Assessment of appropriate medication use by 2015 Beers criteria among elderly critically ill patients in Jordan

Background: Inappropriate prescribing can cause significant morbidity and mortality in geriatric patients. Studies implementing the updated 2015 American Geriatrics Society (ACG) Beers Criteria in the identification of potentially inappropriate medications (PIM) are lacking. In addition, there is limited information regarding PIM use in critically ill older adults.

Objective: To investigate the prevalence, patterns and determinants of PIM among elderly critically ill patients in Jordan.

Setting: critical care unit (surgical, medical, cardiac) at Jordan University Hospital, Amman, Jordan

Method: A cross-sectional study conducted over a 5- month period. Patients 65 years and older, taking at least one medication and admitted to critical care unit, were included. PIM were identified and classified in accordance with the American Geriatrics Society 2015 Beers Criteria.

Results: One hundred and fifty-four patients were included (55.8% males), the mean age was 75.4 ± 7.1 years. The median number of prescribed medications was 11 (IQR=6). The use of at least one PIM was identified in 51 (33.1%). In 90 cases (58.4%), medications to be used with caution in older adults were also evaluated. Patients who received at least one PIM were prescribed a higher total number of medications in the hospital (13 vs. 11.5, P<0.05). Diabetes was also significantly associated with PIM prescription (84.3% vs. 49.5%, P<0.005).

Conclusion: PIM prevalence among ICU elderly patients was high (every third patient). The factors associated with PIM prescription included the total number of medications and presence of diabetes mellitus.

Keywords: potentially inappropriate medications, elderly, Beers Criteria, critically ill patients, Jordan

Introduction

Ageing is accompanied by changes in drug absorption, distribution, metabolism, excretion and sensitivity to adverse effects. All these changes challenge the selection of an appropriate pharmacotherapy.

Inappropriate prescribing can cause significant morbidity and represents a clinical and economic burden to patients and society [1,2].

Results from clinical research revealed an association between inappropriate prescribing and different aspects of health and economic including but not limited to: mortality, the need for additional health care services, adverse drug events and lower quality of life [3-7]. For these reasons, spreading the culture of appropriate prescribing for geriatric patients in different clinical settings is important.

Appropriate prescription can be assessed both by explicit (criterion-based) and implicit (judgment-based) criteria [8]. Explicit criteria of inappropriate prescribing are defined as a list of drugs which are considered inappropriate in general or for older adults with certain chronic conditions. In contrast, implicit criteria of inappropriate prescribing are statements that are used to evaluate the appropriateness of individual drugs prescribed for older patients.

The American Geriatrics Society (ACG) Beers Criteria [9] and the STOPP/START [10] (Screening Tool of Older People's Prescriptions/ Screening Tool to Alert to Right Treatment) stand out among the most commonly used explicit criteria.

These criteria are arranged by body system or therapeutic category and their implementation is not time-consuming [11].

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These major criteria have been updated recently, and their relative applicability in practice is a major area of research in the geriatric literature [9-12]. A recent version of Beers Criteria has been published by the American Geriatrics Society in 2015 [9].

The 2015 Beers Criteria include a list of potentially inappropriate medications (PIMs) for the use in elderly that are categorized into three groups: (1) potentially inappropriate medication use in older adults regardless of medical conditions (2) potentially inappropriate medication use in older adults due to drug–disease or drug–syndrome interactions that may exacerbate the disease or syndrome (3) potentially inappropriate medications to be used with caution in older adults [9].

Two tables were added to the 2015 Beers Criteria: one for potentially clinically important non-anti-infective drug–drug interactions that should be avoided in older adults and the other for non-anti-infective medications that should be avoided or have their dosage reduced with varying levels of kidney function in older adults.

In addition, five new medications or drug classes were added including proton pump inhibitors, desmopressin, antipsychotics, non-benzodiazepine hypnotics and opioids.

However, several recommendation or rationale statements were altered – for example, exceptions for antipsychotic agents were added to allow for use in schizophrenia and bipolar disorder or as short-term antiemetic during chemotherapy [9].

