

PHARMACOVIGILANCE IN ASU DRUGS: NECESSITY OF TODAY

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ABSTRACT

Ayush system of medicine is age old medical system of our country in today's scenario when the world is fighting with pandemic like covid 19, ayush system has emerged like a boon for all in prevention, curing and managing post covid complications also, but on the other side of the coin some side effects of taking ASU drugs has also caught lime light and again need of pharmacovigilance in ASU drugs gaining huge momentum. as self medication and wide spread online purchase has increased need to understand pharmacovigilance in ASU drugs has expanded.

KEYWORDS: *Ayush system, ASU drugs, pharmacovigilance.*

INTRODUCTION

India is the country of rich heritage and culture, had its own medical system known as *Ayurveda* and *siddha* that has been practiced by our ancestors for alleviation of diseases. Because of its caducity and use of herbs as a source of medicine people has a wrong notion about its safety. As the demand of ASU drugs leaped in the global market, certain safety issues has also been raised by authorities.

Its been said 'it is difficult to deal with two diseases one which is nature made and another which is doctors made'

So, from here pharmacovigilance comes into play, pharmacovigilance is the science of detection, understanding, assessment and prevention of adverse drug reactions and related untoward effects.^[1]

It performs various task like detecting adverse drug reaction, assessing its intensity providing guidelines for safe use of ASU drugs and management of A.D.R.

History of Pharmacovigilance

National Pharmacovigilance Program under the control of Central Drug Standards Control Organization (CDSCO) has initiated during 2003. WHO emphasizes that, traditional medicines are to be included into pharmacovigilance system and has published guidelines on safety monitoring of herbal medicines in pharmacovigilance systems in 2004.

The nationwide programme under central sector scheme funded by Ministry of AYUSH, New Delhi for ASU & H drugs to establish and manage a data base of Adverse Drug Reactions (ADR) for developing system wise database of adverse drug reactions and evolving evidence based recommendations towards clinical safety of ASU & H Drugs. Besides this; the program also undertake surveillance of objectionable or misleading advertisements.^[2]

Since ages *Ayurveda*, *Siddha* and *Unani* systems are being practiced in India. In this era of globalization, concerns are being raised with regards to their clinical safety. *Ayurveda* has categorized toxic plants separately and for their use special processing is essential. There is a wide spread misconception that all drugs of "natural" origin are "safe".^[3]

Glossary Used In Pharmacovigilance

Adverse Drug Reactions (ADRs) -A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.

Adverse Event/Experience (AE) - Any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with the treatment.

Side Effect(SE) - Any unintended effect of a pharmaceutical product occurring at doses normally used in human which is related to the pharmacological properties of the drug.

Serious Adverse Event (SAE) – Any adverse event which is fatal, life-threatening, permanently disabling or which results in hospitalization.

Expected adverse reaction - As opposed to “unexpected”, an event that is noted in the brochure or labeling.

Unexpected adverse reaction - The nature or severity of which is not consistent with the domestic labeling or market authorization, or expected from characteristics of the drug.^[4]

Need of Pharmacovigilance of Asu Drugs

Worldwide movement for the improvement of patient safety gains momentum, the subject of drug safety becomes even more prominent. Pharmacovigilance is the science dedicated to reduce the risk of drug-related harms to the consumers. Looking into the conditions prevailing in the present scenario, it is high time to deliberate regarding the concerns over traditional and classical *Ayurvedic, Siddha, Unani* and Homoeopathy products and practices. Thus the program is initiated to collect, collate and analyze data to establish evidence for clinical safety of ASU & H drugs in a scientific manner for documenting clinical evidence of safety and to undertake surveillance of misleading advertisements of ASU & H drugs and improper advertisements of ASU & H drugs for regulatory actions.

It is observed that few of these ASU drugs are being consumed, by patients, as OTC drug. These are sold as either herbal medicines or herbal products in different health-care settings. Due to inadequate regulatory measures, largely uncontrolled distribution channels either in form of mail order or internet sales and poor quality control systems, improper administration, some adverse events has also been reported.^[5]

National Pharmacovigilance Programme

First National Consultative meet of National Pharmacovigilance Programme for ASU Drugs was organized at Dept. of AYUSH, Ministry of Health & FW, New Delhi on August 2008, sponsored by WHO. Based on the feed back received from the meet, National Pharmacovigilance Programme for ASU drugs was launched on 29th Sept 2008. The purpose of the programme is to collect and collate data, analyse it and use the inferences to recommend informed regulatory interventions, beside communicating risks to healthcare professionals and the public.

