

POST MARKETING SURVEILLANCE: METHODS AND REPORTING SYSTEMS- AN OVER VIEW**Sarvan Kumar G. *, Kiran Kumar Y.¹ and Suresh K.²**

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ABSTRACT

The safety profile of a drug cannot be made complete before it placed in to the market. Because of limited information, and scope of the clinical trial. A clinical trail is a biomedical or behavioral research study of human subjects which are used to determine whether new drug interventions are safe, efficacious and effective. The post marketing studies are designed to monitor effectiveness of the approved new interventions in the general population and gather the information about adverse effects associated with the new drug interventions. Post marketing studies are carried out under the functions of Pharmacovigilance. Post marketing surveillance is a scientific study which analyzes the information of new drug after it has been marketed. the present review of Post marketing surveillance shows the selective use of reporting methods in appropriate conditions

which makes awareness among the clinicians, clinical pharmacist and other health care professionals about serious, potentially drug induced events and will begin to address the problems of reporting , prevention of events.

KEYWORDS: Post marketing surveillance, Methods, Reporting, Recently Banned Drugs.

INTRODUCTION

Post-marketing surveillance is a trial designed to estimate the frequency of uncommon side effect, toxicity or interaction and often this is called expanded safety. Safety of medicine being used by patients upon prescription by a medical practitioner. It is the Phase IV of a clinical trial and takes place after FDA has approved a drug for marketing. First three phases of trial is conducted on maximum of 4000 patients under defined condition in limited time period. A 1998 report in the journal of the American Medical Association estimated that 1,06,000 fatal drug reactions occur each year. So Post-marketing surveillance studies have to strengthen to screen adverse effect and to compare the relative efficacy of alternative drugs.

FDA's Involvement in Post marketing Surveillance

- ✚ FDA monitor approved drug use
- ✚ FDA monitor serious Adverse Drug Reaction associated with the use of approved drugs
- ✚ FDA initiates selected epidemiological studies to estimate the risk of test specific hypothesis.

Importance of Post marketing Surveillance

- ✚ Post marketing surveillance plays critical role to screen the real world effect of prescription drugs because pre-marketing clinical studies used to conduct for short duration (maximum 7 years) and small sample size (usually 4000 subject)
- ✚ Post marketing surveillance studies are helps to analyze the questions that occur during process of phase I to phase IV studies, which have not yet been completely answered or adequately addressed. These include comparison with other drugs, cost-effective studies, risk minimization studies and mechanism of action etc.
- ✚ It helps to evaluate the effective use of drug in special population like pediatrics, pregnant women, lactating women, geriatrics and other elderly patients.
- ✚ This is important because it has been estimated that as many as 50% of people over 85 experience adverse drug reaction each year and will increase the rehospitalisation rates. It may help to screen out newer indication of already existing drugs.
- ✚ Manufacturers may give importance to specific indication for use of drug during pre-marketing studies. For example statins, which are developed to lower cholesterol, have shown beneficial effect in treatment of some cancer, Alzheimer's disease, multiple sclerosis.

- ✚ Some pharmaceutical companies have started to conduct clinical trials abroad in order to minimize the cost. So it is important to conduct Post marketing surveillance to verify the study result.
- ✚ Due to increased concern of biased result of clinical trial
- ✚ Since pharmaceutical companies are sponsoring the clinical trial,
- ✚ Post-marketing surveillance plays an important role to check whether the study of drug is safe and effective.

Components of Post-marketing Surveillance

- ✚ Once drug is approved for marketing some type of post marketing surveillance are operating in almost all developed countries.
- ✚ The typical modes of surveillance describe the stepwise progression from suspicion of a problem to the actual verification, as follows:
- ✚ **Signal generation and collection**, almost always by spontaneous reports of suspected drug reaction
- ✚ **Signal verification, hypothesis strengthening and evaluation of potential public health significance**, carried out by evaluating the supporting information in reports on the same or related drugs, careful evaluation of the pharmacology and biological possibility and finally, in some cases, an initial epidemiological study, such as use of automated population data base, or examination of trends in the suspected disorder relative to expected trends. All of may contribute to this evaluation of the verification and significance of the signal.
- ✚ **Hypothesis testing and quantification**, by one or more structured studies, either epidemiological and/or experimental depending upon the questions.

Methods of Phase IV Studies

Qualitative methods

- ✚ Drug utilization review (DUE): DUE is an ongoing, authorized and systemic quality improvement process, which is designed to:
- ✚ Review the drug use and/or prescribing patterns
- ✚ Provide feedback of results to clinicians and other relevant groups.
- ✚ Develop criteria and standards that describe optimal drug use.
- ✚ Promote appropriate drug use through education and other interventions.

- ✚ DUE is a discipline, which aims to understand how and why drugs are used as they are, so that drug use and health outcomes can be improved.
- ✚ DUE can play a key role in helping the health care system to understand, interpret and improve the prescribing, administration and use of medications.
- ✚ The concept of drug utilization review was developed in the hospitals to assess how well the drugs were being used. These studies are conducted on drug with high cost; drugs that are widely used, drugs with narrow margin of safety or that are prone to misuse or over use.
- ✚ Criteria for DUE are developed after literature review and from the input of clinical experts and after official approval, criteria are applied to a sample of exposures to a drug in question and rate of appropriateness is determined
- ✚ In most of the case, feedback is provided in the form of report, educational intervention and restriction on use.
- ✚ DUE information will help physicians to compare their approach to treating certain diseases with their peers. The peer pressure generated by these comparisons may be useful in motivating physicians to change their prescribing habits in an effort to improve care.

