



Emerging Issues in Pharmacovigilance of Herbal Medicines in India

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ABSTRACT

Pharmacovigilance encompasses the science and practice related to the detection, assessment, understanding and prevention of adverse effects of drugs or any other possible drug-related problems. Recently, its purview has been widened to include herbal, traditional and complementary medicines, with the goal to comprehensively detect, assess, understand with the unanimous goal of preventing occurrence of adverse effects in those individuals undergoing therapy. This process of pharmacovigilance of herbals in India has come a long way since its initiation. The objective of the present article is to provide a succinct review on the recent trends and challenges posed in the practice of pharmacovigilance of herbal drugs especially in the Indian context and to shed light on the importance of pharmacovigilance practice in establishing and maintenance of rational use of drugs within the ambit of pharmacotherapy. The methodology adopted in the undertaken work comprises extensive topic related search of contemporary scientific articles and complementary review of bibliographies from selected publications on the subject. The promotion of systematic and rational use of drugs requires the reporting of adverse events possibly caused by herbal and traditional medicines also. Proper reporting of suspected adverse drug reactions from herbal medicines has assumed a greater role today and requires proper and careful implementation from everyone in the healthcare sector. Thus, in summary this review attempts to stress that systematic pharmacovigilance is essential to build up reliable information network on the safety of herbal medicines to boost confidence about their safety.

Keywords: Adverse drug reactions, Herbal drugs, Pharmacovigilance.

INTRODUCTION

Pharmacovigilance is the science dedicated to reduce the risk of drug-related harms to the consumers. Pharmacovigilance refers to the process of identifying side effects of drugs, their treatment, documentation, reporting and regulatory decisions based on these findings. In general Pharmacovigilance is the science of collecting, monitoring, assessing and evaluating information from health care professionals and consumers on the undesired effects of medications including herbal and traditional drugs. The worldwide movement for the improvement of patient safety is gaining momentum so the subject of drug safety becomes even more prominent in the present day scenario. In India also, pharmacovigilance practice is gaining pace in keeping with time.

These days, herbal medicines are being used by various communities throughout the world. Herbal formulations have reached widespread acceptability as therapeutic agents like cough remedies, hepatoprotectives, anti diabetics etc. Herbal medicines are traditionally considered harmless since these belong to natural sources. However, this is not true as there are several case reports of adverse reactions of herbal drugs mentioned in published literature. Although most traditional therapies are presumed to be safe, there is still the problem of how to assess and quantify the possibility of very rare adverse events. Serious event is enough to tip the scales against use of the alternative medicine therapy. If the benefit for any alternative medicine therapy is

modest or unproven, then the presence of even a very small increased risk for a serious event is enough to tip the scales against use of the alternative medicine therapy^{1,2}.

ADVERSE DRUG REACTION OF HERBAL MEDICINES

An adverse reaction (ADR) is defined as a noxious and unintended response to a marketed health product, which occurs at doses normally used or tested for the diagnosis, treatment, or prevention of a disease or the modification of an organic function⁴. It is undeniable that plants have an important role in the development of modern medicines. More than 60 to 70% of modern medicines in the world market are directly or indirectly derived from plant products.

Widely reported issues such as adverse drug reactions associated with Ephedra and Aristolochia have shown that herbal medicinal products can produce toxicity in human beings. The most common adverse effects reported are hepatic and renal problems. However, it is difficult to identify the causative agent associated with the ADRs encountered because traditional herbal preparations often contain multiple ingredients. A list of some suspected and known herbal drug associated with adverse effects is given in Table 1. In addition, a separate list of some herbal drug associated adverse drug interactions is mentioned in Table 2. The WHO database has over sixteen thousand suspected herbal case reports. Due to the lack of clinical trials for most herbal medicinal products, post marketing pharmacovigilance becomes a critical source of safety information. However, the



assessment of adverse reactions associated with herbal medicinal products offers unique challenges in the quantity and quality of available information^{5,6}.

Herbs with suspected or known adverse effects

Table 1 listed Herbs with suspected or known adverse effects.

Table 1: List of Herbs with suspected or known adverse effects.

Herbal drug	Adverse effects
Ginkgo biloba	Bleeding
St. John's wort	Gastrointestinal disturbances, allergic reactions, fatigue, dizziness, confusion, dry mouth, photosensitivity
Ephedra (Ma Huang)	Hypertension, insomnia, arrhythmia, nervousness, tremor, headache, seizure, cerebrovascular event, myocardial infarction, kidney stones.
Kava (<i>Piper methysticum</i>)	Sedation, oral and lingual dyskinesia, torticollis, oculogyric crisis, exacerbation of Parkinson's disease, painful twisting movements of the trunk, rash
<i>Aristolochia sp.</i> (Found use in Chinese medicine)	Kidney toxicity, Carcinogenicity.

Herbs with Adverse Drug Interactions⁷

Table 2 listed specific herbal drugs and their adverse interactions.

Table 2: List of specific herbal drugs and their adverse interactions.

