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(REVIEW ARTICLE)

Advances in molecular biomarkers for pharmacovigilance: Early detection of drug toxicity

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Abstract

The importance of molecular biomarkers leading to early drug toxicity detection as well as drug safety monitoring leading to the strengthening of pharmacovigilance. Hence, spontaneous reporting systems and cohort studies commonly used for the purposes of traditional pharmacovigilance are not effective and timely enough in identifying Adverse Drug reaction (ADR). Molecular biomarkers (genomic, transcriptomic, proteomic or metabolomic and epigenetic) lastly provide a more targeted and mechanistic understanding of drug induced toxicities. There has been evolution in the last few years in discovering biomarkers by next generation sequencing (NGS), artificial intelligence (AI), by organ on a chip technology, allowing us to go beyond personalized medicine/toxicology to predict its outcomes. The organ specific toxicities, i.e., hepatotoxicity, nephrotoxicity, cardiotoxicity and neurotoxicity are assessed by biomarkers and can be used as basis to institute early intervention and choice of strategy thus. Though the first of these seem to be advancements, they have done much on the surface in standardization, validation, ethical issues, etc. and most of all, all this has to do with the cost. Biomarker analysis with AI and machine learning, however, helps to integrate the higher drug safety assessment accuracy and efficiency. Like in the case of pharmacovigilance, global collaboration and regulatory framework for harmonized biomarker applications and routine clinical applications are also needed in the biomarker applications. In the future, predictive toxicology will be made by improving the prediction of toxicology through personalized biomarkers, the second improvement of its AI based biomarker discovery and the span between biomarker research and clinical practice. Placed in future, the assumption of pharmacovigilance can transition to a reactive, data driven discipline from reactive, and become another proactive, safer discipline to enhance global patient safety and therapeutic outcomes.

Keywords: Molecular biomarkers; Pharmacovigilance; Adverse Drug Reaction (ADR); Next-generation sequencing (NGS); Artificial intelligence (AI)

1. Introduction

The role of pharmacovigilance includes ensuring drug safety, monitoring, and evaluating adverse drug reactions (ADRs) during the lifespan of a drug. It is important in this field to identify possible risks not disclosed in clinical trials, enabling the protection of public health [1]. Due to the complexity of drug interactions and wide variability in patient responses, robust pharmacovigilance systems are needed that will be able to respond to new data based on emerging signals of safety [2].

Molecular biomarkers are biological molecules that can be measured in (biological) samples and are indicative of biological state or a biological condition. These biomarkers can serve as key information for the mechanisms of the

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adverse reactions and contribute to the more precise monitoring and drug safety management [3]. Thus, specific molecular changes associated with drug toxicity could be identified leading to targeted interventions to improve patient safety and therapeutic efficacy [4].

The rationale for early detection of drug induced toxicity is supported by the time for early intervention to reduce the severity of the adverse effects and to improve the outcome for the patient. Molecular biomarkers allow for the early identification of at-risk patients and thereby enable personalized medicine approaches applicable to treating patients according to their own genetic profile and thereby minimizing risks of adverse reactions [5]. Particularly in the setting of complex disease in which the treatment response is determined by a combination of factors, responses to this proactive strategy are important [6].

In this review we synthetize recent progress in molecular biomarkers useful in early identification of drug toxicity, and their applications. Objects are to analyze the current context of biomarker research, to discuss the integration of molecular data into pharmacovigilance systems and discuss future paths for improvement of the drug safety criteria via biomarker led approaches.

2. Pharmacovigilance and the Role of Molecular Biomarkers

2.1. Concept of Pharmacovigilance and Its Challenges

Pharmacovigilance: the science and activities that detect, assess, understand and try to prevent adverse effects or any other drug related problems defined [7]. It is a vital part in guaranteeing drug security and effectiveness in a pharmaceutical's lifespan particularly after a pharmaceutical is approved for public use. Pharmacovigilance is an important issue, however, there are several challenges which must be overcome, such as reporting of adverse drug reactions (ADRs) [8,9] and the integration of new technologies and methodologies [8]. Drug interactions are further compounded by the complexity of the human patient population and the identification of safety signals becomes an intractable problem due to the complexity of drug interactions [10,11].

