MANTECH Publications

Journal of Pharmacovigilance and Quality Assurance
Volume 4, Issue 2, July-December, 2022

Pharmacovigilance- Concerns Regarding Drug Safety and it's Future

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Abstract

Medicines and vaccines are critical components of the nation's healthcare system. Deadly episodes in the past, such as the thalidomide catastrophe in 1950, the usage of lash lure mascara, and ethylene glycol toxicity in children, mandated and highlighted the necessity of medication and vaccination safety. Pharmacovigilance is a rigorous procedure that deals with medication safety throughout the medicine's life cycle. Intrinsic limitation up to phase III of the drug discovery process underlines the importance of pharmacovigilance. The current essay attempts to emphasise crucial aspects of the safety process during medication development and its future, and it will aid drug prescribers and users to some extent concerning the effective and safe use of pharmaceuticals in daily life.

Keywords*: - Drug Safety, Pharmacovigilance, Nation Healthcare System, Drug Discovery Process*

INTRODUCTION

Medicines and vaccines are at the heart of the healthcare system, and they have altered our lives via illness prevention and treatment. Medicinal products, in addition to their advantages, may have side effects, some of which may be unwanted and/or unexpected (Who.int). Medicine safety is critical, and monitoring is a constant and dynamic process that occurs throughout all phases of a drug's life cycle (Trifir and Crisafulli, 2022). Deadly incidents in the past, such as the thalidomide tragedy in 1950, the use of lash lure mascara, and

ethylene glycol poisoning in children due to Elixir Sulphanilamide, paved the way for the assessment of chemical safety prior to their direct authorization for use (National Research Council (US) Committee, 2004). Pharmacovigilance is the discipline of medicine that deals with this issue. Pharmacovigilance is the science and practises concerned with the detection, evaluation, comprehension, and prevention of adverse effects or other medicine/vaccine-related problems (Who.int). Interindividual variation accounting for diversity in medication response and adverse impact makes this subject intriguing, as there is rarely a one-size-fits-all solution in global pharmacovigilance. Overall drug safety issues are thus evaluated at various stages of the medication development process.

The medication development process is divided into five stages: discovery and development, preclinical research, clinical research, regulatory authority reviews, and postmarketing safety studies (FDA, 2018). Although all medications and vaccines are subjected to rigorous testing for safety and efficacy in clinical trials before they are approved for use, these trials were done in a limited number of carefully selected individuals over a short period of time (Who.int). As a result, a true picture of a medicine, including its adverse effects, can be obtained only after it has been used by a diverse population, including individuals with other concomitant ailments, over a lengthy period of time. This article seeks to emphasise major aspects of the safety process followed during drug development and its future, and will inform drug prescribers and users to some extent regarding the effective and safe use of pharmaceuticals in daily life.

Safety Evaluation of Drug in Drug Development Process

Following target identification and validation, medication safety was evaluated in pre-clinical investigations, with the major aim of safety evaluation being the identification of safe dosage safety parameters in humans for clinical monitoring (Trifir and Crisafulli, 2022). In line with this, the FDA launched a new initiative called "Project Optimus" in May 2022, replacing the previous maximum tolerated dose approach used for cytotoxic chemotherapeutics, to emphasise the importance of characterising the dose and schedule of anti-cancer drugs in order to maximise efficacy and safety (FDA, 2022). Preclinical safety studies were conducted on two separate animal species, with animals receiving the novel medicine at the maximum tolerated dosage (MTD)

for 30 or 90 days (National Research Council (US) Committee, 2004). Throughout the trial, animals were carefully assessed for any negative effects. Following the trial period, the toxicity potential of the medicine was evaluated by conducting a post mortem examination, if necessary. All of these processes were carried out in accordance with FDA or other regulatory agencies' requirements.

