The Effect of Beers Criteria-Based Training in General Practitioners on Prescribing Potentially Inappropriate Medications in Elderly Patients

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Background:
Pharmacotherapy in elderly patients has become a major concern due to their physiological changes, pharmacokinetic and pharmacodynamics variations and poly-pharmacy. In considering the global trend in population aging, we aim to evaluate the effect of “Beers Criteria” education on prescribing medications for elderly patients by General Practitioners (GPs).

Methods:
Thirty GPs with the highest number of prescriptions were included in this pilot study. All prescriptions written over a three-month period were considered, then prescriptions for geriatric patients were selected and evaluated. The GPs were trained using pamphlets and booklets which were prepared based on Beers 2015 explicit criteria. In order to evaluate the effect of education, appropriateness of prescriptions was analyzed before and 1 month following training.

Results:
Of 15,447 prescriptions selected during the first step, 1,281 prescriptions were related to geriatric patients in which the prevalence of inappropriate drug prescriptions was 37.3%. The most inappropriate medications identified were Bisacodyl, Alprazolam, and Hyoscyamine. While in the second step 1,055 of 15,154 prescriptions concerned the elderly and inappropriate drug prescription rate was noted as 23.6%. The most common inappropriate medications included Alprazolam, Amitriptyline, and Hyoscyamine. Based on our results, the prevalence of prescribing potentially inappropriate medications (PIMs) for elderly patients is high among GPs and educational interventions that raise awareness about “Beers Criteria” significantly reduce the prescribing PIMs.

Conclusion:
Given the importance of GP training programs in reducing inappropriate prescription rates among geriatric patients, it will be necessary for the National Committee of Rational Use of Drugs (NCRUD) to consider undertaking comprehensive educational strategies for reducing the prevalence of inappropriate medication use in elderly people.

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Introduction
Inappropriate prescription of medication includes prescribing a medicine with high risk of adverse effects (AEs) instead of alternative therapies that have significantly lower risk. It also contains prescribing medications at higher or lower required doses or several medications with drug-drug interactions (1). Increase in the share of the elderly population has become a worldwide concern (2). The higher incidence of chronic disease in older adults leads to the higher prevalence of polypharmacy and it increases adverse drug reactions (ADRs) and drug-drug interactions (DDIs). On the other hand, the physiological changes that take place with aging, affect the pharmacodynamics and pharmacokinetics (absorption, distribution, metabolism and excretion) properties of medications. The above mentioned reasons
render the appropriate selection of medications to be more challenging in elderly patients (1, 3, 4).

Previous studies have shown that approximately half of all prescriptions belong to elderly patients (4-7). Almost 20% to 27.6% of administered medications are considered to be inappropriate for elderly patients in developed countries and Middle Eastern populations, respectively (6). Inappropriate drug use is known to increase the risk of hospitalization (OR=1.46) and mortality (HR=1.15) in elderly patients as well as costs associated with hospitalization compared to patients without inappropriate drug use (7).

In 1997, Beers et al., established a list of criteria with the main purpose of preventing inappropriate medication use in adults aged 65 years and older. Since then, the list has been modified several times and the newest updates became available in 2019. Today, this list is one of the most recognized and referenced tools for evaluating the appropriateness of medication use in older adults (8-10). Given the importance of education and its significant impact in prescribing appropriate medications (11) as well as the vital role of GPs in the Iranian health care system, we aim to evaluate the effect of Beers Criteria-based training on prescribing medications for elderly patients by GPs.