Despite the use of spontaneous reporting systems, one major obstacle in pharmacovigilance is that spontaneous reporting systems tend to have low reporting rates and do not capture the whole spectrum of ADRs [7, 12]. The second possible barrier for reporting is that healthcare professionals generally do not know or understand pharmacovigilance processes [13,14]. Lack of resources is another hurdle to the integration of pharmacovigilance into clinical practice: the process is constrained by shortage of funds, especially in the low- and middle-income countries where healthcare systems can be starved of resources [10,15,16].

2.2. Current Methods for Drug Toxicity Monitoring

At present, monitoring drug toxicity is still made using spontaneous reporting system, cohort study and case control study. The backbone of pharmacovigilance is still spontaneous reporting, allowing the collection of real-world data on ADRs [12, 7]. Yet, this method is sometimes criticized as being biased and under an invalid report. The rigor of cohort studies allows researchers to define populations to be followed over time and assess drug safety [8]. However, case control studies compare patients with ADR to those without identifying causal relation [7].

Yet, despite these methods, more innovative ways to improve drug safety monitoring are now recognized as necessary. Real-world evidence (RWE) as well as the use of electronic health records (EHR) have been portrayed as promising tools for improving the detection of ADRs and more generally facilitating more comprehensive safety assessment [17,18]. Additionally artificial intelligence (AI), and machine learning (ML) technologies are being applied to pharmacovigilance systems to add to data analysis and signal detection [19,18].

2.3. Emergence of Biomarkers as a Tool for Safety Assessment

Pharmacovigilance has emerged as a critical tool in pharmacovigilance that has the potential of a more precise safety assessment with the help of the molecular biomarkers. They can further help identify individuals at risk of having ADRs, based on their genetic, proteomic or metabolomic profiles [20]. Biomarkers are used to help catch drug toxicity early, for adverse events to be taken care of early and personalized treatment strategies [20, 22].

Recent studies have demonstrated the importance of biomarkers for explaining the mechanism of drug induced toxicity for more complete risk stratification and management [20,21]. So, for instance, genetic biomarkers associated with different drug responses can help clinicians assess patients' likelihood of adverse reactions and thus help make

treatment decisions [23,20]. Integrating biomarker data into pharmacovigilance frameworks can facilitate application of biomarkers into pharmacovigilance process that is more proactive than reactive [20].

2.4. Advantages of Molecular Biomarkers Over Traditional Methods

Numerous are the advantages of using molecular biomarkers in place of traditional pharmacovigilance. Biomarkers can, firstly, provide an objective, quantifiable data, leading to an improvement of safety assessment reliability [20,21]. Biomarker data is more accurate than the spontaneous reporting, which often relies on bias and is subjective [22,20].

Secondly, biomarkers allow them to identify at risk populations prior to the occurrence of ADRs and thus initiate preventive measures and personalized medicine approach [23,20]. Since complex diseases are also governed by multiple factors of treatment response [22,20], this proactive strategy is especially helpful. Additionally, biomarkers can be integrated into pharmacovigilance to reduce the monitoring process by enabling the real time analysis of such data and quicker identification of safety signals [18,19].

In the end, biomarkers can better facilitate communication and collaboration between stakeholders involved in pharmacovigilance in addition to regulatory agencies, healthcare providers and the pharmaceutical companies. These entities can work together with sharing biomarker data to improve monitoring and response strategies to drug safety, [21,19].

