

Pharmacovigilance: Future Need of Ayurveda

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Abstract

Ayurveda or Indian system of medicine has been serving mankind since time immemorial and now it is spreading worldwide. The commonest myth prevailed regarding Ayurveda medicine is that these medicines are completely safe and do not have any side effects. Improper manufacturing, self-medication, failure of proper dosing etc are leading to disappointing end results and adverse effect. It is necessary to incorporate new system of safety and awareness towards Ayurveda which is known as Pharmacovigilance. Pharmacovigilance is the science dedicated to the monitoring, detection, assessment, evaluation and prevention of adverse effects or any other medicine related problems. The increasing global acceptance of Ayurveda led regulators to implement a similar program for Ayurveda particularly when some scientists, medical professionals, and patients reported cases of adverse drug reaction of Ayurveda medicines. In order to promote Ayurveda as global medicine and meet global healthcare standards there is urgent need to equip Ayurveda with tool of Pharmacovigilance. Government of India has implemented a Pharmacovigilance program for Ayurveda, as a measure to ensure safety and efficacy of Ayurvedic medicines. Pharmacovigilance helps in monitoring of adverse drug reaction thus help to protect public health. This review article provides an overview of the need of the Pharmacovigilance and future aspects of Pharmacovigilance for Ayurvedic system of medicine.

Keywords

Pharmacovigilance, Ayurveda, ADRs, Safety, Efficacy



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INTRODUCTION

Ayurveda, Siddha and Unani medicine makes up an important module towards alternative healthcare in India out of which Ayurveda or Indian system of medicine is most prevalent. Ayurveda is a classical preventive and curative holistic system of medicine originating from the Vedas thousand years ago and currently practiced in India and many countries¹. It is the most commonly practiced form of non allopathic medicine in India comprising a wide range of herbs, minerals, dietary and lifestyle advices, and their combinations with various nondrug treatment approaches. About 80-90% of Indian population is using Ayurveda medicines for their medical needs². The increasing popularity of Ayurveda in the Western world health care facilities creates need for regulation of Ayurveda education and research³. This increasing worldwide use of Ayurvedic medicines has increased concern regarding their safety. Various international publication raises their concern about the safety of Ayurveda medicines^{4,5,6}. In the age of modern technology, scientific advancements, and consumer safety, there is very sparse documentary evidence supporting safety of Ayurveda drugs except the fact that Ayurveda has been practiced

from hundreds of years and there is rarely any adverse effect reported. Serious question has been raised in western publications regarding toxic level of heavy metal in Ayurveda medicine⁷.

With increased demand of Ayurveda drugs scope for adulteration, preparation of low quality drugs and formulations without standard reference has increased. Further with respect to change in environmental conditions, increasing use of synthetic pesticides, cultivation of medicinal plants with laboratory generated species, adulteration of herbs and concomitant use of herbs with drugs of other system of medicine has increased. These changes may have deep impact on the safety and efficacy of the ASU drugs hence, safety monitoring has become very essential. Mechanism is required to put in place to address these problems and Pharmacovigilance program establishment is the first step towards solving these problems. Pharmacovigilance is dedicated to reduce risk of drug-related harms to patients. In era of increasing global acceptance of Ayurveda, there emerges need to implement similar program for Ayurveda particularly when some scientists, medical professionals, and patients reported cases of adverse drug reaction of Ayurveda

medicines. In order to promote Ayurveda as global medicine and meet global healthcare standards there is urgent need to equip Ayurveda with tools that will provide answers to the modern scientific world and providing more acceptability of Ayurvedic drugs.

The number of cases reported of adverse reactions caused due to ASU drugs in India is negligible. The strong belief about safety of ASU medicines is major cause of this situation. Additionally there is lack of knowledge about Pharmacovigilance among ASU practitioners. While improvement of patient safety is gaining momentum worldwide, subject of drug safety becomes even more prominent in the present day scenario. More and more countries are regulating herbal medicines⁸. With the increased concern related to safety of Ayurvedic medicines, National Pharmacovigilance Program in ASU drugs has been founded by Department of AYUSH, Ministry of Health and Family Welfare, Government of India⁹.

