



Tools to Improve Reporting of Adverse Drug Reactions – A Review

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ABSTRACT

Pharmacovigilance is a process that needs time, vision, dedication, expertise and continuity. Underreporting of spontaneous adverse drug reaction (ADR) is a threat to pharmacovigilance. The major factors found to be responsible for underreporting of ADR include inadequate risk perception about newly marketed drugs, fear factor, diffidence, lack of clarity of information on ADR form about reporting, lethargy, insufficient training to identify ADRs, lack of awareness about existence of pharmacovigilance program and ADR monitoring center in the institute and inadequate risk perception of over-the-counter (OTC) product and herbal medicines. ADR reporting is an important aspect of an efficient and effective pharmacovigilance program. Despite comprehensive and stringent phases of clinical trials and surveillance efforts, unexpected and serious adverse drug reactions (ADRs) repeatedly occur after the drug is marketed. Although Medwatch, Yellow Card, CDSCO form, etc. are the protocol forms of ADR collection and reports, a number of countries design and use their respective ADR forms. The reporting of adverse drug reaction may start locally, perhaps in one hospital, then extend to other hospitals and family practices in the region, and progress step by step into a national activity. The present study focuses on the different tools or ways to improve ADR reporting so as to decrease the physical and economic burden due to ADRs. If any of these methods were implemented there could be a significant change in the reporting level.

Keywords: Pharmacovigilance, CDSCO, Adverse Drug Reaction, ADR Reporting.

INTRODUCTION

To summarize tools to improve ADR reporting. The World Health Organization (WHO) defines adverse drug reactions (ADRs) as "a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function".¹ ADRs lead to considerable morbidity and mortality worldwide. ADRs were shown to be directly or indirectly.² In addition to the human costs, ADRs have a major impact on public health by imposing a considerable economic burden on the society and the already stretched health-care systems.^{3,4} The contribution of health professionals, in this regard, to ADRs databases is enormously significant and has encouraged ongoing ascertainment of the benefit-risk ratio of some drugs.^{5,6} as well as contributed to signal detection of unsuspected and unusual ADRs previously undetected during the initial evaluation of a drug.^{7,8} In spite of these benefits, under-reporting remains a major draw-back of spontaneous reporting concluded by Lexchin and Lopez.^{8,9}

It is estimated that only 6–10% of all ADRs are reported.^{10,11} in a study conducted by Lopez et alit was found that the high rate of under-reporting can delay signal detection and consequently impart negatively on the public health. Many factors are associated with ADRs under-reporting among health professionals. These factors have been broadly classified as personal and professional characteristics of health carers, and their knowledge and attitudes to reporting.⁹ ADRs have a major impact on public health, reducing patients' quality of life and increasing mortality and morbidity, whilst at the

same time imposing a considerable financial burden on health care systems. Although some ADRs become apparent during clinical trials, many ADRs are not identified until the post-marketing stage. The sample sizes in most clinical trials are often too low for the detection of rare ADRs, and are unable to detect ADRs with long latency periods. Most systems utilized for post-marketing drug surveillance rely primarily on spontaneous reporting. Examples of such systems include the Yellow Card scheme in the UK, which is managed by the Medicines and Healthcare products Regulatory Agency (MHRA), Medwatch in the US, managed by the Food and Drug Administration (FDA) and the Uppsala Monitoring Centre in Sweden, which is the base for the WHO program for International Drug Monitoring. Typically, signals are identified using disproportionality measures such as the reporting odds ratio (ROR) which can be used to estimate relative risk, or the proportional reporting ratio (PRR): proportion of spontaneous reports for a selected drug related to a specific adverse outcome, divided by the corresponding proportion for all or several other drugs.

There are several limitations with spontaneous reporting databases. Although spontaneous reporting provides data on a broad spectrum of patients, the absence of a control group and lack of denominator data mean rate of ADRs cannot be accurately calculated.^{12,13} New opportunities involve computer-based surveillance methods particularly for hematological, renal, or hepatotoxic ADRs from either secondary or primary care. The key advantages are systematic flagging of abnormal results which warrant further investigation by the responsible physician. Despite the efforts of DCGI (Drug Controller General of India), and



ICMR (Indian Council of Medical Research) in establishing ADR monitoring centers in many hospitals in the major cities of India and the presence of a large tertiary care facilities, pharmacovigilance is still in its infancy in India. Gross underreporting is the cause of concern for which there may be many causes.^{14,15} The prescribers are aware of the ADRs and the importance of their reporting. However, under reporting and lack of knowledge about the reporting system are clearly evident. Creating awareness about ADR reporting and devising means to make it easy and convenient may aid in improving spontaneous reporting.¹⁶ Pimpal khute et al concluded that increasing awareness about pharmacovigilance will be helpful in improving the status of ADR reporting. Other measures such as making ADR reporting guidelines available in the form of booklets and displaying posters can also play a useful role.¹⁷ In order to improve the reporting by nurses who are primary watchers since they are able to observe the untoward reactions directly they should be well versed in managing and documenting and also reporting them to the reporting centers. A study conducted by Hanafi et al regarding the knowledge attitude and practice on reporting adverse drug reporting on nurses showed that they had little knowledge and poor practice regarding the pharmacovigilance and spontaneous reporting system. Interventions such as holding pharmacovigilance workshops in the hospitals focusing on the aims of pharmacovigilance, completing the Yellow Card and clarifying the reporting criteria are strongly recommended.¹⁸ Although there are some differences in the way various countries handle patient reports of ADRs, the importance of giving the public the opportunity to report and the additional scientific value of the collected data is widely recognized by the countries who participated in the survey conducted by Van Hunsel et al.¹⁹ A closer relationship between doctors and the pharmacovigilance centre and the feedback of the Pharmacovigilance activities in the hospital are also suggested. Attitudinal and cultural changes, whereby ADR reporting is seen as an integral part of the clinical activities of the doctors, are very necessary for a long term improvement of ADR reporting.²⁰

