Trigger Tools for Monitoring and Reporting of Adverse Drug Reactions
A Scientific Tool for Efficient Reporting

Madiwalayya S Ganachari¹, Tarun Wadhwa¹, Shashikala walli¹, Dishu A Khoda¹ and Atul Aggarwal*¹
¹KLE University, India
²RAK College of Pharmaceutical Sciences, UAE

Abstract

Background: Adverse drug reactions (ADRs) are the leading cause of morbidity, mortality and increased healthcare cost. 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. The objective of our research was to study and assess the trigger tools for detection and analysis of ADRs.

Method: This prospective study was conducted in internal medicine department of a tertiary care hospital for duration of 3 months. Patients aged ≥ 18 years of either gender admitted were included. Subjects treated on OPD basis, emergency cases, and ICU cases were excluded. Patients and their medical records were reviewed for trigger tools (if any) to monitor and further report ADRs.

Result: A total of 220 subjects were enrolled into the study. Out of them, 40 subjects experienced 93 ADRs. Eighty three trigger tools were identified in 40 subjects. Out of which, 63 trigger tools were utilized to report 80 (86.02%) ADRs. The incidence of ADRs was found to be 18.1%. Male 132 (62.85%) preponderance was observed over females 88 (41.90%). Polypharmacy (67.74%) was one of the most prominent predisposing factors reported. Majority of ADRs were found to be of probable 64 (68.8%) in nature. On severity analysis, 21 (22.5%) ADRs were of moderate (Level3) severity and 75 (80.6%) were probably preventable.

Conclusion: Our results showed incidence of 18.1%. Trigger tools proved to be one of the best scientific tool in identification and reporting of ADRs in our study. Scientific validation of trigger tools is required to further utilize in large scale studies.

Keywords: Trigger tool; Adverse drug reactions


Introduction

Adverse drug reactions (ADRs) are the leading cause of morbidity, mortality and increased healthcare cost [1-4]. Despite of drastic improvement in healthcare practices, ADRs are contributing towards poor clinical outcome, hospitalization, prolongation of hospital stay, and enhanced economic burden [5-8].

The mishaps like medication error occurs frequently and portrays a real image of adverse effects at a rate comparative to the growing population of India [9,10]. Along with multiple uses of drugs or multiple complications; inappropriateness in the dosage or dose interval makes patient care contraindicated in all way around. The National Coordinating Council for Medication error Reporting and Prevention (NCCMERP) defines medication error as "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professionals, patient or consumer" [11-14].

Americans are injured every year by medication error in hospitals, nursing homes and doctor’s offices (IOM 2006) which puts impairment of trust from the Health care professionals. It should be preventable by definition through education and effective system controls involving pharmacists, prescribers, nurses, administrators, regulators and patients [15,16].

Adverse drug reaction detection continues to be an important tool for ensuring patient safety [17,18]. An ADR is a harmful response in the patient caused by the drug itself given in the recommended manner (dose, frequency, route, and administration). For example, allergic reactions effect from withdrawal or reactions caused by interactions with other medications. An Adverse event (AE) defines as “any untoward occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relation to the treatment [2,4,7,8,19].

Who defines a serious ADR “as any reaction that is fatal, life-threatening or permanently or significantly disability, requires or prolongs hospitalization or relates to misuse or dependence”. Improvements in the ability to precisely identify ADR include thorough review of patient medication order, prognosis, anti-dote and while readmission.[19] The concurrent or real time evaluation of triggered alerts has been used to guide clinical interventions to prevent emerging ADR and mitigate actual ADRs [20].

In terms of identifying the medical error and adverse events in both the adults and pediatric, traditionally many of the systems have been adopted including chart review, voluntary reporting by health

*Corresponding author: Atul Aggarwal, 24, Rajendra Nagar, Saharanpur-247001r, UP, India, Tel: 9456018555, 7353262628; E-mail: singhail1507atul@gmail.com

Received May 03, 2013; Published June 24, 2013


Copyright: © 2013 Ganachari MS, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
A trigger is defined as an "occurrence, prompt or flag found on review of the medical record that 'triggers' further investigation to determine the presence or absence of an adverse event" [30-32]. A trigger may include Lab trigger, Medical trigger, and Clinician trigger [33-35].