Compared to Beers Criteria which concerns only drugs that are inappropriate, STOPP–START tool gives recommendations for drugs that should be started for geriatric patients with certain medical conditions (for example, aspirin or clopidogrel for coronary, cerebral or peripheral vascular disease) [10].

However, the successful application of STOPP–START criteria relies on a clinician's skills in reviewing patients' medication list in relation to medical history, duration of drug use, drug–drug and drug–disease interactions and the completeness of patient's records for such data.

Studies that compared between the Beers and STOPP–START criteria suggested that the updated version of Beers criteria could detect more PIMs than both the older versions of Beers and STOPP–START criteria. As an example, the Italian REPOSI trial elucidated that the 2012 Beers criteria identified more PIMs (23.5%) than the 2003 version (20.1%) [13].

Another study conducted in Spain revealed that the 2012 Beers criteria detected higher number of PIMs (44%) when compared to the 2003 Beers and the 2008 STOPP–START criteria (24.3 and 35.4%, respectively) [14].

To date, studies implementing 2015 AGS Beers criteria in the identification of PIMs are lacking. Different evaluation studies of the prevalence of patients with inappropriate prescribing have been conducted resulting in values that range between 15 and 79%, depending on the type of population studied [13,15-17].

Compared to the general ambulatory and hospitalized elderly patients, critically ill patients are at increased risk of potentially inappropriate medications (PIMs) use. Data on appropriateness of prescribing among these patients, however, is limited.

There are several studies that assessed PIM prescription among elderly patients in different clinical settings including ambulatory care or home care centers [18,19] and hospitals [13,20], but very few studies addressed PIM prescription in critically ill patients [21,31].

Aim of the study

The aim of this study was to evaluate the appropriateness of medication use among critically ill geriatric patients using 2015 Beers criteria and to identify the factors associated with inappropriate prescribing. To the best of our knowledge, this is the first study that evaluates prescribing of potentially inappropriate medicines in critically ill older adults using 2015 Beers criteria.

Methods

■ Study design and data collection

This was a cross sectional study conducted over a five-month period between September 2016 and January 2017 at the Jordan University Hospital.

This study consequently enrolled critically ill patients over the age of 65 who were

admitted to medical, surgical or cardiovascular intensive care units. The study started after obtaining approval from The Jordan University Hospital Institutional Review Board (IRB) Committee. Data collection and determination of inappropriate prescribing was performed by two clinical pharmacists with at least two years of experience using a structured questionnaire. Data collected included demographic and clinical characteristics of patients (comorbidities, admission diagnosis, length of hospital stay), and details related to medications prescribed including total number of medications, indications and doses.

Informed consent: "Informed consent was obtained from all individual participants included in the study

■ Determination of potentially inappropriate medication

PIMs were analyzed using 2015 Beers Criteria for potentially inappropriate medication use in older adults. In addition, medical records were assessed in order to identify factors in favor for prescription of a PIM and, based on this information; appropriateness of each PIM prescribed was re-assessed.

All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) 23. Categorical and continuous values were expressed as frequency (percentage) and mean ± SD, respectively.

The comparison between the patients prescribed PIMs and their counterparts was conducted using independent-sample t test for continuous variables and Chi square test for categorical variables. For data that were non-normally distributed, corresponding non-parametric tests were applied. A two-sided P value<0.05 was considered to be statistically significant.

Results

■ Demographic and clinical characteristics of participants

One hundred and fifty four patients were included, of whom males accounted for 55.8% (N=86). Patients had mean age of 75.4±7.1 years, median length of ICU stay of 3 days (IQR=2) and received median number of prescribed medications of 11 (IQR=6).

The most common comorbidities in the studied patients were hypertension, 83.8% (N=129), diabetes, 61.0% (N=94) and congestive heart failure, 44.8% (N=69).

Cardiogenic shock, myocardial infarction and atrial fibrillation collectively comprised the most common reason for ICU admission, 44.8% (N=69), followed by sepsis and adult respiratory distress syndrome (ADRS), 22.1% (N=34), collectively.