Quantitative methods

Cohort studies

A cohort study is one into which patients are entered according to their exposure status. That is, between two groups of people one group is exposed to the drug and other is unexposed comparison group similar to them in all other important aspects.

The two groups are followed through time and outcomes are observed and recorded. When the trail is completed, rates are compared between the two groups, and hypotheses may than be tested.

Advantages

- ✚ Being able to actually measure outcome incidence.
- ✚ With one study, many different outcomes to a single exposure may be explained.
- ✚ Effectiveness data can be collected.

Limitations

- ✚ Need sample size. Expensive, can take years to complete.

- ✚ Incomplete record and missing data due to longer duration of studies.

Cross sectional studies

- ✚ These are called as surveys or prevalence studies and usually involve a statistically based random sampling of a target population. Data are classified according to reported exposure to the drug and observed outcomes.
- ✚ Results since studies were conducted retrospectively. It may be unclear whether exposure truly preceded outcome.

Descriptive studies

- ✚ These studies provide the information on the pattern of the disease occurrence in population according to demographic and prognostic Characteristics.
- ✚ The data used are from routinely collected epidemiological intelligence, which is analyzed to identify the occurrence of rare adverse reactions or to generate a hypothesis.
- ✚ Passive, monitoring of events and reports is an important method for collecting data include in descriptive studies.

Limitations

- ✚ Physicians generally unaware of the unusual event appeared due to drugs as there are no such documented reports for the new drugs.
- ✚ The event cannot be attributed to general population.

Case control studies

- ✚ These are retrospective studies. Cases have the disease and the controls not data are collected by looking back ward in the time to determine differences between the two groups in the past.
- ✚ Each case is matched for specific confounding factors like age, sex with one or more controls. But some situations it is difficult to find appropriate controls and the information obtained is often incomplete and subject to recall biases.

Limitations

- ✚ Do not estimate the frequency of exposure.
- ✚ Do not estimate the frequency of disease in whole population.
- ✚ Only allow estimation of relative risk of disease or event in the exposed versus that in non-exposed person.

Controlled clinical studies and trials

- ✚ Control refers to strict adherence to the protocols. The purpose of which is to reduce the variability of the many factors and biases that might influence the results.
- ✚ Control features include the double blind procedure. Where neither the patient nor the investigator is aware of which treatment the patients is receiving. But are not confined to this others include the adequacy of the group used as controls.

Limitations

- ✚ Reports directly to the health authority centers. This is most often the traditional system in many countries.
- ✚ The intermediary model. This is a predominant in the USA where reports are obtained via detail persons or letters and calls to the manufacturer. Since all events are to be reported this results in a large number of notifications.

Meta-Analysis

- ✚ It is the combination result from group of studies to arrive at a summary estimate of effect. These results may be used when there are controversies when there are conflict results in literature.

Spontaneous reporting

- ✚ Most of the developed and developing countries are practicing this. Clinician is encouraged to report any and all reaction that they believe may be associated with drug use. Usually given importance to new drugs and serious ADR.

Prescription-Event Monitoring.

- ✚ This method was developed in UK. This is to generate or test hypothesis about ADRs
- ✚ In defined population of users. It has advantage of providing incidence or event over a defined follow-up period.

Case reports

- ✚ These are weakest form of clinical evidence. These are usually published after a clinician notice a problem and associate that problem with exposure drug. A case report can be strengthened by a relating ADR to drug concentration in the body.

Case series

- ✚ Case series is a group or cluster of case reports that may be generated by a single clinician, group of clinician, a hospital, pharmaceutical company or a regulatory agency.
- ✚ These reports allow a closer examination of the problem, but provide little insight into the rates of occurrence or extent of the problem.

Some of the Drugs Banned Drugs In India Recently

SNO	DRUG NAME	ACTUAL USE	REASON FOR BANNED
1	Rosiglitazone	Type II DM	Increased heart attacks
2	phenformin	Anti Diabetic	High risk of Lactic Acidosis
3	Fenfluramine Dexfenfluramine	Used to treat Obesity	Diseases of heart valves, pulmonary hypotension, fibrosis
4	Gatifloxacin	AntiBiotic	Risk for Hyperglycemia/ High blood sugar levels in the elderly
5	Terfinadine	Anti Histamine	Polymorphic Ventricular Tachycardia
6	Sibutramine	Weight Loss	Heart related side effects
7	Rimonabant	Weight Loss	Depression, suicidal tendencies,

CONCLUSION

Post Marketing Surveillance is an Important tool for the detection and development of Adverse Drug Reaction after drug placed in to the Market under governed by pharmacovigilance. In India The pharmacovigilance programmed was constituted in the year 2010 under Ministry of Health and Family Welfare, Government of India. The Present Review Article shows the Importance of Post Marketing Surveillance, Methods for reporting and Development of adverse drug reactions. This study will useful for the providing awareness among health care Professionals which includes Clinicians, Nurses, Clinical Pharmacists and Other Health Care Professionals to Increased the health Related Quality Of Life of patients as well as Patient Care Takers.

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