REVIEW ARTICLE

Adverse drug reactions and pharmacovigilance of herbal medicines in India

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Abstract

The use of Ayurvedic medicines is popular in India and in recent times has become accepted in other countries. This paper discusses, in brief, the Ayurvedic concepts of adverse reactions to medicines, the need for pharmacovigilance of Ayurvedic medicines, challenges in introducing pharmacovigilance in Ayurveda, and some recommendations to successfully implementing these activities. Pharmacovigilance is the science and practice related to the detection, assessment, understanding, and prevention of adverse effects of drugs or any other possible drug-related problems. The objective of the present article is to review 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 these drugs. There is increasing awareness of the need to develop pharmacovigilance for herbal medicines. Applying standard pharmacovigilance techniques (WHO guidelines) presents additional challenges, related to the ways in which herbal medicines are regulated, used, named, and perceived. Proper reporting of suspected adverse drug reactions to herbal medicines is currently the main method of detection. However, there is under-reporting for herbal medicines, since users do not seek professional advice about their use of such products, or report adverse effects. Herbal medicine practitioners are not recognized as reporters to spontaneous reporting schemes. Several other conventional pharmacovigilance tools, such as prescription-event monitoring and the use of computerized health record databases, are currently of little use for evaluating the safety of herbal medicines although modified methods have been developed. This process of pharmacovigilance of herbals in India has come a long way since its initiation. The promotion of the systematic and rational use of drugs requires the reporting of adverse events possibly caused by herbal and traditional medicines also.

Key words: Adverse drug reactions, pharmacovigilance, herbal medicines

INTRODUCTION

Pharmacovigilance is the science dedicated to reducing 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 healthcare 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 such as cough remedies, hepatoprotectives, and antidiabetics. 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

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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. A serious event is enough to tip the scales against the 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 the use of the alternative medicine therapy.[1,2] Increasing uses of these drugs are growing concerns about the safety of Ayurvedic medicines.[3]

ADVERSE DRUG REACTION (ADR) OF HERBAL MEDICINES

Charaka says, "that even a strong poison can become an excellent medicine if administered properly. On the other hand, even the most useful drug can act as a poison if handled carelessly." An 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 function.[4] It is undeniable that plants have an important role in the development of modern medicines. More than 60-70% of modern medicines in the world market are directly or indirectly derived from plant products. Widely reported issues, such as ADRs 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.

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]

Need for Pharmacovigilance of Ayurvedic Medicines

The number of adverse reactions to Ayurvedic drugs reported or recorded in the National Pharmacovigilance Program in India is negligible. The strong belief that Ayurvedic medicines are safe contributes to a large extent to this situation. To compound this matter is the lack of knowledge about the concept and importance of pharmacovigilance in Ayurveda among Ayurvedic practitioners. Several challenges that preclude identification and reporting of adverse reactions to Ayurvedic drugs can be identified related to detection, assessment, and prevention of adverse reactions.[7,8]

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 (*P. methysticum*)	Sedation, oral and lingual dyskinesia, torticollis, oculogyric crisis, exacerbation of Parkinson's disease, painful twisting movements of the trunk, rash
Aristolochia sp. (found use in Chinese medicine)	Kidney toxicity, carcinogenicity

P. methysticum: Piper methysticum

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

Herb	Drug	Adverse effect
Ginkgo biloba	Drugs such as aspirin, warfarin, ticlopidine clopidogrel, dipyridamole, garlic, Vitamin E	With aspirin - retards aspirin, absorption
Psyllium seed	Coumarin derivatives	Retards absorption of drug
Ephedra	Caffeine, decongestants, stimulants	Maybe additive in nature
Feverfew	Aspirin	Additive effects

Detection of Adverse Reactions to Ayurvedic Medicines

Perhaps because of the firm belief among doctors and prescribers alike, that Ayurvedic drugs are safe, the detection of adverse reactions to these medicines is a major challenge. From obtaining a correct history to diagnosis and to pinpointing the causal medicine, the path is full of obstacles including:

1. The concept and terminologies related to adverse reaction monitoring are not covered in the Ayurvedic curriculum precluding accurate identification of adverse reactions
2. Methods to study drug safety problems have not evolved adequately in Ayurved
3. Although information related to medicines exists in the stanzas in the ancient treatises of Ayurveda, it is not easily accessible

4. Signal detection is difficult because there is an inherent belief about the safety of Ayurvedic medications leading to the lack of reporting and collection of reports relating to any formulation
5. Patients often use medicines from different systems of medicine concomitantly leading to difficulties in assigning causality
6. Lack of quality assurance and control in the manufacture of Ayurvedic medicine, which acts as a confounding factor in diagnosing the adverse reaction
7. The informal sector manufacturing and selling Ayurvedic drugs on a small-scale is large, and this often makes it impossible to identify the medicine that may be causing the adverse reaction
8. The problem of counterfeit and spurious drugs is serious.