3. Types of Molecular Biomarkers Used in Drug Toxicity Monitoring

Drug toxicity monitoring uses molecular biomarkers which are key in the monitoring of drug toxicity as they reveal ADR mechanisms and allow identification of pre toxicities ones. It discusses different molecular biomarkers such as genomic, transcriptomic, proteomic, metabolomic, and epigenetic biomarkers and the importance of biomarkers in pharmacovigilance.

3.1. Genomic Biomarkers

3.1.1. Role of Single Nucleotide Polymorphisms (SNPs)

Single nucleotide polymorphisms (SNPs) are the most prevalent type of genetic variation within the population and are a significant factor to drug metabolism and response. Interindividual variability of drug efficacy and toxicity is achievable at the level of SNPs within genes responsible for drug metabolism, transport and drug receptors. For example, the CYP450 gene family, which metabolizes many drugs, can vary such that clearance of drugs is changed and ADR risk is increased [24]. By identifying SNPs associated with drug response, personalized medicine approaches can be guided to use tailored therapies around the same time that potentially minimize toxicity [23].

3.1.2. Pharmacogenomics and Toxicogenomic Approaches

Pharmacogenomics and toxic genomics are the fields that have to do with hereditary variations and the impact of genetic factors on responses to drugs and their toxicity. Pharmacogenomics studies the relationship between genetic variations and pharmacological response while toxicogenomic explores the effects of toxic substance on gene expression [24, 25]. High through put sequencing technologies are used to identify genetic markers for predicting drug induced toxicity leading to improved safety [24].

3.2. Transcriptomic Biomarkers

3.2.1. RNA Expression Profiles in Drug-Induced Toxicity

Biomarkers of transcriptomic make use of analysis of RNA expression profiles to identify changes associated with drug induced toxicity. Gene expression alterations imply cellular responses to toxicants and provide information on modes of toxicity, [26, 27]. For example, gene expression signatures have been shown to be correlated with liver injury arising from drug treatment, thus permitting early identification and intervention [28]. These are commonly used to profile RNA expressions following drug exposure.

3.2.2. miRNAs, lncRNAs as biomarkers

miRNAs and lncRNAs, as noncoding RNAs, are important biomarkers in drug toxicity monitoring, in (regulating gene expression) post transcriptionally, they have been implicated in various drug responses and toxicities [29,30]. For example, there have been exemplary identification of specific miRNAs that are potential biomarkers of skeletal muscle

injury caused by drugs. Just as lncRNAs have been shown to extend predictions of drug response beyond traditional protein coding genes, they are promising candidates for use in pharmacogenomics [30].

3.3. Proteomic Biomarkers

3.3.1. Protein Expression Patterns in Drug Toxicity

Proteomic biomarkers focus on evaluating toxicity of drug based on protein expression. This could reflect cellular responses to drug exposure and allow the mechanism of toxicity [31,32]. Specific proteins, for example, such as cystatin C and interleukin [18] are known biomarkers for drug-induced kidney toxicity [32]. Techniques like mass spectrometry can be used to identify and quantify proteins that are associated with [31,32] adverse drug reactions.

3.3.2. Mass Spectrometry and Biomarker Discovery

Mass spectrometry (MS) is a great method for biomarker discovery in proteomics. It enables the respective identification and quantification of proteins in complex biological samples and thus it allows the detection of changes in protein expression related to drug toxicity [31,32]. High throughput analyses are now possible due to the advances in MS technology that have permitted us to discover novel biomarkers for early drugs toxicity detection [31,32].

3.4. Metabolomic Biomarkers

3.4.1. Metabolic Pathway Alterations Due to Drug-Induced Toxicity

Metabolomic biomarkers deal with the study of small molecules (metabolites) in biological samples regarding the detection of changes related to drug induced toxicity. Metabolic alterations can lead to insights into the biochemical mechanisms of drug toxicity [33,34]. For example, specific metabolomic profiles are associated with liver toxicity caused by environmental contaminants, so metabolomics could have a role in toxicity testing [33, 34].

