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PHARMACOVIGILANCE;
A PARADIGM SHIFT FROM CARE TO SAFETY

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ABSTRACT: The solution for safe and rational medication use to improve patient care as well as to enhance public health status is Pharmacovigilance (PV). Optimal care of patient and appropriate medication utilization in secure way with respect to various conditions is an imperative function of pharmacovigilance system. PV mainly involves in the adverse drug reactions (ADRs) identification, system of reporting, scrutinizes the effectiveness of treatment, reduces the adverse consequences to utmost level and guarantees the patient wellbeing. The safety of drug is highly essential factor when it comes from the healthcare provider to the patient. For a drug to be successful in market, it is crucial for it to be efficacious as well as safe and secure for the patients. Hence, adherence toward pharmacovigilance activities and system is now based on a paradigm change from care to safety.

Key words: rational medication, pharmacovigilance, paradigm shift, safety, adverse drug reactions

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INTRODUCTION

Pharmacovigilance has been defined by World Health Organization (WHO) as a discipline as well as actions concerning recognition, evaluation, perception, deterrence and avoidance of undesirable effects (adverse events) along with additional issues regarding medications.[1]

Individualized Pharmacovigilance system are highly needed for every country since medication related problems and associated adverse drug reactions and events seems to be variable because of the differences among formulation designs, distinct genomic natures as well as variation in local practices. Development of localized centers for activities of Pharmacovigilance is greatly emphasized by World Health Organization. There must be a firm controlling infrastructure from each country to regulate pharmacovigilance and to strive for achieving the goals from set objectives that ought to reflect all concerned authorities and personnel's efforts that are significantly indulged in the pharmacovigilance system.[2]

Drug based problems and their respective undesirable incidents reports may be diverged in nature from various regions of the world because of manufacturing variability, genetic variety, physiological variations and local medical trends/practices. For these reasons development of local pharmacovigilance system in each country is recommended. World renowned regulatory bodies supports for the effective implementation of suitable regulatory procedures and development of Pharmacovigilance hubs. Furthermore regulation of these systems requires a strapping system framework to accomplish preferred objectives with the pledge that all pertaining authorities and personnel's are appropriately implicated in the system.[2-4]

For International monitoring of drugs and other medicinal products, a strong Pharmacovigilance system has been formed in 1987 by Malaysia and it had become a member of the program organized by World Health Organization for monitoring medications in the year 1990.[3]

A setup was established in the year 2009 among various partners from Asia, Europe and Africa

named as the Monitoring Medicines project (MM), with the objective to optimizing drug safety monitoring to enhance patient safety and achieve better health outcomes. This project had been supported by European Union framework. And it was conceded out during the period of 5 years starting from 2009 till the year 2013.[4]

Globally, major health concerns are growing due to the life threatening effects of drugs owing to their varied classification, irrational medication use and lack of drug utilization reviews. Worldwide, the most essential standards for any drug product to fulfill the registration process as well as to achieve successful market, factors such as quality, efficacy and most important safety of the medication product is indispensable.

The overdose as well as under dose of every drug product has been associated with several types of adverse events which may arises due to irrational use of that medication and therefore Adverse Drug Reaction is one of the major public health concern which affects approximately 5-20% of hospital admissions. To ensure quality health of every person, one of the most essential component of pharmaceutical care system is Pharmacovigilance which has now become center of attention to the health authorities as well as regulatory bodies. A multidisciplinary team of health care professionals can prove to be milestone in detection, prevention, reporting and minimizing such adverse drug events and reactions.[5]

To display various implementations of pharmacovigilance, centers for national pharmacovigilance programs serves to be important medium to increase public awareness and their responsiveness towards safer drug use practices. Main headquarters in various developed countries which have been instituted for dynamic supervision of drug related events using record and evidence associated with prescription incident monitoring method which helps in data compilation of epidemiological collection of information associated with adverse effect to particular medicine. Table-I summarized the common drug interactions/effects of selected drugs.[6]

ROLES AND ACTIVITIES

Pharmacovigilance had always been the part of reducing the risk of unfavorable treatment response and medication error; conversely the Erice Manifesto in March 2007 also conveyed the innovative approach of patient wellbeing that has to be considered as the leading challenge for national Pharmacovigilance objectives.[7]

Drug Category	Undesirable effects
Benzodiazepine	Sleep abnormality & respiratory restraint
Barbiturates	Muscular weakness, impaired consciousness/
Miconazole	Decreased blood sugar levels
Tetracycline	reduced drug absorption
Theophyllines	sleeplessness, seizures, agitation
Ethanol Additive	CNS abnormalities, loss of consciousness and Death
Phenytoin	Respiratory &CNS depression
Predmisone	Swelling
Warfarin	Bleeding
Methotrexate	Suppression of bone marrow
Alprazolam, Diazepam	depression, Excessive sleep, Drowsiness
Anti-diabetic	Hypoglycemia
lithium	Low body temperature (hypothermia)
Aminoglycoside	Hearing abnormalities, kidney function impairment

Table-I. Common drug undesirable effects

Henceforth A healthcare professional team that embraces pharmacovigilance as main structure of activity that must guarantee safety and wellbeing by reducing the incidence of adverse reactions of medicines and decrease consequential fatalities from them. Furthermore endow with a forewarning network amongst the different healthcare contributors, controllers, regulator, producers and consumers of drugs to provide the effective remedial action plans for execution in a judicious and methodical manner.