TABLE 1 describes the demographic and clinical characteristics of the study population.

Table 1. Demographic and clinical characteristics of critically ill elderly patients (N=154).

Gender, [N (%)]	
Male	86 (55.8)
Age (mean ± SD)	75.4 ± 7.1
65-69	32 (20.8)
70-74	46 (29.9)
75-79	37 (24.0)
80-84	21 (13.6)
>85	18 (11.7)
Median (min-max)	74 (65-98)
Length of hospital stay from the admission to the index day [median days (IQR)]	3 (2) (1-24)
Intensive care unit type at admission, [N(%)]	
Medical ICU	60 (39.0)
CCU	63 (40.9)
Surgical ICU	31 (20.1)
Reason of hospitalization, [N(%)]	
Cardiogenic shock, MI, atrial fibrillation (AFib)	69 (44.8)
Sepsis or (ADRS)	34 (22.1)

Surgery	14 (9.7)
Upper gastrointestinal bleeding (UGIB)	4 (2.6)
Infection without sepsis [including cholangitis, pneumonia , cellulitis, pancreatitis, urinary tract infection (UTI) and diabetic foot infection (DFI)]	17 (11.0)
Ischemic or hemorrhagic stroke	2 (1.3)
Status epilepticus	11 (7.1)
Others (road traffic accident, acute kidney injury (AKI))	2 (1.3)
Total number of drugs received in the hospital [median (IQR)]	11 (6)
Number of inappropriate drugs prescribed during hospital stay, [N(%)]	
None	103 (66.9)
1	43 (27.9)
2	8 (5.2)
Comorbid conditions, [N(%)]	
Hypertension (HTN)	129 (83.8)
Atrial fibrillation (Afib)	33 (21.4)
Ischemic heart disease (IHD)	68 (44.2)
Myocardial infarction (MI)	44 (28.6)
Congestive heart failure (CHF)	69 (44.8)
Cerebrovascular disease	24 (15.6)
Chronic obstructive pulmonary disease (COPD)	17 (11.0)
Diabetes mellitus	94 (61.0)
Uncomplicated	37 (24.0)
Complicated (end organ damage)	57 (37.0)
Moderate-to-severe chronic kidney disease	61 (39.6)
Charlson co-morbidity index score [median (IQR)] Mean ± SD	6 (3) 6.8 ± 2.0
Number of prescribed drugs to be used with caution, [N(%)]	
0	64 (41.6)
1	61 (39.6)
2	27 (17.6)
3 or 4	2 (1.2)
Presence of a drug interaction that should be avoided, [N(%)]	
Yes	7 (4.5)
No	5.5)
	147

Table 2. Potentially inappropriate medications identified by 2015 Beers Criteria.

Drug/drug class	N (%) *
Anticholinergics	9 (5.8)
Atropine	3 (1.9)
Chlorpheniramine	3 (1.9)
Orphenadrine	1 (0.6)
Scoplolamine	2 (1.2)
Antiparkinsonism	1 (0.6)
Carbidopa/levodopa	1 (0.6)
Alpha blocker (doxazosin)	2 (1.3)
Digoxin	13 (8.4)
Inappropriate prescribing of digoxin	2 (1.3)
Amiodarone (appropriately prescribed for: ventricular arrhythmia, second line treatment for AFib, pulseless CPR)	15 (9.7)
Nifedipine immediate release	1 (0.6)
Antidepressant (citalopram)	2 (1.3)
Antipsychotic	8 (5.2)
Short- and intermediate-acting benzodiazepines Bromazepam, midazolam)	6 (3.8) 3 (1.9) 3 (1.9)
Long-acting benzodiazepines (diazepam)	2 (1.3)

