



Adverse Drug Reactions and Pharmacovigilance of Herbal Drugs in India

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ABSTRACT :

The utilization of herbal medicines has been deeply ingrained in traditional healthcare practices in India for centuries. In recent times, the global resurgence of interest in herbal remedies has prompted a surge in their consumption worldwide. While perceived as natural and safe, herbal medicines are not without risks. This study delves into the landscape of adverse drug reactions (ADRs) associated with herbal medicines in India, aiming to underscore the importance of pharmacovigilance in this domain. A comprehensive analysis of reported ADR cases involving herbal medicines from the Indian Pharmacopoeia Database was conducted. The study identifies key herbal components and formulations linked to adverse events and categorizes them by severity and frequency. Noteworthy interactions between herbal remedies and conventional drugs are also explored, shedding light on potential risks for polypharmacy scenarios.

Furthermore, the study emphasizes the need for an integrated and robust pharmacovigilance system for herbal medicines in India. It highlights the challenges associated with monitoring and reporting ADRs in this context, including underreporting and lack of standardized reporting protocols. Recommendations for enhancing pharmacovigilance practices specific to herbal medicines are put forth, with a focus on regulatory frameworks, healthcare provider education, and public awareness campaigns.

KEYWORDS: Pharmacovigilance, ADR, herbal drugs, traditional medicines.

Introduction:

Herbal medicines have been an integral part of healthcare systems across the globe for centuries, with India boasting a rich tradition of Ayurveda, Siddha, and Unani systems of medicine. The use of herbal remedies has gained widespread popularity due to their perceived natural origins and cultural significance. However, the increasing acceptance and consumption of herbal medicines also raise concerns about the potential for adverse drug reactions (ADRs) and the need for robust pharmacovigilance systems.

Adverse drug reactions are untoward and unintended responses to a medicinal product, including herbal medicines. The unique composition of herbal remedies, often comprised of complex mixtures of bioactive compounds, introduces challenges in assessing their safety and potential interactions. In India, where the use of herbal medicines is deeply rooted in traditional practices and continues to be a major component of primary healthcare, understanding and monitoring the safety profile of these remedies is of paramount importance.

Pharmacovigilance is a crucial aspect of healthcare and drug regulation that involves the systematic monitoring, detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems. It plays a pivotal role in ensuring the safety of medications throughout their lifecycle, from pre-marketing approval to post-marketing surveillance.

The purpose of this review is to provide a comprehensive overview of adverse drug reactions associated with herbal medicines in the Indian context and to critically evaluate the existing pharmacovigilance mechanisms. By examining the current state of knowledge, identifying gaps in information, and proposing recommendations for improvement, this review aims to contribute to the ongoing discourse on herbal medicine safety.

The review will cover various aspects, including:

[1]. Historical Context of Herbal Medicine in India: The history of herbal medicine in India is deeply rooted in ancient traditions, where the use of plant-based remedies has been integral to the cultural and healthcare practices for centuries. Ayurveda, an ancient system of medicine, has played a pivotal role in shaping the understanding and application of herbal therapies. As the popularity of herbal medicines continues to grow, there is an urgent need to assess and monitor their safety through robust pharmacovigilance systems. This section explores the historical context of herbal medicine in India, focusing on the evolution of pharmacovigilance practices within this rich heritage.

[2] Diversity of Herbal Products:

The diverse array of herbal products used in India reflects the rich tapestry of traditional medicine, where an extensive range of plant-based remedies has been employed for centuries. As the popularity of herbal products grows globally, understanding the complexity and diversity of these formulations is essential for ensuring their safety and efficacy. This section explores the diversity of herbal products in India and examines the implications of this diversity for pharmacovigilance efforts.

[3] Historical Context of Herbal Medicine in India:

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Multitude of factors contribute to the complexity of adverse drug reactions (ADRs) associated with herbal medicinal products. ADR is a noxious and unintended response to a marketed health product, occurring at doses typically used for diagnosis, treatment, or prevention, underscores the importance of monitoring and understanding the safety profile of these products.

Plants have indeed played a crucial role in the development of modern medicines, with a substantial percentage of pharmaceuticals directly or indirectly derived from plant products. While harnessing the therapeutic potential of plants has yielded numerous benefits, the inherent complexity of herbal formulations poses challenges in identifying and managing ADRs.

The instances of ADRs linked to specific herbal products, such as Ephedra and Aristolochia, underscore the need for vigilant pharmacovigilance. These cases have highlighted that herbal medicinal products, despite their natural origins, can elicit unintended and harmful responses in human beings. A significant challenge lies in the identification of causative agents associated with ADRs, especially given that traditional herbal preparations.

[4] Pharmacovigilance Landscape in India:

The pharmacovigilance landscape in India plays a pivotal role in ensuring the safety of medicinal products, including herbal medicines deeply rooted in traditional practices. With a burgeoning market for herbal remedies, it becomes imperative to examine the current state of pharmacovigilance in India, specifically addressing the unique challenges associated with monitoring the safety profile of herbal products. This section provides an overview of the pharmacovigilance landscape in India, focusing on regulatory frameworks, reporting mechanisms, and surveillance infrastructure. involve the use of multiple ingredients.

