



REVIEW ARTICLE

Stimulated adverse drug reaction reporting in pharmacovigilance: Indian perspectives

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ARTICLE INFO ABSTRACT



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Introduction: The voluntary reporting of adverse drug reactions requires continuous stimulation and motivation.

Methods: It is achieved by the development of a positive approach towards pharmacovigilance among healthcare professionals so that adverse reaction reporting becomes an accepted and understood routine.

Results: In summary, the various strategies developed and made available in India to stimulate reporting, promotion, educational interventions/ awareness program/academics, hospital-based ADRs reporting, establish a culture of reporting.

Conclusions: These exclusive strategies progress the reporting rate in India by altering the mindset of healthcare professionals, undergraduates, and consumers towards safety reporting.

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Introduction

Pharmacovigilance is known for drug safety monitoring. Spontaneous reports are the only source of safety information in almost all countries including India. The current reporting status in India is very low in comparison to developed countries like the US, UK, and Canada. There are less than 8000 monthly reports to the Pharmacovigilance Programme of India for over a billion population in India.¹ Information received through the spontaneous reporting system is not adequate both quantitatively and qualitatively. Under-reporting is the major issue that affects the quantitative estimates of adverse drug reactions (ADRs). This might have an impact

on patient safety in clinical practice. Spontaneous reporting systems have the problem of under-reporting and this has been seen globally. In spontaneous systems, serious ADRs are more likely to be identified, and there are high chances of missing non-serious ADRs. Only about 5-10% of serious ADRs are reported globally (Hazell *et al.*, 2006). The underreporting may due to heavy workload, lack of interest, poor knowledge on reporting form, professional obligations, fear to report, conflicts, unsure of causal association, lack of awareness and beneficence, respect for autonomy, diffidence, lethargy, personal benefit, and ignorance (Khan *et al.*, 2013). Correspondingly, ADRs often go unnoticed as it is difficult to distinguish the adverse event and the



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symptoms of certain diseases, sometimes withdrawal symptoms of disorder mask the adverse event as well (Klopotoska *et al.*, 2013). Additionally, another important challenge is about quality of reports. Current reporting systems are hampered by inadequate information such as action is taken and the outcome of the reaction, which limits our ability to find the causal relationship between drugs and ADR.

Importance of Reporting

Clinical trials are not able to explain all adverse reactions associated with medication due to limited sample size, controlled environment, and limited time of drug exposure. Additionally, special types of the population are not exposed to the drug in clinical trials. Therefore, post-marketing safety surveillance systems are needed to find out unreported safety concerns during the pre-marketing phase⁵. Prompt reporting is important for drug safety monitoring. Under-reporting delays early detection of drug safety issues. For instance, about seven million patients were exposed to fenfluramine before identification of valvular heart disease (VHD) associated with this medication, which subsequently led to the withdrawal of

the drug from the market (Pillarset *al.*, 2008). From the Indian database of ADRs from January to December 2018, only 0.01% were new safety alerts^{7,8}. Few new drug safety alerts namely artemether+lumifantrine induced Steven Johnson Syndrome (SJS), and lamivudine induced hearing loss were identified as global drug safety signals by World Health Organization. However, these alerts are still not accepted as safety signals in the Indian context due to underreporting.⁹ Furthermore, reporting helps to detect or hypothesize rare and delayed potential hazards with medications. Contributing large database will in turn help to enhance patient care and also help healthcare professionals better understanding the rational use of medications. In light of the under-reporting of ADRs being an important concern, we aim to discuss strategies that can improve reporting by stimulating healthcare professionals and substantiate.

Methods to stimulate reporting rates

Various strategies have been proved to stimulate the reporting from healthcare professionals as summarized in **Table 1**, and the advantages and disadvantages of these models are presented in **Table 2**.

Table 1: Strategies to stimulate reporting of adverse drug reactions from healthcare professionals.

