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The Prevalence of Potentially Inappropriate Prescribing in Geriatric Patients with Psychiatric Disorders in Iraq

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Abstract

Potentially inappropriate prescribing is the prescribing of a medication that may cause more harm than benefit. The elderly population aged 65 years or older is more prone to potentially inappropriate prescribing because of the alterations in their physiology, pharmacokinetics, and pharmacodynamics as well as polypharmacy and comorbidities. Beers list is a screening tool that helps doctors to detect potentially inappropriate prescribing in geriatric patients and is designed to solve this problem. The aim of this study was to measure the prevalence of potentially inappropriate prescribing among psychiatric geriatric patients using the Beers criteria as an assessment tool and to find the relationship between PIP and the duration of hospitalization, comorbidities, and polypharmacy in elderly.

This cross-sectional study was carried out using electronic medical records in Ibn Rushd psychiatry and addiction hospital in Baghdad and 369 patients were included. The mean age of the patients was (68.59 ± 3.75 years) and 177 (48%) of them had comorbidities, 100 (27.1%) of them had polypharmacy and 17 (4.6%) stayed in the hospital for more than 3 weeks, the most used drug classes were antipsychotics in (39.9%) of patients and benzodiazepines in (17.6%) of patients.

The prevalence of potentially inappropriate prescribing according to Beers criteria was found to be 74.3% among study patients, the most prevalent inappropriately used drug class was benzodiazepines, and there was a significant association between the prescribing of a potentially inappropriate medication with gender (p=0.018), with comorbidities (p=0.022), and a very significant association with polypharmacy (p<0.001)

Keywords: Potentially inappropriate prescribing, Potentially inappropriate medication, Beers criteria, Geriatric patients.

انتشار الوصف الدوائي الغير ملائم لمرضى كبار السن المصابين بامراض نفسية في العراق

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الخلاصة

الوصف الدوائي المحتمل عدم ملائمته هو وصف اي دواء من الممكن تسببه بضرر يفوق نفعه. ان شريحة كبار السن للاعمار ٦٥ سنة او اكثر هم اكثر عرضة للوصف الدوائي الغير ملائم بسبب تغيرات في الفارماكوكاينتك و الفارماكودينامك و بالاضافة الى الافراط الدوائي و الامراض المصاحبة. لائحة بيرز هي اداة فحص تساعد الاطباء لكشف الوصف الدوائي المحتمل عدم ملائمته لكبار السن. الهدف من هذه الدراسة هي قياس انتشار الوصف الدوائي الغير ملائم لكبار السن المصابين بامراض نفسيه باستخدام لائحة بيرز كاداة تقييم و ايجاد العلاقة بين استخدام الادوية الغير ملائمة و فترة الرقود بالمستشفى, الامراض المصاحبة و الافراط الدوائي.

اجريت هذه الدراسة المستعرضة بالاعتماد على سجلات المرضى الالكترونية في مستشفى ابن رشد للامراض النفسية و الادمان في بغداد و شمل في هذه الدراسة ٣٦٩ مريض, متوسط اعمارهم كان (٦٨,٥٩ ± ٣,٧٥ سنة) و ١٧٧ (٤٨%) منهم كانوا يعانون من امراض مصاحبة, ١٠٠(٢٧,١%) منهم كانوا يعانون من الفرط الدوائي و ١٧ (٤,٦%) منهم رقدوا في المستشفى لاكثر من ٣ اسابيع. اكثر صنف ادوية استخدم كان مضادات الذهان في (٣٩,٩%) من المرضى و البينزوديازبينات في (١٧,٦%) من المرضى.

وجد ان الانتشار للوصف الدوائي المحتمل عدم ملائمته لكبار السن استنادا الى معيار بيرز هو ٧٤,٣% بين المرضى المشاركين في هذه الدراسة, اكثر صنف دوائي غير ملائم استخدم كان البينزوديازبينات, و كان هناك علاقة احصائية ذات اهمية بين وصف دواء من المحتمل عدم ملائمته لكبار السن مع جنس المريض (p=0.018), مع الامراض المصاحبة (p=0.022), وعلاقة ذات اهمية احصائية عالية مع الفرط الدوائي (p<0.001).

