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EVOLUTION AND DEVELOPMENT OF PHARMACOVIGILANCE ACROSS WORLD

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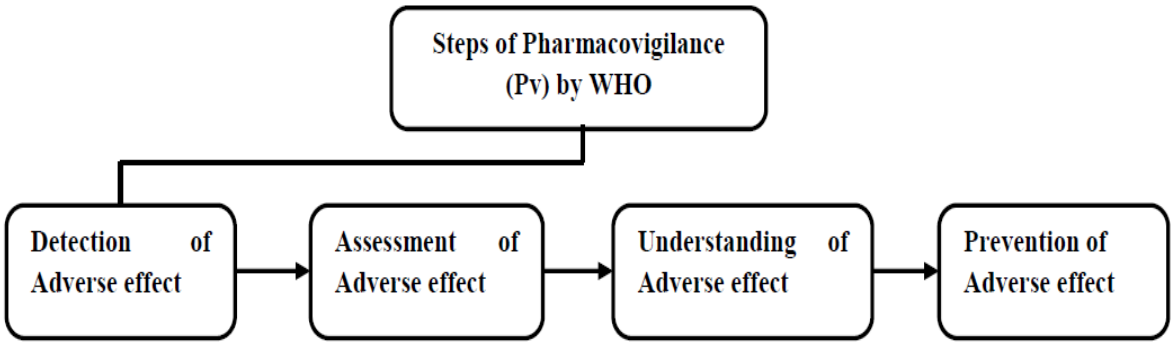
ABSTRACT

In simple terms the definition defines pharmacovigilance as the processes and science of monitoring drug safety and taking action to reduce risk and maximize profits. Safety-related monitoring is needed to identify known and non-invasive backdrops and to assess the safety and efficacy of medical products during clinical trials and during shipping. Pharmacovigilance is the arm of patient care. It aims to achieve the best possible outcome with medication. Nobody wants to harm patients, in any case, sadly, due to many different factors, any medicine sometimes does this. History of pharmacivigilance started 170 years ago on Jan 29 1848. The recorded stages help us to comprehend why pharmacovigilance helped us to accomplish such significant outcomes for man's health and for pharmacology itself, and to distinguish the difficulties that anticipate Pharmacovigilance in future years. In this article it is mentioned the achievements that prompted the advancement of Pharmacovigilance exercises in the only remaining century.

KEYWORDS: Pharmacovigilance, drug safety, efficacy, history.

1. INTRODUCTION

The safety concern about drug is now a top priority, and is actually the first hurdle to deal with a pharmaceutical company to make any drug on the market. To ensure the security of another medication item after a marketing authorization, there are provisions to safely monitor drug safety as part of regulatory requirements.[1] Pharmacovigilance emerged after a largely neglected area of drug safety.[2] Pharmacovigilance is a combination of two port names; Pharmakon is a word that means drugs or drugs substance and vigilare is a latin word that means to keep a watch, so pharmacovigilance is to keeping a watch on a drug.[3] According to WHO's definition of pharmacovigilance is characterized as "the science and exercises related to the detection, testing, comprehension and counteraction of unfavourable impacts or other drug-related problem".[4]



In simple terms the definition defines pharmacovigilance as the processes and science of monitoring drug safety and taking action to reduce risk and maximize profits.[5] Safety-related monitoring is needed to identify known and non-invasive backdrops and to assess the safety and efficacy of medical products during clinical trials and during shipping. Pharmacovigilance is the arm of patient care.[6] It aims to achieve the best possible outcome with medication. Nobody wants to harm patients, in any case, sadly, due to many different factors, any medicine sometimes does this.[7] A good pharmacovigilance will identify the risk within a very short time after the drug has been sold and will help stop and / or identify risk factors. If successfully passed, this information allows for a conclusions based on evidence-based support that may prevent side effects and will ultimately help each patient receive higher-cost treatment in the health system.[7] Pharmacovigilance is nothing new in India and infact have been going on since 1998.

2. Origin of pharmacovigilance

A new Step forward in this field happened after an incident occurred in 1937. In that year, Sulfanilamide (Prontosil) was launched as a syrup containing diethyleneglycol as solvent, it was used since 1932 for the treatment of streptococcal infections.[8] Before launching safety and efficacy was not evaluated resulting death of 105 individuals (34 children and 71 adult). Diethyleneglycol was found as cause of this tragic incident. This tragedy fetched Food Drug and Cosmetic Act which was approved in 1938. According to this Act each pharmaceutical product manufacturers would have to show significant safety of the drug product before releasing them in market.[9]

The Thalidomide disaster is another breakthrough in the beginning and establishment of pharmacovigilance.[10] In 1957 thalidomide was introduced and it was widely prescribed as an supposedly harmless treatment for morning sickness and nausea.[11] It was examined in approximately 300 patients without toxicity. Soon it was resulting congenital abnormality which known as phocomelia and caused several severe birth defects in children of women who had prescribed this medicine during pregnancy in west Germany.[12] In 1962 thalidomide was discontinued after reports of several cases of phocomelia. Later the Kefauver-Harris amendment was passed in same year; according to amendment there should be scientific evidences of safety and efficacy before administering any drug to humans.[13] In 1968 WHO's drug monitoring program started at worldwide level. At first 10 countries established national reporting systems for reporting of adverse drug reactions (ADRs) at pilot project scale. Presently 86 countries have participated in this program, which is harmonized by WHO at its collaborating centre in Uppsala, Sweden. All collaborating centres are responsible for maintaining worldwide adverse drug reaction database. The current database contain more than 4 million ADR reports.[14]

