Review Article.

International Research Journal of Ayurveda & Yoga

An International Peer Reviewed Journal for Ayurveda & Yoga

Adverse Drug Reaction – A Significant Cause of Morbidity and Mortality

Madhu Parihar,[1] Ritu Kapoor,[2] Manoj Adlakha[3]

VOLUME 4 ISSUE 9

1. MD Scholar, P.G. Department of Agad Tantra Evam Vyavahar Ayurveda, Dr. S. R. Rajasthan Ayurved University, Jodhpur.
2. Associate Professor & HOD, P.G. Department of Agad Tantra Evam Vyavahar Ayurveda, Dr. S. R. Rajasthan Ayurved University, Jodhpur.
3. Associate Professor, P.G. Department of Dravya Guna Vigyana, Dr. S. R. Rajasthan Ayurved University, Jodhpur.

Corresponding Author :- Dr. Madhu Parihar, H. No. 6-T-31, Mahaveer Nagar Ext. Kota (Raj.) Mob. No.- 7014686663
Email id- sirfmadhu89@gmail.com

Article received on 17th August 2021 Article Accepted 26th Sept. 2021 Article published 30th Sept.2021

ABSTRACT: -

An Adverse Drug Reaction (ADR) as "An appreciably harmful or unpleasant reaction" after taking a medicine at normal doses, during normal use. Adverse drug reactions are a significant cause of morbidity and mortality and it is considered non preventable. The term **Adverse Drug Effect** is convertible with **Adverse Drug Reaction**. The meaning of ADR is different from the word **side effect** because side effects are beneficial as well as harmful. The field under which ADR is studied is known as **Pharmacovigilance**. An **Adverse Drug Event** (ADE) is an injury resulting from medical intervention related to a drug. The Adverse drug reactions are classified into six types. Timing, the pattern of illness, the results of investigations, and rechallenge can help idiosyncrasy causality to a suspected adverse drug reaction. If possible in management, you can stop that drug and treat its effects. Suspicious adverse drug reactions should be reported so that such cases can be prevented in the future.

Key-words- ADR, Side effect, Pharmacovigilance, ADE.

This work is licensed under a creative attribution -Non-commercial-No derivatives 4.0 International License commons

How to cite this article: Parihar M, Kapoor R, Adlakha M; Adverse Drug Reaction – A Significant Cause of Morbidity and Mortality ; IRJAY. [Online] 2021;4(9):203-207. Available from: http://irjay.com ;**DOI: https://doi.org/10.47223/IRJAY.2021.4926**

INTRODUCTION

In today's world, medicines have become very important for the health system because medicine saves lives. The aim of medicines is to relieve pain and suffering, promote health and prevent disease and if possible the cure of disease and take care of those who cannot be cured [1].

Any substance can cause undesirable or adversarial effects along with the therapeutic effect. These undesirable effects can range from zero to high. Here all the terms related to adverse drug reaction such as definition, classification, diagnosis and how to manage them are described[2].

ADR is made up of two words i.e. Adverse and Drug, which are described as below-

Adverse

Adverse means acting against or in a contrary direction: hostile hindered by adverse winds, opposed to one's interests an adverse verdict heard testimony adverse to their position especially: unfavourable adverse criticism and causing harm: harmful adverse drug effects. (**Definition of adverse by Merriam – Webster**)

Drug

According to the WHO, a drug is a substance that can change how a living organism works. Food is usually not seen as a drug, even though some foods may have such properties. Most of the time drugs are taken to treat a disease or other medical condition. An example for such drugs may be Aspirin or Paracetamol.

Definition

The World Health Organization (WHO, 1972) defines an ADR as "Any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function[3]."

This simple concept encompasses all clinically administered doses, but excludes unintended or intentional overdosing. The 'unexpected' sub classification was included to help identify the types of adverse reactions that are most important to disclose to drug screening organisations.

In other words, ADR is the direct damage caused by the normal dose of medicine during normal use [4], which causes normal functions of the body to be disturbed and adverse effects on the body [5]. ADR not only show major effects but also minor effects, but it is not properly defined in ADR definition. This does not make this definition complete.

Laurence's definition specifically excludes minor unwanted reactions (ex- a slight dryness of the mouth): "A harmful or significantly unpleasant effect caused by a drug at doses wilful for therapeutic effect (or prophylaxis or diagnosis) which warrants reduction of dose or withdrawal of the drug and predict hazard from future administration [6]."

Unexpected Adverse Reaction [7]

Not consistent with applicable product information or characteristics of drug.