Assessment of Adverse Reactions to Ayurved Medicines

Although several scales are available for causality assessment, applying them for Ayurved medicines and ascribing causality is perhaps the greatest challenge for several reasons including:

1. Information related to adverse effects is scattered in Ayurvedic literature and not in electronic form, hence making it is difficult to access. Many publications are not in peer-reviewed journals, and the quality of available publications is questionable
2. Most Ayurved formulations are multi-ingredient-fixed dose formulations rarely prescribed alone
3. In additional, there is the confounding factor that the patient is often receiving allopathic medicines at the same time
4. Dose-related responses are rarely measured and reported
5. One of the most challenging aspects is the lack of expertise in performing causality analysis with Ayurved medicines. A person trained in pharmacovigilance rarely understands Ayurved while an expert in Ayurved is not trained in the science of Pharmacovigilance.

Prevention of Adverse Reactions to Ayurved Medicines

The success in any pharmacovigilance system is in the ability to prevent further adverse reactions successfully by understanding and using the information collected. With Ayurvedic medicines, the challenges would be at multiple levels.

1. Communication between the practitioners and policy makers of orthodox Western medicine and traditional Indian medicine is not adequate. Ayurvedic practitioners are not aware of the need to report and where to report
2. Patients are not adequately aware that Ayurvedic medicines can cause adverse reactions and can take medicines for years on end with no monitoring as they believe that these medicines can do no harm. Hence, they do not even give a history of taking these medicines
3. Education in Ayurveda or modern medicine at both under-graduate and post-graduate levels does not cover pharmacovigilance of Ayurvedic medicines, thus never exposing the young physicians to this concept
4. The Ayurvedic pharmaceutical industry is not motivated to focus on pharmacovigilance of Ayurvedic medicines. Hence, there is no attempt at generating safety data - either before or after marketing of the formulation.

Recommendations

Based on these observations, there are several ways to attempt to embrace pharmacovigilance systems into Ayurveda.

1. Encourage pharmacovigilance concepts into the curriculum of Ayurved at the under-graduate and post-graduate level
2. Encourage studies on drug safety
3. Make reporting of adverse reactions to regulators mandatory for Ayurvedic formulations
4. Make unbiased and easily accessible drug information available
5. Development and validation of scales to assess the causality of the reported reactions to Ayurvedic medicines
6. It will be necessary to train Ayurvedic experts in the science of pharmacovigilance and include them not only in reporting but also assessment of the adverse reactions.

CONCLUSION

Why is pharmacovigilance of herbal drugs important?

Medicinal herbs as a potential source of therapeutics aids have attained a significant role in health care system all over the world for human beings not only in the diseased condition but also as a potential material for maintaining proper health.[9,10] 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.[11,12]

REFERENCES

1. Gadre GK, editor. Ashtang Hridaya. 13th Adhyaya. 2nd ed. Pune: Aryabhushan Printing Press; 1910. p. 65.
2. Thatte UM, Rege NN, Phatak SD, Dahanukar SA. The flip side of Ayurveda. J Postgrad Med 1993;39:179-82.
3. Gogtay NJ, Bhatt HA, Dalvi SS, Kshirsagar NA. The use and safety of non-allopathic Indian medicines. Drug Saf 2002;25:1005-19.
4. Trikramji AJ, editor. Charak Samhita. 8th Adhyaya. 5th ed. Varanasi: Chaukhambha Sanskrit Sansthan; 2001. p. 275.

5. Trikramji AJ, editor. Charak Samhita. 8th Adhyaya. 5th ed. Varanasi: Chaukhambha Sanskrit Sansthan; 2001. p. 276.
6. Shastri PK, editor. Rasantarangini. 2nd Adhyaya. 11th ed. New Delhi: Sri Jainendra Press; 1994. p. 22-4.
7. Saper RB, Kales SN, Paquin J, Burns MJ, Eisenberg DM, Davis RB, *et al.* Heavy metal content of ayurvedic herbal medicine products. JAMA 2004;292:2868-73.
8. Parab S, Kulkarni R, Thatte U. Heavy metals in 'herbal' medicines. Indian J Gastroenterol 2003;22:111-2.
9. Trikramji AJ, editor. Charak Samhita. 1st Adhyaya, 5th ed. Varanasi: Chaukhambha Sanskrit Sansthan; 2001. p. 23.
10. Malik V, editor. Drugs and Cosmetic Act, 1940. Part I. 14th ed., Ch. 4. Lucknow: Eastern Book Company; 2002. p. 37-44.
11. Dahanukar SA, Thatte UM. Can we prescribe Ayurvedic drugs rationally? Indian Pract 1998;51:882-6.
12. Parab SM, Kalele SS, Verma S, Kulkarni RA, Shinde VJ, Bhalerao SS, *et al*. Safety issues with medicines from alternative system of medicine. In: Proceedings of Workshop on Pharmacovigilance: Promoting Drug Safety through Collaboration. Parel, Mumbai: Seth GS Medical College, December, 5-6; 2003. p. 22.

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