

Editorial

SIGNIFICANCE OF PHARMACOVIGILANCE AND ITS CLINICAL IMPLICATIONS

Drug is the single active chemical entity present in a medicine that is used for diagnosis, prevention, treatment / cure of a disease. World Health Organization has given a more comprehensive definition—“Drug is any substance or product that is used or is intended to be used to modify or explore physiological systems or pathological states for the benefit of the recipient.” Pharmacodynamics is what the drug does to the body. This includes physiological and biochemical effects of drugs and their mechanism of action at organ system /subcellular / macromolecular levels. Pharmacokinetics is the effect; the body does to the drug. This refers to movement of the drug in and alteration of the drug by the body; includes absorption, distribution, biotransformation and excretion of the drug (Tripathy 2013).

Adverse drug reactions

The term adverse drug reaction (ADR) has been defined as ‘any noxious change which is suspected to be due to a drug, occurs at doses normally used in man, requires treatment or decrease in dose or indicates caution in the future use of the same drug’. Another term ‘adverse drug event’ (ADE) has been used to mean ‘any untoward medical occurrence that may present during treatment with a medicine, but which does not necessarily have a causal relationship with the treatment’ (Tripathy 2013). The idea is to record all adverse events first, and then searching for causality only while analyzing pooled data.

Adverse drug effects may be categorized as side effects, secondary effects, toxic effects, intolerance, idiosyncrasy, drug allergy (humoral and cellular), photosensitivity, drug dependence (abuse, addiction and habituation), drug withdrawal reaction, teratogenicity, mutagenicity and drug induced iatrogenic diseases.

Pharmacovigilance

Pharmacovigilance mainly deals with adverse drug reactions, “a response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function”. It identifies the risk associated with a marketed drug and minimizes the chance of ill effects that it may have on patients. When a drug is marketed, its pharmacological activity is known. However, clinicians are less aware of the adverse effects it may cause in patients. Pharmacovigilance is thus aimed to address these issues (WHO 2004).

Procedure

Pharmacovigilance centres have been set up in most countries. The Uppsala Monitoring Centre (Sweden) is the international collaborating centre. In India, the Central Drugs Standard Control Organization (CDSCO) is coordinating the pharmacovigilance programme, under which peripheral, regional and zonal monitoring centres have been set up along with a National Pharmacovigilance

advisory committee. The pharmacovigilance centres collect, communicate and disseminate ADR data by linking with hospitals as well as practitioners and are also expected to provide expertise for assessing causality and severity and preventability of ADRs by using standard algorithms and rating scales like the 'Naranjo algorithm' (causality assessment) and modified Hartwig scale (severity grading).

Causality assessment

When a patient undergoing drug therapy experiences an adverse event, it may be due to the drug, or the disease, may be due to the patient or some other causes. Causality assessment is the probability evaluation, that a particular treatment is the cause of an observed adverse event (WHO-UMC). It assesses the relationship between a drug treatment and the occurrence of an adverse event. It is an important aspect of pharmacovigilance, which helps to evaluate the risk-benefit profiles of medicines better. A number of algorithms or decision aids have been published including the Jones' algorithm, the Naranjo algorithm, the Yale algorithm, the Karch algorithm, the Begaud algorithm, the Australian ADR advisory committee and the World Health Organization-Uppsala Monitoring Center (WHO-UMC) criteria (WHO-UMC; Srinivasan and Ramya 2011). Causality assessment is the pivotal issue in assessing the relation of ADRs and culprit drug.

Causality is assessed on the basis of

- Temporal relationship: How the time-sequence of the event is related to drug administration.
- Previous knowledge: Whether the drug is known to produce the event in earlier recipients with a certain degree of consistency.
- Dechallenge: Whether the event subsided on stopping the drug.
- Rechallenge: Whether the event reappeared when the drug was administered again after a gap during which the event had subsided. Many times rechallenge is unethical/dangerous and not done.

Assessed on the basis of the above criteria, causality has been graded as

1. Definite: Causality is proven.
2. Probable: Though not proven, drug is the likely cause of the event.
3. Possible: Drug as well as other causes could be responsible for the event.
4. Doubtful: Drug unlikely to be the cause, but cannot be ruled out.

Clinical Implications

It has an important role in the rational use of medicines, as it provides the basis for assessing safety of medicines. The information generated by pharmacovigilance is useful in educating physicians about ADRs and helps in the official regulation of drug use. It is a sophisticated system to provide surveillance of drugs in the post marketing phase. Pharmacovigilance is an important part of clinical research ranging from drug discovery to post marketing surveillance (Simon 2002; Harmark and Van Grootheest 2008). Pharmacovigilance involves evaluating the information provided by health care providers, pharmaceutical companies and patients in order to diagnose the risk and benefits involved with respect to particular drug (Patel *et al.* 2011; Rohilla *et al.* 2012). Establishing good pharmacovigilance is foremost required in order to understand the drug safety issues during drug development process, thus patients can be provided with safe and effective innovative drugs.

Significance of pharmacovigilance and its clinical implications

Limitations

Limitations of the Pharmacovigilance are

- i. It works on ADRs or harmful effects of drugs but not efficacy or beneficial effects of drugs.
- ii. Patient are not involved in this process, only doctor, nurses, pharmacist are involved.
- iii. Drugs when shows ADRs, it can be confirmed by re-challenging, but it is not possible to start re-challenge due to some problem.
- iv. The awareness and concern related to Pharmacovigilance is yet to spread globally.

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