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Mitigating the burden of adverse drug reactions in older inpatients: short commentary

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Background

Studies have consistently identified older age as a predictor of adverse drug reaction (ADR) and the related adverse outcomes [1, 2]. The safety data collected during the premarketing phase is lacking due to the omission of distinctive groups of patients including the elderly [3]. In the US, approximately 100,000 emergency hospital admissions of older adults, 65 years of age or older, was attributed to ADRs every year. Among the hospitalized older patients, significant proportion (15% to 35%) incurs an ADR during their hospital stay [4–6]. The culprit medications, however, were largely among the commonly used ones rather than medications typically identified as high-risk or inappropriate [7]. A significant increase in elderly population was apparent over the past decades [8].

Moreover, multiple diseases in elderly account for polypharmacy which increases the risk of ADRs by mounting the probability of drug interactions [6, 9]. Incidence of ADRs in elderly (11%–32%) is much higher as compared to general population [10, 11].

ADRs are difficult to detect in older populations and are more often presented acutely with symptoms that are highly prevalent in people with multiple comorbidities, for example, dizziness, delirium or falls [12]. Timing, the pattern of illness, the results of investigations, and re-challenge can help attribute causality to a suspected ADR [13].

This review aimed at identifying and summarizing the findings of the relevant studies thereby enabling the health facilities and the respective health professionals to implement the recommendations and thus, to effect mitigation in the incidence of ADRs among hospitalized older patients.

This review was performed according to Preferred Reporting Items for Systematic Reviews and Meta Analyses guidelines [14]. A comprehensive systematic literature search focusing on the incidence and predictors of ADRs in hospitalized elderly patients was conducted using PubMed, Scopus and Google Scholar to recover articles published in English from 2000 to 2020. A combination of the following keywords were used: “risk factors”, “determinants”, “predictors”, “associated factors”, “contributing factors”, “incidence”, “prevalence”, “occurrence”, “burden”, “adverse drug reactions”, “drug related side effects”, “adverse drug events”, “adverse drug effects”, “drug toxicity”, “adult patients”, “elderly patients”, “older adults”, “older patients”, “geriatric patients” combined with “hospitalized”, “admitted”, “inpatients”, “hospital admission”, “acute care admission” and “hospitalization”. The search was conducted latest of 25th February, 2020 and limited to English language.

Reducing the occurrence of ADRs in hospitalized elderly patients

General measures to detect and prevent ADRs among elderly inpatients

Currently, there is scarce standardized method for ADR prediction,

detection, causality assessment and avoidance in older people. Without such tools, a reliable and dependable prediction of ADRs is difficult to achieve. The emphasis on the most frequently involved culprit drugs in ADRs among older hospitalized patients may possibly help in predicting the ADR occurrence better than patient characteristics alone [13].

The proportion of preventable ADRs ranged from 18.7% to 92.1% [15, 16]. Given that ADRs represent an enormous burden for older populations, any attempt should be made to prevent them. Fortunately, more serious ADRs are more likely to be preventable [15]. However, this objective can be pursued not only by limiting the number of prescribed drugs but also by using the minimal effective doses. Moreover, recognizing patients with impaired renal function is an obvious condition for optimal dosing. Thus, glomerular filtration rate should be obtained in older people before prescribing or reevaluating drug therapy [17].

Good clinical practice for detecting and predicting ADRs in susceptible patients, including the elderly, comprises of thorough documentation and consistent evaluation of prescribed and over-the-counter medications as well as herbal remedies through standardized medication reconciliation [18]. Strategies that precisely address the management of complex drug regimens are required [18–21].

Specific interventions to mitigate the incidence of ADRs among elderly inpatients

There are several strategies with promising outcomes in preventing ADRs. Most of the elderly patients used at least one potentially inappropriate medication (PIM) as categorized by Beers criteria; and up to 40% of them experienced ADRs [22]. Accordingly, a routine use of Beers criteria to identify and avoid PIMs can significantly reduce the incidence of ADRs in these patients. Focusing on high-risk medications and patients with multi-morbidity may advance prediction of ADR [13].