3. History of pharmacovigilance

Pharmacovigilance began around 170 years back, despite the fact that it was not yet named as such around then. Pharmacovigilance era in India began in 1986. An official Adverse Drug Reaction (ADR) monitoring process was initiated with 12 regional centres, each regional centre covers a population of 50 million.[10] However the impact was not too significant. Later in 1997, India got connected with World Health Organization (WHO) and Adverse Drug Reaction (ADR) inspection programs based at.[15] Uppsala, Sweden. The impact,

however, was not as significant as expected. In 2005 India became part of World Bank Funded National Pharmacovigilance (NPPV) and started functioning.[15,16,17]

In 2005 the National Pharmacovigilance program (PvPI) was launched and oversee by the National Pharmacovigiance Advisory Committee (NPAC) in Central Drugs Standard Control Organization (CDSCO), New Delhi India.[10] It is divided in two zonal centers, first is North-East zonal centre which located in Department of Pharmacology, All India Institute of Medical Science New Delhi India and second is South-West zonal centre which located in Department of Clinical Pharmacology, Seth GS Medical College and KEM hospital, Mumbai India.[18] These zonal centers were established to gather information from all over countries and dispatch it to the committee as well as to the Uppsala monitoring centre (Sweden). There were three regional centers that who had to Mumbai or New Delhi centre. Presently the Number of Peripheral centre is 26; who has to report the data to corresponding regional centre.[19] Patient safety was first time discussed when the Biologics Control Act was passed, 1902.

Table 1: Historical event of pharmacovigilance.

Year	Historic timeline
1747	First known clinical trial conducted by James Lind, demonstrate usefulness of lemon juice in impeding scurvy.
1848	**Accidental chloroform death**[20] Hannah's death was caused by chloroform
1902	**Biologics Control Act**[21,22] It passed in 1902 by the USA because many deaths were caused by vaccination with tetanus diphtheria.
1906	**Pure Food and Drug Act**[23] Approved by the US Congress, to prohibit the manufacture, sale, or transportation of food that is warmed or ill-treated or poisonous or illegal, drugs, drugs, and alcohol, and to control overcrowding there, and for other purposes. The bill was passed after much public pressure came from the novel by journalist Upton Sinclair exposing bad practices in the meat business in Chicago.
1937	**Sulphanilamide Elixir**[24] USA (sulfanilamide) with solvent diethyl glycol tragedy. Sulphanilamide result death of more than 100 children due to toxicity.
1938	**Federal food, drug and cosmetic act**[25] It was introduced and the public health system was redesigned.
1949	**Council for International Medical Sciences Organizations (CIOMS)**[26] It has been developed together by WHO and UNESCO to promote also, advance worldwide exercises in the field of biomedical science, particularly where the participation of international organizations and national organizations is considered appropriate.
1950	Apalstic anemia disclose due to chloramphenicol toxicity.

1955	The Gastrointestinal toxicity of ASA was confirmed.
1961	**Thalidomide Tragedy**[12] McBride's report on thalidomide poisoning
1962	**Kefauver-Harris**[27] This amendment was passed to the US Congress as a response to the thalidomide disaster. The law required evidence of drug activity and safety before selling.
1963	16th world health congregation recognize essential to quick action on Adverse Drug Reaction (ADRs).
1964	**Yellow Card Scheme**[28] The yellow card was edited in the UK
1965	European law was introduced (EC Directive 65/65).
1967	**WHO resolution**[29] WHO launched a worldwide drug monitoring program Resolution 20.51 laid the foundation for the international ADR monitoring program.
1968	**Medicines Act**[30] Established the UK to administer control of human and animal medicine, including manufacturing and distribution. International Drug Monitoring project research by WHO (Pilot Scale).
1973	**Pharmacovigilance System**[31] The French Pharmacovigilance system was implemented.
1982	**Benoxaprofen**[32] Removed from the market in the UK and USA after being linked to 3500 adverse effects and 61 deaths. To show that despite the progress and efforts to prevent disasters, this is still possible and great care is needed to ensure the safety of patients.
1986	India's ADR monitoring system is proposed (12 regional centers)
1990	**CIOMS – 1**[33] CIOMS - 1: International detailing of unfavorable medication occasions issued.
1991	**European Rapid Alert System**[34] This system signed to have the power to determine early exchange of information relating to safety risks related to medical products. Reduced the delay in operation of safety features such as Sulfanilamide elixir in 1937.
1995	**European Medicines Agency** EMA was established
1996	At global standard level clinical trials conducted in India.
1997	India tied with WHO Adverse Drug Reaction inspection Program.
1998	Beginning of Pharmacovigilance in India.
2001	**EU Clinical Trial directives**[35] Eudravigilance was supported
2002	67th National Pharmacovigilance centre was established in India.
2004-05	National Pharmacovigilance program successfully launched in India.
2005	Achievement of structured clinical trials in India.
2009	**Black Triangle**[36] The MHRA Black Triangle scheme to report all suspected drug reactions to selected drugs. Pharmacovigilance Program (PvPI) Started in India.
2012	**Good Pharmacovigilance Practice (GvPs)**[37] New European Pharmacovigilance law (directive 2010/84 / EU)

