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Essentials of Pharmacovigilance



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CHAPTER 3

Aim and Importance of Pharmacovigilance

KEYPOINTS

- *Aim of Pharmacovigilance*
- *Objective of Pharmacovigilance*
- *Definition of Adverse Drug Reaction (ADR) and its Types*
- *Importance of Pharmacovigilance*
- *International Response to Drug Safety Issues*
- *Major Challenges*

AIM OF PHARMACOVIGILANCE

To identify new information about hazards associated with medicines.

OBJECTIVE OF PHARMACOVIGILANCE



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- Improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions
- Monitor the adverse effects of drugs from preclinical to postmarketing phase and then for many years



- Contribute to the assessment of benefit, harm, effectiveness and risk of medicines, encouraging their safe, rational and more effective (including cost-effective) use
- Promote understanding, education and clinical training in pharmacovigilance and its effective communication to the public

DEFINITION OF ADVERSE DRUG REACTION (ADR) AND ITS TYPES

Adverse Drug Reaction

It is an unintended and noxious effect of drug which occurs at normal doses used in humans for prophylaxis, diagnosis or therapy of disease or for modification of psychological functions.



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Types of ADR

The types of ADR are as follows (Table 3.1):

A. Serious adverse reaction
B. Unexpected adverse reaction

Table 3.1: Types of adverse drug reaction under various conditions.

	Type A (augmented)	***Type B (bizarre)***
Pharmacologically predictable	Yes	No
Dose-dependent	Yes	No
Frequency	Common	Rarer
Incidence	High	Low
Mortality	Low	High
Treatment	Adjust dose	Stop the drug



Side effect: An unintended effect of a pharmaceutical product occurring at normal dosage which is related to the pharmacological properties of the drug.

IMPORTANCE OF PHARMACOVIGILANCE

Safety Monitoring of Medicinal Products

- Drug monitoring
- Pharmaceutical preparations—adverse effects
- ADR reporting
- Product surveillance and postmarketing

A new medicine must pass three hurdles before its approval by the national drug regulatory authority. Sufficient evidence is required to show the new drug to be of good quality,

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effective and safe for the purpose or purposes for which it is proposed, whereas the first two criteria must be met before any consideration can be given to approval, the issue of safety is less certain. Safety is not absolute, and it can be judged only in relation to efficacy, requiring judgment on the part of the regulators in deciding on acceptable limits of safety.

Postmarketing Safety Monitoring



- It is now generally accepted that part of the process of evaluating drug safety needs to happen in the postmarketing (approval) phase, if important innovations are not to be lost in an unduly restrictive regulatory net.
- Judgment as to whether and how this might happen lies within the regulators.
- The stronger the national system of pharmacovigilance and ADR reporting, the more likely it is that reasonable regulatory decisions will be made for the early release of new drugs with the promise of therapeutic advances.
- Legislation governing the regulatory process in most countries allows for conditions to be placed on approvals, such as a requirement that there should be detailed pharmacovigilance in the early years after a drug's release.
- Careful safety monitoring is not confined, however, to new drugs or to significant therapeutic advances. It has an important role to play in the introduction of generic medicines and in review of the safety profile of older medicines already available, where new safety issues may have arisen.
- In a developing country, these latter considerations are likely to be more important than the benefits a novel therapeutic entity might bring to an already pressed health service.
- Spontaneous reporting remains a cornerstone of pharmacovigilance in the regulatory environment and is indispensable for signal detection.
- Without information on utilization and on the extent of consumption, spontaneous reports do not make it possible to determine the frequency of an ADR attributable to a product or its safety in relation to a comparator.

More systematic and robust epidemiological methods that take into account the limitations of spontaneous reporting are required to address these important safety questions. They need to be incorporated into postmarketing surveillance programs. There are other aspects of drug safety that have been rather neglected until now, which should be included in monitoring

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latent and long-term effects of medicines. These include detection of drug interactions, measuring the environmental burden of medicines used in large populations, assessing the contribution of "inactive" ingredients (excipients) to the safety profile systems for comparing safety profiles of similar medicines surveillance of the adverse effects on human health of drug residues in animals, for example, antibiotics and hormones. A more difficult question is whether pharmacovigilance has resulted in inappropriate removal of potentially useful medicines from the market as a result of misplaced fears or false signals. Pharmacovigilance in drug regulation the Council for International Organizations of Medical Sciences report on benefit–risk assessment of medicines after marketing has contributed to a more systematic approach to determining the merit of available medicines. Systematic medical and prescription record linkage, with drug utilization studies, would contribute to greater accuracy. This is a responsibility that falls outside the strict traditional terms of reference of national pharmacovigilance centers.



