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SAFETY SIGNAL IN PHARMACOVIGILANCE

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ABSTRACT

Every drug has a potential to produce adverse effects. Pharmacovigilance focuses on adverse drug reaction (ADR) signals of medicinal product. It ensures that the patients get safe drugs. More than a single report of ADR is required to generate a valid signal. Information in the reports should be of good quality. Identifying signal with the help of event data from any source called as signal detection. It is the process of monitoring safety data. Detection of new risk can have great impact on the benefit-risk profile of the drug. Detection of signal in post marketing is a crucial task. Signal detection depends on the variety of data sources. These sources are analyzed for signal detection purposes. Different ADRs requires different strategies for detection.

Keywords: Pharmacovigilance, Signal, Signal detection, ADR.

INTRODUCTION

WHO defines Pharmacovigilance as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects and any other drug related problem" [1, 2]. Pharmacovigilance assess the risk and benefits of the medicine in order to improve public health. Signal can arise at any time throughout the life cycle of a drug. Thalidomide tragedy happened because of late signal detection in 1960s [3]. Late signal detection affects public health as well as pharmaceutical companies. Main objective of signal detection is to understand benefit-risk profile of drug, protect patients and public health. It is an important activity in Pharmacovigilance, performed to find out whether there are novel or unidentified risks associated with a medicinal product based on data sources. Continuous monitoring of drug is essential to ensure patient safety. Post market monitoring of drug is important because data from pre-marketing study is not sufficient to predict all ADRs [4].

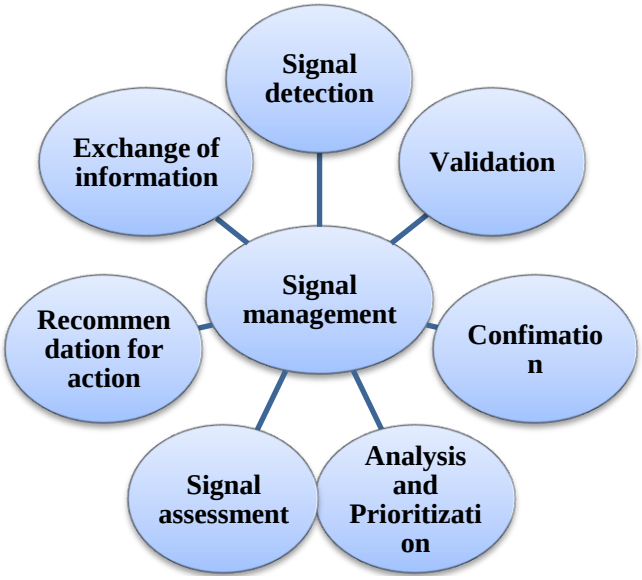
SAFETY SIGNAL

It is the most important activity of Pharmacovigilance. A safety signal is defined as "Any information that is new or previously unknown, which represents a causal relationship between a drug and an event" [5, 6]. Safety signal may be generated from different types of data sources [7]. Signal identification helps in minimizing the risk associated with the use of marketed medicine [8]. Identification of signal is the main aspect in post marketing drug surveillance [9]. When a new signal is detected, it requires further evaluation to determine whether an actual causal relationship exists [10]. . Early signal detection plays essential role to protect public health. To generate a valid signal, more than one report of adverse events is required [11].

SIGNAL MANAGEMENT

Signal management is a multistep process. It is the most critical process. It involves signal detection, validation, confirmation, analysis and prioritization, signal assessment,

recommendation for action and exchange of information [12]. It helps in identifying new or altered hazards related to the drug. It prevents the outbreak of serious adverse reactions before harming the community. All the relevant data needs to be recorded and documented in a consistent manner.



Signal detection

Signal detection is the complex process in Pharmacovigilance. It helps in identifying signal as early as possible. Its aim is to recognize potential harm relating to the use of particular drug [13]. Signals have qualitative and quantitative aspects [14]. Accurate and careful signal identification is extremely important. It plays an important role to assess the safety of drug [15]. The process of identifying signal follows a specific methodology to monitor safety data. To protect public health against the adverse effects of drugs it is necessary to quickly detect the signal [16]. Signal detection is an effective approach used in the supervision of drug safety. Continuous monitoring of drug safety is done to determine whether there has been any change in its safety profile or not [17]. Detection of signal is based on the analysis of reports received from various sources [18].

Data sources for Signal Detection

1. **Spontaneous Reports-** This serves as an effective source in Pharmacovigilance. Spontaneous reporting plays vital role in early detection of safety signal [19]. It helps in identifying serious and rare ADRs [20]. Reporting of ADRs mainly relies on the healthcare professionals [21]. These reports provide essential data regarding ADRs of marketed drug [22].

2. **Individual Case Safety Reports (ICSRs)-** Individual case safety report is a report that describes adverse event in an individual patient [23]. It shows first line of evidence by determining causal association between drug and adverse event [24]. ICSR is the primary basis to identify the unknown risk associated with medicine [25]. A valid report must include an identifiable patient, a reporter, suspect drug and an adverse event [26]. All reports are stored in WHO database i.e. Vigibase.

3. **Periodic Safety Update Report (PSUR)-** Periodic Safety Update Report is a report on safety information of a registered medicinal product which is submitted to the regulatory authority over a specific period of time [27]. It is an important tool for

identifying new signal [28]. It provides an update on risk-benefit profile of a medicinal product [29].

4. **Record linkage**-Record linkage is the linkage of various records relating to same individual [30]. It is the process of assembling the outcomes of drug exposure into a single database [31]. It helps to access the relationship between drug exposure and outcome.

Signal validation

It is the process of assessing the facts that supports identified signal. This is done to prove that there is enough information to express the presence of a new possible causal association [32]. This known association may give rise to a new signal.

Signal confirmation

Validated signals are entered into European Pharmacovigilance Issues Tracking Tool (EPITT) [33]. It undergoes further examination to ensure that the validated signal is confirmed or not. Confirmed signal should be examined by Pharmacovigilance Risk Assessment Committee (PRAC) [12].

Analysis and Prioritization

This step is done to determine the signal which may have a harmful effect on public health. It also helps to identify signals which affect the benefit-risk profile of the drug [34]. It helps to determine the seriousness of the association of drug and event.

Signal Assessment

This step involves assessment of all available information relating to safety signal to determine whether or not there is a relationship between the drug and adverse event [35]. It step determines whether additional data is required or not. It includes assessment of the available pharmacological, non-clinical and clinical information.

Recommendation for action

Pharmacovigilance Risk Assessment Committee (PRAC) determines whether there is need for further investigation and risk minimization activities [12]. Additional information is required for prioritising and assessment of signals. This step involves activities to verify signals.

Exchange of information

All the information on signal needs to be managed and documented in an appropriate and consistent manner. The marketing authorization holder receives information on validated signals and updates the product information. It is the responsibility of MAH to provide such information to the competent authority, health care professionals, patients and the public.

CONCLUSION

Signal detection is the main aspect of Pharmacovigilance. Different sources are used to detect safety signal. It provides early warning of serious adverse reaction of new drugs. Information arise from different sources should be of good quality. Even a single report of an unexpected adverse reaction may contain sufficient data to raise a signal. It includes monitoring of adverse events which are actually related to the medication being provided. Signal detection does not depend on the single method. It requires planning in which various activities are involved. These activities are required for patient safety. Overall goal of signal detection is to protect patient and public health.

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