Serious Adverse Reaction or Event [8]

`Any untoward medical occurrence that at any dose;

1. Results in death
2. Life threatening
3. Requires inpatient hospitalization or prolongation of existing hospitalization
4. Results in persistent of significant disability or incapacity

Frequency of adverse drug reactions (CIOMS) [9]

1. Very common > = 1/10
2. Common (frequent) > = 1/100 and < 1/10
3. Uncommon (infrequent) > = 1/1000 and < 1/100
4. Rare > = 1/10000 and < 1/1000
5. Very rare < 1/10000

Classification:-ADRs can be classified into six types (according to WHO) [10]-

1) Type A reactions (dose-related) - These reactions are an exaggerated, but otherwise normal pharmacological responses to the effects of the medicines given in therapeutic dose, cause significant morbidity but are rarely severe. The reaction is treated by reducing the dose or withholding the medicine and considering alternative therapy. Examples of such reactions include-

- Pharmacodynamics (e.g., bronchospasm from beta-blocker administration)
- Toxic (e.g., deafness from overdosing of aminoglycosides)

Management: Reduce dose or withhold & Consider effects of concomitant therapy.

2) Type B reactions (non-dose related) - These reactions are bizarre and unpredictable with no relation to dose or pharmacological action of the medicine and are often allergic in nature. They are uncommon but are often severe and cause high mortality. The reaction is treated by stopping the medicine and avoiding it in the future. Examples of such reactions include-

i. Medicine-induced diseases (e.g. antibiotic-associated colitis)
ii. Allergic reactions (e.g. anaphylactic reaction to penicillin administration)
iii. Idiosyncratic reactions (e.g. irreversible aplastic anaemia caused by chloramphenicol)

Management: Withhold and avoid in future

3) Type C reactions (dose-related and time-related) - These reactions are chronic (long term) and related to cumulative dose. The reaction is treated by reducing the dose or withholding the medicine, which may have to be withheld for a long time. Examples of such a reaction include-

Osteoporosis with oral steroids
Hypothalamic-pituitary-adrenal axis suppression by corticosteroids

Management: Reduce dose or withhold; withdrawal may have to be prolonged

4) Type D reactions (time related) - These reactions are delayed (i.e., have a lag time) after the use of a drug. They are uncommon but their treatment is often intractable. Examples of such reactions include-

i. Teratogenic effects with anticonvulsants or lisinopril
ii. Carcinogenesis
iii. Tardive dyskinesia

Management: Often intractable

5) Type E reactions (withdrawal) - These reactions occur soon after the end of use (i.e. withdrawal) and are uncommon. The reaction is treated by reintroducing the medicine and then withdrawing it slowly. Examples of this reaction include-

i. Withdrawal syndrome with benzodiazepines
ii. Opiate withdrawal syndrome
iii. Myocardial ischemia after beta-blocker withdrawal

Management: Reintroduce and withdraw slowly

6) Type F reactions (unexpected failure of efficacy) - These reactions occur when there is a failure of efficacy. Such reactions are common, may be dose-related and are often caused by drug interactions. The reaction is treated by increasing the dose and considering the effects of concomitant therapy. Examples include-

Resistance to antimicrobials

Inadequate dosage or oral contraceptives, particularly when used with specific enzyme inducers.

Management: Increase dosage & Consider effects of concomitant therapy.

Ayurvedic texts have explained various causes for ADR such as excessive effects, drug interactions, drug aversion in susceptible patients, idiosyncrasy and drug allergy. Although the term ADR is not present in *Ayurvedic* literature, the principles and safety issues are prevalent in *Ayurvedic* texts.

Ayurveda has given priorities to patient protection and care at any step of treatment, including selection of raw drugs, collection, various preparation procedures and careful administration of properly diagnosed patients [11].

Acharya Charaka has explained the importance of drugs in the *Sutrasthana* [12]-

1. The goatherds, shepherds, cowherds and other forest dwellers know the drugs by name and form.
2. No one can know the principles governing correct application of drugs simply by knowing their names and forms.
3. A drug not known is likened to poison; weapon, fire and thunderbolt while the one known, to be the nectar.
4. A drug known in respect of its name, form and properties or even if known, improperly administered, leads to bad consequences.
5. Even an acute poison can become an excellent drug if it is properly administered. (On the other hand) even a drug, if not properly administered, becomes an acute poison.

Proper application of drugs depends upon their proper knowledge. Unless the physician knows the drugs properly he cannot cure a patient; his prescription would rather kill his patient. The drugs unknown, might act as poison which kills after bringing about unconsciousness or as a weapon which kills after piercing through the vital organs, or like fire which kills by causing boils, etc. or as a thunderbolt which kills instantaneously. It is only when a physician knows all the three aspects, viz. name, form and properties of drugs; he can treat his patients successfully.

Pharmacovigilance [13]

Also known as drug safety. Derived from 2 words

Pharmakon - Drug

Vigilare - To keep watch

Definition [14]

Pharmacological is defined by the WHO as "science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine or vaccine related problem".

Scope of Pharmacovigilance

The scope of Pharmacovigilance has grown remarkably in recent times and is now considered to include the following domains:

i. ADRs or events
ii. Medication errors
iii. Counterfeit or substandard medicines
iv. Lack of efficacy of medicines
v. Misuse and abuse of medicines
vi. Interaction between medicines
vii. The products under consideration go beyond conventional medicines and also include

herbal medicines, other traditional and complementary products, biological, vaccines, blood products and possibly medical devices.

