Integrative Pharmacovigilance: Monitoring Adverse Events in Herbal, Nutraceutical, and Conventional Therapies

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ABSTRACT

Pharmacovigilance (PV) is responsible for monitoring the safety of allopathic(drugs), herbal (medicines) and nutraceutical (food-based products). Given the increasing use of traditional and natural therapies, UV reports of adverse events and herb-drug interactions are also on the rise. Yet. PV systems are ill-positioned to effectively monitor non-conventional therapies due to regulatory gaps, a lack of standardization, and underreporting. Integrative PV approaches- through better regulatory harmonization, the development of standardized adverse drug reaction (ADR) reporting, Artificial Intelligence (AI) tools, inter-professional and collaborative approaches, and education – are a useful and effective way to monitor consumer safety. An integrated and inclusive approach to PV will improve patient safety and lead to better-informed therapeutic choices in all health care systems.

Keywords: Adverse drug reactions (ADRs), AI in pharmacovigilance, Complementary and alternative medicine (CAM), Drug safety monitoring, Herb-drug interactions, Herbal medicine safety, integrative pharmacovigilance

INTRODUCTION

Pharmacovigilance(PV) is a rapidly evolving field in the pharmaceutical industry, playing a key role in ensuring drug safety across clinical trials and post-marketing phases. Originating in the 1950s following adverse events linked to chloramphenicol, PV gained formal structure through the 1962 Kefauver-Harris Amendments. Core functions include case management, signal detection, and benefit- risk assessment. PV has since expanded to encompass patient safety in trials, dose selection, safety communication, product monitoring, and regulatory readiness With the rise of AI and data analytics, future PV professionals will require advanced skill sets to support the safe use of medicines [1]. In addition to allopathic treatments, many individuals opt for ayurvedic and herbal remedies to manage their health conditions, mainly because they believe these alternatives are safer. However, improper use of these herbal drugs could also lead to adverse drug reactions and toxicity [2].

Herbal therapies are widely used for conditions like diabetes, rheumatism, and liver disorders. Although some herbal treatments have demonstrated effectiveness, many lack proper testing and oversight, resulting in sufficient understanding of their action, potential side effects, contraindications, and interactions with conventional medications. Ongoing safety concerns emphasize the necessity for regulatory bodies to enforce standards that guarantee the safety and quality of these products [3]. Current pharmacovigilance systems, designed for synthetic

drugs, face challenges in monitoring herbal medicine safety due to their unique toxicological profiles and interactions [4].

Various herbal medicines cause variety of adverse reactions, such as Kava, Black cohosh, and Germander have been linked to liver damage, while Ginkgo biloba may trigger seizures and St. John's Wort can cause serotonin syndrome when combined with antidepressants [5] [6] [7]. Cardiovascular risks have been noted with Ephedra and Yohimbe, while Echinacea may cause allergic reactions [8] [9]. Ginger and Ginkgo increase bleeding risk, especially with anticoagulants. Additionally, St. John's Wort interacts with several drugs, reducing their effectiveness [10] [11] . Therefore, systematic pharmacovigilance is essential to accurately assess risks and develop guidelines for the safe and effective use of herbal and traditional medicines.

Nutraceuticals and dietary supplements are products taken in addition to the regular diet to provide extra nutrients as defined by the Dietary Supplement Health and Education Act(DSHEA) of 1994. Unlike allopathic and herbal medicines, nutraceuticals do not require pre-market approval or clinical trials [12]. Common reasons for its use include to improve general health, especially among women. Majority of these nutraceutical is used by individual's choice and only 25% of supplements use is based on medical advice. Clear indication of these supplements exists only in cases of vitamin deficiency diseases (e.g., Vitamin C deficiency, Vitamin B12 deficiency) [13] [14]. These are considered safe but are not risk-free. Some nutraceuticals like vitamins, omega-3s, plant antioxidants, weight loss and body-building products shows adverse reactions [15]. Lack of clinical trials leads to limited systematic evidence on adverse effects.

Therefore, continuous pharmacovigilance and careful evaluation of case reports are essential for identifying and managing adverse reactions related to conventional drugs, herbal medicines, and nutraceuticals. Strengthening these systems ensures safer use, informed decision-making, and better protection of public health.

REGULATORY FRAMEWORK IN PHARMACOVIGILANCE

The pharmacovigilance regulatory framework is a comprehensive system designed to monitor and ensure the safety of medicines after they have been approved for public use. It includes a set of legal requirements, guidelines, and procedures enforced by both national and international regulatory bodies. At the global level, the world Health Organization (WHO) plays a key role through the Uppsala Monitoring center(UMC), which manages the international ADR database known as VigiBase. The International Council for Harmonization(ICH) also supports pharmacovigilance by developing standardized guidelines like ICH E2E. On a national scale, each country has its own system. For instance, in India, the Central Drugs Standard Control Organization (CDSCO) oversees pharmacovigilance activities through the pharmacovigilance Programme of India (PvPI), coordinated by the Indian Pharmacopoeia Commission(IPC) .

Herbal medicine and nutraceutical product pharmacovigilance is also governed by global and national regulatory frameworks aimed at ensuring safety through adverse drug reaction (ADR) monitoring. Organizations like WHO advocate integrating herbal products into national pharmacovigilance systems, with data reported to global databases such as VigiBase. Regulatory bodies (e.g., FDA, EMA) require manufacturers to conduct post-marketing surveillance [16].