3.4.2. Role of LC-MS and NMR Spectroscopy in Toxicology

The techniques used in metabolomics to investigate metabolic changes in the presence of drugs are key technologies in LC-MS and NMR spectroscopy. The separation and identification of metabolites in complex mixtures can be carried out using LC-MS, whereas NMR yields structural information about metabolites [33, 34]. Thus, these techniques allow for a complete profiling of metabolic alterations and allow the identification of potential biomarkers for drug toxicity [33, 34].

3.5. Epigenetic Biomarkers

3.5.1. DNA Methylation and Histone Modifications

Epigenetic biomarkers are a direct change in the genome that would alter the expression of the genes without the DNA codon getting altered. Drug exposure can induce these modifications, and they may contribute to toxicity induced by drug [35,25]. For instance, particular patterns of DNA methylation have been linked to the enhanced susceptibility to drug toxicity, indicating the role importance of epigenetic factors in pharmacogenomics [35, 25].

3.5.2. Epigenetic Regulation in Drug Response and Toxicity

Epigenetic regulation is critical in directing how an individual will respond to a drug and its associated toxicities. Because the epigenetic landscape defines how effects of drugs affect expression of genes and contribute to adverse reactions [35,25], understanding this landscape can be informative. In this area, research is growing, and it may lead to the discovery of new epigenetic biomarkers that can predict drug responses and harmful effects, thereby improving patient safety [25,35].

4. Applications for Molecular Biomarkers in Early Drug Toxicity Detection

Early detection of drug toxicity using molecular biomarkers allows for timely interventions and tailored treatment strategy. Next, this section discusses applications of several biomarkers in detection of hepatotoxicity, nephrotoxicity, cardiotoxicity, neurotoxicity, and drug induced immune responses in personalized medicine and in prediction of adverse events.

4.1. Biomarkers in Hepatotoxicity Detection

As a result of severe adverse effects and withdrawal for hepatotoxicity, liver toxicity is a major concern in drug development. There have also been identified several biomarkers for early detection of drug induced liver injury (DILI). For example, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are traditional biomarkers to assess liver function but are not precise and sensitive markers for doing it [36]. More recent studies have emphasized that more specific biomarkers, microRNAs (miRNAs) or proteins, for example, keratin 18, can even give earlier indications of liver damage [35,36]. Due to the integration of these biomarkers in clinical practice, the monitoring of liver safety on drug therapy can be improved, and timely interventions for hepatotoxicity can be achieved once it is identified [37].

4.2. Biomarkers in Nephrotoxicity and Cardiotoxicity

Biomarkers are also important in another critical area: nephrotoxicity, or kidney toxicity. One [38], traditional markers such as serum creatinine and blood urea nitrogen (BUN) are not always good enough to detect the process of acute kidney injury (AKI). Other novel biomarkers like cystatin C and kidney injury molecule-1 (KIM-1) have proved to be useful new markers for sooner and more exact appraisals of renal workhorses. These biomarkers may be used to identify when drugs have begun to cause nephrotoxic effects so that possibly more safe treatment can be provided before serious injury has occurred.

Similarly, its cardiotoxicity is a major concern of cancer therapies. Troponins and natriuretic peptides have been biomarkers used to monitor cardiac function during treatment [39]. Contemporary developments in circulating miRNAs characteristic of cardiac injury have also surfaced as promising investigative modalities for the early diagnosis of drug induced cardiotoxicity [40]. Use of these biomarkers in clinical practice could assist in identification of at-risk patients and will help to implement timely modifications in treatment regimens.

4.3. Neurotoxicity Biomarkers in Drug Safety Monitoring

However, neurotoxicity has been a major issue in drug development in general, and in those drugs directed to the central nervous system. Such biomarkers as neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) are identified as indicators of neurotoxicity [41,42]. Various neurodegenerative diseases are associated with elevated levels of NfL in serum 44 and these levels have been demonstrated to be sensitive markers of neuronal damage. These biomarkers are useful in biomonitoring neurotoxic effects in clinical settings to improve monitoring of toxicity and help in early intervention and improved patient outcomes.

