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An Evaluation of Trigger Tool Method for Adverse Drug Reaction Monitoring at a Tertiary Care Hospital in Andhra Pradesh

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Abstract: ***Objectives: Trigger tool method (TTM) is an active surveillance method for adverse drug reaction (ADR) monitoring. The study aimed to evaluate TTM for ADR monitoring in in-patients of the surgery department. Material and Methods: This prospective, observational study was conducted at the Department of Surgery of a Tertiary Care Teaching Hospital in Kakinada, Andhra Pradesh. Preliminary trigger tool list (PTTL) comprising 13 drug triggers (DTs), 13 patient triggers (PTs), 9 laboratory triggers (LTs), and 12 surgical module triggers (STs) were used. Patients were followed up till discharge to monitor the occurrence of triggers and adverse events. Results: A total of 400 patients were included (male: female ratio of 2.3:1; mean age: 43.07 ± 16.4 years; and mean length of hospital stay: 5.75 ± 3.12 days). Of 400 patients, triggers were present in 359 patients (89.75%) and no trigger was observed in 41 patients (10.25%). Of the 47 triggers in PTTL, 24 triggers were observed 1155 times, of these 14 triggers lead to the detection of 49 ADRs in 43 patients. The rate of adverse drug events was 12.25/100 patients. DT was the most common trigger identified (81.64%). Positive predictive values (PPV) for PTs, STs, DTs, LTs were 26.88%, 23.07%, 10.3%, and 5.55%, respectively. The comprehensive PPV of PTTL was 11.97%. Modified trigger tool list consists of 14 triggers. Conclusion: TTM is an effective method of ADR monitoring in the surgery department. An awareness of TT helps better detection of ADRs.***

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

1. 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).

The IHI Global Trigger Tool was published in 2003 and revised in 2009 which consists of 15 cares module triggers, 13 medication module triggers, 11 STs, 4 intensive care module triggers, 8 perinatal module triggers, and 2 emergency department module triggers. Most studies evaluated TTM retrospectively to detect ADR. Furthermore, the IHI global trigger tool consists of surgery module triggers which can be evaluated in the surgery department, and limited data were available for the evaluation of TTM in the surgery department. Hence, the present study was conducted to evaluate effectiveness of trigger tools to detect ADRs in Surgery Department of a Tertiary Care Teaching Hospital in Kakinada, India.

2. Materials and Methods

This prospective, observational study was conducted in the Department of Surgery of a Tertiary Care Teaching Hospital in Kakinada, India. Permissions to conduct the study were sought from the Institutional Ethics Committee (IEC/RMC/2020/37 and Head of the Department of Surgery. You should use Times Roman of size 10 for all fonts in the paper. Format the page as two columns:

Validation of preliminary trigger tool list

After evaluation of two reference trigger tool list (TTL), IHI Global TTL[2] and Pérez Zapata et al. list[3] for the presence of triggers, preliminary trigger tool list (PTTL) was prepared based on observation of pilot study and opinion received from clinicians which include 47 triggers: 13 DTs, 13 PTs, 12 STs, and 9 LTs.

Indoor patients of either gender and more than 18 years of age admitted to two selected surgery units were enrolled after prior written informed consent. Case papers of the patient, laboratory investigations, patients' complaints, and discharge forms were observed and evaluated for the detection of triggers until the discharge of the patient. All detected triggers and adverse events were recorded in pretested case record form and analyzed in terms of positive triggers (triggers related to ADRs) and negative triggers (triggers not related to ADRs). Positive predictive value (PPV) of the trigger was calculated. All ADRs were collected in the central drugs standard control organization

(CDSCO) ADR reporting form and assessed for causality, severity, seriousness, and preventability using the WHO-UMC scale,[4] Modified Hartwig and Siegel scale,[5] criteria mentioned in the CDSCO ADR reporting form,[6] and Modified Schumock and Thornton criteria,[7] respectively. Data were entered in Microsoft Excel 2007, and $P < 0.05$ was considered statistically significant [Figure 1].

