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Original Research Article

A Hospital-Based Assessment of the Trigger Tool Method for Adverse Drug Reaction Monitoring

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Abstract

Aim: The objective of this study is to evaluate the trigger tool method (TTM) in detection, monitoring, and reporting of adverse drug reactions (ADRs) at teaching hospital, Gaya, Bihar, India.

Methods: The present study was conducted at a teaching hospital ANMMCH, GAYA, Bihar, India for a period of 12 months. A total of 200 patients who fulfill the selection criteria were enrolled and male were 70% and female 30%. The mean age of patients was 42.08 ± 16.4 years, and the mean length of hospital stay was 5.75 ± 3.12 days.

Results: DT (800 times) was the most commonly observed trigger followed by PT (80 times), ST (80 times), and LT (16 times). One or more DT was observed 800 times in 285 patients, of which 40 patients had ADRs. Hence, the PPV of DT was 10.3%. Similarly, PT was observed 100 times in 150 patients and 50 patients had ADRs. While ST was observed 80 times in 70 patients, of which 15 patients had ADRs. The use of thrombophob gel has the highest PPV (100%), followed by rash (84.16%), other complaints not related to disease (48.96%), antihistamines (40.50%), and laxatives (35.5%).

Conclusion: Trigger tool approach is highly effective in the identification of ADRs in comparison to traditional approach. This method enables health care professionals including pharmacists for easy identification and reporting of ADRs.

Keywords: Adverse drug reaction, adverse drug reaction monitoring, pharmacovigilance, trigger tool method

Introduction

Adverse drug reactions (ADRs) are one of the leading causes of morbidity and mortality. It has been estimated that around 2.9–5.6% of all hospital admissions are due to ADRs and as many as 35% of hospitalized patients experience an ADR during their hospitalization [1] Spontaneous reporting of ADRs is a common method of detecting undesirable responses to the drugs. [2] In some developing countries, the importance of ADR reporting is just being recognized. In Iran, a national ADR-reporting system was established by the Ministry of Health in June 1998. Despite the existence of the national ADR-reporting system in Iran, a major problem of voluntary surveillance by healthcare professionals has been the high level of under-reporting. [3] Under-reporting, a major drawback of spontaneous

ADR reporting, is prevalent even in developed countries with a long history of a functional ADR-reporting system. [4]

Among various methods to monitor adverse drug reaction (ADR), the most popular method of ADRs reporting is spontaneous or voluntary reporting. However, spontaneous method has major drawbacks such as under reporting, bias in reporting, and incomplete data. [5] ADR incidence has been reported in the range of 5.9 to 22.3% of all emergency department admissions in India. It has been reported that deaths due to ADRs contributed for 1.8% of total of deaths in India. [6]

Several methods are used to monitor ADRs. These can broadly be categorized as: voluntary reporting, record review, triggers, direct observation, interviews, targeted reporting, cohort event monitoring, and electronic health record mining. [7] The most popular method of ADRs reporting is spontaneous or voluntary reporting. However, under reporting, bias in reporting, and incomplete data are the major drawbacks of this method. [5]

These problems can be overcome by one of the active surveillance methods like the trigger tool method (TTM). 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." [8] A trigger may be a laboratory trigger (LT) or a drug trigger (DT) or a patient trigger (PT).

TTM is a lesser evaluated method in India. Most studies conducted worldwide have used TTM retrospectively to detect ADR. This has several limitations such as sole dependence on documentation and the lack of details at the time of the assessment of causality and preventability. To overcome these problems, we used TTM prospectively, which allow real-time review of cases to detect ADR. The present study was, therefore, undertaken to evaluate the efficacy of trigger tools to detect ADRs at a teaching hospital GAYA, Bihar, India. It also aims to compare the conventional existing spontaneous reporting with the underused TTM.

Materials and Methods

The present study was conducted at a teaching hospital ANMMCH, GAYA, Bihar, India for a period of 12 months. A total of 200 patients who fulfill the selection criteria were enrolled and male were 70% and female 30%. The mean age of patients was 42.08 ± 16.4 years, and the mean length of hospital stay was 5.75 ± 3.12 days.