Objectives

Short-term objectives - To develop the culture of notification.

Medium-term objectives - To involve healthcare professionals and professional associations in the drug monitoring and information dissemination processes.

Long-term objectives - To achieve operational efficiencies that would make NPP for ASU drugs a benchmark for global drug monitoring endeavors.^[6]

Pharmacovigilance Centers of Asu Drugs

Taking the WHO guidelines for the safety issues of herbal medicines into consideration and to put pharmacovigilance system for ASU drugs in proper place, the Department of AYUSH, Ministry of Health and Family Welfare, Govt. of India, New Delhi, took initiation basing upon the activities on pharmacovigilance, recognized by the Institute for Post Graduate Teaching and Research in Ayurveda (IPGTRA), Gujarat Ayurved University, Jamnagar, as National Pharmacovigilance Resource Centre for Ayurveda, Siddha and Unani Drugs (NPRC-ASU) in India under the Central sector scheme for upgradation to Centre of Excellence since 2008-09 and sanctioned an amount of Rs 57.66 Lacs in this regard. As per the protocol, the NPRC-ASU Drugs is coordinating this National Pharmacovigilance Program (NPP-ASU) under the aegis of Department of AYUSH, Ministry of Health and Family Welfare, Govt. of India, under the guidance of the National Pharmacovigilance Consultative Committee.

For ASU Drugs (NPCC-ASU), which comprise mainly of administrative heads of National Institutes, regulatory authorities and technical persons and have responsibility of monitoring and regulating administrative and financial aspects related to the program. Further this program is also guided by National Pharmacovigilance Technical Advisory Committee (NPTAC-ASU), a technical committee mainly concerned with reviewing and analysing the ADRs reported at different levels and to suggest proper remedial measures.

Under NPRC-ASU drugs, there are eight Regional Pharmacovigilance Centre (RPC) for ASU drugs. There are 30 Peripheral Pharmacovigilance Centre (PPC) for ASU drugs, which are working under these eight RPCs, across the country. Adverse drug reaction related to any ASU drugs is being reported to these PPC, in a specially designed ADR reporting form.^[7]

The Structure Of India's Pharmacovigilance Program For Asu Drugs

India's National Program of Pharmacovigilance for ASU drugs was adopted under the following blueprint in accordance with recommendations of the expert group made at its meeting on 28-29 August, 2008.

What to report?

The National Pharmacovigilance Programme for ASU drugs (NPP ASU) shall encourage reporting of all suspected drug related adverse events, including those

suspected to have been caused by interaction with any other drugs or food incompatibilities. Reporting of seemingly insignificant or common adverse reactions may be important, since it could highlight a widespread prescribing problem.

The program particularly solicits reports of all adverse reactions suspected to have been caused by ASU drugs either alone or in conjunction with other drugs all suspected drug interactions reactions to any other drugs suspected of significantly affecting a patient's management, including reactions suspected for events in the following categories:

1. Death
2. Life threatening (real risk of dying)
3. Hospitalization (initial or prolonged)
4. Disability (significant, persistent, or permanent)
5. Congenital anomaly
6. Required intervention to prevent permanent impairment or damage.

Who can report?

Any health care professional may report suspected adverse drug events. The program does not accept reports from lay members of the public, nor others than health care professionals. Others can report through the physician under whom they have undergone treatment.

Where to report?

Reporting should be done in a prescribed format through a local pharmacovigilance center.

Direction of submitted information

Information in the forms is to be handled in all confidentiality. Peripheral pharmacovigilance centers forward the form to their regional pharmacovigilance centers where causality analysis is carried out. The information is then forwarded to the National Pharmacovigilance Resource Centre, where it is consolidated, statistically analyzed, and forwarded to the Dept of AYUSH.^[8]

Highlights Of some articles published regarding a.d.r of the of asu drugs

1. *Panchakarma* (procedural therapies) and their role in ADR (Edwards RI et al) recent definition of ADR includes any unintended response from drug or materials used to diagnose or treat. Thus, any unintended responses from *Panchakarma* (Procedural therapies) can be included in this category of ADR.