An ADR trigger tool makes chart review more efficient by identifying suspected AE via laboratory values, text phrases or automated 'values' available in medical records, which is more time effective than complete chart review and more sensitive than voluntary reporting [35]. Therefore, the use of triggers promotes more focused chart review and thus may help to identify ADRs [36].

This study is undertaken to utilize the existing trigger tools in practice for identification of ADRs and also to develop and validate new trigger tools for effective monitoring and reporting of ADRs. The main objective of the research is to study and assess the trigger tools for detection and analysis of ADRs. Secondary objectives of the research are to identify trigger tools likely to provoke ADRs, to develop new trigger tools, to analyze reported ADRs using standard scales (causality, severity and preventability).

Material and Method

Study setting

It is a tertiary care teaching hospital which is providing healthcare services to patients in and around Belgam district. It is a prospective surveillance and observational study, data collected for 3 months, analyzed in 1 month.

Inclusion criteria of the study, Subjects aged ≥ 18 years of either gender admitted to medicine wards and who agree to participate voluntarily with written consent form and those who refused to participate, or admitted to intensive care units or emergency department or visiting on OPD basis and likely to withdraw or lost to follow up as per discretion of investigator are excluded from the study.

Procedure

Ethical clearance has been obtained from institutional ethics committee (IEC) before initiating the study. Informed consent (in vernacular language) will be administered by the investigator to the subjects (based on inclusion/exclusion criteria) before enrolment in the medicine department for specified period. Trigger tools developed by researchers will be utilized by investigator for the detection, monitoring, reporting and analysis of ADRs. New trigger tools will also be developed during the study period. Subjects will be intensively monitored for the occurrence of ADRs and identification of trigger tools. Suspected ADRs will be notified and documented in a specified format (designed for study purpose) after discussion with physicians.

Subjects will be regularly monitored from the day of admission till discharge. Reported ADRs will be characterized based on demographics, drug class implicated, organ system affected, reaction occurred, management and outcomes aspects, treatment, de-challenge, re-challenge, and analysis of ADRs using standard scales for causality (WHO probability scale), severity and preventability (Modified Schumock and Thornton scale). Adverse drug reaction information will be discussed with physicians in internal medicine department to know their opinion regarding utilization of trigger tools in clinical practice. Suggestions would be considered (if appropriate) for implementations of developed ADR trigger tools.

Results

A total of 220 subjects were enrolled into the study. Out of them, 40 subjects experienced 93 ADRs. Eighty three trigger tools were identified in 40 subjects. Out of which, 63 trigger tools were utilized to report 80 (86.02%) ADRs. The incidence of ADRs was found to be 18.1%. Male 132 (62.5%) and female 88 (41.90%) were observed over females 88 (41.90%). Poly-pharmacy (67.74%) was one of the most prominent predisposing factors reported. Majority of ADRs were found to be of probable 64 (68.8%) in nature (Figure 1). On severity analysis, 21 (22.5%) ADRs were of moderate (Level3) severity and 75 (80.6%) were probably preventable.

Management and outcome of ADRs

The ADR is managed in various ways for the better outcome of patient for that Physician, Nurses and clinical pharmacists are involved in and out day over time. In our study an investigator (Clinical Pharmacist) involved over a time with the respected unit Physician and PG (students) that gives management of ADRs data as Drug Withdrawn (53, 56.9%) followed by the No Change in medication (36, 38.7%), Dose Altered for suspected drug (4, 4.3%). Outcome of the following subjects for the suspected ADRs are 52 of the subjects recovered (55.9%) followed by the continuing of the reaction (28,
and 13 (13.9%) were unknown due to lots of follow-up or discharge (Table 1).

