities provided by digitalisation, monitoring and evaluation processes on drug and product safety become more effective and efficient. Digital platforms facilitate reporting and tracking of adverse events by enabling easy and fast communication between patients, healthcare professionals and pharmaceutical manufacturers. This allows

potential risks to be identified more quickly and urgent action to be taken. At the same time, digital technologies such as big data analytics and artificial intelligence can more comprehensively assess trends and patterns of adverse events and develop an in-depth understanding of drug safety. Digitalisation of pharmacovigilance is becoming an important tool to protect public health by enabling health authorities to make better-informed decisions. It also increases responsibility in the pharmaceutical industry by supporting the efforts of pharmaceutical companies and drug manufacturers to make their products safer. In this respect, the digitalisation of pharmacovigilance is a critical process that contributes to the public health by better ensuring the safety of medicines and products.

The Role of Artificial Intelligence: Data Analysis and Predictive Power

In the dynamic realm of medicine, where complexity abounds, there is an inherent understanding that processes which can learn from data hold significant potential compared to those relying solely on pre-defined rules[6]. In this context, the field of pharmacovigilance (PV) emerges as a crucial guardian of patient safety, dedicated to the noble goal of ensuring physicians' "do no harm" tenet. PV's vital mission involves diligent post-licensure monitoring of pharmaceutical products, encompassing continuous surveillance of known drug side effects while diligently sifting through vast troves of data to detect and respond to emerging, previously unknown side effects[11].

Given the immense volume of data, the inherent uncertainty, and the imperative to learn from such data, the synergy between artificial intelligence (AI) and machine learning (ML) appears inherently harmonious for PV tasks[11]. The potential of AI/ML in pharmacovigilance lies in its ability to leverage the power of advanced algorithms, equipping healthcare professionals with the means to analyse and interpret data comprehensively, contributing to improved patient outcomes and a safer healthcare landscape.

In contemporary times, the widespread adoption of AI is evident across diverse domains, including pharmacovigilance, security operations, signal management, and the identification of target populations. As AI's presence expands, it becomes imperative to comprehend the current landscape of AI in pharmacovigilance and explore the potential opportunities for advancing this field even further.

Within the realm of pharmacovigilance, AI's influence is becoming increasingly prevalent. It aids in efficiently processing and analysing massive datasets, facilitating early detection of adverse drug reactions and emerging safety concerns. Furthermore, AI-powered algorithms enable the identification of at-risk patient populations, optimizing drug safety monitoring, and fostering precision medicine approaches[12].

Despite these remarkable strides, the potential for growth in AI-powered pharmacovigilance remains vast[13]. There is a pressing need to explore the integration of real-world data and electronic health records, enhancing AI's ability to predict and prevent adverse events more effectively. Moreover, harnessing natural language processing and advanced machine learning techniques can further augment signal detection and automated case processing capabilities.

Detection of Drug Interactions and Drug Safety

Digital pharmacovigilance is also very important in detecting and evaluating possible interactions that may occur when multiple drugs are used together[14]. By analysing drug interactions, AI can warn healthcare professionals and patients about potential risks and improve drug safety[15].

The implementation steps of an AI-based case flow example for the detection of drug interactions and drug safety are as follows[14,16].

Data Collection: The first step is to collect the necessary data to detect drug interactions. This data can be obtained from various sources such as hospitals, pharmacies, electronic prescription systems, patient health records and pharmacovigilance databases. This large data pool is used by the AI model to analyse interactions and extract important information.

Data Pre-processing: The collected data is processed in the preprocessing step to remove irregularities and keep it in a suitable format. Data cleaning and editing operations are performed, which are necessary for the AI model to understand and interpret the data more efficiently.

Artificial Intelligence Model Application: AI model is used to detect drug interactions and improve drug safety. Artificial intelligence analyses the large dataset and looks for clues about potential interactions of drugs. Various AI technologies such as Natural Language Processing (NLP) algorithms, machine learning techniques and deep learning methods can be used.

Interaction Detection: The AI model generates warnings about potential interactions or side effects of medicines. The model can alert users to identify patients with specific symptoms or signs or groups at risk.

Automatic Notification and Alerts: The AI model can automatically send notifications and alerts to relevant healthcare professionals when drug interactions are detected. In this way, rapid intervention is provided and possible damages are prevented.

Continuous Update: The AI model is continuously updated from pharmacovigilance databases and new research. This ensures that drug interactions and side effects are kept up to date based on new information.

Patient Reporting Systems and Smart Drug Use

"Brain-Boosting Compounds" have garnered significant attention in response to our modern, demanding lifestyles. These substances are commonly referred to as "Smart Drugs" because they can enhance various aspects of brain performance. Among their impressive benefits are improvements in memory, focus, creativity, intelligence, and motivation. The term "Smart Drugs" traces its origins back to the Greek language, where it signifies the concept of bending or shaping the mind to achieve heightened cognitive abilities[17,18].

Smart drugs include devices that can continuously collect data on patients' drug use and health status. Thanks to these devices, patient reporting systems can be created and patients can directly report side effects. Artificial intelligence and data analytics can evaluate this data to provide rapid feedback to healthcare professionals and optimise treatment processes.