الكلمات المفتاحية : الوصف الدوائي المحتمل عدم ملائمته،الادوية المحتمل عدم ملائمتها،لائحة بيرز، مرضى كبار السن.

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Introduction

Potentially inappropriate prescribing (PIP) can be defined as the prescribing of a medication that the risk of adverse drug reaction may outweigh the benefit of the medication especially if there is a safer alternative available[1].

The elderly population which is aged 65 years or older has been increasing rapidly, since the last century are very susceptible to the problem of PIP because of the alterations in their pharmacodynamics and pharmacokinetics as well as other drug-related problems such as polypharmacy and having multiple co-morbid diseases [2,3].

There are many consequences of PIP, including increased adverse drug events such as cognitive impairment, falls and fractures which can lead to increase emergency room visits and prolonged hospitalization and increased health care use and cost[4–6].

It is challenging to prescribe for geriatric patients with mental disorders because there are many factors influencing prescribing options that can cause alterations in pharmacokinetics such as changes in renal clearance, liver metabolic activity, brain volume, lean body mass and albumin binding this can lead to increased sensitivity to drugs effect especially in the central nervous system [7]. In addition, geriatrics with psychiatric disorders usually take several medications for the treatment of their mental disorders as well as other diseases, which increases the risk of drug-drug and drug-disease interactions.[8]

Patients with mental disorders may be less able to express their discomfort or drug-related problems such as side effects especially in patients with dementia, therefore they may communicate their discomfort as aggression or agitation[9]. This miscommunication may be perceived as worsening of their mental disease rather than a drug-related adverse effect. Lastly, the geriatric population are often excluded from most clinical trials, typically clinical trials conducted in adult population include patients between the ages of 18 and 64 years which causes a limited evidence base for medication use and safety in this population[10,11].

This fact leads to the need of a screening tool that helps doctors to measure the appropriateness of the medications to be prescribed to the elderly and the first list for potentially inappropriate medications (PIMs) made was called the Beers criteria and was created in 1991 making it the longest-running criteria for detecting PIMs in the elderly, the criteria were revised and updated many times over the years and adopted by the American geriatric society, the criteria consist of five categories including drugs to be avoided regardless of condition and drugs to be avoided due to a certain disease/syndrome and drug interaction and drugs to be avoided due to drug-drug interaction[12].

The aim of this study was to measure the prevalence of PIP among psychiatric geriatric patients using the Beers criteria as an assessment tool and to find the relationship between PIP and the duration of hospitalization, comorbidities, and polypharmacy in such patients.

Patient and Methods

Study design

This cross-sectional observational study was carried out using the medical records of patients admitted to Ibn Rushd psychiatry and addiction hospital which is a large psychiatric teaching hospital in Baghdad, Iraq. The researcher retrospectively reviewed inpatient medical records over several years (from July 2011 to September 2018) and recorded any inappropriately prescribed cases.

Inclusion criteria

For this study, the inclusion criteria were:

1- Patient aged 65 years or older
2- Patient admitted for more than 24 hours
3- Patients received pharmacological therapy
4- Patients information was included in the hospital electronic medical record.

Data collection

The research reviewed medical records using a data collection sheet that was specifically designed by the research team to match study goals and it included the following information:

1- The age at the time of admission
2- Gender
3- Diagnosis
4- Administered medications
5- Length of stay
6- Comorbidities

Screening tool

To assess the appropriateness of prescribed medications the 2015 Beers list was used, the following table 1 shows a summary of the criteria used in this study for a medication to be considered inappropriate and was directly derived from the 2015 Beers criteria, these criteria were selected to measure the inappropriateness of psychotropic medications only.