Inclusion criteria

- Patients with age greater than 18 years old
- Patients agreed to participate voluntarily with written consent form
- Patients who were admitted as inpatients in the study duration

Exclusion criteria

- Patients who were hospitalized less than 48 h
- Patients admitted to pediatrics and gynecology ward

Study Procedure

A total of 200 patients, who met the inclusion criteria, were recruited into the study. A suitable data collection form was designed for use in the study. The sources of data were patient case sheets and laboratory data. All the recorded data was reviewed independently to identify 'triggers' and when a trigger was found, patient record was investigated in depth to determine whether an ADR occurred. If an ADR was discovered incidentally when going through the patient charts, without the presence of a specific trigger, this ADR was also considered and recorded as a "non-triggered" or "spontaneous" ADR, in accordance with the IHI methodology.

Harm categorization and causality were assessed for observed ADRs using National Coordinating Council for Medication Error Reporting and Prevention Index (NCC

MERP) and Naranjo scale respectively. Positive Predictive Value (PPV) was calculated for each trigger as, number of ADRs identified with the trigger/number of triggers found in the patient charts.

Identification of Triggers

The (IHI) simplified the manual medical record review process and developed (GTT) consisting of 19 triggers to monitor adverse events rates in a way that was easy to replicate in hospitals, with or without computerized records.8 But, in our study, modified IHI trigger tool consisting of 16 triggers was used. List of modified IHI global triggers were presented in Table 1.

Table 1: List of modified IHI Global Triggers followed in the study

T1–Abrupt Medication Stop	T9-WBC count <3000 cells/cu.mm
T2–Glucose Less than 50 mg/dl	T10-Elevated ALT/AST levels
T3–Anti-Emetic Administration	T11-Hypokalemia
T4–Vitamin K Administration	T12-Hyperkalemia
T5–International Normalized Ratio (INR) Greater than 6	T13-Hyponatremia
T6–Rising BUN or Serum Creatinine Two Times (2X) over Baseline	T14-Decrease in Haemoglobin or Haematocrit of 25% or Greater
T7-Rash	T15-Platelet Count Less than 50,000
T8-Antidiarrheals	T16-Hypotension

Clinical Outcomes

The primary outcome was to assess incidence of ADRs using trigger tool and traditional approach. The secondary outcome was to identify the factors associated with them.

Results

Table 2: Positive predictive value of triggers

Trigger	Total triggers observed	Positive triggers	Negative triggers	PPV (%)
DT	**800**	**100**	**700**	
DT1 - Sudden stoppage of drug	25	5	27	10.40
DT2 - Antihistamines	23	15	10	40.50
DT3 - Antiemetic	300	7	310	1.44
DT4 - Antidiarrheal	25	5	25	16.24
DT5 - Laxatives	20	10	15	35.5
DT6 - Blood/blood product transfusion	15	5	16	11.6
DT7 - IV fluid started	12	15	0	0
DT8 - Thrombophob gel	5	5	0	100
DT9 - New drug administration	90	10	75	20.40
DT10 - Antacids	285	23	222	0.84
PT	**100**	**30**	**75**	
PT1 - Rash	7	5	2	84.16
PT2 - Pruritus	15	5	10	34.6
PT3 - Patient fall/lethargy/over sedation	8	0	8	0
PT5 - Transfer/reference to other center	35	0	40	0

PT6 - Other complains	25	15	10	48.96
PT10 - Readmission within 30 days	10	5	5	0
ST	**80**	**16**	**70**	
ST2 - Change in procedure or procedural complications	65	10	55	20
ST6 - Death postoperatively	5	0	5	0
ST7 - Mechanical ventilation >24 h postoperatively	5	0	5	0
ST11 - Any operative complications	2	3	3	0
ST12 - Wound dehiscence	3	3	2	0
LT	**16**	**2**	**17**	
LT6 - Positive blood culture	4	0	4	0
LT8 - Decrease HB or hematocrit >25%	4	0	3	0
LT9 - Serum electrolyte abnormality	8	2	10	7.50

DT (800 times) was the most commonly observed trigger followed by PT (80 times), ST (80 times), and LT (16 times). One or more DT was observed 800 times in 285 patients, of which 40 patients had ADRs. Hence, the PPV of DT was 10.3%. Similarly, PT was observed 100 times in 150 patients and 50 patients had ADRs. While ST was observed 80 times in 70 patients, of which 15 patients had ADRs. The use of thrombophob gel has the highest PPV (100%), followed by rash (84.16%), other complaints not related to disease (48.96%), antihistamines (40.50%), and laxatives (35.5%).

