

# Research in Pharmacy and Health Sciences

## Review Article

### Importance of Literature in Pharmacovigilance: A Review

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#### ABSTRACT

Pharmacovigilance is to track and detect new adverse drug reactions mainly due to drugs or due to any other chemical substance or similar entity. The knowledge of a drug's adverse reactions can be increased by various means, including spontaneous reporting, intensive monitoring and literature searching. But, in this review, we discuss how the medical literature plays a crucial role in pharmacovigilance. It is necessary to improve systematic reviews of adverse drug reactions. As literature is one of the vital sources of signal detection, it is essential for pharmaceutical companies to establish pharmacovigilance programs that capitalize on the best available information from multiple data sources. So, it is important to develop a prototype that first reproduces and standardizes search strategies to have a better information retrieval. Marketing-authorization holders (MAH's) are encouraged to be aware of publications in their local and international journals frequently or according to local regulation and to bring attention to the company safety departments also.

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#### INTRODUCTION:

Pharmacovigilance is defined by the World Health Organization (WHO) as 'the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem' [1]. The Pharmacovigilance has been known to possess various roles like, identification, estimation and documentation of adverse drug reaction; contribution towards reducing the risk of drug-related problems in healthcare systems and understanding of factors and mechanisms which are responsible for drug-related injuries [2]. A properly working pharmacovigilance system is essential if medicines are to be used safely. However, despite all their benefits, evidence continues to get those bigger adverse reactions to medicines which are common, yet often preventable, cause of illness, disability and even death. Pharmacovigilance depends on targeted, up to date product information and adverse event reporting to meet regulatory requirements. The spontaneous reporting system is a major contributor in drug safety information. But, the other sources of information are of interest to improve our knowledge of adverse drug reaction [3]. The medical literature is one of them, which include medical journals, reference books, national adverse drug reaction bulletins etc.

The scientific and medical literature is a significant source of information for the monitoring of the safety profile and of the risk-benefit balance of medicinal products, particularly in relation to the detection of new safety signals or emerging safety issues [4]. This review article discusses about the importance of literature in Pharmacovigilance.

#### Current scenario

Pharmacovigilance procedures are necessary for evaluation of medicine. Pharmacovigilance thought to be based on spontaneous reporting but it is more than spontaneous reporting alone [5]. Currently, with widespread use of internet, information retrieval, extraction and analysis of individual cases reports or of other information (Literature cases) are a challenge for pharmacovigilants [6].

The worldwide experience includes published scientific and medical literature that could impact on the risk-benefit assessment of the product under evaluation. This information is used to update the benefit/risk analysis, the Investigator Brochure (IB), report expedited cases to regulatory authorities [4]. The ICH E2D Guidelines provides guidance for literature search are as [7]:

- Accessing of systematic literature reviews or reference databases.
- Frequency of literature search should be in every 2 weeks.
- Abstracts from meetings and drafts manuscripts should be included.
- Awareness of publications in local journals.

Medical literature for safety information seems to still be confusing to companies as inferred by Pharmacovigilance audits and inspection. The main challenges while literature reviews are [8]:

- Search strategies with different keywords is main challenge
- Search in local journals, published letters and meeting abstracts of adverse drug reaction

- Search in different international journals like PubMed, Empirica Trace, Embase etc.

Articles relevant to the safety of medicinal products are usually published in well-recognized scientific and medical journals [9]; however, new and important information may be first presented at international symposia or in local journals.

### Importance of literature for Pharmacovigilance

Pharmacovigilance system plays a vital role in increasing public awareness of drug safety. Literature has been widely accepted to possess a significant role in early observation of the risk associated with the drug. The drug Withdrawal from the market for safety reason is a serious and sometimes complex decision [10]. The scientific evidence supporting drug withdrawals in the past years is critically appraised. Usually literature reports have more detailed information and being medically confirmed for signal detection.

Publish case reports and case series are very important source of signals, the letter from McBride to 'The Lancet' in 1961 raising concern about the teratogenicity of thalidomide is an excellent example [11-12]. Screening of Abstracts from the literature helps in identification of potential, new and significant safety findings for inclusion in PSURs. PSURs also includes lack of efficacy, asymptomatic overdose, abuse or misuse and medication error cases which provides only by the literature. Early detection of safety signal from literature is necessary to identify the risk associated with the products [13]. Number of recent high profile drug withdrawals point towards this fact.

TABLE 1: List of Withdrawal drug from the market due to Literature reporting [14].

### Future Scope of literature

Literature reporting has been shown to be a useful tool in generating signals [15], but the relatively high number of reports received for a specific adverse drug reaction makes it most useful in providing key information of patient's diagnoses, lab tests performed, medications prescribed, and their outcome that would facilitate the sound clinical decision making in a timely manner [16]. In the past few years there has been a major push in trying to change the existing pharmacovigilance systems in order to meet the demands of the future. Scientific support of pharmacovigilance is needed to ensure that it will develop as a scientific discipline and thereby contribute to the innovation needed in this field [17]. The pharmacovigilance of tomorrow must be able to identify new safety issues without delay.

### Advantages

- The literature reports are detailed and contain enough information for appropriate assessment [18].
- Literature will help to collect accurate information on areas of particular interest e.g. pregnancy, children and the elderly [19].
- The chances of biasness are very rare in literature cases.
- It is the method that provides complete lab information including physical examination, Diagnosis of particular disease etc.
- The data relevant to drug abuse, misuse, overdose and death are easier to find in literature search.

- It allows getting more than one case reports for a particular drug in a published article.
- The causality is already mentioned in some cases.
- Case series in literature provides interesting characteristics in a group of patients.

### Disadvantages

- One of the key challenges in literature searching is to ensure that the strategy used for searching is robust enough to capture all relevant hits.
- Authors may have published the case in local journals followed by publication in a peer reviewed journal and also reported prior to regulatory authority. So, it will enhance the chances of duplicacy.

### CONCLUSION

Although spontaneous reporting is a major data contributor but, literature is still a major source of information to evaluate drug safety. Usually, Signal detection activities have also mainly been performed on spontaneous reporting from healthcare professionals and national health regulatory agencies, but the other relevant source of information is scientific literature that helps in evaluation of the benefit-risk assessment. Content is sourced from journals, scientific meetings, media releases, regulatory agency websites, and bulletins from the National Centers that participate in the WHO International Drug Monitoring Program. Literature could play a role in identifying individual risk factors for the occurrence of certain ADRs. So, to compensate the limitation of spontaneous reporting the literature searching should be more focused.

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**Table No: 1 List of drugs withdrawal from the market due to literature reporting**

Sr. No.	Drug (INN)	Adverse Reaction	Year of withdrawal
1.	Pirprofen	Liver toxicity	1990
2.	Terodiline	Cardiac arrhythmias	1991
3.	Cinchophen	Liver toxicity	1992
4.	Glafenine	Hypersensitivity reactions	1992
5.	Bendazac	Liver toxicity	1993
6.	Naftidrofuryl	Cardiac and Neurotoxicity	1995
7.	Zipeprol	Abuse and Dependence	1995
8.	Minaprine	Abuse	1997
9.	Mibefradil	Drug-drug interactions	1999

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