AI IN HERBAVIGILANCE

Machine learning shows promise in predicting adverse drug reactions(ADRs), but limited external validation hinders clinical reliability. Externally validated models showed better accuracy, emphasizing the need for diverse data and robust validation to strengthen AI- driven pharmacovigilance across all therapy types [16]. AI algorithms, particularly machine learning (ML) and natural language processing (NLP), can analyze diverse data sources such as spontaneous reporting systems, electronic health records, social media, and published literature to detect adverse drug reactions (ADRs) related to herbal products. These technologies help identify safety signals, uncover patterns in real-world usage, and assess herb-drug interactions. By automating and enhancing signal detection, AI contributes

to more timely and accurate pharmacovigilance of herbal medicines, ultimately supporting regulatory oversight and improving patient safety [17]. Thus, AI enhances the efficiency of analyzing diverse herbal and nutraceutical data sources to detect adverse drug reactions of nutraceutical products and herb-drug interactions. This enables earlier identification of safety signals, improves monitoring accuracy, and supports better regulatory decisions to ensure patient safety [18].

CHALLENGES IN HERBAL AND NUTRACEUTICAL PHARMACOVIGILANCE

Pharmacovigilance in the realm of herbal medicines faces a constellation of hurdles. There's a pervasive assumption that "natural" automatically equals "safe," which often leads to unsupervised self-medication and a noticeable lack of adverse event reporting [19]. Unlike conventional pharmaceuticals, herbal remedies frequently lack rigorous scientific validation, standardized labeling, or consistent quality control. This inconsistency—whether it's in sourcing, preparation, or even potency—complicates efforts to monitor and assess potential side effects [20].

Current pharmacovigilance frameworks? Honestly, they're tailored for synthetic medications and don't quite accommodate the unique complexities or interactions herbal products can present . Add to this the widespread lack of awareness among both healthcare providers and the general public, and you're left with underreporting and a serious gap in safety data. In short, our systems are not yet equipped to keep up with the growing popularity and diversity of herbal medicines [21].

INTERGRATIVE PHARMACOVIGILANCE STRATEGIES

1. ***Regulatory harmonization and policy integration***

   As the utilization of complementary and alternative medicine(CAM) rises globally, the need for an integrative pharmacovigilance(PV) effort to assess the safety of all therapeutic modalities, including herbal and nutraceutical products, is growing. Historically, PV systems have focused on pharmacovigilance of allopathic medications alone. However, these commonly used herbal and nutraceutical agents are similarly linked to adverse events and drug interactions, on despite unproven assumptions that they are safe solely based on their natural origins. To protect patient safety and support therapeutics efficacy, it is imperative to develop a harmonized and inclusive PV framework [22].

   A fundamental requirement is the development of a unified regulatory framework that brings allopathic, herbal, and nutraceutical products under a single umbrella for safety monitoring. National regulatory bodies should revise existing laws to include mandatory ADR (Adverse Drug Reaction) reporting for herbal and nutraceutical products. International harmonization with WHO, ICH, and EMA guidelines is also necessary, especially to standardize definitions, risk categories, and reporting methods. Regulatory reforms must clearly define these products, ensure that they follow good manufacturing practices, and are subjected to post-marketing surveillance similar to that mandated for allopathic drugs [23] [24].

2. ***Standardized ADR reporting systems***

   A successful integrative PV system relies on standard and inclusive ADR (adverse drug reaction) reports. Reporting tools should be established with as much details as possible with respect to herbal and nutraceutical products, and include aspects such as botanical names, methods of preparation, and whether or not they are standardized, and sources of purchase. Digital platforms and mobile applications should be enhanced to obtain all ADR's regardless of the nature of therapy, and include multilingual features to improve usability and accessibility. These systems should facilitate, or at minimum promote, ADR reporting for health care professionals, the public, and those practitioners engaged in traditional practice, who are often the first contact for CAM therapies [25].

3. ***Education and awareness programme***

   Education and awareness are vital components that can build capacity for effective integrative pharmacovigilance. Many health professionals — including allopathic and traditional health care providers — are not sufficiently trained in the adverse effects of herbal and nutraceutical products. By integrating drug safety training in the education of strengthened human resources in medical, pharmacy and AYUSH professions, professionals will better recognize

and report ADRs across the disciplines. Education campaigns must also be used for the general population to raise awareness and dispel myths about assumed safety of "natural" products and to encourage ADR reporting [26] [27].

4. Inter-System Working

Forming collaborative teams among difference systems of medicine is required. Pharmacovigilance committees and working groups must include representatives from allopathic, AYUSH, nutrition, and toxicology backgrounds. Health institutions with the provision of health care, including hospitals and AYUSH dispensaries, must develop bridging processes to allow for ethno medical care under the same roof to facilitate real-time ADR sharing and discussions. Only by facilitating inter-system-cooperation, can we address the complex care issues related to polypharmacy that involve herbs, supplements and prescription medications [28].

CONCLUSION

With the global health environment becoming more integrative, pharmacovigilance coverage needs to be extended from traditional medicines to herbal remedies and nutraceuticals. Though commonly used and felt to be safe, they also pose risks and are capable of inducing severe adverse effects when used in conjunction with allopathic medications. Current pharmacovigilance systems based mainly on synthetic medications fail to capture the specific safety profiles of herbal and dietary supplements.

To promote public health and patient protection, a coordinated and open pharmacovigilance strategy is essential. This involves regulatory harmonisation, harmonized ADR reporting systems, improved education among professionals and the public, and efficient inter-system communication between healthcare professions. Utilizing AI and digital technologies can further enhance early signal detection and data assessment, culminating in earlier intervention.

Finally, integrative pharmacovigilance will make healthcare systems able to monitor and manage risks in every type of therapy, allow safer therapeutic options, informed regulatory decisions, and comprehensive patient care.

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