Furthermore, miRNAs have also been suggested as neurotoxic biomarkers through the premise that they are easy to detect in biofluids and regulate neuronal function [42]. They are of course useful tools to monitor drug induced neurotoxicity because of their ability to reflect changes in neuronal health [43].

4.4. Biomarkers for Drug-Induced Immune Responses

Severe adverse effects induced by drug mediated immune responses can be hypersensitivity reactions and autoimmune disorders. Based on [44, 45], biomarkers such as specific autoantibodies and inflammatory cytokines are recognized as potential indicators of an immune mediated drug reactions. For example, the occurrence of anti-drug antibodies can indicate an immune response to biologics so that they have lower efficiency or increased risk of adverse events [45]. Since the identification and monitoring of these biomarkers can help to identify these immune related adverse events earlier, adjustments in therapy can be made earlier.

4.5. Role of Biomarkers in Personalized Medicine and Risk Prediction

Molecular biomarkers integrated into personalized medicine is a breakthrough in monitoring drug safety. Healthcare providers can tailor treatments to their patient's unique genomes, reduce their patient's risk of adverse effects [46], by identifying genetic, proteomic and metabolomic profiles correlating with drug responses. For example, pharmacogenomic biomarkers can predict how patients metabolize some drugs and predict dosage adjustments that lessen the chances of toxicity [47,48].

Likewise, biomarkers added to the risk prediction models can improve the ability to identify patients at higher risk of drug induced toxicities. An example is the combining of clinical data with biomarker profiles thus improving the accuracy of risk assessments and facilitating proactive management strategies [48, 49]. By identifying potential safety issues earlier in clinical trials what is also achieved is greater patient safety as well as saving time and costs in drug development processes.

This brings us to conclude that molecular biomarkers are applied in the early detection of drug toxicity and thus greatly changing the practice of pharmacovigilance and personalized medicine. These biomarkers enable the early detection of adverse effects and thus help improve patient safety and increase therapeutic effectiveness.

5. Recent Advances and Technological Innovations

Advancement made in molecular biomarkers field and its technological innovations to improve detection of drug toxicity and pharmacovigilance. This section also presents recent advances in both endogenous and exogenous approaches to NGS, CRISPR-based, artificial intelligence (AI) and machine learning (ML), organ on a chip technology, as well as multi-omics and systems drug safety assessment.

5.1. Next-Generation Sequencing (NGS) in Biomarker Discovery

Next generation sequencing (NGS) has completely revolutionized the field of genomics by fast throughput sequencing of DNA and RNA, impacting from the discovery novel biomarkers of drug toxicity. The limitations of GSE correlating profiling of genetic variations, gene expression level and epigenetic modifications are overcome and grant insight of the molecular mechanism underlying drug induced toxicities using NGS. For example, NGS has been used to identify genetic variants linked with bad drug reactions enabling personalized medicine practice in view of patient's genetic profiles [50]. With the ability to rapidly analyze gigantic amounts of genomic data, NGS is becoming increasingly pertinent to discover and validate biomarkers.

5.2. CRISPR-Based Approaches for Biomarker Validation

The capability of precise genome editing with CRISPR technology thus served as a powerful tool to validate the biomarkers, permitting genetic modification of specific biomarkers on the cell line or animal model to study its functional role in drug toxicity [50]. For example, CRISPR can be used to eradicate or genetically modify genes associated with drug metabolism or toxicity, to learn more of what genes are implicated in an adverse drug reaction [50]. Based on CRISPR application in biomarker validation, biochemical pathways involved in drug carcinogenicity and pathways that one can expect from drug induced toxicities are better known to develop better therapeutic strategies.