A study by Bandekar et al reveals that the spontaneous reporting form from different countries is inadequate to capture detailed information. Therefore, there should be international guidelines and checklists for the inclusion of mandatory information needed for causality assessment for drafting and designing of spontaneous reporting form by countries. Spontaneous ADR reporting form is a major tool of the pharmacovigilance system of any country. The ADR reporting forms is different for different countries thus leading to a lot of discrepancy in data captured by it. The WHO ADR monitoring centre collates information it receives from different countries. Non-uniformity of the form leads to WHO database itself being incomplete. Thus there is a need to harmonize the ADR reporting forms of all the countries to capture complete adverse event-related information.²¹ A new scientific tool has been developed to monitor and report ADRs. Trigger tool is one

of the active data collection process which triggers to identify the ADR in a quicker fashion. Use of this tool showed incidence of 18.1% increase in identifying and preventing ADRs. Trigger tools proved to be one of the best scientific tool in identification and reporting of ADRs in this study. Scientific validation of trigger tools is required to further utilize in large scale studies.²² Good levels of reliability were obtained between independent nurse reviewers at the case-level for both the occurrence of any trigger and the identification of an adverse event. Nurse reviewer agreement for individual triggers was much more varied. Higher agreement appears to occur among triggers that are objective and consistently recorded in selected portions of the medical record. Individual triggers also varied on their yield to detect adverse events. Cases with adverse events had significantly more triggers identified (mean 4.7) than cases with no adverse events (mean 1.8). The trigger methodology appears to be a promising approach to the measurement of patient safety. However, automated processes could make the process more efficient in identifying adverse events and has a greater potential of improving care delivery and patient 'outcomes'.²³ A multidisciplinary expert panel was able to reach consensus agreement on a list of signals to detect potential ADRs in nursing home residents. The results of this study can be used to prioritize an initial list of signals to be included in paper or computer-based methods for potential ADR detection.²⁴

To ensure patient safety, each patient with an ADR was provided with an 'ADR alert card' at the time of discharge, which was kept by the patient and presented to other health care providers when needed in the future. To get sustained results from this strategy for reporting ADRs, there should be strong collaboration between the Department of Pharmacology and other clinical departments. ADR monitoring should be a compulsory part of training for postgraduate students in the Department of Pharmacology, as a part of their M.D. curriculum. Lectures should be taken at the undergraduate level on the importance of pharmacovigilance and ADR reporting. Students could be given an exercise such as to report three ADRs in their term which they can do during their ward postings. Interns can be taught about ADR reporting during their Internship Orientation Programme, so that they too can assist the resident doctors working in various clinical departments. The Department of Pharmacology should provide pharmacovigilance awareness programmes to all the nurses and other allied health staff working in the hospital. Assistance should be provided by the CDSCO to sponsor ADR boxes, notification forms and ADR alert cards many developed countries but may be a challenge for public hospitals in developing countries like India under the National Pharmacovigilance Programme (NPP). This strategy if adopted by all the government hospitals as well as government medical colleges could be a useful stepping stone in generating a genuine ADR database for our population. All marketed drugs could be monitored



simultaneously. Another way could be a computer based online reporting system which is utilized by many developed countries but may be a challenge for public hospitals in developing countries like India.^{25,26} A study conducted by Mrinmoy and Vijay suggested few techniques through which ADR reporting can be increased and made accessible to all. Easy and free availability of prepaid reporting forms and other modes of reporting, Duly acknowledging the receipt of ADR reports telephonically or through personal communication Providing journal articles, ADR bulletins, newsletters to reporters, Actively involving the PV center staff in scientific meetings, undergraduate and postgraduate education Collaborating with other PV committees, Collaborating with professional associations, Utilizing PV data for development of clinical pharmacy and clinical pharmacology.²⁷

CONCLUSION

Even though there are many methods through which reporting of ADRs can be improved, it is the duty of the health care professionals to feel the responsibility and understanding its importance. Continuous awareness programmes, maintaining a healthy relationship with the department of pharmacovigilance, making ADR reporting mandatory, providing drop box, having intercom to reporting centers enhances ADR reporting rates. Providing identifying trigger tools can also be implemented which has shown drastic improvement in the ADR reporting rate. Local government should announce awards for the reporters so as to encourage reporting. WHO should provide uniform ADR reporting form throughout the world which should be easy and take less time.

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