PHARMACOVIGILANCE – A REVIEW

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ABSTRACT
Pharmacovigilance is the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects, particularly long term and short term side effects of medicines. Generally speaking, pharmacovigilance is the science of collecting, monitoring, researching, assessing and evaluating information from healthcare providers and patients on the adverse effects of medications, biological products, herbalism and traditional medicines with a view to identifying new information about hazards associated with medicines and preventing harm to the patients.

Key words: Pharmacovigilance, Risks of medical treatment, Adverse reactions.

INTRODUCTION
Pharmacovigilance starts from the clinical stage and continues throughout the product life cycle of the drug, mainly divided as pharmacovigilance during pre-marketing (that is clinical phase) and post marketing. The process of collection of such information about a drug begins in phase I of the clinical trial, before approval of the drug, and continues even after approval; several post-market safety studies are conducted, with many made mandatory by drug regulatory agencies around the world.

Pharmacovigilance is particularly concerned with adverse drug reactions, or ADRs, which are officially described as: A response to a drug which is noxious and unintended, and which occurs at doses normally used for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function. Pharmacovigilance is gaining importance for doctors and scientists as the number of stories in the mass media of drug recalls increases. Because clinical trials involve several thousand patients at most; less common side effects and ADRs are often unknown at the time a drug enters the market. Even very severe ADRs such as liver damage are often undetected because study populations are small. Postmarketing surveillance uses tools such as data mining of spontaneous reporting systems and patient registries, and investigation of case reports to identify the relationships between drugs and ADRs.

Risks of medical treatment
While medicines have led to major improvement in the treatment and control of diseases, they also produce adverse effects on the human body from time to time. While many drugs are precisely targeted to the causes and mechanisms of disease, they may also have minor or distressing effects on other parts of the body, or interact negatively with the systems of the particular individual or with other drugs or substances they are taking, or not work well or at all for some, many or all of those who take them for illness. There are risks in any intrusion into the human body, whether chemical or surgical. Nothing in this field is entirely predictable as the interaction between chemicals and the human body may produce surprises.

Terms commonly used in drug safety
Benefits are commonly expressed as the proven therapeutic good of a product, but should also include the patient’s subjective assessment of its effects. Risk is the probability of harm being caused, usually expressed as a percent or ratio of the treated population; the probability of an occurrence. Harm is the nature and extent of the actual damage that could be caused. It should not be confused with risk. Effectiveness is used to express the extent to which a drug works under real world circumstances, i.e., clinical practice (not clinical trials). Efficacy is used to express the extent to which a drug works under ideal circumstances (i.e., in clinical trials).

Finding the risks of drugs
Pharmaceutical companies are required by law in all countries to perform clinical trials, testing new drugs on people before they are made generally available. The manufacturers or their agents usually select a representative
sample of patients for whom the drug is designed – at most a few thousand – along with a comparable control group. The control group may receive a placebo and/or another drug that is already marketed for the disease. The purpose of clinical trials is to discover:

- if a drug works and how well
- if it has any harmful effects, and
- its benefit-harm-risk profile - does it do more good than harm, and how much more? If it has a potential for harm, how probable and how serious is the harm?

Clinical trials do, in general, tell us a good deal about how well a drug works and what potential harm it may cause. They provide information which should be reliable for larger populations with the same characteristics as the trial group - age, gender, state of health, ethnic origin, and so on. The variables in a clinical trial are specified and controlled and the results relate only to the population of which the trial group is a representative sample. A clinical trial can never tell you the whole story of the effects of a drug in all situations. In fact, there is nothing that could tell you the whole story, but a clinical trial must tell you enough; enough being determined by legislation and by contemporary judgements about the acceptable balance of benefit and harm.