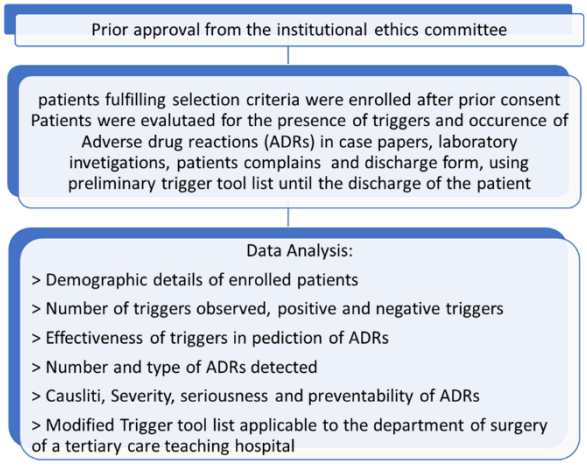

Figure 1: Study design and analysis

A total of 400 patients who fulfill the selection criteria were enrolled. Male: female ratio was 2.3:1 (male [69%] and female [31%]). The mean age of patients was 43.07 ± 16.4 years, and the mean length of hospital stay was 5.75 ± 3.12 days.

Of 47 triggers (PTTL), 24 triggers were found 1155 times in 359 patients; of these, only 14 triggers detected 49 ADRs in 43 patients. The rate of adverse drug events (ADE) was 12.25/100 patients. Neither a trigger nor an ADR was observed in 41 (10.25%) patients.

DT (943 times; 81.64%) was the most commonly observed trigger followed by PT (104 times; 9%), ST (90 times, 7.8%), and LT (18 times; 1.56%). One or more DT was observed 943 times in 359 patients, of which 37 patients had ADRs. Hence, the PPV of DT was 10.3%. Similarly, PT was observed 104 times in 93 patients and 25 patients had ADRs. The PPV of PT was 26.88%. While ST was observed 90 times in 78 patients, of which 18 patients had ADRs. Hence, the PPV of ST was 23.07%. LT was observed 18 times in 18 patients, and one patient had ADR. Hence, the PPV of LT was 5.55%. Among 359 patients, 43 patients had ADRs. Hence, The PTTL had PPV (overall) of 11.97% with sensitivity of 100% and specificity of 11.48%. The PPV for individual triggers ranged from 0% to 100%. The use of thrombophob gel has the highest PPV (100%), followed by rash (83.33%), other complaints not related to disease (48.38%), antihistamines (45.45%), and laxatives (37.5%) [Table 1].

Table 1: Positive predictive value of triggers evaluated at the department of surgery of a tertiary care teaching hospital in Kakinada, India

Trigger	Total triggers observed	Positive triggers	Negative triggers	PPV (%)
DT	943	61	882	
DT1 Sudden stoppage of drug	29	3	26	10.34
DT2- Antihistamines	22	10	12	45.45
DT3 - Antiemetic	348	5	343	1.44
DT4- Antidiarrheal	29	5	24	17.24
DT5 - Laxatives	24	9	15	37.5
DT6- Blood / blood product transfusion	18	2	16	11.1
DT7 - IV fluid started	13	0	13	0
DT8 Thrombophob gel	4	4	0	100
DT9 New drug administration	97	20	77	20.62
DT10 - Antacids	359	3	356	0.84
PT	104	25	79	
PT1 - Rash	6	5	1	83.33
PT2 - Pruritus	14	5	9	35.7
PT3 Patient fall / ethargy / over sedation	7	0	7	0
PT5 - Transfer / reference to other center	43	0	43	0
PT6- Other complains	31	15	16	48.38
PT10 - Readmission within 30 days	3	0	3	0
ST	90	18	72	
ST2 - Change in procedure or procedural complications	75	18	57	24
ST6- Death postoperatively	6	0	6	0
ST7 - Mechanical ventilation > 24 h postoperatively	6	0	6	0
ST11 - Any operative complications	1	0	1	0
ST12 - Wound dehiscence	2	0	2	0
LT	18	1	17	
LT6- Positive blood culture	3	0	3	0
LTB Decrease HB or hematocrit > 25 %	2		3	0
LT9 – Serum electrolyte abnormality	13	1	12	7.69

DT= Drug trigger, PT= Patient Trigger, ST== Surgical module Trigger, LT= Laboratory Trigger, PPV= positive productive value, HB= Hemoglobin

Among positive triggers, nine DT were detected 61 times. While three PT, one ST, and one LT were detected 25 times, 18 times, and 1 time, respectively. Hence, 14 triggers were observed 105 times which related to 49 ADRs [Table 2].