Pharmacovigilance is science of monitoring, detection, assessment, understanding, and prevention of adverse effects of drug. This definition covers the AYUSH program objectives and its coverage area as per the

WHO guidelines¹⁰. To be specific Pharmacovigilance program aims to collect data regarding ADR and to identify and quantify the noxious and unintended effects associated with the use of drugs including lack of efficacy which occurs at doses normally used for prophylaxis, diagnosis or therapy of disease. Inferences drawn from analysis of data are used to suggest regulatory measures and provide management skills to health care professionals and the public. The major activity under Pharmacovigilance is reporting of side effects (SE), adverse drug events (AE) and adverse drug reaction (ADR). Side effect is any unintended effect of a pharmaceutical product used at recommended dose. Adverse drug event is any unusual occurrence of events that may appear during treatment with a drug but which does not necessarily have a relationship with this treatment. Adverse drug reactions according to WHO Technical Report No 498 (1972); “Noxious and undesirable responses to a drug occurring at standard doses used for the prophylaxis, diagnosis, or therapy of disease.” An ADR is a harmful response reflected in patient due to drug given by standard dosing, frequency and administration technique.

NEED OF PHARMACOVIGILANCE IN AYURVEDA

Ayurveda always had inherent spirit of pharmacovigilance within. Texts focus on rational use of medications and safety during treatment to improve patient care and safety^{11,12}. Ancient texts clearly define that if a drug is used without proper knowledge of its pharmacological action, drug would act as a poison¹³. Drug if prepared according to its GMP and used in the prescribed dose, then the adverse reactions can be minimized to a great extent. Guidelines for identification of drug, harvesting technique, storage, detoxifying, manufacturing, therapeutic dosage and its combination with other drugs, shelf life of drug, contraindications are some of the core principles and tools of Pharmacovigilance are used in Ayurveda since ancient time. Determination of drug and dose based on precise evaluation of the *roga* (disease), *rogi bala*, *aushadha kala*, (time of administration of drug) its *desh* (place), *satwa*, *satmya*, *ahara Shakti*, *vyayam Shakti* also minimizes the ADR¹⁴. Scientific assessment of the AE's and ADR's on objective parameters would definitely help Ayurveda proves its

worth globally. Practice of Pharmacovigilance will enable us to make more safer and authentic medicines and making Ayurveda more rational and reliable. From ancient times, Ayurvedic physicians used to prepare medicines for their patients themselves. Today, only few practitioners follow this. Now production and sale of Ayurvedic drugs has become changed into a full-scale industry. Manufacture and marketing of Ayurvedic drugs is regulated by the Drugs and Cosmetics Act¹⁵. There are mainly two categories of Ayurvedic medicine are available in the market, classical Ayurvedic and proprietary formulations. Classical medicines are made as per descriptions in Ayurveda *samhitas* whereas proprietary formulations are made from herbal extract¹⁶. This commercialization produces new challenges about safety of Ayurvedic drugs resulting into need of Pharmacovigilance program implementation. Perception that ASU drugs are always safe and innocuous is likely to be change due to reports of ADR during their use. Increased global use increases chances of interaction of these drugs with different genomic profiles. This led to more incidences of unexpected effects. This is the right time to evolve a mechanism to record

ADR of ASU drugs. There is a need to engage health-care professionals and the public at large for monitoring adverse drug reactions caused due to ASU medicines. The purpose of the program is to collect data, analyze it and use the inferences to recommend regulatory measures to healthcare professionals and the public.

CHALLENGES IN IMPLEMENTING PHARMACOVIGILANCE IN AYURVEDA

After establishment of National Pharmacovigilance Program, Steps are taken to promote awareness and educational training. Several challenges are associated with detection, reporting and assessment of adverse reactions.

1. Signal detection is difficult because there is an inherent faith in safety of Ayurvedic medications resulting into ignorance of ADR reporting. Patients keep taking medicines for years with no monitoring hence they do not even give history of taking these medicines.
2. The concept and terminologies of Pharmacovigilance are not included in the Ayurvedic curriculum both at under-

graduate and post-graduate levels, thus never exposing the young physicians to concept of Pharmacovigilance in Ayurveda.

3. There is lack of awareness regarding Pharmacovigilance among ASU practitioners.
4. Methods to study drug safety problems have not evolved adequately in Ayurveda.
5. The Ayurvedic pharmaceutical industry is not encouraged to work on concept of Pharmacovigilance in Ayurvedic medicines. Hence, there is no attempt at generating safety data related to Ayurveda formulations.
6. Information related to medicines are described in form *shloka* in the Ayurveda which is not easily accessible due to poor documentation
7. Information related to adverse effects is not systematically arranged and are not in electronic form making it is difficult to access. Many journals are not peer-reviewed hence quality of publications is questionable.
8. Lack of quality assurance and control in manufacturing of Ayurvedic medicine make it difficult to diagnose the source of adverse reaction.