Strategies	Salient points
Promotion	Public awareness among healthcare professionals and consumers about safety surveillance programs and their importance can increase reporting rates.
	Modes of publicity: website, advertisements, social media (Facebook, Twitter, Flipboard, LinkedIn, YouTube, Flickr, Pinterest), news media (newspapers and television networks), newsletters, posters, job aids, scientific publications, abstracts, and posters at national and international events and social networking sites.
	Black box advisory on safety alerts by the regulatory authority
Educational Interventions/ Awareness programme/ Academics	Undergraduates can be educated during academics by changing their curriculum.
	Educational interventions can be taken to clinical and non-clinical healthcare professionals related to identifications of ADRs, reporting methods, filling reporting forms and channels of reporting
	Conducting lectures/ workshops/ conferences on the importance of spontaneous reporting procedure to catchment areas includes medical institutes, educational institutions, and healthcare facilities to enhance stimulation or sensitization among healthcare professionals and undergraduates.
Stimulation strategies to improve hospital-based reporting ADRs	Training session: Regular training session on adverse events reporting to reminisce by health-care professionals. Online training modules can help more healthcare professionals to participate, and according to time suitable for them. Information of updates on ADRs to physicians, pharmacists, and nurses can make them clinically aware of the newly reported ADRs.
	WhatsApp messages/Emails: Frequent reminder messages through these modes might increase the chance of adverse event/ adverse drug reaction reporting.
	Simplifying reporting process: Adverse reaction reporting forms shall be customized in such a way that everyone can fill them feasibly and timely. Reporting ADRs doesn't alter

their clinical care. Forms should inquire for essential elements (for example, the onset date of adverse reaction, age, and suspected drug and suspected reaction are noted). If required follow-up information shall be collected by the resource person during the evaluation of adverse reactions.

Linking medical records: ADR forms can be attached with medical records, so that healthcare professionals can fill the ADR forms where and when noticed.

Dear doctors letters: Serious, unlisted safety alerts shall be made aware by sending ADR information letter particular to the topic of concern.

A regular visit to outpatient and inpatient services: Responsibility of resource personnel to visit outpatient and inpatient wards regular to increase the interest among healthcare professionals about ADR reporting

Acknowledgment/feedback/token of appreciation: One of the most important attributes is to appreciate the reporter by sending thank you emails, phone calls, messages, and letters. Acknowledging them by newsletter, journals, and bulletins. Encourage them to participate and present in pharmacovigilance conferences and scientific meetings.

Rewarding the reporters: Introducing a new aspect of token of appreciation or rewarding the reporters may enhance reporting trends.

Establishing a culture of reporting

Establishing a reporting culture environment can help care providers to openly discuss, record, and report adverse reactions without any obligations. This may help to establish a robust pharmacovigilance system in any healthcare setup. Ensuring no legal obligation in reporting can make them more confident in reporting. Furthermore, staff can be motivated to speak openly about safety concerns without fear.

Table 2: Advantages and disadvantages of various models of stimulating reporting of ADRs

Strategies	Advantages	Disadvantages
Promotion	Information can be communicated to a large number of the targeted population regarding drug safety monitoring systems, and what, where, when, why, and whom to report the safety concerns. Publicity on drug safety information by regulatory and media can give a call for intervention to risk minimization. Publicity through the social-networking system requires less financial resources gives high output	At times false information can be communicated to the general population through social networking sites. Attention should be paid before publicizing drug-related safety concerns. Some forms of dissemination may be resource-intensive. One has to guard against making consumers and healthcare professionals apprehensive of treatment options.
Educational Interventions/Awareness programme/Academics	Best way to stimulate and promulgate safety information reporting system to the large population through educational activities particularly to undergraduates	Technical and financial assistance is required for proper continuous medical education on pharmacovigilance Required adequate trained and motivated team for dissemination of pharmacovigilance activities Curriculum change may require sustained focus

Stimulation strategies to improve hospital-based ADR reporting	Continuous and frequent motivation can enhance reporting rate. Stimulating healthcare professionals on regular basis can minimize the reporting obligation and thereby increase reporting rate. Developing feasible reporting methods like simplified reporting forms can help in reporting. Also, it can reduce the workload of healthcare professionals for ADR reporting	Classroom training is not possible for practicing doctors due to their busy schedules. Availability of resource person in each hospital setting requires financial assistance. Repeated reminders can be construed as an intrusion Although rewarding techniques may increase reporting rate but may increase the chances of duplicate reports and false reporting.
Establishing culture	Changing mindset towards the reporting sustain the pharmacovigilance reporting	Require high technical and financial assistance is required to establish robust pharmacovigilance culture