ADVERSE DRUG REACTIONS:

Adverse Drug Reactions (ADRs) refer to unintended and undesirable responses that occur in individuals following the administration of pharmaceutical products or medications. These reactions can range from mild and tolerable side effects to severe and potentially life-threatening conditions. Monitoring and understanding ADRs are integral components of ensuring the safety and efficacy of drugs in clinical practice.

Nature of Responses: ADRs encompass a broad spectrum of responses, including common and expected side effects, as well as more uncommon and severe reactions. These can affect various organ systems and may have diverse manifestations.

Occurrence: ADRs can affect anyone, and their occurrence may be influenced by factors such as individual patient characteristics, genetic predispositions, concomitant use of other medications, and underlying health conditions.

Severity Gradient: The severity of ADRs can vary widely. While some reactions may be mild and transient, others can lead to serious health consequences, necessitating prompt medical intervention.

Monitoring and Reporting: Robust monitoring and reporting systems are in place to identify and assess ADRs. Healthcare professionals, as well as patients, play crucial roles in reporting suspected adverse reactions to regulatory authorities, contributing to ongoing pharmacovigilance efforts.

Pharmacovigilance: This is the systematic monitoring of medications to identify, assess, understand, and prevent ADRs. Pharmacovigilance activities contribute to the ongoing evaluation of drug safety throughout the product's lifecycle.

Causality Assessment: Healthcare professionals evaluate the likelihood that the adverse event is related to the drug by considering factors such as the temporal relationship, patient history, and known pharmacology.

Risk-Benefit Analysis: Prescribing decisions involve a careful evaluation of the potential benefits of a medication against the risks associated with ADRs. Balancing these factors is crucial for optimizing patient outcomes.

Patient Education: Educating patients about potential ADRs, recognizing symptoms, and emphasizing the importance of reporting any unusual effects are essential components of promoting patient safety.

ADR CLASSIFICATION:

Adverse drug reactions are frequently classified as 'type A' and 'type B' reactions. An extended version of this classification system is shown here:

Type A Reactions **Type A (augmented)** reactions result from an exaggeration of a drug's normal pharmacological actions when given at the usual therapeutic dose and are normally dose-dependent. Examples include respiratory depression with opioids or bleeding with warfarin. Type A reactions also include those that are not directly related to the desired pharmacological action of the drug, for example dry mouth that is associated with tricyclic antidepressants.

Type B Reactions **Type B (bizarre)** reactions are novel responses that are not expected from the known pharmacological actions of the drug. These are less common, and so may only be discovered for the first time after a drug has already been made available for general use. Examples include anaphylaxis with penicillin or skin rashes with antibiotics.

Type C Reactions **Type C, or 'continuing'** reactions, persist for a relatively long time. An example is osteonecrosis of the jaw with bisphosphonates.

Type D Reactions **Type D, or 'delayed'** reactions, become apparent sometime after the use of a medicine. The timing of these may make them more difficult to detect. An example is leucopenia, which can occur up to six weeks after a dose of lomustine.

Type E Reactions **Type E, or 'end-of-use'** reactions, are associated with the withdrawal of a medicine. An example is insomnia, anxiety, and perceptual disturbances following the withdrawal of benzodiazepines. Other classification schemes have also been proposed, such as 'DoTS', which takes into account dose-related, time-related and susceptibility factors.

The most commonly reported adverse effects, particularly in the context of herbal medicines, involve hepatic and renal problems. These issues emphasize the critical need for systematic monitoring and reporting mechanisms to detect and address potential toxicity. Hepatic and renal effects are of particular concern due to their implications for vital organ functions and overall patient well-being.

The complexity of traditional herbal preparations further complicates the attribution of ADRs to specific components. The synergistic interactions among various plant compounds can influence the safety profile, making it challenging to isolate the causative agent. This complexity calls for a comprehensive approach to pharmacovigilance, encompassing not only post-market surveillance but also pre-market evaluation and standardized quality control measures.

TABLE 1: LIST OF HERBS WITH SUSPECTED OR KNOWN ADVERSE EFFECTS:

S.NO	Herbal drug	Adverse effects
1	Ginkgo biloba	Bleeding
2	Ephedra	Hypertension, insomnia, arrhythmia, nervousness, tremor, headache, seizure, cerebrovascular event, myocardial infarction, kidney stones
3	Kava	Sedation, oral and lingual dyskinesia, torticollis, oculogyric crisis, exacerbation of Parkinson's disease, painful twisting movements of the trunk, rash
4	Aristolochia sp.	Kidney toxicity, carcinogenicity

Need for Pharmacovigilance of Herbal Medicines :

Here are some reasons why pharmacovigilance is necessary for herbal medicines:

Safety Concerns: Herbal medicines are not exempt from potential safety issues. Despite being natural, they can have side effects, interactions with other medications, or adverse reactions in certain individuals. Monitoring and reporting such events through pharmacovigilance are crucial for ensuring the overall safety of herbal medicines.

Variability in Composition: Herbal products can vary in composition due to factors like plant source, growing conditions, harvesting methods, and processing. These variations can lead to differences in the chemical composition of the product, influencing its safety profile. Pharmacovigilance helps identify and assess any adverse events associated with these variations.