	Best practice of Pharmacovigilance (GvPs) Release of this volume 9A. It has expanded and clarified the PV obligation of trademark owners. Regularly renewed and available for public consultation.
2014	**New Clinical Trial Regulation**[38] Strongly signed to replace 2001 EU-CTD. Scheduled implementation of all member states.
2016	**BIA 10-2474**[39] A BIA study of 10- 2474 in France led to deaths and hospitalization in five healthy volunteers, following an increase in capacity in the new group. The ANSM Committee, made six recommendations, and invited European and international regulators for consideration.
2017	**EudraVigilance**[40] New Eudravigilance format

Table 2: Progress of pharmacovigilance in india according to year.

Progress of pharmacovigilance in India[41]	
2010-2011	First phase
2011-2012	Expansion and Consolidation Phase
2012-2013	Expansion and maintenance phase
2013-2014	Expansion and optimization phase
2014-2015	Excellence phase

4. Need of pharmacovigilance

Pharmacovigilance is referred to as drug monitoring, drug surveillance and post-marketing surveillance. Operation in pharmacovigilance including; detection and reporting of ADRs, data input in software (Vigiflow), analysis of data local, national, and worldwide level, signal generation and gathering information related newly detected adverse outcome from health care provider through various sources.[42] Pharmacovigilance is self-supporting field; it starts from clinicians and ends at clinicians.

5. Aim of pharmacovigilance

5.1 General aim

- Improve patient consideration and wellbeing comparable to the utilization of drugs and all clinical and paramedical mediations.
- Enhance general health programs by gathering great data on the impacts of medicines and grow early admonition of issues which may influence the achievement of the program.
- Improve general health and safety comparable to the utilization of medications.
- Detect issues identified with the utilization of prescriptions and convey the discoveries in an ideal way.

- Contribute to the appraisal of advantage, mischief, viability and danger of prescriptions, prompting the anticipation of damage and expansion of advantage.
- Encourage the protected, judicious and more powerful utilization of medications.
- Promote understanding instruction and clinical preparing in Pharmacovigilance and its compelling correspondence to general public.

5.2 Specific Aim

- The distinguishing proof of signs of serious adverse drug reactions (ADRs) following the presentation of new medication or medication combination.
- The appraisal of signals to assess causality, clinical significance, recurrence and conveyance of ADRs specifically population groups.
- The fast recognizable proof of events those are probably going to influence adherence to treatment and assurance of their rates and the hazard factors that make these events almost certain with the point of diminishing their occurrence.
- The computation and assessment of paces of events so that: hazard can be estimated.
- The safety of medicines can be looked at and educated decisions made.
- Risk components can be obviously distinguished.
- The interchanges with and suggestions to authorities and the general public.
- The appropriate reaction or activity as far as medication enrollment, drug use as well as preparing and training for health professionals and in general population.
- The estimation and assessment of result of reaction or of activity taken.
- The appropriate input to the clinicians who gave the data.

6. Objectives of pharmacovigilance[18]

The main purpose of pharmacovigilance is to identification of the unpredictable response of pharmaceutical products after the presentation of the product is important.

6.1 Short-term objective: To promote the ADR notification culture.

6.2 Medium-term objective: Involve healthcare professionals and organizations working with drug monitoring and information dissemination processes.

6.3 Long-term objective: To achieve operational efficiencies that would enable ASU's drug NPP to become a benchmark for worldwide medication testing activities.

7. Scope of pharmacovigilance[43]

- Long-term monitoring of drug safety to detect previously unknown risks
- Measure changes in profit and risk
- Provide relevant information to users
- Take action to promote safe use
- Monitoring the effect of the action taken (black boxed warning for use of patient categories and drug withdrawals)

8. The uppsala monitoring centre

The primary function of Uppsala monitoring centre include management of international database of ADR reports which are received from national centres.[14] The Uppsala monitoring centre has established systematized reporting system for all national centres to facilitate communication between countries to encourage rapid identification of signals.

9. CONCLUSION

Pharmacovigilance is the best way to guarantee the safety of medication all through the lifecycle. Its significance is a lot of pivotal as the clinical trials have confinement to distinguish the uncommon and exceptionally uncommon ADRs. Healthcare professionals are the primary reporters of the ADRs; but, there are high rates of under- reporting revealed comprehensively. It is the significant difficulties. Each reporting by healthcare professionals is significant; despite the fact that, attention on the serious unlabelled kind of ADRs is more significant. There are noteworthy endeavours on the Pharmacovigilance to make it more practical after the idea has risen.

Consent for publication

Not Applicable.

Conflict of interest

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