The prevalence of polypharmacy and drug-drug interactions is much higher among the elderly patients as compared to the general population and up to 97.75% of the prescriptions for older patients were identified with drug-drug interactions using Lexi-Comp version 2.4.1 database tool [9]. Given the strong association established between polypharmacy, drug-drug interactions and ADR, a consistent check for drug-drug interactions and adherence to the Preventable by Adherence to Screening Tool of Older Persons’ Prescriptions (STOPP) criteria to avoid the use of PIMs using standard tools like Lexi-Comp and STOPP criteria might significantly mitigate the high burden of ADRs in this group of patients [6, 10, 11, 23, 24].

Most of the ADRs in the elderly are caused by commonly prescribed drugs like antibacterial and analgesics. Nearly one fourth of the ADRs are due to PIM which can be avoided by careful application of Beer’s criteria [16]. Two randomized controlled trials on application of STOPP/START criteria to hospitalized older patients indicated a

significant decrease in the risk of ADRs [25]. To ensure the cost-effectiveness of such strategies, it would be necessary to target them to those older individuals who are at highest risk of experiencing ADRs [26]. Thus, application of validated ADR prediction tools may significantly reduce the incidence of ADRs among older patients admitted to health care facilities.

Increased comorbid complexity was another consistent determinant of increased risk of ADR [27–29]. Comorbidity from chronic conditions and severity of the disease and comorbid conditions including congestive heart failure, liver disease, and renal failure [30–32]. Isolating these patients and offering unusual screening and monitoring may potentially reduce the incidence and complications of ADRs in elderly inpatients.

Multiple studies identified cardiovascular agents, analgesic medications, anti-diabetic drugs, antibacterials, central nervous system agents, anticoagulants, cytotoxics, anti-rheumatics, hypoglycemic medications, insulin, non-steroidal anti-inflammatory drugs and antimalarials as the drug classes most frequently implicated in ADRs among older patients [5, 19, 23, 33–38]. Whenever possible, older patients should be treated with other alternative drugs. Doctors and pharmacists should closely monitor for the likely ADRs in patients receiving any of these high risk medications.

Studies have shown an increase in the risk of ADR among hospitalized patients who used a herbal medicine preadmission [39]. Comprehensive medication history which includes previous use of herbal medicine enables clinicians to timely identify and manage ADRs in hospitalized patients.

To prevent ADRs associated with misunderstanding and inappropriate use by patients, the universal medication schedule and other individualized strategies should be put in place [40]. This requires special commitment in educating and counseling patients on their health conditions and medications.

Active clinical pharmacist engagement in wards resulted in a significant reduction in ADRs by 35% to 78% among older patients [41, 42]. In wards, pharmacists should give the best priority to older patients, especially those with multiple comorbidities, and closely monitor them for ADRs and proactively intervene when modifiable risks are identified.

Conclusion

Incidence of ADRs in elderly is much higher as compared to the general population. ADRs are difficult to detect in older populations and are more often presented acutely with symptoms that are highly prevalent in this group of population. Most of ADRs in older inpatients are preventable. There are several strategies with promising outcomes in preventing ADRs in hospitalized older patients. Most of them use at least one PIM and thus, a routine use of Beers criteria to identify and avoid PIMs can significantly reduce the incidence of ADRs in these patients. Similarly, given the strong association established between polypharmacy, drug-drug interactions and ADR, a consistent check for drug-drug interactions and adherence to the STOPP criteria to avoid the use of PIMs might significantly mitigate the high burden of ADRs in this group of patients. Moreover, identifying patients with high risk comorbid conditions and on PIMs and offering unusual screening and monitoring may potentially reduce the incidence and complications of ADRs in elderly inpatients. Comprehensive medication history which includes previous use of herbal medicine enables clinicians to timely identify and manage ADRs in hospitalized patients. To prevent ADRs associated with misunderstanding and inappropriate use by patients, the universal medication schedule and other individualized strategies should be put in place. Active clinical pharmacist engagement in wards resulted in a significant reduction in ADRs among older patients.

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Competing interests

The authors declare no conflicts of interest.

Abbreviations

ADR, adverse drug reaction; PIM, potentially inappropriate medication; STOPP, Preventable by Adherence to Screening Tool of Older Persons' Prescriptions.

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