Herb	Drug	Adverse effect
Ginkgo biloba	Drugs like Aspirin, warfarin, ticlopidine, clopidogrel, dipyridamole, garlic, vitamin E	With aspirin - retards aspirin absorption
Psyllium seed	Coumarin derivates	Retards absorption of drug
Ephedra	Caffeine, decongestants, stimulants	May be additive in nature.
Feverfew	Aspirin	Additive effects

METHOD OF PHARMACOVIGILANCE OF HERBAL DRUGS

In order to provide consistency in the naming of herbs in adverse reaction (ADR) reports, the WHO Collaborating Centre for International Drug Monitoring has recommended the use of proper scientific binomial names for herbs used in medicine, including the use of such names (where this information is available) in the coding of ADR reports³. This would ensure comparability between reports from various international pharmacovigilance databases. It is equally important for the authors of published adverse reaction case reports to

identify the specific product involved, including label and manufacturer information, specific ingredients, and dose employed. Published case reports would also benefit from analysis of the suspect product used, for contamination and adulteration, or species identification, where possible.

Various methods in pharmacovigilance practice are passive surveillance including spontaneous reporting and stimulated reporting, active surveillance by sentinel sites, drug event monitoring, registries, comparative observational studies by survey study, case control study, targeted clinical investigations by investigating drug-drug interactions and food- drug interactions⁸.

THE EMERGENCE OF PHARMACOVIGILANCE OF HERBAL MEDICINES IN INDIA

Constitution of the National Pharmacovigilance Programme of India (PVPI)

The National pharmacovigilance programme in India is under the control of Central Drug Standards Control Organization (CDSCO) has already started functioning since 2003. World Health Organisation (WHO) had emphasized that it should include traditional medicines in pharmacovigilance system and has published guidelines on safety monitoring of herbal medicines in Pharmacovigilance systems in 2004. Department of AYUSH, Ministry of health and Family Welfare, Government of India, New Delhi has initiated the national pharmacovigilance programme for Ayurvedic, Siddha and Unani (ASU) drugs. NPCR-ASU is coordinating the country-wide Pharmacovigilance programme for ASU drugs. Worldwide movement for the improvement of patient safety gains momentum, the subject of drug safety becomes even more prominent.

Pharmacovigilance is dedicated to reduce the risk of drug-related harms to the consumers. Looking in to the conditions prevailing in the present scenario, it is high time to deliberate regarding the present scenario, it is the need of the hour to deliberate regarding the burning issues over traditional and classical Ayurvedic, Siddha and Unani Products and practices; it is felt to constitute a National Pharmacovigilance center for ASU Drugs in India. The first national consultative meet of national Pharmacovigilance Programme for ASU Drugs was organized at Dept. of AYUSH, ministry of Health & FW, New Delhi in the month of August 2008, where the draft protocol was technically reviewed and finalized^{9,12}.

PHARMACOVIGILANCE OF HERBAL MEDICINES IN INDIA - CHALLENGES AHEAD⁹

In spite of the many wondrous achievements in the development process of pharmacovigilance of herbal medicines, the practice apparently suffers from many drawbacks in India. Although the National Pharmacovigilance Program has encouraged reporting of all suspected drug-related adverse events including those caused by herbal/traditional/alternative medicines still the number of reports related to Ayurvedic/herbal drugs



has been abysmally low. Several challenges that prohibit identification and reporting of adverse reactions to Ayurvedic drugs can be identified related to the detection, assessment and in the prevention of the adverse reactions.

Among the challenges faced in the detection of adverse reactions may involve one or more of the following such as-Adverse reaction terminology not covered in Ayurvedic curriculum, Drug safety problems, Accessibility of safety information, Signal Detection, Concomitant medication, Lack of Quality Assurance /Quality Control, Informal selling, Counterfeit and spurious herbal drugs to name a few.

The challenges faced in the assessment of adverse reactions include lack of trained professionals, inability in the interpretation of causality assessment reports, lack of information about the active principle and with regards to the mechanism of action of herbal medicines etc

CONCLUSION

Why is Pharmacovigilance of Herbal Drugs Important?

Some countries accept traditional, experience based evidence while others consider herbal remedies as dangerous or of questionable value. Medicinal herbs as potential source of therapeutics aids has attained a significant role in health care system all over the world for human beings not only in the diseased condition but also as potential material for maintaining proper health¹⁰. A major factor impeding the development of the medicinal plant based industries in developing countries has been the lack of information on the social and economic benefits that could be derived from the industrial utilization of medicinal plants.¹¹

The monitoring the safety of herbal medicinal products, in the market or in the pipeline, will definitely go a long way in restoring the confidence of their safety.

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Raja Chakraverty pursued his M Pharm in Pharmacology from Gupta College of Technological Sciences, Asansol affiliated to West Bengal University of Technology (WBUT). Mr. Chakraverty has to his credit published 5 original research articles in various national and international journals in Pharmaceutical Sciences. His research interest lies in the preclinical studies, particularly in the pharmacological screening of antidiabetic drugs in animal models, clinical research of pharmaceuticals and biologicals, in pharmacovigilance of herbal medicines and Toxicological studies.