INTERNATIONAL RESPONSE TO DRUG SAFETY ISSUES



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Certain safety issues are likely to have a global impact with possibly serious consequences for public health. When this happens, a cohesive international assessment and response is needed. Such a system would need to be supported by member countries. Its terms of reference should be quite clear and generally agreed. There would be a need to access all data relating to a product under consideration, including product information protected by secrecy laws and patient case records when necessary. The aggressive marketing of new medicines by pharmaceutical manufacturers and the resultant rapid exposure over a short period of time of large numbers of patients to them warrant the creation of a system for global assessment of drug safety concerns. The World Health Organization (WHO) has supported the creation of an independent advisory panel composed of a broad spectrum of medical disciplines including clinical pharmacologists, regulators, academics and epidemiologists. The functions of this panel will be to provide advice to WHO on safety issues relating to medicinal products, including its Collaborating Centre for International Drug Monitoring (the Uppsala Monitoring Centre) and through it to the Member States of WHO.

MAJOR CHALLENGES



Globalization

The globalization of drug distribution increase exposure of massive populations to large volumes of medicines. These include novel chemical entities used for symptomatic relief and lifestyle modification as well as medicines used in developing countries to curb the prevalence of pandemic diseases such as human immunodeficiency virus/acquired immunodeficiency syndrome, malaria and tuberculosis. The use of medicines on such a large scale and within such a short period of time calls for a better and more efficient level of international pharmacovigilance.

Web-Based Sales and Information

The Internet, in addition to its many benefits, has also facilitated the uncontrolled sale of medicines (including herbal and traditional medicines) across national borders. Drug information in

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all forms and with varying levels of accuracy is distributed internationally through this medium. Such information covers prescription drugs, unregistered medicines, highly controlled substances and traditional and herbal medicines with questionable safety, efficacy and quality.

Broader Safety Concerns

The scope of pharmacovigilance continues to broaden as the array of medicinal products grows. There is a realization that drug safety is more than the monitoring, detection and assessment of ADRs occurring under clearly defined conditions and within a specific dose range. Rather, it is closely linked to the patterns of drug use within society. Problems resulting from irrational drug use, overdoses, polypharmacy and interactions, increasing use of traditional and herbal medicines.

Public Health Versus Pharmaceutical Industry Economic Growth

There may be shortcomings and, at times, conflicting interests within the pharmaceutical industry when dealing with public health concerns arising from drug safety issues. The industry needs to overcome weaknesses in safety monitoring during clinical trials and postmarketing surveillance.

Monitoring of Established Products

The generic sector of the pharmaceutical industry has not fully recognized its responsibility to continuously monitor the safety of its products throughout the world. There is the erroneous belief that generic drugs are inherently safe even when they interact with other medicines. The generic sector is the largest supplier of essential drugs.

Outcomes and Impact

Along with increased public awareness over safety of medicines, there is an increasing public gaze on the performance of the health professions, industry and regulators. Increased accountability must lead to more research into the effectiveness of pharmacovigilance and its place in improving public perception. A major focus must be to empower health practitioners and patients themselves with useful information that improves individual therapy, aids the diagnosis and management of medicine-induced disease and generally leads to a reduction of iatrogenic diseases.

True challenges lie in recognizing at the earliest possible stage, the adverse effects that a drug may induce, so that the risk (unfavorable results) never becomes disproportionate to benefit (favorable results). We have to balance risk–benefit ratio of drug by strictly monitoring drug therapy on continuous basis by well-trained and qualified pharmacovigilance personnel because risk–benefit assessment is vital during the whole life cycle of products. All risks must be considered in the context of benefits. The underlying principles of assessment are the same whether pre- or postmarketing. For each medicine, there is a balance between risk and benefit, but the perspective of different stakeholders (regulator, marketing authorization holder, academic, patient or prescriber) may vary. The risk–benefit assessment in pharmacovigilance

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course enables delegates to explore the relationship between risk and benefit, and review the integration of appropriate strategies within risk management plans.

FURTHER READING

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Essentials of Pharmacovigilance

Essentials of Pharmacovigilance is a unique blend of basic and fundamental aspects of Pharmacovigilance. It is complete guide of all basic guidelines and practical case studies for hand on training and experience in Pharmacovigilance practices. The book is specially designed for students as well as for Pharmacovigilance professionals. The layout of book is simple, attractive and reader friendly.



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