Insulin sliding scale	19 (12.3)
Glyburide (glibenclamide)	3 (1.9)
Metoclopramide	11 (7.1)
Proton pump inhibitors (PPI)	116 (75.3)
Inappropriate prescribing of PPI **	1 (0.6)
Meperidine	4 (2.6)
NSAIDs (diclofenac)	1 (0.6)
Drugs to be used with caution, [N(%)]	
Carbamazepine	4 (2.6)
Furosemide	70 (45.5)
Haloperidol	6 (3.9)
Indapamide	6 (3.9)
Isosorbide dinitrate	19 (12.3)
Others	13 (8.4)
Categories of drug interactions that should be avoided, [N(%)]	
Anticholinergic with anticholinergic	1 (0.6)
Warfarin with amiodarone	4 (2.6)
Benzodiazepine with two or more CNS active drugs	2 (1.3)

*Valid percent
**appropriate prescribing of PPI is defined as prescription of PPI for stress ulcer prophylaxis according to the American Society of Health System Pharmacists. The guidelines recommend stress ulcer prophylaxis for ICU patients with any of the following characteristics: Coagulopathy, mechanical ventilation for more than 48 hours, history of GI ulceration or bleeding with the past year, and two or more minor risk factors. Minor risk factors include sepsis, ICU admission lasting >1 week, occult GI bleeding lasting ≥6 days, and glucocorticoid therapy.

Table 3. Predictors of PIM prescription in critically ill patients.

Variables	Predictors of PIM prescription in critically ill patients.		
	Yes (N=51)	No (N=103)	P*
Continuous variables	**Mean ± SD**		
Age	76.2 ± 6.9	75.0 ± 7.2	0.348
Total number of drugs received in hospital	13.0 ± 4.5	11.5 ± 4.2	0.043
Length of hospital stay	4.4 ± 4.7	3.9 ± 3.0	0.372
Charlson co-morbidity index score	6.9 ± 1.9	6.8 ± 2.1	0.741
Categorical variables	N (%)		P**
Intensive care unit type			
Medical ICU	20 (39.2)	40 (38.8)	0.432
CCU	18 (35.3)	45 (43.7)	
Surgical ICU	13 (25.5)	18 (17.5)	
Gender			
Males	24 (47.1)	62 (60.2)	0.122
Females	27 (52.9)	41 (39.8)	
Reason for hospitalization			
Cardiogenic shock, MI, AFib	19 (37.3)	50 (48.5)	0.046
Sepsis or ARDS	9(17.6)	25 (24.3)	
Surgery	8 (15.7)	7 (6.8)	
UGIB	3 (5.9)	1(0.9)	
Infection without sepsis	5 (9.8)	12 (11.7)	
Ischemic or hemorrhagic stroke	0 (0)	2 (1.9)	
Status epilepticus	7 (13.7)	4 (3.9)	
Others	0 (0)	2 (1.9)	
Comorbid conditions			
HTN	46 (90.2)	83 (80.6)	0.128
AFib	8 (15.7)	25 (24.3)	0.222
Ischemic heart disease	24 (47.1)	44 (42.7)	0.61
Myocardial infarction	13 (25.5)	31 (30.1)	0.551
Congestive heart failure	17 (33.3)	52 (50.5)	0.044
Cerebrovascular disease	11(21.6)	13 (12.6)	0.150

COPD	3 (5.9)	14 (13.6)	0.151
Diabetes Mellitus	43 (84.3)	51(49.5)	<0.005
Moderate-to-severe chronic kidney disease	18 (35.3)	43 (41.7)	0.441

* calculated using independent-sample t-test, ** calculated using Chi-square test MI: myocardial infarction, AFib: atrial fibrillation, ARSD: adult respiratory distress syndrome, UGIB: upper gastrointestinal bleeding, HTN: hypertension, COPD: chronic obstructive pulmonary disease

■ Potentially inappropriate medications

The use of at least one PIM was identified in 51 (33.1%) of elderly patients treated in ICUs according to 2015 Beers Criteria.

Prescription of insulin sliding scale (12.3% of PIMs) accounted for the greatest number of PIMs detected, followed by amiodarone (9.7%), digoxin (8.4%) and metoclopramide (7.1%). Proton pump inhibitors were prescribed for 75.3% of patients but their use was justified for prevention of stress ulcer.