**Spontaneous reporting**

Spontaneous reporting is the core data-generating system of international pharmacovigilance, relying on healthcare professionals (and in some places consumers) to identify and report any suspected adverse drug reaction to their national pharmacovigilance center or to the manufacturer.[3] Spontaneous reports are almost always submitted voluntarily. In many parts of the world these are submitted electronically using a defined message standard. One of this system’s major weaknesses is under-reporting, though the figures vary greatly between countries and in relation to minor and serious ADRs. Another problem is that overworked medical personnel do not always see reporting as a priority. If the symptoms are not serious, they may not notice them at all. And even if the symptoms are serious, they may not be recognised as the effect of a particular drug. Even so, spontaneous reports are a crucial element in the worldwide enterprise of pharmacovigilance and form the core of the World Health Organization Database, which includes around 4.6 million reports, growing annually by about 250,000.

**Other reporting methods**

Some countries legally oblige spontaneous reporting by physicians. In most countries, manufacturers are required to submit, through its Qualified Person for Pharmacovigilance (QPPV), all the reports they receive from healthcare providers to the national authority. Others have intensive, focused programmes concentrating on new drugs, or on controversial drugs, or on the prescribing habits of groups of doctors, or involving pharmacists in reporting.

All of these generate potentially useful information. Such intensive schemes, however, tend to be the exception.

**International collaboration**

The principle of international collaboration in the field of pharmacovigilance is the principal basis for the WHO International Drug Monitoring Programme, through which over 100 member nations have systems in place which encourage healthcare personnel to record and report adverse effects of drugs in their patients. These reports are assessed locally and may lead to action within the country. Through membership of the WHO Programme one country can know if similar reports are being made elsewhere.

Member countries send their reports to the Uppsala Monitoring Centre where they are processed, evaluated and entered into the WHO International Database. When there are several reports of adverse reactions to a particular drug this process may lead to the detection of a signal – an alert about a possible hazard communicated to member’s countries. This happens only after detailed evaluation and expert review.

**European Union**

The pharmacovigilance effort in the European Union is coordinated by the European Medicines Agency (EMA) and conducted by the national competent authorities (NCAs). The main responsibility of the EMA is to maintain and develop the pharmacovigilance database consisting of all suspected serious adverse reactions to medicines observed in the European Community. The system is called EudraVigilance and contains separate but similar databases of human and veterinary reactions.

EMA requires the individual marketing authorisation holders (drug companies), to submit all received adverse reactions in electronic form (save in exceptional circumstances). The reporting obligations of the various stakeholders are defined in the Community legislation, in particular:

Regulation (EC) No 726/2004


Reporting can be performed with software developed for the purpose or with a web utility called EVWEB accessible through the EudraVigilance homepage. Registration for use of EVWEB is necessary.

In 2002 Heads of Medicines Agencies agreed on a mandate for an ad hoc Working Group on establishing a European risk management strategy. The Working Group considered the conduct of a high level survey of EU pharmacovigilance resources to promote the utilisation of expertise and encourage collaborative working.

**Japan**

In Japan, pharmacovigilance is regulated by the PMDA and MHLW.
United States

Three primary branches of pharmacovigilance in the U.S. include the FDA, the pharmaceutical manufacturers, and the academic/non-profit organizations.

Latin America

Most Latin American countries have high or medium levels of regulatory pharmacovigilance requirements, in line with international standards.

Kenya

In Kenya, pharmacovigilance is regulated by the Pharmacy and Poisons Board.

Pharmacovigilance of Herbal Medicines

The safety of herbal medicines has become a major concern to both national health authorities and the general public. The use of herbs in Traditional medicines continues to expand rapidly across the world. Many people now take herbal medicines or herbal products for their health care in different national health-care settings. However, mass media reports of adverse events tend to be sensational and give a negative impression regarding the use of Herbal medicines in general rather than identifying the causes of these events, which may relate to a variety of issues.

CONCLUSION

Despite receiving attention and necessary action by regulatory agencies like FDA and the European Union, there is a lack of substantial procedures regarding impending monitoring of drug concentrations in the environment and the palpable adverse effects. In 2006 a new concept of pharmacovigilance in environmental pharmacology, entitled as 'Pharmacoenvironmentology' was suggested by Syed Ziaur Rahman. It is a form of pharmacovigilance which deals specifically with those pharmacological agents that have impact on the environment via elimination through living organisms subsequent to pharmacotherapy.

REFERENCES