**The need of Pharmacovigilance**

**Introduction:**

* The treatment of diseases changed a lot with the help of modern medicines.
* However, despite all their benefits, evidence continues to mount that adverse reactions to medicines are a common, yet often preventable, cause of illness, disability and even death.
* It’s the time to:

1. prevent or reduce harm to patients and thus improve public health and safety.
2. Evaluate the harm and monitor the safety of medicines in clinical use.

Definition:

“Pharmacovigilance is defined as the science and activities related to the detection, assessment, understanding and prevention of adverse effects or any other drug related- problem”.



*“This applies throughout the life cycle of a medicine equally to*

*the pre-approval stage as to the post-approval.”*

The Pharmacovigilance not only includes the modern medicines, but it also extended to Herbals, traditional and complementary medicines, blood products, biologicals, medical devices, vaccines.

It involves many other issues:

* Substandard medicines,
* medication errors,
* lack of efficacy reports,
* use of medicines for indications that are not approved and for which there is inadequate scientific basis,
* case reports of acute and chronic poisoning,
* assessment of drug-related mortality,
* abuse and misuse of medicines,
* adverse interactions of medicines with chemicals, other medicines, and food.

Life cycle of a drug:



**Brief description of clinical trials:**

1. **Preclinical Studies:**

**Animal studies tested for**

* Acute toxicity
* Organ damage,
* Pharmacokinetics
* Carcinogenicity
* Mutagenicity

1. **Phase- I**

* Healthy volunteers
* Limited number of subjects
* 20-50 subjects

1. **Phase- II**

* 150-350 subjects with disease.
* No healthy volunteers.
* Controlled study only

1. **Phase-III**

* 250-4000 subjects with disease
* Large number of general population

**Why Pharmacovigilance?**

**Reason 1:**

* Humanitarian grounds –
  1. Insufficient evidence of safety from clinical trials
  2. Animal experiments
  3. Phase 1 – 3 studies prior to marketing authorization

Limitations in Clinical trials:

* 1. Limited size: no more than 5000 and often as little as 500 volunteers
  2. Narrow population: age and sex specific
  3. Narrow indications: only the specific disease studied
  4. Short duration: often no longer than a few weeks

**Reason 2**

* Medicines are supposed to save lives

*Dying from a disease is sometimes unavoidable; dying from a medicine is unacceptable.*

*Lepakhin V. Geneva 2005*

UK:

It has been suggested that ADRs may cause 5700 deaths per year in UK.

*Pirmohamed et al, 2004*

US:

ADRs were 4th-6th commonest cause of death in the US in 1994

*Lazarou et al, 1998*



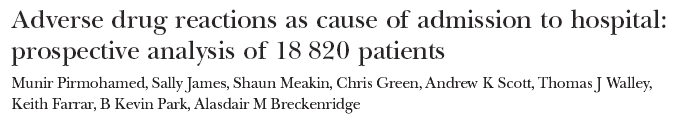
* 125 Patients

(59%) wereavoidable

* 24 Patients experienced ADRs (19%)

**Reason 3:**

* **ADRs are expensive!!**



* 6.5% of admissions are due to ADRs
* Seven 800-bed hospitals are occupied by ADR patients

Cost £446 million per annum

* Cost of drug related morbidity and mortality exceeded $177.4 billion in 2000

(*Ernst FR & Grizzle AJ, 2001: J American Pharm. Assoc)*

**Reason 4:**

Promoting rational use of medicines and adherence

**Reason 5:**

**Ensuring public confidence**

**Reason 6:** Ethics

To know of something that is harmful to another person who does not know, and not telling, is unethical.

**Examples of product recalls due to toxicity**

|  |  |  |
| --- | --- | --- |
| **Medicine** | **year** | **Examples of serious and unexpected AE leading to withdrawal of medicine** |
| Thalidomide | 1965 | Phocomelia |
| Practolol | 1975 | Sclerosing peritonitis |
| Clioquinol | 1970 | Subacute nephropathy |
| Benoxaprofen | 1982 | Nephrotoxicity, cholestatic jaundice |
| Terfenadine | 1997 | Torsade de pointes |
| Rofecoxib | 2004 | Cardiovascular effects |
| Veralipride | 2007 | Anxiety, depression, movement disorders |

**Drugs and the adverse reactions identified after the drug marketed.**

|  |  |
| --- | --- |
| **Medicine** | **Adverse reaction** |
| **Amino phenazone (Amidopyrine)** | **Agranulocytosis** |
| **Chloramphenicol** | **Aplastic anemia** |
| **Clioquinol** | **Myelo-optic neuropathy** |
| **Erthromycin estolate** | **Cholestatic hepatitis** |
| **Fluthane** | **Hepatocellular hepatitis** |
| **Methyl dopa** | **Hemolytic anemia** |
| **Oral contraceptives** | **Thrombo embolism** |
| **Practolol** | **Sclerosing peritonitis** |
| **Reserpine** | **Depression** |
| **Statins** | **Rhabdomyolysis** |
| **Thalidomide** | **Congenital malformations** |

**The Purpose of Pharmacovigilance system is:**

* Collection of medication related errors.
* Analyze the errors
* Evaluate and implement any further course of action and implement the interventions.
* Protects and promotes the Public safety
* Prevents the preventable errors.

**Pharmacovigilance in Europe:**

* Pharmacovigilance system in Europe is coordinated by the European Medicines Agency (EMA) and conducted by the National Competent Authorities (NCAs).
* The EMA maintains and develops the pharmacovigilance database comprising all suspected serious adverse drug reactions observed in the European region.

**Pharmacovigilance in United States**

* It’s a Multifaceted approach in USA.
* The US Food and Drug Administration (FDA) receives reports about adverse drug reaction and takes appropriate actions for drug safety.

Finally: Am I safe with medicines?