The list of medications to be used with caution in older adults was also evaluated; they were identified in 90 (58.4%) cases. The most frequently prescribed drugs to be used with caution were furosemide, 45.5% (n=70) and isosorbide dinitrate, 12.3% (N=19).

Drug interactions that should be avoided were found in 7 (4.5%) of older patients. These data are shown in detail in **TABLES 2 and 3**.

Patients who received at least one PIM were prescribed a higher total number of medications in the hospital (13 vs. 11.5, P<0.05). Diabetes was also significantly associated with PIM prescription (84.3% vs. 49.5%, P<0.005).

Type of ICU (medical vs. surgical vs. cardio), patient gender, age, Charlson comorbidity index and comorbid conditions other than diabetes were not significantly associated with PIM prescription.

Discussion

Elderly, a vulnerable population, represents the fastest growing up group treated in the ICU and is frequently prescribed PIM [21].

As opposed to massive efforts exerted towards reducing PIMs in community-dwelling elderly adults, inpatients, particularly those who are critically ill, received lower attention. Different rates of PIM prevalence among elderly patients are seen according to the clinical setting that include ambulatory care [22,23], home care [24-26] hospitalized non-critically ill [27-29] and critically ill brain injury patients [21].

In this study, the rate of PIM prescription among critically ill older patients was 33.1% which is comparable to that reported in Ireland (32%) [15], however, for the latter assessed generally acutely ill elderly patients using Beers 2003 Criteria.

The prevalence of PIM prescription in other countries was much higher. In Brazil the prevalence of PIM prescription in generally hospitalized patients was 95.5 % [30], while in critically ill patients it was 98.2% [31], while in USA it occurred in 81.3 % of critically ill patients with neurological injury [21].

The high grade of variability in PIM prescription might be related to different categories of patient (critically ill vs. hospitalized in general, neurological injury vs. critically ill in general), differences in prescribing habits, etc.

Similar to situation with elderly hospitalized patients, among home care elderly residents, the prevalence of PIM was found to be 20% in Europe [32], 38% in USA [24], 38.2% in Qatar [25] and 40% in Japan [26].

What makes this study unique among the few studies conducted in critically ill elderly patients is that we used both explicit measures (Beers Criteria 2015) and clinical judgment to identify PIM and factors predicting their use. Clinical judgment is usually needed in geriatric medicine because evidence-based aspects of treatments are frequently absent.

All studies assessing PIM prescription in critically ill patients [21,30,31] applied only explicit criteria that focused on a drug or a disease rather than on a patient. Although The AGS Beers Criteria were shown to significantly affect patient care [13,14], it represents only a part of the complex system to improve medication use in elderly in order to optimize health outcomes.

The current study demonstrated that the significant predictors of PIMs use were the total number of medications received in the hospital and the presence of diabetes mellitus. Several

other studies identified a positive association between the total number of medications prescribed and the PIM use [15,23,3334].

As compared to this study findings, Galli et al. (2016) [31] demonstrated that the number of prescribed PIMs was significantly associated not only with the total number of medications received but also with ICU length of stay.

An interesting finding in our study is the high percentage of PIMs classified as medications to be used with caution (48.4 %), - that should draw clinicians' attention and needs frequent assessment of risk against anticipated benefit of using these PIMs. Noticeably, this class consists of medications that can be potentially misused or harmful, yet the consensus view of the panel explored that their use can be adequately justified in some patients, especially in the setting of critically ill patients where many of these drugs are used intermittently [9].

In this study, sliding scale insulin (12.3%), amiodarone (9.7%), digoxin (8.4%) and metoclopramide (7.1%) were the most commonly prescribed PIM in critically ill older patients. In Brazil study, among critically ill patients, metoclopramide prescription was responsible for the greatest number of PIMs detected (28.6%), followed by benzodiazepines (8.4%), antipsychotics (8.3%) and amiodarone (7.8%) [31].

Among critically ill elderly patients with neurological injury in USA, the most common PIMs prescriptions involved barbiturates (23%), opioids (18 %), and H2RAs (12%) [21].