Panchakarma (Procedural therapies) are detoxification (*Shodana*) therapies used to treat various diseases and many rules and precautionary measures are listed in Ayurveda. These are termed as inadequate (*Ayoga*), excess administration of therapy (*Atiyoga*), Contraindications (*Anarha*) and Complications (*Vyapad*) while carrying out these procedures. Such consequences are mostly because of faulty preparation of drug and

improper assessment of patient resulting in failure of treatment or by iatrogenic.

These can be classified into materialistic, Drug-induced (*Dravyataha*), iatrogenic, and patient faults (*Rogisambandi*).^[9]

Materialistic causes include faulty preparation of *Basthi* (enema procedure) instrument (*Basthi Yantradoshas*) as defective nozzles and defective enema can.

Drug-induced (*Dravyata*) examples can be quoted as inferior substitute of *Operculina turpethum* this administration will lead to drastic purgative and aggravating the disease condition (*Utkarshana*), unconsciousness, fainting, burning sensation, giddiness.

Iatrogenic events include wrong selection of drug with respect to pathology, complications from therapist and improper patient examination with respective drug administration.

Rogisambandi (patient related) includes improper observance of treatment by patient, faithless patient (*Abhishakvasya*) and reprehensive pursue of diet restriction (*Apatyasevana*) leading to failure of respective drugs or therapy.

2. Rasaushadi (mineral drugs) and their role in Ayurvedic ADR. It is a common notion among the public and modern doctors that mineral drugs are toxic since they are heavy metals. These sayings have been potentiated by the recent article, but later Dept. of AYUSH (Ayurveda, Unani and Siddha) has found various flaws and bias in reported results against Ayurvedic medicines. If at all these consequences persist it is due to administration of substandard drugs (*Ashoditadravya/hina dravyaprayoga*), over dose and lack of textual knowledge. Few examples are death, abdomen pain, loss of lustre, chest pain, intoxicating and GI bleeding by administration of Improper prepared of iron calyx (*Apakva Lohabhasma*) Over dose is one of major saddle in drug events of Ayurvedic mineral drug. Many a times, this over dose could be unintentional in nature since it is common to prescribe multiple Herbo-mineral drugs in combination. Hence, more possibility of combining the similar drugs in different formulations thus, tendency of additive greater drug dose are more. Ayurveda uses deadly poisons as medicine which are Arsenic, mercury,^[10] lead etc. these therapeutic administration dose is minimal. Slight changes in dose could lead to dire event or death e.g. over dose of arsenic^[11] Hair fall property of orpiment.^[12]

2. A study was conducted in ayurvedic collage regarding A.D.R OF Ayurvedic drugs. And following were the findings:^[13]

Drug/ medication type	Reaction detail	Total number (%) (n=52)
Panchakarma	Skin rashes 02, diarrhea 03, vomiting 03, headache/nausea 02, constipation 01, rectal prolapse 01, fever 03, pain abdomen 03, duodenal ulcer 01, local pain and swelling 01, boils 01 and other 02	23 (44.23)
<i>Rasaushadhis</i>	Skin rashes 02, diarrhea 03, vomiting 01	06 (11.53)
Classical herbal preparations	Skin rashes 07, diarrhea 02, vomiting 01, fever 01, pain abdomen 01, throat pain 01	13 (25.00)
Proprietary	Skin rashes 01, vomiting 01, fever 03, irritability 01	06 (11.53)
Material/ environmental	Vomiting 01, boils 01	02 (03.84)
<i>Pathya</i> (restricted diet)	Diarrhea 01, headache/ nausea 01	02 (03.84)