Table 1 .Summary of the criteria used in this study[12]

Beers criteria for potentially inappropriate medications regardless of patient condition		
1	Antidepressants, alone or in combination	Amitriptyline Clomipramine Imipramine Paroxetine
2	Antipsychotics	typical and atypical
3	Benzodiazepines	Short- and intermediate- acting Alprazolam Lorazepam
		Long-acting Chlordiazepoxide Clonazepam Diazepam
4	Nonbenzodiazepines	Zolpidem

Beers criteria for potentially inappropriate medications due to drug-drug interaction		
1	Anticholinergic	Anticholinergic
2	Antidepressants (i.e., TCAs and SSRIs)	≥2 other CNS-active drugs
3	Antipsychotics	≥2 other CNS-active drugs
4	Benzodiazepines and nonbenzodiazepine	≥2 other CNS-active drugs

Beers criteria for potentially inappropriate medications due to drug-disease interaction		
1	Syncope	Tertiary TCAs Chlorpromazine Olanzapine
2	Chronic seizures or epilepsy	Chlorpromazine Clozapine Olanzapine
3	Delirium	Anticholinergics Antipsychotics Benzodiazepines Chlorpromazine
4	Dementia or cognitive impairment	Anticholinergics Benzodiazepines Zolpidem Antipsychotics
5	History of falls or fractures	Anticonvulsants Antipsychotics Benzodiazepines Zolpidem TCAs SSRIs
6	Parkinson disease	All antipsychotics (except aripiprazole, quetiapine, clozapine)

CNS –active agents defined as:

antipsychotics; benzodiazepines; nonbenzodiazepine, benzodiazepine receptor agonist hypnotics; tricyclic antidepressants (TCAs); selective serotonin reuptake inhibitors (SSRIs); and opioids

Administrative arrangement and ethical approval

The study proposal was approved by the Ethical Committee at the University of Baghdad - College of Pharmacy and permission from Ibn-Rushd Hospital was obtained before conducting this study.

The college ethical committee decided that informed consent is not required from patients in case of de-identification patients' names, addresses and date of birth in addition to lacking direct researcher-patient contact.

Statistical analysis

Data were subjected to statistical analysis; data were expressed as mean± standard deviation (SD) of samples. The Statistical significance of the differences between various groups was determined by chi-square test using SPSS software version 22. Differences were considered statically significant for p-value < 0.05.

Results

A total number of 6129 medical records were reviewed for the period from July 2011 to September 2018 and 369 patients met the criteria for this study.

Demographic data

Mean ± SD of age was 68.59 ± 3.75 years ranging from 65 to 95 years with a male to female ratio of 1.13:1 and 77% of the study patients were aged ≤ 70 years.

They have been prescribed a total of 1376 medications with a median of 4 drugs per patient and polypharmacy defined as receiving five or more medications were found in 100 (27.1%) of patients

The most frequent diseases that were diagnosed among patients were schizophrenia (33.06%), psychosis with depression (15.44%), then by bipolar disorder (11.32%), psychotic episode due to alcohol consumption (8.94%), and Alzheimer disease (4.06%).

The most prescribed drugs were quetiapine (13.44% of all prescribed drugs), procyclidine (9.3%) and haloperidol (7.92%).

Table 2. Patients characteristics and administered medication

Age: mean (SD) years	68.59(3.75)
Females: n (%)	160 (43.4%)
Benzodiazepines: n (%)	239 (17.6%)
Antipsychotics: n (%)	550 (39.9%)
Antidepressant: n (%)	213 (14.79%)
Antiepileptics as mood stabilizer: n (%)	138 (13.28%)
Anticholinergics for EP*: n (%)	128 (9.3%)
other medications: n (%)	63 (4.56%)
Drugs prescribed per patient: median, (IQR)	4, (2)
Patients with comorbidities	177 (48%)
Patients prescribed with 5 drugs or more: n (%)	100 (27.1%)

*Extrapyramidal side effect.

The duration of hospitalization in 216 patients (58.5%) was less than one week, 136 (36.9%) from one week to three weeks and 17 (4.6%) stayed for more than three weeks.

Among the 369 patients, 177 patients (48%) were complaining from comorbidities the most prevalent diseases were hypertension (63.8%) and diabetes mellitus (35.6%).

Prevalence of PIP

PIMs regardless of patient condition

In this study, the overall number of *PIMs that were prescribed inappropriately regardless of patient condition* was 323. The most frequent inappropriately prescribed medications were: Diazepam (18.27%), Quetiapine (16.72%) and Alprazolam (10.84%). The distribution of non-conditional PIMs is shown in table .