5.3. Artificial Intelligence and Machine Learning in Biomarker Analysis

Artificial intelligence (AI) and machine learning (ML) have revolutionized biomarker data analysis by being able to find complex patterns and relations that are not discoverable using classical statistical methods. The AI algorithms can analyze large datasets generated via the multi omics approaches such as genomic, transcriptomic, proteomic or metabolomic, for the identification of potential drug toxicity biomarkers [51]. Meanwhile, there are recent studies that prove the application of machine learning for prediction of drug responses and toxicities from biomarker profiles in pharmacovigilance precision [51]. AI driven tools to biomarker analysis are now rapidly developed towards early diagnosis, planning of the treatment, and risk assessment [52].

5.4. Organ-on-a-Chip and In Vitro Biomarker Testing Models

Organ on a chip technology that are new represents a potentially huge step forward in drug toxicity testing as they bring toxicity testing closer to the relevant physiological conditions they cannot replicate with other technologies. In these microfluidic devices, human organs can be mimicked in terms of architecture and function and the resultant drug toxicity can be evaluated in a controlled manner. These models incorporate human cells and therefore allow researchers to figure out just how drugs affect specific tissues, and which markers of toxicity are produced [52]. The approach allows the utility of the in vitro testing to predict the response to a drug while reducing reliance on animal models, as this is in the spirit of responsible ethical research in biomedical sciences.

5.5. Integration of Multi-Omics Approaches for Drug Safety Evaluation

Over the past decade, multi-omics approaches (generally genomic, transcriptomic, proteomic and metabolomic data) have increasingly become applied as an advanced method for assessing drug safety in a systems manner. Researchers can use multiple layers of biological information to work out how difficult it is to find the right drug at the right time (therapeutically to be targeted at a particular disease). In terms of the identification of biomarkers that are correlated with drug toxic effects and understanding the pathogenesis of toxic adverse drug reactions, this global strategy will help [52]. Pharmacovigilance applications using multi-omics help in prediction and mitigation of drug induced toxicities leading to a safer patient care.

6. Challenges and Limitations

Molecular biomarkers and related technologies are at least well developed, but these and many other challenges and shortcomings prevent the use of these types of techniques.

- Lack of standardization and validation problems: The issue of standardization and validation problems has been addressed owing to lack of standardized protocols for biomarker discovery and validation which makes it so that results obtained in the discovery of biomarkers are not reproducible and reliable. Consensus guidelines are needed, however, to create robustness of biomarker assays [52].
- Biomarker Application: Ethical and Regulatory Challenges: The utilization of advanced biomarker technology has important ethical and regulatory challenges in pure and applied ethics concerning the ethical obligation to secure patient's consent, protect patient privacy and avoid misuse of the genetic information. Regulatory frameworks need to evolve to address these challenges and promote innovation [52].
- Cost and Accessibility of Advanced Biomarker Technologies: NGS and AI driven analyses like them are very expensive enough and hence very inaccessible to even those in lower resource settings. This calls for widespread adoption [53], with the effort to make costs go down and at least to achieve as much access as possible.
- Data Interpretation and Reproducibility Concerns: There are some aspects regarding complexity connected to multiple omics data and AI algorithms which might bring in issues of data interpretation and reproducibility. Trust in biomarker applications necessitates the incorporation of transparency and interpretability of AI driven analysis [54].

7. Future Directions and Perspectives

Industrial interest and technological advances along with expanding knowledge of personalized medicine are spurring the development of the molecular biomarkers pattern in the landscape of the drug's toxicity detection. Here we discuss the use of personalized biomarkers for predicting toxicology, recent advancements in biomarker discovery using AI, what has been achieved on biomarker research to clinical practice and pharmacovigilance global policy making and collaborations.