Létinier et al.[19] focused on developing a system to identify ADRs using a combination of a knowledge base about drugs and supervised machine learning (ML) models trained on patients' reporting data. To train their models, they collected data from patients who reported ADRs to a French Pharmacovigilance Centre through a national web-portal between March 2017 and March 2019, totalling 2,058 reports. The researchers tested both conventional ML models and deep-learning models to identify the most effective approach for detecting ADRs. For external validation, they used a separate dataset containing a random sample of ADRs reported to the Marseille Pharmacovigilance Centre during the same period, comprising 187 reports. The results indicated that the gradient boosting trees model (LGBM) outperformed other models in terms of area under the curve (AUC) and F-measure. The LGBM model achieved an AUC of 0.93 and an F-measure of 0.72 for identifying ADRs in the original dataset. For the external validation dataset, the LGBM model achieved an AUC of 0.91 and an F-measure of 0.58. The success of this artificial intelligence pipeline in correctly identifying ADRs from unstructured data was evident. This finding is promising as it demonstrates the potential for using AI-driven tools to efficiently manage drug safety information. With these encouraging results, the researchers plan to conduct a new study using even more data to further enhance the system's performance and provide a practical tool for drug safety management.

A systematic literature review by Choudhury and Asan[20] aimed to examine quantitative studies that have an impact on the safety of patients at the clinical level using AI. Articles published in English between January 2009 and August 2019 from PubMed, PubMed Central and Web of Science databases were searched and quantitative studies focusing on AI-based machine learning algorithms and natural language processing, reporting positive, negative or intermediate outcomes on the safety of patients were identified. This review, in which studies were classified according to subcategories such as clinical alarms, clinical reports and medication safety, shows that, when implemented correctly, AI-assisted decision-making systems can help to improve error detection, patient classification and medication management. However, a strong validation study in prospective and real-world clinical settings is needed in future studies to better understand the effectiveness of these systems in predicting safety in healthcare settings.

In the study by Salas et al.[12] they aimed to examine quantitative studies that have an impact on the safety of patients at the clinical level using AI. In the study, a systematic search was conducted using Embase and MEDLINE databases, using search terms such as "pharmacovigilance," "patient safety," "artificial intelligence," and "machine learning" among articles published from January 2015 to July 2021. As a result, 66 articles were evaluated and most of these articles focused on artificial intelligence-based machine learning techniques. To improve the safety of patients, AI was used in the detection of adverse drug effects (ADE) and adverse drug reactions (ADR) (57.6%), processing of safety reports (21.2%), extraction of drug interactions (7. 6%), identification of populations at high risk of drug toxicity or personalised care guidance (7.6%), prediction of side effects (3.0%), simulation of clinical trials (1.5%) and integration of prediction uncertainties into diagnostic classifiers (1.5%). AI has been used to identify safety signals with automated processes and machine learning models; however, the generalisability of the results may be limited as different data types are used in different sources. The results of the study showed that artificial intelligence enables the processing and analysis of large amounts of data and can be applied to various disease states. However, further research is required to determine its impact on the quality of safety analyses. The role of AI in the prediction of side effects and ADRs is expected to be important in future developments

Studies in the literature show the importance of artificial intelligence and machine learning methods in pharmacovigilance, patient management and patient safety. It is also seen that artificial intelligence is widely used in the field of pharmacovigilance. This technology has had a major impact on the detection of adverse events such as adverse drug effects (ADEs) and ADRs, processing safety reports and inferring drug interactions. It is also reported that AI has a valuable role in areas such as treatment guidance based on patients' personal characteristics and prediction of side effects. The ability of AI to identify safety signals with automated processes and machine learning models has also been a remarkable finding.

The findings of these studies suggest that AI can optimise pharmacovigilance processes and improve patient safety more effectively and efficiently. However, there are also some challenges, such as limitations of generalisability and lack of quality analyses. Further research and development work is necessary for AI to be fully utilised as a reliable tool in the field of pharmacovigilance.

Conclusion

The digitalisation of pharmacovigilance is an essential step toward enhancing healthcare quality and assuring medication safety. Artificial intelligence and data analytics play an important role to detect drug side effects more quickly and effectively, evaluate drug interactions and improve drug safety by processing large data sets. The digital transformation makes it easier for patients to receive healthcare services and allows healthcare professionals to make more informed decisions. Furthermore, the use of artificial intelligence provides important information for predicting and avoiding potential future drug side effects.

Digital transformation in healthcare and drug development processes provides an important opportunity to strengthen pharmacovigilance and improve patient safety. Artificial intelligence and data analytics technologies should be expanded for more effective and faster implementations of pharmacovigilance process. The healthcare industry may make enormous progress in recognizing and preventing drug side effects more quickly and accurately by active utilization of artificial intelligence, which has the capacity to scan large data sets and uncover important information. Therefore, healthcare institutions and pharmaceutical firms should build the necessary infrastructure for pharmacovigilance digitalisation and make the best use of these technologies to maximize patient safety by incorporating artificial intelligence - based solutions.

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Correspondence Address / Yazışma Adresi
Algül Dilara Dokumacı
Çukurova Üniversitesi Tıp Fakültesi
Tıbbi Farmakoloji Ana Bilim Dalı
Adana, Turkey
e-mail: dilaradokumaci@gmail.com

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