ADVERSE DRUG REACTIONS (ADRs)

For keeping an eye on drug safety and monitoring, WHO conjointly initiated program with International Drug Monitoring, Uppsala in the year 1961 for promotion of Pharmacovigilance[8] According to data provided by WHO, there is high prevalence rate of ADRs which constituents approximately 4.6million reports on annual basis which furthers raised up to 250,000.[9] For development of a sound Pharmacovigilance system as well as processing new ideas along with identifying infrequent outcomes, exploration of the data from distinct global areas of social as well as medical population is very necessary and influential.[10]

Pharmacovigilance has been involved in post marketing studies having focus on clinical reporting of unfavorable drug reactions which is in the transition phase of approval process by united state food and drug administration, for the continuous updates and amendments regarding safety issues of the medication therapy. The process of pharmacovigilance has always been indulged in triggering food and drug administration for implementation of these regulations of safety of drugs[11] and timely withdrawal of Roficoxib is an example that reflects the importance of drugs safety and it was made possible by the efforts of trial board that the drug has been involved with cardiovascular risks.[12] Likewise several other medications had been withdrawn from the market for similar reasons which lead to severe adverse drug reactions. Primarily adverse drug reactions were not fully identified till a large group of people administered the drug product. Thalidomide in the year 1961 is one of the examples which was found to be associated with congenital limb abnormalities, similarly in the year 1982, Phenormin was withdrawl due to lacticacidosis, hepatotoxicity was resulted from benoxafen as well as many valvular abnormalities were resulted by use of fenfluramine in the year 1997 and Haemmorhagic stroke was associated to be caused by phenylpropanolamine.[13]

MAJOR CONSIDERATIONS

Drug safety is a matter of utmost concern in health care system. Health care providers along with patients must be ensured about safety of the medication to get optimal benefits from the medication therapy and this purpose is achieved by establishment of a completely robust PV system that must be centered for an uninterrupted development of safety issues and profiles of the medications[14] The science of Pharmacovigilance came into existence after the Thalidomide disaster in 20th century. Since then, heath care sectors in various developed countries initiated efforts for ensuring safety of drugs.[15] An active Pharmacovigilance system encompasses the following critical issues such as ADRs, medication errors, counterfeit or substandard medicines, lack of efficacy of medicines, misuse and/or abuse of medicines, interaction between medicines. Among all these problems, highest rates of mortality and morbidity has been associated with Adverse Drug Reactions which is fourth to sixth leading cause of death in USA.[16-17]

PREVALENCE OF ADR AND ECONOMIC BURDEN

ADRs are defined as multifaceted events by World Health Organization (WHO). It is symbolizes as a reaction of a remedial moiety that is injurious and inadvertent. The occurrence of these events are associated with normal doses utilized for diagnosis, prophylactic and therapeutic purposes for the improvisation of physiological responses.[18]

Results of various studies reveal that 0.2-24% of hospital admission are results of ADRs.[19-20] Cost associated with ADR also one of the major concerns as they create a very high financial burden on patient in terms of cost associated with prevention as well as treatment of adverse drug reactions and its consequences.[21] According

to the results of a German micro costing study, reporting economic burden of approximately 1 Billion Euro for the account of ADRs.[22]

Pharmacovigilance ensures the safety, efficacy as well as eminence of medicines and medical devices consumed and utilized by the communities of respective regions. Thus it is the foremost conscientiousness of drug regulators to observe the feat of medicines after their marketing. Essential drugs are predominantly vital as their consumption by larger group of people has been reported with significant rationale of Adverse Drug Reactions (ADRs) upshots.

