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Original Research Article

An Observational Study to Evaluate 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 ANMMCH, Gaya, 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 350 patients were admitted during the Phase I (6 months) of which 200 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 in 100 patients. DT (140 times) was the most commonly observed triggers followed by LT (100 times) and PT (50 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

Adverse drug responses, also known as ADRs, are described as "a response to drug that is noxious, unintended, and occurs in doses used in human beings for the purpose of disease prophylaxis, diagnosis, and therapy, or for the modification of physiological function.". [1] Approximately 2.9-5.6% of all hospitalizations were attributed to adverse drug reactions (ADRs), and as many as 35% of hospitalized patients encountered an ADR during their stay, according to research that was carried out in the United States of America. [2] A research that was carried out in southern India found that while adverse drug reactions were responsible for 0.7% of hospital admissions, 3.7% of hospitalized patients suffered an adverse drug reaction, and 1.8% of hospitalized patients encountered a fatal adverse drug reaction while they were in the hospital. [3] Monitoring adverse drug reactions (ADRs) may be accomplished using a variety of approaches, including but not limited to: voluntary reporting, record review, triggers, direct observation, interviews/surveys, targeted reporting, cohort event monitoring, and HER mining (an acronym for electronic health record mining). [4]

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 ANMMCH, Gaya, 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, [11] Abideen [12] 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	140	20	120	-
DT1 - Sudden stoppage of drug	14	7	7	52.048
DT2 - New drug administration	22	2	20	739
DT3 – Antihistamines	6	2	4	22
DT4 – Antiemetics	26	1	25	0.314
DT5 – Antidiarrheal	12	2	10	18.86
DT6 – Antacids	31	1	30	0.720
DT7 – Laxatives	6	1	5	4.16
DT8 - Vitamin K	3	0	3	0
DT14 – Steroids	1	0	1	0
DT15 - IV fluids started/dose increased	6	1	5	12
DT19 - Thrombophob gel	2	2	0	105
DT20 - Blood/blood product transfusion	11	1	10	4.40
LT	100	5	95	-
LT1 - PTT >100 seconds	1	0	1	0
LT4 - Abrupt drop in hemoglobin	7	2	5	10.5

LT5 - ESR increased	1	0	1	0
LT9 - ECG	13	0	13	0
LT11 - Hypocalcemia	4	0	4	0
LT13 - Hypokalemia	17	2	15	3.40
LT14 - Hyperkalemia	3	0	3	0
LT15 - Hyponatremia	12	0	12	0
LT16 - Hypernatremia	1	0	1	0
LT17 - Abnormal acid-base balance	8	0	8	0
LT18 - Hypoglycemia	2	0	2	0
LT19 - Hyperglycemia	1	0	1	0
LT20 - High cholesterol	2	0	2	0
LT23 - Abnormal LFT	15	0	15	0
LT24- Increased serum creatinine	13	1	12	4.36
PT	50	10	40	-
PT1 – Rash	3	2	1	62.5
PT2 – Pruritus	3	1	2	33.33
PT3 - Drowsiness/falls/lethargy	3	1	2	25
PT4 – Death	4	0	4	0
PT5 - Transfer/reference to other center	21	1	20	3.84
PT6 - Weight gain	3	1	2	50
PT7 - Other complaints	13	4	9	48.3

A total of 350 patients were admitted during the Phase I (6 months) of which 200 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 in 100 patients. DT (140 times) was the most commonly observed triggers followed by LT (100 times) and PT (50 times).

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

Number of triggersdetected	Number of patients (*n*=200), *n* (%)	Patients without adverse events (*n*=100), *n* (%)	Patients with adverse events (*n*=50), *n* (%)	*P*
0	34 (17)	17 (17)	0 (0)	-
1	20 (10)	16 (16)	4 (2)	0.1530
2	40 (20)	34 (34)	6 (3)	0.0001
3	24 (12)	18 (9)	6 (3)	0.0184
4	32 (16)	26 (26)	6 (3)	0.1262
5	20 (10)	12 (12)	8 (4)	0.1005
6	10 (5)	7 (7)	3 (3)	0.6827
7	6 (3)	4 (4)	2 (1)	1.00
8	6 (3)	4 (4)	2 (1)	1.34
9	4 (2)	3 (3)	1 (0.50)	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	2
	Gastritis	1
DT2 - Antihistamines	Rash	6
	Pruritus	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) refers to a harmful and unanticipated response to a medication, which happens at levels typically administered to males for disease prevention, diagnosis, treatment, or physiological function alteration. Pharmacovigilance encompasses the scientific and practical aspects of identifying, evaluating, comprehending, and averting any negative effects or potential issues associated with drugs. [12] Epidemiological studies conducted in India indicate that over 50% of hospital admissions are linked to Adverse Drug Reactions (ADRs). [13] PPV, sensitivity, and specificity are often used metrics for evaluating the precision of the trigger instrument. The current investigation found that the TT has a sensitivity of 100% and a specificity of 11.48%. In a study conducted by Pérez Zapata et al [14], the sensitivity and specificity of the TT were determined to be 86% and 93.6% respectively, in a sample of 350 surgical patients in Spain. The variation in sensitivity and specificity of TT may be ascribed to disparities in the health-care environment.

In Malaysia, Sam et al [15] did a retrospective analysis where they observed nine triggers occurring 45 times in 38 patients. Using these triggers, they were able to discover 29 adverse drug events (ADEs). DTs were discovered more often than PTs and LTs in all of the aforementioned investigations. Riffin and Classen [16] documented an adverse drug event (ADE) rate of 16 AE per 100 patients in retrospective research that closely resembles the current investigation. In research conducted by Pérez Zapata et al [14], a significantly higher incidence of Adverse Drug Events (ADEs) was discovered, with 51.1 AEs occurring per 100 patients. This might perhaps be

attributed to the absence of a causal relationship between the reported ADEs. Matlow et al. [7] discovered that the TT had a high sensitivity of 85% but a low specificity of 44%. Karpov et al [17] found that the trigger instruments had a sensitivity ranging from 2.6% to 15.8% and a specificity ranging from 99.3% to 100%.

A total of 350 patients were admitted during the Phase I (6 months) of which 200 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 in 100 patients. DT (140 times) was the most commonly observed triggers followed by LT (100 times) and PT (50 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. Kennerly et al [18] using TTM observed PPV of triggers to be between 0% and 100% with an overall PPV of 17.1%. 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 functioning well at the research site, and Adverse Drug Reactions (ADRs) are being documented using a standardized form. The majority of adverse drug reactions (ADRs) experienced by patients after discontinuing the suspected medication were minor. The TTM may serve as a supplementary tool to enhance the identification of adverse drug reactions (ADRs) in the pharmacovigilance program, when used in conjunction with current techniques such as the spontaneous approach, specifically for healthcare professionals. However, more investigation is necessary to examine the practicality and level of approval for TTM.

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