7.1. Potential of Personalized Biomarkers for Predictive Toxicology

The predictive toxicology based on individual's biomarkers holds promise in adopting specific strategies in the drug safety assessments. Integration of genomic, transcriptomic and proteomic data can also direct the identification of single susceptibility to drug induced toxicities leading to improved risks predictions [54]. For instance, testing for genetic variants affecting the way drugs are metabolized with the intention of guiding clinicians in selecting appropriate therapies and doses for that patient can be performed with pharmacogenomic testing [55]. By having more information about the genetic and molecular underpinnings of responsiveness to drugs, we should either be able to design biomarkers for personal prediction of toxicology and subsequently patient safety and therapeutic outcome both.

7.2. Advances in AI-Driven Biomarker Discovery

Artificial intelligence (AI) and machine learning (ML) use permit that biomarker discovery is done on large and complex data sets. Integration of multiple -omics data can identification new biomarker related with drug toxicity through recent development on AI algorithm [56]. AI driven approaches can further improve biomarker discovery efficiency with a reduction of manual analysis, automating the data analysis and identification of patterns which would otherwise be not visible [57]. Moreover, in prediction of adverse drug reactions from biomarker profiles, AI can be used to develop predictive models that are expected to estimate the probability of an adverse drug reaction [58]. The same are expected to give insight into drug safety during biomarker discovery as AI technologies advance.

7.3. Biomarker Research in Translation towards Clinical Practice

Although I still facing a critical hurdle of translating biomarker research into clinical practice, the idea of pharmacovigilance continues [58]. This shall be important to bridge the gap between research and clinical application of biomarkers using standardized protocols for validation. For biomarkers to be integrated into routine clinical practice, collaboration of researchers and clinicians together with the regulatory bodies is needed [59]. Finally, staff trained in biomarkers use in drug safety monitoring need to be educated to help them realize the potential of biomarkers in drug safety monitoring [60]. Creating the collaborative and standardization environments for the transition from biomarker research to clinical application will better the safety monitoring of drug.

7.4. Global Initiatives and Collaborations in Pharmacovigilance

Pharmacovigilance is a global initiative and collaboration, which facilitates improvement in the monitoring of drug safety across the globe. The activities of harmonizing pharmacovigilance practices from the point of view of countries are underway by the World Health Organization (WHO) [60] and International Council for Harmonizing (ICH). These initiatives will bring together the national pharmacovigilance system, data sharing and encourage best practices of adverse event reporting among the member states. However, in the field of pharmacovigilance it is important to collaborate in the low- and middle-income regions country for building the capacity and improving the effectiveness of the system gradually [61]. International cooperation can be fostered for promotion of the improvement of drug safety outcomes at the global level.

8. Conclusion

Subsequently, molecular biomarkers have revolutionized the detection of drug toxicity for early detection of adverse drug reactions in addition to significant enhancement of pharmacovigilance detection. Advance has made the prediction and monitoring of the drug safety with genomic, transcriptomic, proteomic, metabolomic and epigenetic biomarkers. By means to next generation sequencing (NGS), artificial intelligence (AI) and organ on a chip models, biomarker discovery has been accelerated at a faster pace to enable personalized medicine by prediction of individual drug response. These biomarkers are important in determining the safe dose of drug that should be done for a healthy person to avoid or to decrease the side effects in the absence and the amount of disease affected person can tolerate without jeopardizing the treatment success. Second, they support the practice in real time pharmacovigilance and improved drug safety monitoring and response strategies. However, challenges with biomarker standardization and validation make these easy except that we have no recourse other than to produce consensus guidelines for the reliability of biomass in clinical practice. The translation process to become routine medical application requires collaboration of researchers, regulatory bodies, healthcare providers to research for biomarkers. Artificial intelligence (AI) and machine learning have tremendous application for biomarker discovery and refinement of implementation. In the future, biotechnologies will play a major role in the transposition of pharmacovigilance with their ability to predict drug toxicity and optimize therapeutic strategies in personalized medicine. It will be important to standardize pharmacovigilance practices and effective drug safety monitoring globally for global collaboration. In the future, the present challenges could be addressed and the best utilized of the technological advancements in pharmacovigilance to go a long way.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this review article.

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