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RESEARCH ARTICLE

Implementation of a pharmacovigilance system to detect adverse events and improve medication appropriateness in a hospital in Indonesia

Dewi Susanti Atmaja^{1,2} , Yulistiani Y³ , Suharjono S³ , Elida Zairina^{3,4,5} 

¹ Doctoral Programme of Pharmaceutical Science, Faculty of Pharmacy, Universitas Airlangga, Surabaya, Indonesia

² Department of Pharmacy, Faculty of Health, Universitas Sari Mulia, Banjarmasin, Indonesia

³ Department of Pharmacy Practice, Faculty of Pharmacy, Universitas Airlangga, Surabaya, Indonesia

⁴ Innovative Pharmacy Practice and Integrated Outcome Research (INACORE) Group, Universitas Airlangga, Surabaya, Indonesia

⁵ Centre of Excellence for Patient Safety and Quality, Universitas Airlangga, Surabaya, Indonesia

Keyword

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Correspondence

Elida Zairina
Department of Pharmacy Practice
Faculty of Pharmacy
Universitas Airlangga
Surabaya
Indonesia
elida-z@ff.unair.ac.id

Abstract

Background: The growing elderly population has led to an increased occurrence of adverse drug reactions (ADRs) due to the various drugs they are prescribed, posing the problem of potential drug interactions. The application of causality instruments combined with trigger tools and the competency of healthcare professionals has yielded better results in detecting ADRs. **Objective:** To evaluate the implementation of a pharmacovigilance system to detect ADRs, potentially inappropriate medications, and potential prescription omissions. **Methods:** An observational, descriptive, prospective study was conducted over six weeks at one of the largest hospitals in Indonesia. The pharmacist and the physicians collaborated in reviewing patient medication records using the pharmacovigilance system. **Results:** The study enrolled 144 patients. The 163 positive triggers identified helped detect 28 Adverse Drug Events (ADEs) caused by at least one high-alert medication. These ADEs occurred in 25 patients. Additionally, 62 potentially inappropriate medications and 41 potential prescription omissions were detected. **Conclusion:** The pharmacovigilance system could reduce the frequency of ADEs caused by medications used in elderly patients.

Introduction

According to the 2015 data from the World Health Organisation, the elderly population is consistently growing each year. Predictions suggest an increase from 900 million to two billion people between 2015 and 2050 (WHO, 2015). Physiological body changes that occur in the elderly lead to decreased organ function, making older individuals more susceptible to various diseases and reducing their quality of life. There is an increased need for both prescription and over-the-counter medications to manage these conditions. The number of prescribed drugs for older individuals varies, ranging from 2 to 5 routine prescriptions on average. The use of significant medication doses in the elderly often causes polypharmacy, affecting 20-50% of

patients, and poses a high risk of drug interactions and adverse drug reactions (ADRs) (Nojiri *et al.*, 2019).

The prevalence of hospitalised elderly patients due to ADRs related to polypharmacy is 86%, with suspected drug-drug interactions occurring in 49% of cases (Pedrós *et al.*, 2016). ADRs that occur in the hospital contribute to a 9% increase in the length of stay and a 20% increase in treatment costs, including hospital stay and laboratory and overall treatment expenses. Death caused by ADRs in hospitalised patients ranges from 0.1% to 4.7% in patients aged 55 years. The risk of ADR-related mortality becomes even higher in patients aged 75 years and older (Lavan and Gallagher, 2016).

In pharmacovigilance, assessing the causality of ADRs helps understand the risks and benefits of using drugs

and serves as an early warning system for possible ADR events. Optimising ADR detection is accomplished by combining the use of causality instruments and trigger tools while relying on the competence of healthcare professionals. Trigger tools serve to identify ADRs (Pandya *et al.*, 2020). In addition, using relevant tools tailored for elderly patients also helps identify inappropriate drug use, ensuring a safe therapy for the elderly (Santos-Garcia *et al.*, 2020). This study aimed to evaluate the implementation of a pharmacovigilance system (PoSt) to detect adverse drug events (ADEs), potentially inappropriate medications (PIMs), and potential prescription omissions (PPOs).

Methods

Design

This prospective observational study was conducted over six weeks (3 May to 14 June 2023) in one of the largest public hospitals in South Borneo, Indonesia. The study was approved by the ethics committee of the study hospital in South Borneo, Indonesia (approval number 93/IV-Reg Riset/RSUDU/23).