9. Patients often use multiple medications from different systems at a time leading to difficulties in finding exact cause of ADR and casualty.

10. The informal sector manufacturing and selling Ayurvedic drugs makes it impossible to identify the medicine because of no labeling on formulations. These drugs may cause of adverse reaction

11. The problem of counterfeit and spurious drugs is serious. There are reports of using orthodox modern medicines as “Ayurvedic” drugs.

12. Most Ayurvedic formulations are multi-ingredient and multiple drug are consumed at the same time. Pharmacokinetics and Toxicokinetics of multi ingredient Ayurveda drugs are difficult to describe

13. Lack of personal having expertise in evaluating causality analysis due to Ayurvedic medicines. Pharmacovigilance are unable to understand Ayurveda principals and expert in Ayurveda find it hard to understand science of Pharmacovigilance.

NATIONAL PHARMACOVIGILANCE PROGRAM (NPP) FOR ASU DRUGS¹⁷

The National Pharmacovigilance Program for ASU drugs was discussed in December 2007 in workshop sponsored by WHO organized at IPGT and RA, Jamnagar, India on possibility of applying concepts of Pharmacovigilance program to ASU drugs. The protocol and ADR reporting forms were prepared and discussed by the Department of AYUSH of India in a meeting held in August 2008. It was on 29 September 2008 that a formal Pharmacovigilance program was finalized to be implemented. IPGT and RA, Jamnagar, India has been assigned as National Pharmacovigilance Resource Centre for ASU drugs in India.

There are three levels of Pharmacovigilance centre. National Pharmacovigilance Resource Centre for ASU Drugs or tertiary Pharmacovigilance centre is large healthcare facilities attached ASU medical colleges identified by Dept. of AYUSH, Ministry of Health and FW, Govt. of India. It would act as National administrative body of the NPP for ASU in India. Govt. of India has declared Institute for Post Graduate Teaching and Research in Ayurveda (IPGT & RA), Jamnagar as National Resource centre for this program. Regional Pharmacovigilance Centers or Secondary Pharmacovigilance centers for ASU. Are

relatively larger healthcare facilities attached ASU medical colleges identified as RPC - ASU. They are assigned as second level centers in the administrative structure of the NPP. Peripheral Pharmacovigilance Centers for ASU or Primary Pharmacovigilance centres are relatively small ASU medical Colleges including individual ASU medical practitioners' clinics, nursing homes private hospitals, pharmacies etc. They will function as first contact ADR data collection unit at a health care facility.

What to report under NPP-ASU

- Reporting of all suspected ASU drugs associated adverse reactions either alone or in combination with other drugs
- Suspected drug interactions of ASU drugs
- Reactions to any other drugs suspected to affect a patient's management to major extent, including reactions suspected for events like Death, Life threatening risk requiring hospitalization and medical interventions

Who can Report?

Health care professional may report suspected cases of adverse drug events. The cases reported by lay members and other than healthcare professionals not accepted

directly however they may report through their physician.

Where to Report?

Reporting should be done in a prescribed format through a local Pharmacovigilance centre.

Aim of PV

- To improve patient care and safety
- To maintain efficacy of drug which will improve patient wellbeing
- To develop the culture of notification and ADR reporting
- To involve healthcare professionals expert in the drug monitoring and information dissemination processes.
- To achieve operational skills that would make National Pharmacovigilance Program for ASU drugs as standard model for global drug monitoring endeavors.

DISCUSSION

Ayurveda has been a wonderful system of medicine serving mankind from centuries ago. Effectiveness and safety of Ayurveda is not at all questionable but some circumstances and definitions have changed over the period of time. One the one side practice, production and sale of Ayurvedic drugs has become a thriving industry due to which there emerges scope for adulteration,

preparation of counterfeit drugs, development of formulations which do not have conceptual basis and use of Ayurveda with drugs of other system of medicine has increased. Further changed environment, use of insecticides and cultivation of medicinal plants with laboratory generated species creates impact on the quality of raw material and formulations hence affecting safety and efficacy of the Ayurveda drugs in the market. In these circumstances, safety monitoring has become very essential. A Mechanism is required to put in place to deal problem with efficacy and safety of drug. On the other hand Ayurveda is getting global popularity due to its great results on non-infectious, chronic and lifestyle related disorders. The increasing global acceptance of Ayurveda led regulators to implement Pharmacovigilance program for Ayurveda particularly when some scientists, medical professionals, and patients reported cases of adverse drug reaction of Ayurveda medicines.

