Review Article

PHARMACOVIGILANCE AND USE OF TECHNOLOGIES

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ABSTRACT

Introduction: *Pharmacovigilance is the science of monitoring the effects of medicinal products with the aim of identifying and evaluating potential adverse reactions. Recent technological advances in the areas of artificial intelligence automation have profound implications for medicine and in the discovery, development and post-marketing phases of life cycle of pharmaceutical medicines. Pharmacovigilance systems are supported by secure closed relational databases. These databases are often linked to data ware house and advanced tools to enable the retrieval reporting and visualization of data in support of signal detection and risk management.*

Objectives: *Significant challenges and opportunities when designing, deploying and utilization of IT in pharmacovigilance systems*

Methods and materials: *Articles about Pharmacovigilance in PUBMED, GOOGLE SCHOLAR using the keywords Pharmacovigilance, Information technology, Artificial intelligence*

Result: *The technologies identified has potential to yield efficiencies and improvements of quality not only for ICSR, also in the context of aggregate reporting, signal detection, risk management and the Quality Management System for the pharmacovigilance systems*

Conclusion: *Rapid development of technologies has the potential to reduce cycle times, improve quality, create efficacies and reduce costs, all of which lead to better allocation of resource*

INTRODUCTION:

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug related problems. In India, Adverse Drug Reaction centers were established in 1980 by Indian Council of Medical Research (ICMR) and Drugs Controller General of India (DCGI) but their activities were limited to only a handful of institutions and the majority of the healthcare practitioners were unaware of these developments. The Pharmacovigilance Programme of India (PvPI) was initiated by the Government of India in July 2010. All India Institute of Medical Sciences (AIIMS) was designated as the National Coordination Centre for monitoring Adverse Drug Reactions (ADRs) in the country. In the year 2010, 22 ADR monitoring centers including AIIMS, New Delhi was set up under this Programme. Later the National Coordination Centre was shifted from the All India Institute of Medical Sciences (AIIMS), New Delhi to the Indian Pharmacopoeia Commission, Ghaziabad, Uttar Pradesh on 15th April 2011.

The objectives of this programme are

- To create a nation-wide system for patient safety reporting
- To identify and analyze the new signal (ADR) from the reported cases
- To analyses the benefit - risk ratio of marketed medications
- To generate the evidence based information on safety of medicines
- To support regulatory agencies in the decisionmaking process on use of medications

- To communicate the safety information on use of medicines to various stakeholders to minimize the risk
- To emerge as a national center of excellence for pharmacovigilance activities
- To collaborate with other national centers for the exchange of information and data management
- To provide training and consultancy support to other national pharmacovigilance centers located across globe

PHARMACOVIGILANCE METHODS

Spontaneous report monitoring system (SRS), Prescription event monitoring (PEM), Cohort studies, Case-control studies, Case reports and case series, General Practioners database (GPRD), Medicine monitoring unit (MEMO), Drug utilization studies (DUS)

ADVERSE EVENT REPORTING SYSTEMS

FDA reporting of pharmaceuticals is generally carried out with the help of Adverse Event Reporting Systems (AERS). AI/ML-driven solutions for AERS have helped develop clear explanations for timely FDA reporting of adverse events.

INDIVIDUAL CASE SAFETY REPORTS

The existing process involves a human pharmacovigilance professional manually assessing the validity of each case related to ADRs or events of serious reactions to specific drugs. AI-powered ICSR allows safety departments, and pharmacovigilance executives to ensure better reporting outcomes with highly relevant data at their fingertips

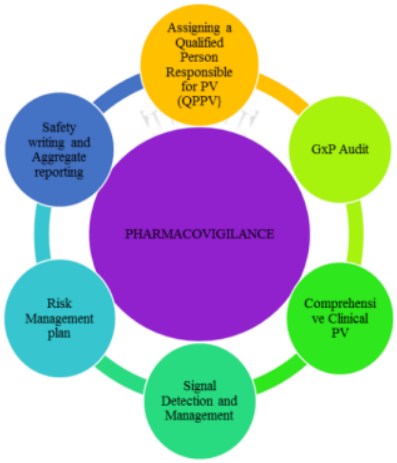
SENTIMENT ANALYSIS AND SOCIAL MEDIA MONITORING

Social media platforms and online forums have become places where individuals often share their healthcare experiences, including adverse drug reactions (ADRs).