Table 3 . Potentially inappropriate medication regardless of patient condition

Potentially inappropriate medication	**No.**	**Percentage (%)**
Antidepressant	**49**	**15.17%**
Amitriptyline	26	8.05%
Clomipramine	19	5.88%
Imipramine	2	0.62%
Paroxetine	2	0.62%
Second generation antipsychotics	**86**	**26.63%**
Quetiapine	54	16.72%
Olanzapine	21	6.50%
Risperidone	11	3.41%
First generation antipsychotics	**27**	**8.36%**
haloperidol	16	4.95%
Flupenthixol	6	1.86%
Chlorpromazine	3	0.93%
Trifluoperazine	1	0.31%
Fluphenazine	1	0.31%
Benzodiazepine	**161**	**49.85%**
Diazepam	59	18.27%
Alprazolam	35	10.84%
Clonazepam	30	9.29%
Chlordiazepoxide	24	7.43%
Lorazepam	13	4.02%
Non-Benzodiazepine	**2**	**0.62%**
Zolpidem	2	0.62%
	323	**100.00%**

PIPs due to drug-condition interaction

There was 71 PIMs prescribed to the study patients as follows: Benzodiazepines in patients with delirium (30.99%) and Benzodiazepines in patients with dementia (19.72%), and antipsychotics in patients with dementia (19.72%).

The most frequent class of medications present was benzodiazepines as recorded in 54.94%.

Table 4 .Potentially inappropriate medication regarding patient condition

Potentially inappropriate medication	**No.**	**Percentage (%)**
Syncope	**6**	**8.45%**
Olanzapine	6	8.45%
Delirium	**28**	**39.44%**
Benzodiazepine	22	30.99%
Antipsychotics	5	7.04%
Chlorpromazine	1	1.41%
Dementia	**28**	**39.44%**
Benzodiazepine	14	19.72%
Antipsychotics	14	19.72%
Falls	**7**	**9.86%**
Benzodiazepine	3	4.23%
Antipsychotics	3	4.23%
Anticonvulsant	1	1.41%
Parkinson	**2**	**2.82%**
Antipsychotics	2	2.82%
	71	**100.00%**

The PIMs due to drug-drug interaction

355 PIMs were found and this occurred most frequently by inappropriate prescriptions of benzodiazepines (42.5%), followed by antidepressants and antipsychotics (29.6%, and 26.7%)

Table 5 .Potentially inappropriate medication due to drug-drug interaction

Potentially Inappropriate Medication	**No.**	**Percentage (%)**
Benzodiazepines	151	42.54%
Antidepressants	105	29.58%
Antipsychotics	93	26.20%
Anticholinergics	6	1.69%
	355	**100.00%**

The total prevalence of PIP

The prevalence inappropriate psychotropic medications was 74.3%, while the remaining 25.7% received appropriately prescribing medications.

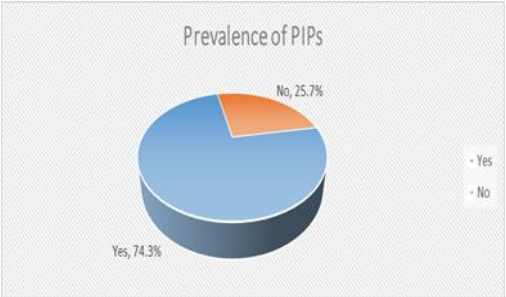

Figure 1 . Prevalence of potentially inappropriate prescribing in this study.

The association of PIPs with certain demographic data, comorbidities, and duration of hospitalization

The study revealed that 78.9% of male patients in this study received psychotropic medications inappropriately, with statistically significant association (P=0.018) between gender of patients and prescription of inappropriate psychotropic medications, this study also found a statistically significant association (P=0.022) between the presence of comorbidities and PIMs prescription, and there was a highly significant association between polypharmacy and being prescribed a potentially inappropriate medication (P<0.001).

