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Original Research Article

A Hospital Based Single Center Study Assessing the Trigger Tool Method (TTM) in Detection, Monitoring, and Reporting of Adverse Drug Reactions (ADRS)

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Abstract

Aim: The aim of the present study was to evaluate the trigger tool method (TTM) in detection, monitoring, and reporting of adverse drug reactions (ADRs).

Methods: This prospective, continuous, single-center study was conducted in the Department of Pharmacology of DMCH, Laheriasarai, Darbhanga, Bihar, India in two phases over 15 months. Phase I (6 months) of the study was observational, whereas Phase II (9 months) was interventional.

Results: A total of 1135 patients were admitted during the Phase I (6 months) of which 500 patients, who met with the inclusion criteria were included. The mean age of patients was 44.36 ± 18.02 years, and mean length of hospital stay was 4.26 ± 3.27 days. Of 55 triggers (PTTL), a total of 34 triggers were found 1202 times in 325 patients. DT (780 times) was the most commonly observed triggers followed by LT (325 times) and PT (105 times). Similarly, LT were observed 325 times in patients. PT was observed in 105 times. It was apparent that more than one trigger was associated with a single ADR. It was further observed that patients in whom more than five triggers were present showed >30% "yield" in terms of detection of an ADR. Among positive triggers, nine DT were detected 65 times. While three PT, one ST, and one LT were detected 24 times, 16 times, and 1 time, respectively.

Conclusion: The reporting system is operational at the study site and ADRs are being reported using a standard form. Patients recovering from the reactions following the withdrawal of the suspected drug, and the majority of ADRs were mild. TTM can be used as an add-on tool to existing methods like spontaneous method for the health-care professionals for better detection of ADRs in the pharmacovigilance program. However, further research is required to explore the feasibility and acceptability of TTM.

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

Introduction

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. [1] Active surveillance methods such as the trigger tool method (TTM) can overcome these problems. 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." [2] A trigger may be a laboratory trigger (LT) or a drug trigger (DT) or a patient trigger (PT) or a surgical module trigger (ST).

Drugs are primarily used for the diagnosis, prevention, treatment of various diseases. But it is sometimes observed, that these drugs have been proved fatal. This could be due to variable person-to-person responses towards a drug. Even at therapeutic doses, people develop adverse effects. [3] Adverse drug reactions (ADRs) are one of the leading cause of repeated hospitalization and they adversely affects the quality of life. [4] 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. Early detection, evaluation and monitoring of ADRs are essential to reduce harm to patients and thereby improving public health. [3] The detection of ADRs has become increasingly significant because of the introduction of many newer medicines in the last two or three decades. 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". [5] A trigger may include laboratory trigger, medical trigger and clinician trigger. Earlier studies report that use of triggers promotes more focused chart review and thus may help to identify ADRs. [6-8] The Institute of Healthcare Improvement (IHI) simplified the manual patient case chart review process and developed the Global Trigger Tool (GTT) consisting of 19 triggers in order to monitor adverse events rates in a way that was easy to replicate in hospitals, with or without computerized records. [9] Studies conducted worldwide show that the TTM improve ADR reporting in terms of both quality and quantity. [10] However, TTM is a lesser evaluated method in India. Most studies conducted worldwide have used TTM retrospectively to detect ADR.

The aim of the present study was to evaluate the trigger tool method (TTM) in detection, monitoring, and reporting of adverse drug reactions (ADRs).

Materials and Methods

This prospective, continuous, single‐center study was conducted in the Department of Pharmacology of DMCH, Laheriasarai, Darbhanga, Bihar, India in two phases over 15 months. Phase I (6 months) of the study was observational, whereas Phase II (9 months) was interventional.

Phase I (evaluation of triggers‐6 months)

After a pilot study by the investigator, a preliminary trigger tool list (PTTL) was prepared based on IHI Global TTL, [6] Abideen [2] List which includes 55 triggers: 20 DTs, 28 LTs, and 7 PTs. A total of 500 patients were enrolled. PTTL was tested in each alternate patient admitted in two selected Medicine units who consented to participate was included. Case papers of the patient, laboratory investigations, discharge form, and patients' complaints were observed by the investigator and evaluated for the detection of triggers until the discharge of the patient. The presence of one or more triggers and adverse event, if any, were recorded in pretested case record form. All detected triggers and adverse events were recorded and analyzed in terms of positive triggers (triggers related to ADRs) and negative triggers (triggers not related to ADRs). For accuracy of TT, the PPV, sensitivity, and specificity were calculated.