RISK BASED MANAGEMENT

The significance of a proficient framework for managing drug dangers and emergencies has turned out to be progressively apparent in recent days. Numerous national authorities have recognized the requirement for building up a hierarchical arrangement for risks supervision and for correspondence and required action during crises and emergencies.[23]

Risk management as the part of pharmacovigilance is responsible for signal detection and to monitor the profiles of drugs with respect to risk-benefit ratios.[24]

SIGNAL DETECTION

A signal comprises of reported data on a conceivable underlying association between an event and medication, the relationship being obscure or not completely recorded already. Typically more than solitary information is required to produce a signal, contingent on the intensity of the incident and the nature of the data.[25] For making judgments on proper association between drug product and associated adverse drug reactions and for this Vigirank is appreciable.[26-28]

RISK/BENEFIT PROFILE OF DRUGS

It is obligatory for Pharmaceutical organizations by law in various regions of the world to conduct clinical trials, before the accessibility and marketing of new drugs to the population. Prior to these trials, prescreening of formulation is carried out for poisonous/undesirable quality attributes and potentials, by using different animal models.[24-25,29]

The intention of clinical trials is to evaluate drug performance, range of activity, and elucidation of toxic potential, acceptable risk benefit ratio, intensity and magnitude of harmful events.[30]

Since Pharmacovigilance is a backbone in drug's market, it is imperative to create a shift from ancient methods of evaluating safety data by keeping rely completely on reports from individual cases accounted by health care practitioners as well as clinical trials to a more comprehensive system utilizing modern computerized technologies not only for pre and post marketing surveillance but to evaluate the signals linked with the safety profiles of that medication throughout its marketed life.[31] The paradigm has now completely transferred from absolute compliance to a devotion to the safety of patients.[32]

POST-MARKETING SURVEILLANCE

It is currently acknowledged that part of the procedure of assessing medication wellbeing should also be performed in the post- endorsement stage of marketing. The more grounded the national arrangement of pharmacovigilance and ADR system, the probability of rational and logical regulatory choices will be made for the early arrival of new medications with the guarantee of restorative character of drug.[31,33,37]

ELUCIDATION OF PRODUCT SAFETY

internationally drug safety criteria is based on two fundaments; satisfaction of the regulatory necessities in the relevant areas where medical devices and products are produced and distributed while secondly, tailoring methods to accomplish regulatory concerns for the exceptional formulations of the individual corporation. Drug makers should guarantee that overall acquiescence objectives are recognized and tackled and that appropriate system of signal recognition, prioritization, and valuation are in position to detect real risks including identified and potential risks.[33-34]

A diverse group of population has been using

Antibiotics, Anticoagulants, Cardiac glycosides such as Digoxin, Diuretics, hypoglycemic, anti-neoplastic agents as well as Non-steroidal anti-inflammatory agents along with various essential medicines, and hence these medications have been contributed about 60% of adverse events which ultimately results in prolong hospitalizations and studies revealed that 70% of Adverse drug reactions have been identified in hospital settings.[8-10] These adverse drug reactions occurring in patients who are hospitalized are distinguishable into two separate entities; the ADRs that causes admission to hospitals while those ADRs that develops in in- patients after they admitted in hospitals. Results from a random-effect model study reveals that there was about 6.7% serious adverse drugs from both categories showing fatality rates of 0.32% which further explained by recently performed Swedish study showed result that the 7th commonest cause of death is Adverse Drug Reactions [31] and results have been showed that Adverse Drug Reactions are leading causes of major clinical issues as well.[32,40]

ROLE OF PHARMACOVIGILANCE IN SPECIALTY PHARMACIES

Exclusive drug stores are assuming an expanding part in patient care and participating actively in disease management activities, which entails consistence with the rules of global pharmacovigilance paradigm.[33-34] Authorities and drug stakeholders anticipate that adverse events highlighted from customer contact are properly documented, verified and reported. It is important to guarantee satisfactory training and guidance of pharmacy personnel's to build the capacity to distinguish, record, and convey the related safety data.[35-36]

During several different stages of drug product development, a comprehensive team must be there for ensuring safety of drug and other medications products and one of the major responsibility of this safety management team is to properly evaluate as well as communicate the data regarding safety of medicines and this group has been constituted by indulging stakeholders from research designing and developmental projects. Hence forth, a team of highly competent personnel is an imperative approach for the risk and safety management of the drug product.[37-39]

CONCLUSION

At conclusive part, it is a need of time to institute a vigilant system with optimal objective of drug performance reporting, which is composed of a team from various sectors of healthcare domain to avert the significant magnitude of patient suffering, associated morbidities and mortality. It has become imperative to initiate concept of pharmacovigilance for cultivating seeds of safety at each and every step of medication therapy as well as for improving public health and safety.

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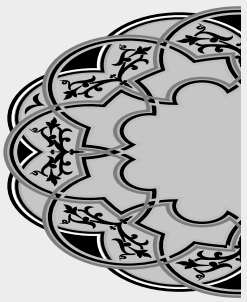

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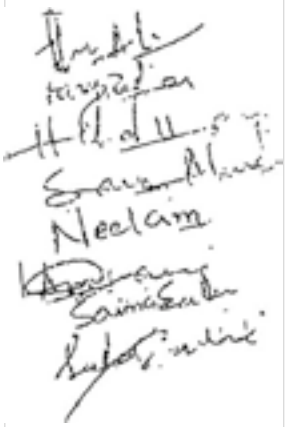
1	Dr. Huma Ali	Equal contribution by all authors	
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