Table 6. Association of PIPs with patient factors

Variable	PIPs		Total (%) n= 369	P- Value
	Yes (%) n= 274	**No (%) n= 95**		
Age (Years)				
≤ 70	213 (74.5)	73 (25.5)	286 (77.5)	**0.857**
> 70	61 (73.5)	22 (26.5)	83 (22.5)	
Gender				
Male	165 (78.9)	44 (21.1)	209 (56.6)	**0.018***
Female	109 (68.1)	51 (31.9)	160 (43.4)	
Comorbidities				
Yes	141 (79.7)	36 (20.3)	177 (48.0)	**0.022***
No	133 (69.3)	59 (30.7)	192 (84.3)	
Duration of Hospitalization (Weeks)				
< One	155 (71.8)	61 (28.2)	216 (58.5)	**0.331**
One - Three	107 (78.8)	29 (21.3)	136 (36.9)	
> Three	12 (70.6)	5 (29.4)	17 (4.6)	
polypharmacy				
≥5 medications	88 (88)	12 (12)	100 (27.1)	**0.0002***
<5 medications	186 (69.1)	83 (30.9)	269 (72.9)	

*Significant difference according to the chi-square test

Discussion

The results of the study shows that the antipsychotics were the most widely used medication by (39.9%) of the total number of geriatric patient enrolled in this study but it wasn't the most frequent inappropriately prescribed medication due to the exception made by the criteria to geriatric patients diagnosed with schizophrenia, bipolar disorder or acute psychotic episodes that threaten to cause harm to self or others[12].

There are several factor that lead to the high prevalence of PIPs in 74.3% of this study patients such as: most patients admitted due to acute psychological conditions or agitation which in turn required aggressive therapeutic plans to improve patient's condition, combined with the lack of safer alternative interventions which lead to the increased use of anxiolytics, hypnotics and antipsychotic injections; other factors that may have caused a false increase in PIPs is due to a flaw in the criteria itself for not providing a rule regarding a duration of medication use to be considered inappropriate which lead to many medications used only once

by the patients to be counted as potentially inappropriate[13–16].

However, the result of the present study is similar to (M Gutiérrez-Valencia et al., 2017)[14] which measured a PIP prevalence of 71.5% in hospitalized geriatric patients in acute setting in Spain, and also similar to (G. Fond et al.,2016)[17] which measured prevalence of PIP of psychotropic medications in hospital setting after discharge in France and found it to be 76.1%, another study measuring PIPs in psychiatric hospital in the Netherlands (S. Rongen et al.,2016)[16] found a much lower prevalence of 47%.

The second major result of this study is that benzodiazepines was the most prevalent PIM used, this is also similar to other studies such as (M Gutiérrez-Valencia et al., 2017)[14] in Spain which measured the impact of hospitalization on PIP and found Benzodiazepines as the most inappropriately prescribed medication, other studies concerning elderly patients treated with psychotropic medications in Spain such as (X. Vidal et al.,2016)[18] found benzodiazepines as the most prescribed medications as well as the most inappropriately prescribed medication, as mentioned before this result is most likely due to the acute nature of most admissions.

It was interesting to notice the differences in prevalence of polypharmacy in geriatric patients among different studies concerning with the subject of potentially inappropriate prescribing ranging from as high as 95% in the study by (MF. Najjar et al,.2018)[13] in Saudi Arabia, 86.5% in the study by (M Gutiérrez-Valencia et al., 2017)[14] in Spain, 79% in the study by (S. Rongen et al.,2016)[16]in the Netherlands to 29% In a study by (H. Cho et al,.2018)[15] in South Korea despite being defined in all these studies as patients receiving 5 or more medications, it was also found to be a significant factor for the prescribing of an inappropriate medication in all of these studies similarly to the result of this study even though we found polypharmacy only in 27% of the study participants which can be explained by the methodology of this study which included only listing the medications in the electronic medical chart which doesn't include medications used for other diseases such as hypertension or diabetes.

Gender and age were considered to be a significant factor in the prescribing of PIM is some studies (G. fond et al.,2016)[17] and (H. Cho et al,.2018)[15], and considered to be insignificant in others (X. Vidal et al.,2016)[18] , this can be explained by differences in study settings, prescribed medications, and discrepancies in other factors.

Conclusions

There is a high prevalence of potentially inappropriate prescribing among geriatric patients with psychiatric disorders in Iraq in addition the factors affecting potentially inappropriate prescribing were gender (male), having a comorbid disease and taking more than 5 medications and found to be strongly associated with being prescribed a potentially inappropriate medication.

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