Success of any system of medicine always depends upon authenticity, safety and efficacy of drugs. Soul of Pharmacovigilance is inherent in Ayurveda. Ayurveda Texts focus on rational use of medications and safety during treatment.

However, scientific assessment of the ADR's on objective parameters is the present need that would definitely help Ayurveda to prove itself worthy to the modern scientific world. A misconception that has been prevailed among the common people is that Ayurveda medicines are always safe. This wrong thinking must be changed. Ayurveda medicines are safer but if a drug is not properly manufactured as per set protocols or improperly prescribed, side effects are bound to occur. Pharmacovigilance is observational study which deals with monitoring, detection and evaluation of safety of medicines and thus helps in identifying risk factors. Very little information about ADR profile of Ayurvedic drugs is available. Establishment of Pharmacovigilance set up is the first required step. It is going to be a long way in creating infrastructure for Pharmacovigilance reporting system for Ayurveda. The Ayurveda practitioner should be given training regarding assessment and procedure for reporting of adverse reactions. Format of assessment forms should be simplified so that easy reporting and close monitoring of all drug prescriptions could be done. Conducting regular seminars and guest lectures among Ayurvedic health

workers and pharmacist to educate about importance of ADR reporting in Ayurveda. Adequate inclusion of Pharmacovigilance may be done in the undergraduate and postgraduate curriculum of Ayurveda. Prescription of Ayurveda drugs along with drugs from different system of medicine should be avoided so that the effect of drugs on human body can be precisely evaluated. Clinical studies on Ayurveda drug safety and efficacy should be encouraged. Improve documentation regarding theoretical concept in text of Ayurveda and observational outcome through clinical trials. Awareness about the science of Pharmacovigilance should be spread among Ayurvedic practitioners, other health care professionals and workers, pharmacists and patients. Direct involvement of Academic Institutions in the NPP would be an appropriate first step in creating human resource. Pharmaceutical industry can also play a major role by following GMP and generating data for safety and efficacy profile of drugs. Data obtained from various clinical or pharmacological studies/trials should be updated in the text books at regular intervals. Human resource development is a most important requirement for the success of the Pharmacovigilance program. It is

necessary to provide proper training to Ayurvedic experts in the science of Pharmacovigilance.. Information gained should be systematically arranged and digitalized so that the knowledge can be made available instantly. More institutes should be involved in the process so as to create a deeper penetration of the concept.

CONCLUSION

The need of the hour is to educate the physicians and encourage them to analyse and report any adverse effects that occur in a patient, no matter how small or irrelevant they may seem. Quality drugs are one of the primary requisite for effective therapy. The onus of providing quality drugs lies with the pharmaceutical houses. The industry should take some concrete steps to generate confidence and reliability for its products. The morality of manufacturing standard drugs can go a long way in minimizing the adverse effects and generating confidence in therapeutic efficacy. Clinical trial data documentation must be done. Further, this shall in long term lead to characterization of Ayurvedic drugs as OTC (over the counter), prescription or scheduled drugs for better safety and acceptance of Ayurvedic medicines. At some stage, there also needs

to be regulation of self-preparation and administration of drugs by clinicians. Data obtained through Pharmacovigilance program will create better confidence in the users of ASU Drugs and will provide some answers to the modern scientific world ultimately boosting global acceptability to Ayurveda system of medicine. In a recent study it was reported that ADR'S are from *Panchkarma* treatment are high in ratio. GI and skin are maximum effected organs due to ADR'S possibly due to oral and skin as most preferred route of administration. There were no CVS, CNS and Urinary system related symptoms suggesting that ADRs due to Ayurvedic medicines are mild in nature , self-limiting and do not affect the major systems¹⁸. The success of Pharmacovigilance system lies in the ability in preventing further adverse reactions successfully by analysing, understanding and using the information collected. We can say pharmacovigilance is future need of Ayurveda which will establish benchmark of safety and efficacy of Ayurveda and will promote Ayurveda as global system of medicine.

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