Table 3: Positive triggers and related adverse drug reactions

Trigger	ADR	Number of ADR detected
DT		
DT1 - Sudden stoppage of drug		
	Diarrhea	4
	Gastritis	2
DT2 - Antihistamines		
	Rash	5
	Pruritis	5
DT3 - Antiemetic	Vomiting	6
DT4 - Antidiarrheal	Diarrhea	9
DT5 - Laxatives	Constipation	3
DT6 - Blood/blood product transfusion	Anemia	
DT8 - Thrombophob gel	Thrombophlebitis	5
DT9 - New drug administration		
	Rash	5
	Pruritus	6
	Constipation	8
	Diarrhea	5
DT10 - Antacids	Gastritis	4
PT		
PT1 - Rash	Rash	6
PT2 - Pruritus	Pruritus	6

PT6 - Other complains	Dizziness	5
	Vomiting	7
	Headache	8
ST		
ST2 - Procedural complications	Constipation	8
	Hypokalemia	2
	Headache	7
	Anemia	1
LT		
LT9 - Serum electrolyte abnormality	Hypokalemia	3

Among positive triggers, nine DT were detected 67 times. While three PT, one ST, and one LT were detected 32 times, 18 times, and 3 times, respectively. Hence, 14 triggers were observed 105 times which related to 49 ADRs

Discussion

In the present study, only 16 triggers (105 times) were related to one or more ADRs. DT (82%) was most frequently detected followed by PT (8%), ST (8%), and LT (2%). A study by Rajesh et al. [8] conducted in 120 case records in the Department of Surgery of a Tertiary Care Teaching Hospital of India, using a trigger list of 77 triggers demonstrated medical module triggers as most frequently detected triggers and commonly associated with adverse events similar to the present study. Furthermore, STs were less frequently detected than medical module triggers in the study by Rajesh et al., similar to the present study. [9]

Approximately 2/3rd (70%) of ADRs were detecteby triggers and 1/3rd (30%) of ADRs were found spontaneously without the presence of a trigger. It implies that number of ADRs identified by trigger tool method is remarkably increased in comparison to the conventional method does. Our result is further supported by numerous studies reported that trigger tool method is more effective than conventional approach. [10,11] It was further observed that patients in whom more than five triggers were present showed >30% "yield" in terms of detection of an ADR in compared to Naessens et al. (50% "yield"). [12] This suggests that the likelihood of detection of ADRs increases with the number of triggers per case.

PPV, sensitivity, and specificity are the most commonly used parameters to assess the accuracy of the trigger tool. In the present study, the TT had a sensitivity of 100% and specificity of 11.48%. Neither trigger nor ADR was present in 10.25% of patients and all the ADRs (n = 49) were detected by TT. Pérez Zapata et al. [13] found sensitivity (86%) and specificity (93.6%) of the TT in 350 surgical patients in Spain. However, difference in sensitivity and specificity of TT can be attributed to the difference in health-care setting.

In the present study, the PPV for individual triggers ranged from 0% to 100% and the triggers with higher PPV were the use of thrombophob gel with the highest PPV (100%), followed by rash (84.16%), other complaints not related to disease (48.96%), antihistamines (45.50%), and laxatives (35.5%). PPV for predicting adverse events can vary for the same trigger in different health-care settings and differences in their existing diagnostic and therapeutic practices. Certain triggers occurred with a relatively lower frequency but were more efficient in identifying ADE.

The final MTTL comprises 16 triggers based on the PPV of individual triggers. Certain triggers which were not observed in the study population do not indicate that these triggers are insignificant. Trigger tools with a limited number of triggers with

higher PPV and clinical relevance have advantage of low burden on the reviewer and better effectiveness.

Using TTM, the rate of detection of ADEs was 12.25/100 patients. Griffin and Classen[9] reported ADE rate (16 AE/100 patients) in a retrospective study similar to the present study. A much higher ADE rate (51.1 AE/100 patients) was observed in a study by Pérez Zapata et al. [14] which can be because of the lack of causal association of reported ADEs.

Conclusion

Trigger tool approach is highly effective in the identification of ADRs in comparison to traditional approach. This method enables health care professionals including pharmacists for easy identification and reporting of ADRs. However, further research is required to explore the feasibility and acceptability of TTM.

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