MATERIALS &METHODS

Search was done using the PubMed, Google scholar and ResearchGate database using keywords such as Pharmacovigilance, PvPI, Information technology, Artificial Intelligence, references of included articles & websites of relevant authorities including CDSCO, Ministry of Health and Family Welfare, Govt. of India

DISCUSSION



The use of AI technologies in pharmacovigilance makes it easier to extract correct data. Nearly every part of Pharmacovigilance can be automated or facilitated by AI tools, including case processing and risk tracking,

- **VigiBase**: A Pharmacovigilance database that stores the data in a structured, orderly fashion to make it simple to analyse recorded data
- **VigiAccess**: It is a freely available web application that allows users to browse and quickly obtain data on adverse medication effects stored in VigiBase
- **VigiLyze**: It is a tool that can be used online to quickly and clearly review VigiBase and be further explored
- **VigiFlow**: It is a web-based ICSR management system for global drug surveillance that facilitates efficient data analysis through data collection, processing, and sharing
- **VigiGrade** :To assess the degree to which each case report's ordered, clinically important information is complete. This is mostly used to communicate with nations on the quality of their data.
- **VigiMatch**: It is an algorithm that uses probabilistic pattern matching to find related individual case reports
- **VigiRank**: It is a novel technique for identifying statistical signals that take into account not only disproportionate reporting patterns but also the geographic distribution, completeness, and recentness of individual case reporting.
- **VigiBase**: This signal production was controlled in India by CDSCO and NCC-PvPI utilising the database . The signals are used by PvPI to review, identify, decide, and conclude the collected data from various national databases

BENEFITS OF ARTIFICIAL INTELLIGENCE IN PHARMACOVIGILANCE

The most important benefits of AI are reduced cycle times. Due to this method, the processing is spontaneous. Improve the quality and accuracy of the information. AI can handle or manage diverse types of incoming data formats. It can be used for the identification of ADRs. AI is useful to reduce the burden and time of case processing. AI tools extract the information from the adverse drug event form and evaluate the case validity without the workforce.

Experts are looking at the use of AI/ML to make the Pharmacovigilance process more effective and efficient (Fig. 2)

1. OCR & NER Augmented Case Intake

In pharmacovigilance, case intake refers to the process of collecting and recording information about adverse events associated with the use of a medication or medical device. Case intake is one of the most common applications of AI.

OCR & NER has the potential to extract data quickly and efficiently with the expanding volume of information and multiple data sources like Medical Literature, Social Media, Electronic Health Records, Regulatory Reporting, News Websites and Papers, Mobile Applications, etc. containing primarily unstructured data including free text narratives and scanned PDFs, avoiding the massive amount of time required for human data entry. OCR can be used to digitize these reports and make the information they contain accessible to automated systems.

Figure 2

NER (Named Entity Recognition) is another technique used in natural language processing that can be applied to case intake to automatically identify and classify relevant entities, such as the name of the drug, the symptoms experienced by the patient, and the outcome of the event. This can help to streamline the case intake process and make it more efficient. There are various NER techniques and models that can be used for this purpose, such as rule-based systems, statistical models, and neural network-based models.

When using OCR for case intake, the first step is to convert the scanned document or image into a digital format that the OCR software can process. Once the image is in a digital format, OCR software can analyse it and recognize the text it contains. The software will then output the recognized text in a machine-readable format, such as a plain text file or a structured data format like XML or JSON.

The next step is to use NER to extract the named entities such as drug name, symptoms and patient details, etc. from the recognized text. This information can then be stored in a structured format for further analysis and reporting.

2. ML & NLP for Cognitive Case Processing

It involves the use of ML techniques to analyse large amounts of text data, such as patient narratives or adverse event reports, to extract relevant information and classify the reports into different categories.

In cognitive case processing, an ML model is trained on a large dataset of labelled adverse event reports. The model learns to identify patterns and relationships in the data that correspond to different categories of reports, such as serious adverse events or non-serious events.

Once the model is trained, it can be applied to new adverse event reports to automatically classify them into the appropriate categories. This can help to streamline the case processing process and make it more efficient, as well as increasing the consistency and accuracy of the classification.

Additionally, this approach can be enhanced with the use of natural language processing (NLP) techniques to extract entities such as drug names, symptoms and patient details from unstructured narratives which can further improve the accuracy and speed of case processing.

3. NLG-Aided Narrative Writing

Narrative writing plays a key role in pharmacovigilance by providing a detailed account of an adverse event, enabling better understanding and communication of the event, and helping to identify patterns or trends that may indicate a safety issue.

According to an ICSR research article in their publication, Perspectives in Clinical Research, resourcing, consistency, timeliness with high-quality and potentially various data sources utilised as input, and considerable variation in the templates are all challenges with narrative writing. there is a high possibility that the story might become fragmented and confusing.

Using Natural Language Generation (NLG) to automate narrative writing increases the quality and consistency of the narratives while decreasing the time required to construct and complete the narrative. The model can extract all necessary information quickly and effectively, produce the narrative, and place it in the required format or template. Built-in audit trails and version control can ensure that each version of the narrative is logged and saved for easy access and comparison.

4. RPA-Based Case Workflow

Robotic Process Automation (RPA) is one of the emerging forms of business process automation technology based on the notion of software bots or artificial intelligence.