Phase II (interventional phase‐9 months)

Resident doctors of the selected medicine units were enrolled after consent to evaluate TTM and spontaneous method after an educational intervention. They were sensitized for 15 days to both methods through personal meetings and lectures. Then, they were observed for ADR reporting and notification over 4 months for each method. The need to report ADRs was reiterated through SMS reminders sent to them every 15 days during the study period. All ADRs reported or notified by resident doctors were collected in CDSCO ADR reporting form and assessed for causality, severity, and preventability using the standard Scales. Following the study, feedback was obtained from the resident doctors about their opinion regarding TTM and its usefulness in ADR reporting. All data are entered in Microsoft Excel 2007® and analyzed using appropriate statistical tests.

Results

Table 1: Positive predictive value of triggers evaluated during Phase I at a tertiary care hospital

Trigger	Total triggers observed	Positive triggers (related to ADRs)	Negative triggers (not related to ADRs)	PPV (%)
DT	780	50	720	-
DT1 - Sudden stoppage of drug	40	21	15	52.048
DT2 - New drug administration	90	7	80	739
DT3 – Antihistamines	15	4	9	22
DT4 – Antiemetics	265	1	265	0.314
DT5 – Antidiarrheal	34	7	28	18.86
DT6 – Antacids	260	2	260	0.720
DT7 – Laxatives	20	1	20	4.16
DT8 - Vitamin K	17	0	13	0
DT14 – Steroids	2	0	2	0
DT15 - IV fluids started/dose increased	13	1	10	12
DT19 - Thrombophob gel	4	5	0	105
DT20 - Blood/blood product transfusion	20	1	18	4.40
LT	325	5	320	-
LT1 - PTT >100 seconds	2	0	2	0
LT4 - Abrupt drop in hemoglobin	15	2	14	10.5
LT5 - ESR increased	3	0	2	0
LT9 - ECG	62	0	62	0
LT11 - Hypocalcemia	10	0	10	0
LT13 - Hypokalemia	43	2	41	3.40
LT14 - Hyperkalemia	9	0	9	0
LT15 - Hyponatremia	49	0	50	0
LT16 - Hypernatremia	2	0	1	0
LT17 - Abnormal acid-base balance	25	0	26	0

LT18 - Hypoglycemia	3	0	3	0
LT19 - Hyperglycemia	2	0	2	0
LT20 - High cholesterol	6	0	6	0
LT23 - Abnormal LFT	55	0	55	0
LT24- Increased serum creatinine	37	1	37	4.36
PT	105	25	90	-
PT1 - Rash	6	6	3	62.5
PT2 - Pruritus	4	2	4	33.33
PT3 - Drowsiness/falls/lethargy	4	1	4	25
PT4 - Death	6	0	9	0
PT5 - Transfer/reference to other center	50	2	51	3.84
PT6 - Weight gain	4	2	3	50
PT7 - Other complaints	30	12	15	48.3

A total of 1135 patients were admitted during the Phase I (6 months) of which 500 patients, who met with the inclusion criteria were included. The mean age of patients was 44.36 ± 18.02 years, and mean length of hospital stay was 4.26 ± 3.27 days. Of 55 triggers (PTTL), a total of 34 triggers were found 1202 times in 325 patients. DT (780 times) was the most commonly observed triggers followed by LT (325 times) and PT (105 times). Similarly, LT were observed 325 times in patients. PT was observed 105 times in the study.

Table 2: Number of triggers observed per patient and their association with adverse drug reactions

Number of triggers detected	**Number of patients (*n*=500), *n* (%)**	**Patients without adverse events (*n*=325), *n* (%)**	**Patients with adverse events (*n*=60), *n* (%)**	***P***
0	85 (17)	80 (16)	0 (0)	-
1	50 (10)	40 (8)	5 (1)	0.1530
2	100 (20)	80 (16)	5 (1)	0.0001
3	60 (12)	50 (10)	6 (1.2)	0.0184
4	80 (16)	60 (12)	20 (4)	0.1262
5	50 (10)	40 (8)	10 (2)	0.1005
6	25 (5)	15 (3)	10 (2)	0.6827
7	15 (3)	10 (2)	5 (1)	1.00
8	15 (3)	10 (2)	6 (1.2)	1.34
9	10 (2)	5 (1)	4 (0.80)	0.6105

It was apparent that more than one trigger was associated with a single ADR. It was further observed that patients in whom more than five triggers were present showed >30% “yield” in terms of detection of an ADR.