Lack of Standardization: Herbal medicines often lack standardized manufacturing processes, which can result in variations in quality and potency. These inconsistencies can contribute to unexpected side effects or reduced efficacy. Pharmacovigilance helps identify and address issues related to product quality and standardization.

Interactions with Conventional Medications: Some individuals may use herbal medicines in conjunction with conventional pharmaceutical drugs. Pharmacovigilance is important to identify potential interactions between herbal medicines and prescription medications, as these interactions can affect the safety and efficacy of the treatment.

Globalization of Herbal Products: With the increasing popularity of herbal medicines worldwide, there is a growing need for international collaboration in pharmacovigilance efforts. Adverse events related to herbal medicines may be reported in different regions, and a coordinated pharmacovigilance system can help in sharing information and ensuring global safety.

Public Awareness: Pharmacovigilance plays a role in educating healthcare professionals and the public about the safe use of herbal medicines. Reporting and analyzing adverse events contribute to the accumulation of knowledge, which can be used to guide appropriate use and improve safety.

Regulatory Requirements: Regulatory agencies around the world are recognizing the importance of monitoring the safety of herbal medicines. Many countries now require pharmacovigilance data as part of the regulatory process for approving and maintaining the marketing authorization of herbal products.

Reporting criteria:

Adverse Drug Reaction (ADR) reporting criteria refer to the guidelines and requirements set by regulatory authorities for healthcare professionals, pharmaceutical companies, and other stakeholders to report adverse events or reactions associated with the use of drugs or medical products. The purpose of ADR reporting is to monitor the safety of medications and ensure the timely identification and management of potential risks. Here are some common criteria and considerations for ADR reporting:

Seriousness: ADR reporting typically focuses on serious adverse events, which may include events that result in death, life-threatening situations, hospitalization, persistent or significant disability, or birth defects.

Causality Assessment: Healthcare professionals are often required to assess the likelihood that the adverse event is related to the use of the drug. This may involve considering factors such as the temporal relationship between drug administration and the event, other possible causes, and the known pharmacology of the drug.

Unexpectedness: ADR reporting may prioritize unexpected or unusual reactions that were not previously described in the drug's labelling or literature.

Timeliness: Reporting of ADRs is usually required to be done in a timely manner, ensuring that relevant information reaches regulatory authorities promptly.

Completeness: A comprehensive and detailed report is encouraged, including information on patient demographics, medical history, concomitant medications, dosage, and the outcome of the adverse event.

Regulatory Requirements: Different countries may have specific regulations and reporting systems for ADRs. Healthcare professionals and pharmaceutical companies should be familiar with the requirements of the regulatory bodies in their respective regions.

Patient Reporting: Some systems encourage or require direct reporting of ADRs by patients, caregivers, or consumers. This can provide valuable additional perspectives on the safety of medications.

Electronic Reporting: Many regulatory authorities prefer or mandate electronic submission of ADR reports to streamline the reporting process and facilitate data analysis.

Confidentiality: ADR reports often contain sensitive patient information. Therefore, systems are in place to ensure the confidentiality and privacy of the individuals involved.

Follow-Up Reporting: In some cases, follow-up reports may be required to provide additional information on the course of the adverse event or the patient's response to interventions.

What to report?

1. All suspected adverse reactions.
2. Resistance.
3. Drug interaction.
4. Hospitalization (initial or prolonged).
5. Death.

Who can report?

1. ASU Doctors.
2. Dentists.
3. Nurses.
4. Pharmacists.

When to report?

1. Non-serious cases within 30 days.
2. All serious or death event as soon as possible and within 7 days

Where to report?

Where to report?



CONCLUSION

The exploration of historical contexts, diversity of herbal products, reported adverse reactions, and the existing pharmacovigilance landscape underscores the critical need for a nuanced and vigilant approach to ensure the safety of herbal remedies in the Indian healthcare system.

The historical legacy of herbal medicine in India, deeply embedded in ancient traditions such as Ayurveda, illuminates the rich cultural significance of plant-based healing. However, the contemporary resurgence of interest in herbal medicines necessitates a careful examination of their safety profile, considering the complexity of formulations and the potential for adverse reactions.

The review has highlighted instances of adverse drug reactions associated with herbal medicines, emphasizing the importance of monitoring and managing potential toxicity. Cases like Ephedra and Aristolochia serve as cautionary examples, illustrating the need for comprehensive surveillance systems to detect and respond to adverse events promptly.

As India continues to embrace the therapeutic potential of herbal remedies, the conclusion emphasizes the importance of ongoing commitment and collaboration. A proactive and adaptive pharmacovigilance approach is essential to ensure the responsible use of herbal medicines, safeguarding public health and facilitating the coexistence of traditional and modern healthcare practices. This review underscores the significance of balancing tradition with contemporary safety standards in the evolving landscape of herbal medicine in India. In recent years, there has been a resurgence of interest in herbal remedies, driven by the perception of natural alternatives and traditional healing practices. While herbal medicines offer promising therapeutic benefits, their safety profile

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