In a study by Morandi et al. (2013) [35], the three most common PIMs prescribed at hospital discharge following medical, surgical, or cardiovascular ICU admission were opioids, anticholinergics, and antidepressants.

Each ICU may have different PIMs that need to be evaluated. Medications regarded as potentially inappropriate in a certain patient population may be appropriate in another one due to difference in risk-benefit ratio or the lack of alternative choices. For example, critically ill patients often experience pain and agitation, therefore the use of evidence-based pharmacotherapy such as neuroleptics and benzodiazepines which may have a higher anticholinergic and sedative effect that are potentially hazardous in the elderly population, may be necessary.

Although there is no evidence that reducing drug burden due to PIMs will lead to improved outcomes in critically ill elderly patients, there is evidence that PIM use increases the chance of a serious avoidable adverse drug event in senior hospitalized patients [36]. The influence of reducing PIMs in critically ill elderly patients on outcomes needs to be scrutinized.

It is necessary to emphasize that, the Beers Criteria are meant to serve as a clinical guide for practitioners which does not preclude the use of certain medications, but restricts them on occasion, depending on the possible interactions between the drugs and the disease or syndrome presented by the individual. Thus, these criteria must be applied carefully, identifying medications that have potential risks outweighing potential benefits for elderly people.

Findings of our study confirm the importance of promoting and strengthening the role of pharmacists participating in critical care units. Improved clinical outcomes for older patients are noticed when pharmacotherapy process involves pharmacists in performing medication reviews proactively and when other healthcare professionals receive active education [37].

Our study has certain strengths. First, it applied Beers criteria 2015, the most updated PIM assessment tool for the elderly at the time of study performance. The criteria were supported by the evidence-based standards of the Institute of Medicine in a partnership with the AGS to regularly update it, which potentially addressed the past criticisms of being less relevant to clinicians and health outcomes.

Second, the study was the first in the Middle East region to evaluate the appropriateness of prescribing in critically ill elderly patients, a population that is highly fragile and clinically complex, yet understudied.

Third, the review process to identify and classify PIMs was carried out by two pharmacists independently which intended to avoid information bias. The study, however, has limitations.

Limitations

First, an association between inappropriate prescribing and clinical outcomes such as medication adverse events, length of ICU and hospital stay, was not established. Second, identification and classification of PIMs was based solely on one tool, Beers criteria which were criticized to have several limitations. Those include overlooking important causes of potential inappropriate prescribing like drug–drug interactions, drug class prescription duplication, and prescribing omission errors compared to other criteria like the STOPP–START developed in United Kingdom and Ireland [10]. However, studies mentioned earlier proved that updated Beers list could detect more PIMs than its older versions [13,38] and STOPP–START [14] tools, as most of the available comparisons were based on the older criteria. In a study conducted in Chile, more PIM prescriptions were identified using the Beers criteria as compared to the STOPP criteria. There were differences in the medications that Beers and STOPP identified as inappropriate; only 41% of the patients were identified as being prescribed PIMs by both criteria. Also, Beers identified 38% of patients prescribed PIMs who were not identified using STOPP. In contrast, STOPP identified PIMs only in 6.8% patients, who were not prescribed PIMs according to Beers criteria [39].

Third, this study was conducted at a single medical center, and the results may not be generalizable to other ICU patients.

Nevertheless, this is a pioneer study as publications regarding PIM use in the critically ill elderly patients in the Middle East are lacking. Our study will allow alerting health care managers and providing data to researchers, health care professionals, particularly drug prescribers, on the use of potentially inappropriate medications among the elderly.

Conclusion

Elderly ICU patients received a high number of medications. Using Beers 2015 Criteria, at least one PIM was prescribed to every third patient. More than half patients received medications that should be prescribed with caution. Two factors were associated with PIM prescription: the number of medications and presence of diabetes mellitus. Further studies are needed to identify the impact of PIM prescription on the clinical outcomes in ICU patients including length of ICU stay and length of hospitalization as well as mortality.

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Informed consent

Informed consent was obtained from all individual participants included in the study.

Conflicts of interest

The authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (The Institutional Review Board at the Jordan University Hospital) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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