Inclusion and exclusion criteria

The study included patients who were 60 years older, hospitalised for a non-emergency degenerative disease, receiving polypharmacy defined as taking five or more drugs), and having a hospital stay of more than 48 hours. Patients were excluded from the study if their admission was related to chemotherapy or cancer diagnosis, had chronic kidney disease, or if they were admitted for surgery and receiving palliative care.

Data collection

The pharmacist and the physicians collaboratively reviewed patient medication records using PoSt, a web-based application described in a previous study and used to detect ADEs and optimise medication appropriateness in elderly patients based on TRIGGER-CHRON and STOPP/START criteria version 2 (O'Mahony *et al.*, 2015; Otero *et al.*, 2021). An electronic form developed for PoSt studies was used to record each detected trigger, ADEs, PIM, and PPO.

Data analysis

Data were analysed with the Statistical Package for Social Sciences (SPSS) 26.0 for Macintosh. Descriptive statistics were used to calculate the frequencies and percentages for the number of patients, triggers, ADEs, PIMs, and PPOs detected by PoSt.

Results

In the six weeks of the study period, 587 elderly patients were admitted to the hospital, but only 144 met the inclusion criteria. Follow-up was carried out until the patient was discharged or died. Table I shows the sociodemographic characteristics of the participants. The most comorbidity identified in the patients is cardiovascular disease (28.9%), followed by neurological disorders (14.4%).

Table I: Sociodemographic characteristics

| Characteristics | Frequency (Percentage) | % |
|---|------------------------|------|
| Age (mean) | 68.3 (6.7) | - |
| Sex | | |
| Male | 74 | 51.7 |
| Female | 69 | 48.3 |
| Number of comorbidities per patient | | |
| 1 | 54 | 37.8 |
| 2 | 46 | 32.2 |
| ≥3 | 43 | 30.1 |
| Polypharmacy (number of medications) | | |
| Major (5 to 9) | 87 | 58.0 |
| Severe (≥10) | 63 | 42.0 |
| Rehospitalisation | 7 | 4.8 |
| Death | 18 | 12.5 |

Prevalence of triggers and ADEs

Using PoSt, 163 positive triggers were identified from the 144 medical records reviewed, leading to the detection of 28 ADEs caused by at least one high-alert medication. These ADEs occurred in 25 patients, noting that one ADE can be identified by one or more triggers. The most frequently detected trigger was the administration of antiemetics with the trigger code D5 (Figure 1). Figure 2 displays medications causing ADEs identified by trigger codes.

Prevalence of PIMs and PPOs

Medication appropriateness in elderly patients was enhanced by detecting PIMs and PPOs using STOPP/START version 2, one of the instruments integrated into PoSt. A total of 62 PIMs and 41 PPOs were detected. The highest number of PIMs (n=27) was in section B, related to the cardiovascular system (Figure 3a), while the highest number of PPOs (n=35) was in section A, related to the cardiovascular system (Figure 3b).