Ayurvedic drug/therapy	Mode of administration	Reported event	Prime ascertained cause after causality assessment
<i>Aragwadadi Kashaya</i> and syrup Talekt	Oral	Skin rashes	Bizarre cause
<i>Mahavatavidvanshini Rasa</i>	Oral	Diarrhea	Drug over dose
<i>Vaishwanara Kalka, Goarka, Mutralakashaya</i>	Rectal	Pain abdomen	Iatrogenic
<i>Sastikasali Pinda Sweda</i>	Skin (external)	Skin rash	Bizarre cause
<i>Erandamoola Niruha Basti</i>	Rectal	Rectal prolapse	Iatrogenic
<i>Haridrakhanda</i> with milk	Oral	Exacerbation of tonsillitis	Bizarre cause
<i>Jaloukavacharana</i> (leech application)	Skin	Pain and swelling	Iatrogenic
<i>Sahacharadi Taila</i>	Rectal	Constipation and pain abdomen	Iatrogenic (<i>Sneha Asiddhi Lakshana</i>)
<i>Karpasasthyadi Taila</i>	Nasal	Headache	Iatrogenic
<i>Erandamoola</i> and <i>Gomutra Arka</i> (distillate of cow's urine)	Rectal	Pain abdomen and diarrhea	Improper <i>koshta</i> assessment
<i>Brihat Saindavadi Taila</i>	Skin (external)	Headache and wheezing	Pseudo allergic reaction
<i>Madana Yoga</i> (a preparation of <i>Randia dumetorum</i>)	Oral	Pain abdomen and dehydration	<i>Koshtha Viruddha Dravya Prayoga</i>
<i>Trivrutta Leha</i> along with milk	Oral	Vomiting and dehydration	Iatrogenic
<i>Sahacharadi Taila</i>	Skin (external)	Ear ache and partial deafness	Bizarre
<i>Agnitundi Vati</i>	Oral	Diarrhoea and vomiting	<i>Prakriti Viruddha Dravya Prayoga</i>
<i>Saraswata Ghrita</i>	Oral	Pain abdomen	Improper <i>Purvakarma</i> (preprocedural therapies)
<i>Gandha Taila</i>	Nasal	Vomiting and headache	Bizarre
<i>Mahatiktaka Ghrita</i>	Oral	Vomiting, diarrhea, and dehydration	Selective drug allergy
<i>Agastya Haritaki Rasayana</i>	Oral	Skin rashes	Bizarre
<i>Asanadikashaya</i> and <i>Tab Histantin</i>	Oral	Vomiting and dehydration	Bizarre
<i>Suvama Bindu Prashana</i>	Oral	Fever, child irritability	Bizarre
<i>Dashanga Lepa</i>	Skin (external)	Skin rash	Bizarre
<i>Shatadouta Ghrita</i>	Skin (external)	Skin rash	Bizarre
<i>Bala Ashwagandha Lakshadi Taila</i>	Skin (external)	Skin rash	Bizarre
Combination of <i>Sutashekararasa</i> and <i>Mayurapiccha Bhasma</i>	Oral	Diarrhea	Over dose
<i>Erandamoola Lekhana Basti</i>	Rectal	Duodenal perforation	Iatrogenic
<i>Gandhaka Rasayana</i>	Oral	Skin rash	<i>Prakriti Viruddha Dravya Prayoga</i>
<i>Sarsapa Lepa</i> (mustard pack)	Skin (external)	Skin rashes	<i>Prakriti Viruddha Dravya Prayoga</i>
Combination of <i>Mahavatavidvanshini Rasa, Tinispora cordifolia</i> and <i>Samirapannagarasa</i>	Oral	Nausea and vomiting	Over dose
<i>Kottamchukadi Taila</i>	Skin (external)	Skin rash and periorbital swelling	<i>Prakriti Viruddha Dravya Prayoga</i>
IR light	Skin (external)	Boil and redness	Over dose
<i>Shatapushpa</i> (<i>Anethum sowa</i>)	Oral	Diarrhea	Bizarre
Decoction of <i>Ricinus communis, Eranda, Vitex negundo</i> and <i>T. cordifolia</i>	Oral	Nausea and oral tingling sensation and vomiting	Bizarre
<i>Mutralakhada</i>	Oral	Nausea and vomit	Drug organoleptic character

ADR: Adverse drug reactions

CONCLUSION

As self medication and unrestricted use of asu drugs have increased many folds so its our responsibility as a common people to report any of the A.D.R of ASU DRUGS that we come to know to the PVPC so that it could be assessed and optimized further pharmacovigilance has been included in postgraduate level of *AYUSH* curriculum need to introduce it on Bachelors' level also, then we can assure safe use of ASU medicaments by professionals.

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