Table 2: Positive triggers and related adverse drug reactions observed at the department of surgery of a tertiary care teaching hospital in Kakinada, India

Trigger	ADR	Number of ADR detected
DT		
DT1 Sudden stoppage of drug	Diarrhea	2
	Gastritis	1
DT2 Antihistamines	Rash	5
	Pruritus	5
DT3 - Antiemetic	Vomiting	5
DT4 Antidiarrheal	Diarrhea	5
DT5 Laxatives	Constipation	9
DT6- Blood / blood product transfusion	Anemia	2
DT8 - Thrombophob gel	Thrombophlebitis	4
E DT9- New drug administration	Rash	5
	Pruritus	5
	Constipation	9
	Diarrhea	5
DT10 Antacids	Gastritis	3
PT		
PT1 - Rash	Rash	5
PT2 - Pruritus	Pruritus	5
PT6 - Other complains	Dizziness	4
	Vomiting	5
	Headache	6
ST		
ST2 Procedural complications	Constipation	9
	Hypokalemia	1
	Headache	6
	Anemia	2
LT		
LT9 - Serum electrolyte abnormality	Hypokalemia	1

DT= Drug trigger, PT= Patient Trigger, ST== Surgical module Trigger, LT= Laboratory Trigger, ADR= Adverse drug reaction

Twenty three triggers (3 of 13 DT, 7 of 13 PT, 7 of 12 ST, and 6 of 9 LT) were not observed in the study population. These triggers were deleted from PTTL for the preparation of a modified TTL (MTTL) that was applicable to the Department of Surgery of a Tertiary Care Teaching Hospital in Kakinada. Triggers with PPV more than 0% were added in the MTTL which consisted of 14 triggers, including 9 DTs, 3 PTs, 1 ST, and 1 LT [Table 3].

Table 3: Modified trigger tool list for the department of surgery of a tertiary care teaching hospital in Kakinada, India

Trigger
DT
Sudden stoppage of drug
Antihistamines
Antiemetic
Antidiarrheal
Laxatives
Blood / blood product transfusion
Thrombophob gel
New drug administration
Antacids
PT
Rash
Pruritus
Other complains
ST
Procedural complications
LT
Serum electrolyte abnormality

DT= Drug trigger, PT= Patient Trigger, ST== Surgical module Trigger, LT= Laboratory Trigger, MTTL= Modified trigger tool list

Gastrointestinal disorders (22, 44.9%) were the most common system organ class affected followed by nervous system disorders (10, 20.4%), skin and subcutaneous tissue disorders (10, 20.4%), vascular disorders (4, 8.16%), blood and lymphatic system disorders (2, 4.1%), and investigation (1, 2.04%). ADRs observed in the study population included constipation (9, 18.36%), headache (6, 12.24%), diarrhea (5, 10.2%), rash (5, 10.2%), pruritus (5, 10.2%), vomiting (5, 10.2%), dizziness (4, 8.16%), thrombophlebitis (4, 8.16%), gastritis (3, 6.12%), anemia (2, 4.1%), and hypokalemia (1, 2%). According to the WHO-UMC scale, 91.8% of ADRs were possibly related to suspect drugs and 8.2% of ADRs were probably associated with suspect drugs. According to Modified Hartwig and Siegel scale, 91.8% of ADRs were moderate in severity while 8.2% of ADRs were mild. Two ADRs (4.1%) were serious, while 95.9% of ADRs were nonserious. All the ADRs (100%) were not preventable according to Modified Schumock and Thornton criteria.

3. Discussion

In the present study, only 14 triggers (105 times) were related to one or more ADRs. DT (81.64%) was most frequently detected followed by PT (9%), ST (7.8%), and LT (1.56%). 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.,[8] similar to the present study.

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.[3] 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 current study, the overall PPV of PTTL was 11.97%. Pérez Zapata et al.[3] reported very high overall PPV (89%) in 350 surgical patients in Spain. A retrospective study lacking causal association with ADEs and less number of triggers used in the study by Pérez Zapata et al.[3] can be the reason for higher PPV. 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 (83.33%), other complaints not related to disease (48.38%), antihistamines (45.45%), and laxatives (37.5%). 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 14 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.[3] which can be because of the lack of causal association of reported ADEs.

4. Conclusion

TTM is an effective method of ADR monitoring in the surgery department. An awareness of trigger tool helps better detection of ADRs. However, further research is required to explore the feasibility and acceptability of TTM.

Conflicts of interest: There are no conflicts of interest.

5. References

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