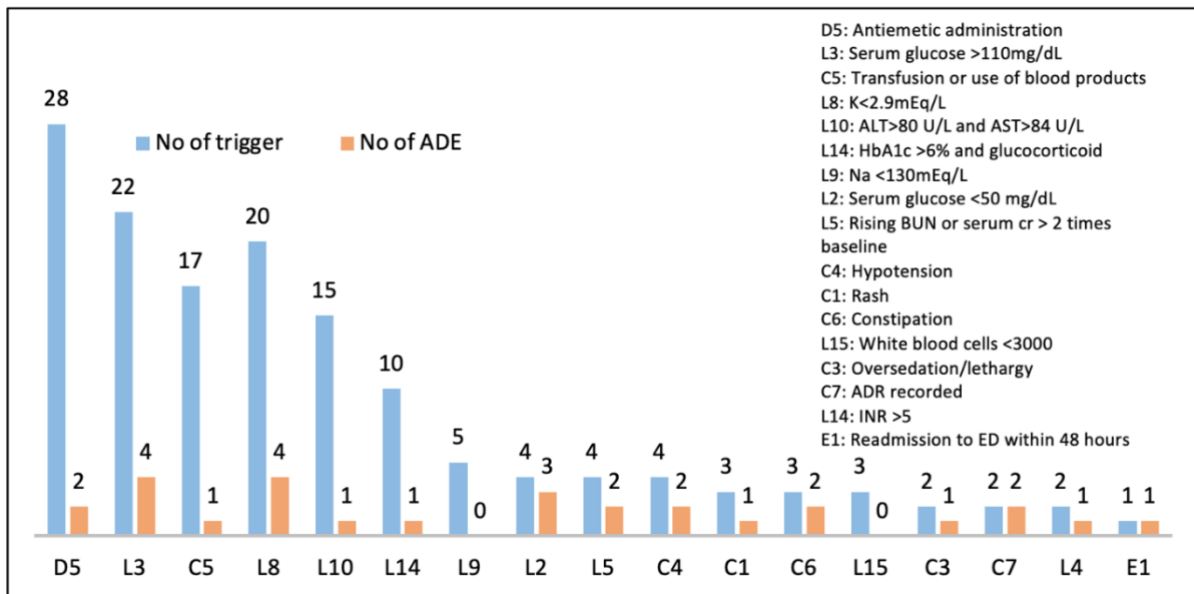


Figure 1: Prevalence of triggers and ADEs detected by PoSt

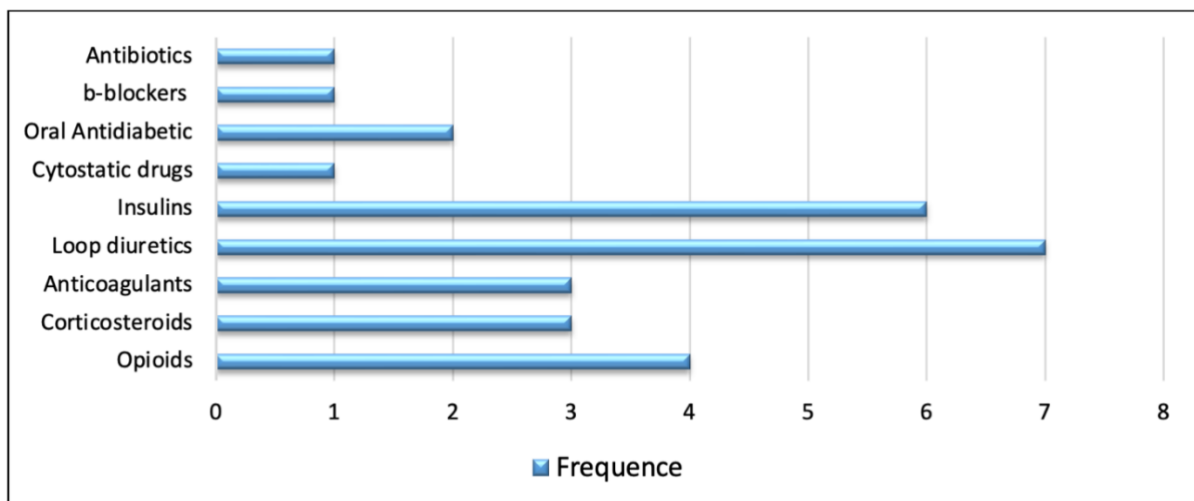


Figure 2: Medications causing ADEs identified by trigger codes

Discussion

ADEs are a common cause of morbidity and mortality, particularly in elderly patients with polypharmacy (Sheikh *et al.*, 2017), defined as taking more than five medications at the same time. The risk of ADRs and drug interactions increases with the number of medicines taken, often leading to additional drug prescriptions to address problems caused by ADRs. This situation indirectly reduces patient adherence to medications (Barclay, 2018). In this study, the implementation of PoSt allowed for the detection of 28 ADEs caused by at least one high-alert drug in the HAMC register, occurring in 25 patients and indicating

a prevalence of ADEs related to high-alert medications of 17.4 per 100 admissions. This result is slightly lower than previous studies, with a majority of 19.3 per 100 admissions (Otero *et al.*, 2021).