Automation is something pharmaceutical companies are eager to implement to save costs and delivery times. Robotic processes that perform repetitive operations can greatly minimise the need for manual effort by enhancing productivity, compliance, and overall quality while also immediately boosting efficiency.

5. ML-Assisted Medical Coding

Medical coding is the classification of a number of similar verbatim phrases using a certified medical lexicon that is either given by the client or granted permission by the relevant licencing authorities, in order to provide a statistically quantifiable count of all related terms.

ML can reduce the risk of coding errors, as it is not subject to the same types of mistakes that humans can make when coding manually. By automating the coding process, it is possible to reduce the effort and cost associated with manual coding.

6. AI-Assisted Literature Monitoring

Pharmacovigilance professionals seek for indications of drug safety risks in research findings, case studies, and other publications. This process typically takes a long time and is prone to human error. AI-enabled solutions could be used to automate the process by ingesting data from an increasing number of scientific sources and automatically flagging possible drug safety risks.

Literature monitoring in pharmacovigilance could use Artificial Intelligence (AI) and Natural Language Processing (NLP) techniques to automate the process of monitoring scientific literature for new information related to the safety and efficacy of drugs and medical devices.

One of the main benefits of AI-assisted literature monitoring is the ability to quickly and efficiently process large amounts of information from a wide range of sources. This can help to identify potential safety issues early on and can be used to inform the development of new safety measures or to make regulatory decisions about a drug or device.

Additionally, AI-assisted literature monitoring can be used to prioritize articles for review by human experts, focusing on the most relevant studies and publications for a given topic, which can save time and resources for the pharmacovigilance teams.

7. Neural Network Models for Seriousness Prediction

The seriousness of adverse events is a critical component in determining reporting timelines, and it is usually handled manually by pharmacovigilance professionals. Because of the huge growth in the amount of safety reports, a neural network approach can provide a precise and scalable solution for potentially enhancing the assessment of the seriousness of adverse events in spontaneous, solicited, and medical literature reports, according to the findings of a research study that was published in Drug Safety, the official journal of the International Society of Pharmacovigilance (ISoP).

Once trained, the model can then be used to predict the seriousness of new Adverse event reports as they come in. This can help to quickly identify and prioritize serious events, which can be important for ensuring the safe and effective use of medications.

8. Automated Causality Assessment

In pharmacovigilance, causality assessment is the process of determining whether an adverse event is causally related to the use of a specific drug or medical device. Machine Learning (ML) models can be used to automate this process, making it more efficient and accurate.

9. AI-Assisted Signal Detection & Monitoring

The increasing complexity of data reporting and regulators' expectations of being more proactive in detecting adverse events is transforming how signals are gathered and managed.

There are several ways that AI and ML can be used to improve signal detection in pharmacovigilance:

- Natural Language Processing (NLP): NLP algorithms can be used to extract information from unstructured text data, such as patient reports of adverse events.
- Predictive Modelling: Machine learning algorithms can be used to predict the likelihood of a particular adverse event

occurring based on a patient's characteristics and their use of a medication or vaccine. This can help to identify high-risk populations and prioritize safety monitoring.

- Data Visualization: AI and ML can be used to create visualizations of data, such as graphs and maps, to help identify trends and patterns that may indicate a safety issue.
- Automated Analysis: Machine learning algorithms can be used to automatically analyse substantial amounts of data, reducing the need for manual review, and allowing for more efficient signal detection.

CHALLENGES WITH AI/ML IN PHARMACOVIGILANCE

- **Data Quality and Availability:** The quality and quantity of data can affect the performance of AI/ML models. In pharmacovigilance, data may be incomplete, inconsistent, or biased, which can lead to inaccurate or unreliable results.
- **Explainability:** AI/ML models can be difficult to interpret and explain, which can be a problem in a regulated field such as pharmacovigilance where decisions may have significant consequences.
- **Legal and Ethical Considerations:** AI/ML models in pharmacovigilance may raise legal and ethical concerns, such as inadvertent bias and liability concerns.
- **Integration with existing systems:** AI/ML models may need to be integrated with existing systems and processes, which can be a challenging task.
- **Validation and Regulatory Approval:** AI/ML models in pharmacovigilance may need to be validated and approved by regulatory bodies before they can be used in practice.

CONCLUSION

Artificial Intelligence and Machine Learning have a lot of potential for safety and pharmacovigilance. These technologies have the ability to change the focus of the pharmacovigilance function from data collecting and reporting to assisting in improving product quality, streamlining treatment regimens, reducing costs, and enhancing patient safety.

The future of pharmacovigilance is in digitalization, AI analytics, and patient-centred data collection, all of which are expected to increase overall medication safety. To ensure performance and generalisation, the AI/ML models should be trained on high-quality, representative, and well-annotated data and evaluated on separate datasets.

The advantages of implementing AI/ML are visible in the long term. It's time for the pharmaceutical business to advance by fast adapting, creating AI/ML use cases, and implementing them at scale.

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