Discussion

A study conducted in the US by (Wong *et al.*, 2018) suggested that intense media publicity resulted in a significant increase in reports related to ADRs of zolpidem. According to (Motola *et al.*, 2008) results suggested there was a five-fold increase in reporting rate of Acetylcholine esterase (ACE) inhibitor-induced cough recorded during 1 year period, more than a four-fold increase in ADR reporting rate with musculoskeletal ADRs, which accounts for 60% of total ADRs reported in that respective year. Increased reporting rate of hepatic ADRs from Spanish and Finnish markets was observed after withdrawal of nimesulide. However, these reporting rates were measured after regulatory intervention. According to a review by (Sloane *et al.*, 2015), social media publicity has few challenges on pharmacovigilance and reporting system and drew attention to the negative connotation of medication use besides the actual benefits. Analysis by (Casselset *et al.*, 2003) demonstrated the response from consumers and healthcare professionals on Canadian newspaper coverage suggests that the benefits are reported nearly five times more often than harm (Moynihan *et al.*, 2000) study on new media coverage on benefit-risk assessment on medications, results suggested that the information received in response to news media is inadequate and inappropriately documented.

As per (Dorsey *et al.*, 2010) regulatory actions minimized the risk associated with targeted drugs. Also, study findings explained the decreased use of prescription medication after the regulatory intervention. A retrospective report by (Cassels *et al.*, 2007) projected through newspapers gave a call for interventions to avoid or to minimize the medication errors. In support of this study, authors opine that regulatory and media intervention on drug safety information could minimize the risk in addition to reporting rate (Yong *et al.*, 2009) showed an increase in motivation towards risk reporting

with quality information through media coverage as compared to FDA alerts.

A study suggested by (Cassels *et al.*, 2003) suggested a good response from consumers and healthcare professionals after newspaper coverage of certain medications. Regrettably, at times information promulgated by regulations is inappropriately delivered by media according to the examination of Italian print media published by (Laboliet *et al.*, 2010), According to (Edwards *et al.*, 2011) and (Gavaza *et al.*, 2011), social networking can be an economical and effective way of communication about patient safety information to improve spontaneous reporting of adverse drug events.

(Herdeiro *et al.*, 2004) presented his opinion on educational interventions about pharmacovigilance activities that might enhance the spontaneous reporting rate. (Williams *et al.*, 1999) and (Rehan *et al.*, 2002) suggest that reporting from both prescribers and undergraduates are low, and enhancing of reporting can be done through education (George *et al.*, 2006) (Ariciet *et al.*, 2015) also suggested the regular training to medical students can enhance the reporting rate. Continuous medical education (CME) can help to sustain reporting culture in pharmacovigilance in developing countries. Thereafter, subsequent changes can be made in the teaching curriculum. Moreover, a periodic update on drug safety information is necessary to prescribers. Hence, regular sensitization on drug safety monitoring and dissimulation of safety information is warranted. In addition to this conducting sensitization programs on reporting systems at various conferences and workshops may also enhance the reporting rate.

(Jha *et al.*, 2015) expressed his view on strengthening reporting rate by implementing few strategies like regular sensitizing on reporting to healthcare staff, and enhancing motivation in terms of reporting. They also opined on awarding or rewarding to reporters which may tackle the

underreporting. Moreover, the author also supported the view on acknowledgment for the reporter on reporting adverse reactions. A study done by (Gony *et al.*, 2010) in France had shown 3 folds improved reporting rate by pharmacovigilance personnel regular visiting treating department (Johansson *et al.*, 2011) suggested that there was a great impact on quality reports rather than improvement in reporting rate after sending repeated ADR information letters to physicians and nurses. In addition to the above-stated strategies, authors express their view on simplifying reporting forms may also increase reporting of adverse reactions, as doctors are busy and already loaded with high work, simplifying reporting may decrease the load, and further increase the chances of reporting. Moreover to avoid the chances of missing the reporting or recording adverse reaction by linking the medical record with the adverse reaction reporting form, thereby we can minimize the underreporting due to lack of reporting form.

Conclusions

Continuous stimulation is required to increase reporting rate about drug-related issues. Regional and peripheral adverse reaction monitoring centers have their important role in Pharmacovigilance for the proper functioning of the safety program. Exclusive strategies progress the reporting rate by altering the mindset of healthcare professionals, undergraduates, and consumers towards safety reporting. The present brief review discusses the various options for stimulating reporting across various centers. Different options would be suited for different settings, and the implementation processes would need to take cognizance of current trends and deficits, available resources, and the aims that need to be achieved. The overall aim of creating a reporting environment in the healthcare setting can improve patient surveillance and medication safety.

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Conflict of Interest

There is no conflict of interest

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