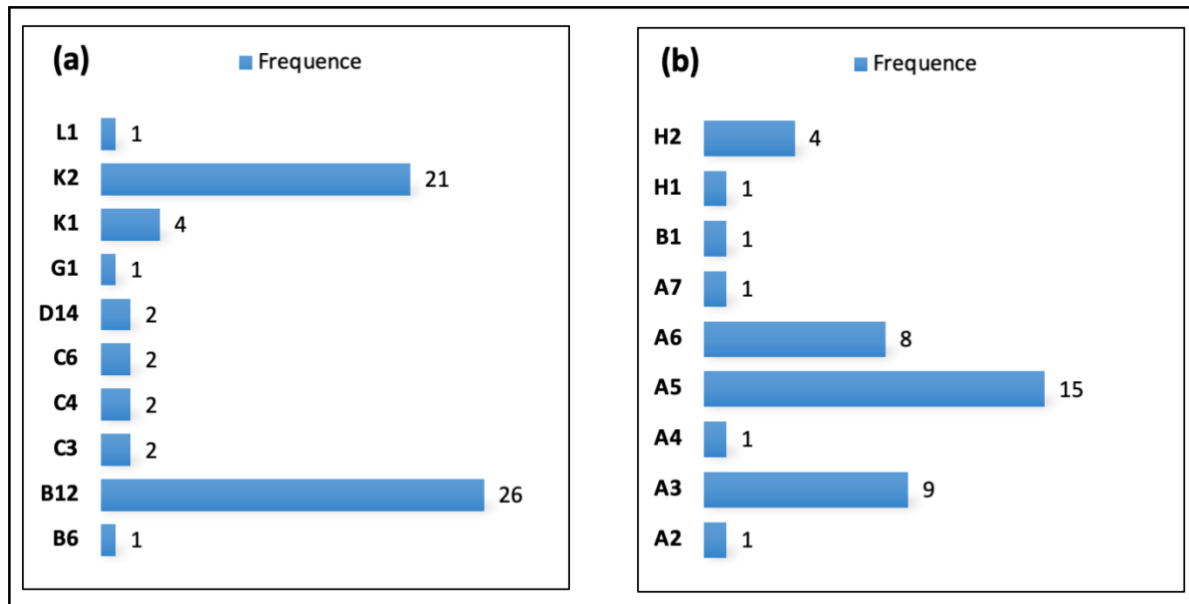
The low detection ability of the TRIGGER-CHRON instrument in this study could be attributed to a difference in the study duration, with this study lasting six weeks compared to the 12 weeks of the previous study. Additionally, the number of medical records reviewed is also different, whereas the previous study involved 720 medical records (Otero *et al.*, 2021). Trigger tools help identify ADRs (Pandya *et al.*, 2020). Their benefits are bound to whether they are

developed according to current field conditions, thereby exhibiting optimal effectiveness in improving patient safety (Davis *et al.*, 2018).

PoSt generated 62 STOPP and 41 START recommendations, with most PIMs and PPOs related to cardiovascular medications. This result aligns with the findings of a previous study, where the implementation of the STOPP/START instrument version 2 yielded 43 STOPP and 49 START recommendations, with a similar emphasis on cardiovascular medications (Herawati *et*

al., 2020). Other studies have also reported similar results, where the detected PIMs and PPOs were associated with the overuse of aspirin and the underuse of both antiplatelets and statins (Fahrni *et al.*, 2019).

Loop diuretics were associated with the most encountered ADEs in this study. Many PIMs and PPOs are still found in prescribing practices for elderly patients in Indonesia (Darmawan *et al.*, 2020).



(a): B: cardiovascular system; C: coagulation system; D: central nervous system; G: gastrointestinal system; K: drug predicted to increase fall risk in the elderly; L: analgesic drugs

(b): A: cardiovascular system; B: respiratory system; H: analgesic

Figure 3: (a) STOPP Recommendation; (b) START Recommendation

Using tools such as the STOPP/START or Beers criteria in medication reconciliation can help identify PIMs in elderly patients and prevent the occurrence of ADRs. The STOPP/START criteria are more recommended for detecting PIMs and PPOs in hospitals, while the Beers criteria are more suitable for detecting PIMs and PPOs for homecare or outpatient care (Fick, 2003; O'Mahony, 2015).

Strengths and limitations

A group of healthcare professionals can use the STOPP/START recommendations when making a clinical judgment on patient treatment. The combination of the TRIGGER-CHRON and STOPP/START instruments with the PoSt application has been shown to be appropriate for detecting ADEs induced by PIMs and PPOs and improving medication appropriateness in

older patients. In addition, a module for pharmaceutical safety in Indonesia has been developed (Ernawati, 2022).

However, this study has some limitations. The constraints on data collection time have resulted in a limited quantity of medical records evaluated. As this study was conducted at a single hospital, the findings may not be representative of the entire Indonesian population. Furthermore, this study is merely observational. Establishing techniques to prevent and mitigate ADEs utilising PoSt is also critical. The deployment of PoSt should be supported by a partnership of healthcare professionals working in interdisciplinary groups to provide the most effective safety solutions for PoSt analysis.

Conclusion

The implementation of PoSt could reduce the number of incidents caused by medications among elderly patients.

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