**Treatment**

Subjects who are enrolled during the study for the suspected ADRs are treated for the better outcome in terms of health, medication related burden to give the disease free environment. The Specific treatment provided to the suspected ADRs was (38, 40.8%), maximum are given No treatment (48, 51.6%) and lastly symptomatically treated subjects are 7 (7.5%).

**Discussion**

**Incidence of ADRs**

The incidence of ADRs calculated over the study period of time was 18.1% and that was a good number to overcome the traditional reporting system of ADRs which was greatly compared to the other studies done by the Vora et al. (5.42%), Arulmani et al. (9.8%) and Sinha et al. (3.31%) [37-40].

The reason for increase in the incidence of ADR was due to the use of Trigger tool reporting system that was largely supported by the authors all over wide across the world like Classen et al., Rozich et al., Sarkar et al., Takata et al., and one of the study by Finney et al., in Surgery stated that the trigger tool uncovered AEs in 14.6% of patients [30,31,35,41,42].

**Demographics**

Vor et al., showed that in internal medicine males and females incidence rate were 3.37% and 2.05% respectively and a similar type of study showed reason of admission due to ADR is higher in female (57%) than male (43%) [37]. Arulmani et al., showed higher incidence of rate in females (78, 64.5%) than males (43, 35.5%) [38]. An Indian study by Gor et al., stated that sex of the patient does not affect the incidence of ADR [39]. In state of the above data our study resulted in Male 132 (62.85%) preponderance over females 88 (41.90%).

**Predisposing factor**

Poly-pharmacy (67.74%) was one of the most prominent predisposing factor reported in the study that was similar to the other study done by the Fattinger et al., [43]. The other predisposing factors which are contributed in the study are Inter current disease (51, 31.48%), Age (23, 14.1%), Gender (7, 4.3%) and others (6, 3.7%).

**Drug class implicated**

In one the study by the by Vora et al., showed that the Anti-microbial agents cause maximum of ADR (40.43%) which equally proved by the other author Arulmani et al., Anti-microbial agents (44, 17.0%) followed by Anti-hypertensive agents (35,14.3%) [37,38].

Sinha et al., showed that the most common drugs associated in the ADR are Anti-hyperglycemias agents, anti-hypertensive, chemotherapeutic agents and insulin [40]. Major of the cardiovascular agents are related to the increase in the liver enzymes (28) showed by the Dormann et al. [44]. In view of above data, our drug class study maximum related to the Anti-hypertensive (35, 37.6%) followed by the Anti-hyperglycaemias (12, 12.9%), 10 each of Steroids, NSAIDs (10.7%) and others (26, 27.9%) (Figure 2).

**Organ system affected**

Maximum of the drugs affecting the organ system was cardiovascular system (CVS, 32.2%), followed by the Endocrine (30.1%), Neurological (8.6%), Gastrointestinal (7.5%), Dermatological (5.3%) and Musculoskeletal, Respiratory, Haematological, Ophthalmic (1 each, 1.07%) in comparison to other studies Piessen CV et al., and Fattinger et al., showed Gastrointestinal was the major affecting organ system [43,45]. Arulmani et al., showed that the most affected organ system was skin (56, 34.1%) followed by the CNS (31, 18.9%) [38] (Figure 3).

**Analysis of ADR**

Depending upon the WHO causality scale the highest ADR falls in the category of probable (64, 68.8%) followed by the certain (21, 22.5%), Possible (7, 7.5%) and unlikely (1, 1.0%) that is similar to the results of Arulmani et al., classified two third of the reactions as probable (102, 62.2%) [38]. Another study by Vora et al., stated that maximum of ADRs occurred as certain (28, 59.57%) [37] (Figure 4).
A Hartwig Scale defined for calculating the severity was used, maximum of ADR come under the category of moderate level 3 (21, 22.5%) which is similar to the other study done by Sinha et al., having severity as moderate (77.12%) [40]. The other two studies by the Takata et al., and Arulmani et al., showed mild as severity having 97% and 53.7% respectively [38,41]. A broad classification in terms of severity reported as mild (35, 37.8%), moderate (65, 69.8%), severe (9, 9.67%). A major finding in the moderate severity was level 4b (20, 21.5%).