Aims [15]

The specific aims of pharmacovigilance are to:

i. To improve patient care and safety.
ii. To improve public health and safety.
iii. To contribute to the assessment of benefit, harm, effectiveness and risk of medicines.
iv. To promote understanding, education and clinical training.
v. To promote rational and safe use of medicines.

Need of Pharmacovigilance …ASU drug perspective

i. Myths
ii. ASU drugs are absolutely safe.
iii. ADRs don't happen with natural drugs.
iv. No need for Pharmacovigilance in ASU.

Reality-

i. ADRs associated with ASU drugs are less but present.
ii. Many Poisons are also natural substances.
iii. Thus, there is a need of Pharmacovigilance in ASU.

PVG in Ayurveda in Contemporary Era

i. Increased gap between physician and drug
ii. Improper manufacturing process
iii. Exponential increase in use of proprietary of *Ayurvedic* medicines
iv. Concurrent use of modern medicine
v. Generalized fall in quality of environmental factors like water, soil, air etc.

DISCUSSION

Drug safety is a basic and essential notion, in medical practise. ADRs play a critical role in determining patient safety, in any system of medicine. The importance of a pharmacovigilance study in understanding treatment outcomes cannot be overstated. The origins and techniques of drug-induced effects, as well as preventative measures, are discussed in *Ayurveda*, an Indian holistic system of medicine. The accessible evidence in ancient literature is fragmented. The notion of medication safety and adverse drug reactions (ADR) is not new to *Ayurveda*. To reduce the occurrence of ADRs, lot of textual expertise is needed while practising. There is also a need for significant study to comprehend the logic and concept underlying the traditional medication administration and safety guidelines [16].

CONCLUSION

In every branch of medicine, drug protection continues to play an important part in health treatment and disease control. When it comes to the question of *Ayurvedic* medicine protection, the issue becomes critical because it casts doubt on patients' perceptions of Ayurveda's protection [17]. It is important to recognise that the use of any medication carries some level of risk. This risk can be significantly minimised by using high-quality medications and observing the different protocols and guidance of drug administration found in *Ayurvedic* literature. To do this, it is important to comprehend and research the ideals of drug control described in *Ayurvedic* classics. Although the term ADR is not present in *Ayurvedic* literature, the principles and safety issues are prevalent in *Ayurvedic* texts. To reduce the frequency of ADRs, you'll need a lot of textual expertise when learning. In this article,

the definition of ADRs, six types and management is described. Also Pharmacovigilance has been described as to how the ASU drug has its need.

Acknowledgment: Nil.
Financial Support: Nil.
Conflict of Interest: Nil

REFERENCES

1. https://www.who.int > tbs > 0…
2. Ralph E, Jeffrey K, Adverse drug reactions: definitions, diagnosis and management, The Lancet, 7 October 2000, Vol.356, Issue 9237, Pg. no. 1255-1259.
3. Drug and Therapeutics Committee Training Course; Session 4. Assessing and Managing Medicine Safety, Participants' Guide, Lancet 356 (9237); 1255-59.
4. Drug and Therapeutics Committee Training Course; Session 4. Assessing and Managing Medicine Safety, Participants' Guide, Lancet 356 (9237); 1255-59.
5. Ralph E, Jeffrey K. Adverse drug reactions: definitions, diagnosis and management, Science Direct, The Lancet, 7 October 2000, Vol. 356, Issue 9237, Pg. no. 1255-1259.
6. Ralph E, Jeffrey K. Adverse drug reactions: definitions, diagnosis and management, Science Direct, The Lancet, 7 October 2000, Vol. 356, Issue 9237, Pg. no. 1255-1259.
7. https://www.who.int > areas > trainingcourses > definitions
8. https://www.who.int > areas > trainngcourses > definitions
9. https://www.who.int > areas > trainingcourses > definitions
10. Drug and Therapeutics Committee Training Course; Session 4. Assessing and Managing Medicine Safety, Participants' Guide, Lancet 356 (9237); 1255-1259.
11. Manjunath A, Adverse drug reaction and concepts of drug safety in Ayurveda: An overview; Journal of Young Pharmcists (2013) 116-120.
12. Sharma R. K Agnivesa's Caraka Samhita based on Cakrapani Datta's Ayurveda Dipika, Sutra sthana, Chapter 01, Verse No. 120-121, Chowkhamba Sanskrit Series Office; Varanasi, 2009.pp. 58-60.
13. https://en.m.wikipedia.org
14. https://www.who.int > teams > phar….
15. https://www.slideshare.net
16. Manjunath A, Adverse drug reaction and concepts of drug safety in Ayurveda: An overview; Journal of Young Pharmcists 5 (2013) 116-120.
17. Manjunath A, Adverse drug reaction and concepts of drug safety in Ayurveda: An overview; Journal of Young Pharmcists 5 (2013) 116-120.