Following the finalisation of the dosage, the medicine enters the clinical phase, which consists of four phases. Phase I investigations are conducted in healthy human volunteers to evaluate the tolerance of the dosage range that will be required for further clinical trials. Phase II studies are conducted in individuals with an illness or condition of interest in order to determine an appropriate dosing range. Phase III clinical trials are big multicenter studies involving a large number of patients with an emphasis on determining the efficacy of the medicine and continuing to monitor for any negative effects. Pre-marketing clinical studies will not be able to comprehensively analyse medication safety profile due to inherent restrictions involving a restricted number of individuals, distorting the overall outcomes of the research (Trifir and Crisafulli, 2022).

The last step is phase IV (post-marketing monitoring), in which the medicine is actually released onto the market. Because the medicine has been exposed to a diverse population, a comprehensive and exhaustive safety study of the drug profile is possible during this phase. This safety profile was reviewed by the medicine manufacturer and the FDA for the occurrence of adverse effects that might occur due to interindividual variation in the population (National Research Council (US) Committee, 2004). Conclusively, phase IV of a trial is vital for better defining medications' safety profiles in real-world settings, which helps to further enhance pre-marketing study results, so closing the evidence gap. Pharmacovigilance is critical.

Thalidomide tragedy in 1950, use of lash lure mascara, ethylene glycol poisoning in the children due to Elixir sulphanilamide created a need for assessment of safely of chemical before their direct authorization for use (National Research Council (US) Committee, 2004). Despite this, in the last two year, with first wave of COVID-19 pandemic further highlights the importance of pharmacovigilance wherein absence of vaccines and drugs for treatment/prevention of COVID-19, lead to repurposing of several drugs. Various

drugs like hydroxychloroquine, ivermectin and azithromycin has been off-label used for the treatment of COVID-19 patients, in the absence of scientific evidence (Sultana et al., 2020a). Risk associated with off label use of these drugs is the important step for pharmacovigilance monitoring. Elucidating further, azithromycin, a macrolide antibiotic that has been widely used, for the treatment of COVID-19 patients despite its proarrhythmogenic activity, led regulatory agencies to issue warnings against the use of this drug, unless in case of bacterial superinfection occurrence (Crisafulli et al., 2021). Global health emergencies like pandemic COVID-19 accelerated the process of drug approval, and of safety evaluation in post-marketing setting with an emphasis on patient safety.

Besides this, role of communication between health care providers and patients in relation to appropriate use of medicines/vaccines, further supports and validate the role of pharmacovigilance as number of studies has reported accelerated inappropriate drug use associated with the risk of serious adverse reactions, the best example being the hydroxychloroquine (Sultana et al., 2020b).

Pharmacovigilance-Conclusion and Future Directions

Pharmacovigilance has played a critical role in the safety of drugs, all of which carry some risk. It has developed in the pharmaceutical sector and is now acknowledged as a discipline. With an emphasis on individual case reporting in the past (Talbot and Nilsson, 1998), we must be prepared for present and future issues in terms of safety and drug laws. Medicinal side effects or related danger can be reduced by using high-quality, effective medications. Aside from that, rational medication usage, improved communication between health experts and the public, and education of health professionals to understand the effectiveness or risk of the medicines they prescribe are also critical steps to take (Jeetu and Anusha, 2010). More stricter controls throughout the medication development process, as well as adequate risk communication across the drug chain, are critical initiatives to adopt. Furthermore, innovative approaches such as artificial intelligence, machine learning, the use of digital therapies, and the generation of electronic healthcare data must be considered ((Trifir and Crisafulli, 2022). This will allow for the optimization of pharmacological benefit-risk profile evaluation in a real-world environment.

Advanced therapeutic pharmaceutical goods based on genes, cells, or tissue engineering (European Medicines Agency, 2021) are an emerging subject that incorporates personalised or precision medicine and need post-marketing surveillance. In recent years, various biologicals such as vaccinations may have required particular pharmacovigilance monitoring in addition to pharmaceuticals. Finally, while a distinct branch termed "Eco pharmacovigilance" (Velo and Moretti, 2010) deals with all of this aspect and is a very important topic these days, harmful effects occurring to nature as a result of the presence of medicines in the environment must be taken into account.

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