Table 3: Positive triggers and related adverse drug reactions observed during Phase I

Trigger	ADR	Number of ADR detected
DT DT1 - Sudden stoppage of drug	 Diarrhea Gastritis	 2 1
DT2 - Antihistamines	Rash Pruritus	6 6
DT3 - Antiemetic	Vomiting	6
DT4 - Antidiarrheal	Diarrhea	5
DT5 - Laxatives	Constipation	8
DT6 - Blood/blood product transfusion	Anemia	3
DT8 - Thrombophob gel	Thrombophlebitis	3
DT9 - New drug administration	Rash Pruritus Constipation Diarrhea	5 5 8 5
DT10 - Antacids	Gastritis	2
PT PT1 - Rash	 Rash	 5
PT2 - Pruritus	Pruritus	5
PT6 - Other complains	Dizziness Vomiting Headache	4 5 6
ST ST2 - Procedural complications	 Constipation Hypokalemia Headache Anemia	 8 1 5 2
LT LT9 - Serum electrolyte abnormality	Hypokalemia	1

Among positive triggers, nine DT were detected 65 times. While three PT, one ST, and one LT were detected 24 times, 16 times, and 1 time, respectively.

Table 4: Modified trigger tool list

DT	LT	PT
Stoppage of drug Antihistamines Antiemetic Antidiarrheal Laxatives Transfusion of blood and blood product IV fluid started Thrombophob gel New drug administration Antacids	Increased serum creatinine Abrupt drop hemoglobin Hypokalemia	Rash Pruritus Patient fall/ oversedation/lethargy Weight gain Transfer to other health-care level Other complaints not related to disease

All PT were observed in the study population. Twenty-one triggers were not observed in the study population.

Discussion

An adverse drug reaction (ADR), is "a response to a drug that is noxious and unintended that occurs at doses normally used in male for prophylaxis, diagnosis, or treatment of disease, or for the modification of physiological function." Pharmacovigilance is "the science and activity relating to the detection, assessment, understanding, and prevention of adverse effects or any other possible drug-related problems." [11] Epidemiological studies in India show that about 50% of all hospital admissions are associated with ADRs. [12] 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%. 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.

The retrospective study conducted in Malaysia by Sam et al. observed nine triggers 45 times in 38 patients; 29 ADEs were detected using these triggers. [14] In all the above studies, DTs were more frequently detected than PTs and LTs. riffin and Classen [15] 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 al13 which can be because of the lack of causal association of reported ADEs. Matlow et al. [7] found high sensitivity (85%) and low specificity (44%) of the TT. Karpov et al. observed the sensitivity of the trigger tools to be between 2.6% and 15.8% and specificity varied from 99.3% to 100%. [16]

A total of 1135 patients were admitted during the Phase I (6 months) of which 500 patients, who met with the inclusion criteria were included. The mean age of patients was 44.36 ± 18.02 years, and mean length of hospital stay was 4.26 ± 3.27 days. Of 55 triggers (PTTL), a total of 34 triggers were found 1202 times in 325 patients. DT (780 times) was the most commonly observed triggers followed by LT (325 times) and PT (105 times). Similarly, LT were observed 325 times in patients. PT was observed 105 times in the study. It was apparent that more than one trigger was associated with a single ADR. It was further observed that patients in whom more than five triggers were present showed >30% "yield" in terms of detection of an ADR. Kennerly et al. using TTM observed PPV of triggers to be between 0% and 100% with an overall PPV of 17.1%. [17] Above findings reflects that PPV for predicting adverse events can be different for the same trigger in different clinical settings because the performance of the trigger may vary over time and is dependent on the existing diagnostic and therapeutic practices in the given health-care setting. Certain triggers occurring with a relatively lower frequency were more efficient in identifying ADE.

Conclusion

The reporting system is operational at the study site and ADRs are being reported using a standard form. Patients recovering from the reactions following the withdrawal of the suspected drug, and the majority of ADRs were mild. TTM can be used as an add-on tool to existing methods like spontaneous method for the health-care professionals for better detection of ADRs in the pharmacovigilance program. However, further research is required to explore the feasibility and acceptability of TTM.

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