An ADR scale used for the calculation of preventability done on the basis of Modified Schumock and Thornton preventability scale which was maximized in terms of probably preventable (75, 80.6%) followed by the not preventable (13, 13.9%) and definitely preventable (5, 5.37%). Davies et al. [2] stated that half of ADR was definitely preventable, in comparison Handler et al., and Wet et al., judged preventability as 42% [46,47].

**Trigger tool**

Naessens et al., resulted in the Anti-emetic (32%) trigger has maximum probability followed by the Diphenhydramine (10%), abrupt medication stop (8%), Transfer to higher level of care (4.9%), Over sedation / Hypotension (3.8%), Vitamin K administration (3.2%), High Serum Creatinine (2.6%), glucose less than 50 mg/dl (2.2%) [48]. In comparison our study relates data maximum of ADR to the cessation of drug trigger tool (37.3%) followed by the Hypotension (13.2%) and others described in the above Figure 5 as follows that is significantly comparable to other study done by the Takata et al., abrupt medication stop (19.7), PTT > 100 s (16.7). Over sedation/ lethargy/ fall/ hypotension (14.9), Diphenhydramine (8.44), Rise serum Creatinine (3.85), Laxative (2.82), Anti-emetic (1.55), glucose less than 50 mg/dl (0.6) [41] (Figure 5).

Eighty three trigger tools were identified in 40 subjects. Out of which, 63 positive trigger tools were utilized to report 80 (86.02%) ADRs and 20 (21.5%) triggers (like Diphenhydramine, Vitamin K, PTT, INR, diphenoxylate and loperamide, Clostridium difficile positive stool) resulted in no ADRs. During the study Trigger number (24) customized to individual institution was used, new trigger are developed like hypertension (4, 4.8%), Steroid (3, 3.6%) and Laxative and Enema (5, 6.0%). In view of above data and practice, according to the Trigger number (24) customized to individual institution, some of the triggers are drop out like vitamin K, Diphenhydramine, diphenoxylate and loperamide, and some of are replaced in simple terms like Clostridium difficile positive stool trigger with Loose stool trigger.

The percentage of contribution by the trigger tool in identification and reporting of suspected ADRs Medication trigger (42, 50.6%) followed by the clinical trigger (16, 19.2%) and laboratory trigger (5, 6.0%). Handler et al., stated that laboratory/ medication signal contribute 75% of preventable ADRs in comparison our study resulted 56.6% [47].

**Limitation and future direction**

Firstly, the use of trigger tool was done only in the in-patients of General medicine. Secondly, the time period for conducting the research was less to make more validated data for that study should be continued further, depending upon this situation the research is still going on to prove trigger tool is better scientific tool for identification and reporting of ADRs than the traditional reporting system. Thirdly, there are new trigger tool was adopted in the study for that validation of Trigger was needed. Fourth, there was a need of training regarding the trigger tool in the Health Care Professionals for better outcomes of patient in both the prospects health and economics. This scientific tool study was mainly done in developed countries, a developing countries like India still behind to overcome and solve the problem of ADRs, there is a need to develop the strategies like trigger tool in all the health care institution for the better patient safety.

**Conclusion**

This is the scientific systemic tool approach to indentifying and reporting of ADRs to overcome the traditional poor approach or we can say a add on therapy to the spontaneous reporting for the Health Care Professionals, a need of vigilant monitoring for the better patient safety that results in indentify of ADR, accounted for incidence of 18.1%. Such type of studies should be continued for the further research in pharmacovigilance program.

**Acknowledgment**

This manuscript is acknowledged to each and every Health care Professional for the betterment of society and no grants or funds were taken from any of the agencies and no conflict of interest by any of the authors.

**References**