Methods

This is a pilot before and after study that was done in Tabriz from October 2015 to April 2016. We received information about the number of prescriptions for all GPs of Tabriz from one of the main health insurance organizations (Taamin Ejtemaeae), then we selected 30 GPs with the highest number of prescriptions during the past 3 months, from different areas of the city. The inclusion criteria were all prescriptions for people older than 65 years, which were prescribed by GPs with the highest number of prescriptions through past months. The prescriptions of specialists, GPs with a lower number of prescriptions, and the prescriptions for patients younger than 65 years were excluded. The prevalence of inappropriate drug prescription was the primary outcome of the study and the efficacy of education considered as the secondary outcome. The study conducted in two main steps; First, we prepared a checklist of potentially inappropriate medications for the elderly population (Table 1) based on Beers 2015 updated criteria (12) and evaluated all included prescriptions according to the prepared checklist. Then we contacted the selected GPs and noted their common errors in prescribing medications for older adults. We explained the aim and method of the study and asked them to participate in our study. 6 GPs refused to participate in the study and replaced by 6 other GPs according to the inclusion criteria. Some educational pamphlets prepared according to each physician’s prescription errors. Furthermore, a general guideline for pharmacotherapy considerations in geriatrics arranged in the form of a booklet and educational pamphlets. The prepared pamphlets, booklets and also necessary information about the beers list gave to the physicians, then they visited and their questions about pharmacotherapy in geriatrics resolved. The second step, conducted after one month. In this step, the GPs prescriptions collected and examined similar to the first step during 3 months. Finally, the data analyzed by spss16. Student’s t-test used to compare the mean of quantitative variables and results reported as average ± standard deviation. The chi-square test used to analyze qualitative variables and the qualitative data reported in the form of numbers or percentages. In the end, the number of inappropriately prescribed medications before and after education, compared by Mc nemar test, data reported in the form of numbers or percentages. In the end, the number of inappropriately prescribed medications before and after education, compared by Mc nemar test.

Table 1. Checklist of potentially inappropriate medications for elderly.

| Analgesics               | Ketorolac | meperidine | pentazocine | propoxyphene |
|-------------------------|-----------|------------|-------------|--------------|
| Antidepressants         | Amtriptyline | Imipramine | Bupropion | Fluoxetine* |
| Antihistamin            | Chlorpheniramine | Cyproheptadine | Deschlorpheniramine | Diphenhydramine |
| Antihypertensives        | Doxazosin | Prazosin | Trazosin | Clonidine | Ethacrynic acid | Guanethidine | Metyldopa | Nifedipine* | Reserpine* | Thiazide* |
| Antiplatelet Drugs       | Dipyridamole | Ticlopidine |
| Antipsychotics          | Mesoridazine | Thiordazine | Chlorpromazine* | Clozapine* | Olanzapine* | Thiothixene |
| Anxiolytics             | Clorazepate | Chlordiazepoxide | Diazepam | Quazepam | Meprobamate | Alprazolam* | Lorazepam* | Oxazepam* |
| Cardiac Drugs           | Amiodarone | Beta-blockers* | CCB* | Digosint* | Dihydropyridine | Chlorpropamide |
| GI Drugs                | Belladonna* | Dicyclomine* | Hyoscyamine* | Propantheline* | Cimetidine* | Diphenoxylate* | Metoclopramid* | Mineral oil |
| Hormones                | Estrogens | Methyltestosterone |
| Hypnotics               | Barbirutus | L.a benzodiazepines | Diphenhydramine | Flurazepam | Triazolam |
| Muscle Relaxants        | Carisopradol | Chlorzoxazine | Cyclobenzaprine | Metaxalone | Methocarbamol | Orphenadrine |
| NSAIDS                  | Aspirin* | Naproxen* | Oxapozin* | Piroxicam* | Indomethacin |
| Respiratory drugs       | Pseudoephedrine* | theophylline* |
| Stimulant Drugs         | Amphetamins* | Methylphenidate* |
| Urinary Drugs           | Nitrofurantoin | Oxybutynin* | Tolterodine* |
Results
30 GPs were assigned in the study and their prescriptions were examined for demographic information of patients, the number of medications in each prescription, and the number of inappropriate medications (drug name and pharmacological category) for older adults in two steps. The descriptive information of study (Table 2) represents that data in two steps of study are uniform in terms of patient’s age, gender and the mean number of medications in each prescription (P>0.05), so the age and gender are not confounding variables in our study. As it is obvious in Table 2 and 3, the number of prescriptions with inappropriate medications and number of inappropriate medications in each prescription is significantly reduced after educating general physicians (P<0.05).

Table 2. The demographic and descriptive information of study

| Variables | Before education | After education | P value |
|-----------|------------------|----------------|---------|
| All prescriptions | 15449 | 15154 | |
| Prescriptions belonged to patients over 65 years old (% of all prescriptions) | 1281 (8.2%) | 1055 (6.9%) | <0.0001 |
| Prescriptions with inappropriate medications (% of all prescriptions belonged to elderly patients) | 478 (37.3%) | 250 (23.6%) | 0.001 |
| Mean age | 72.4±6.1 | 72.3±5.9 | 0.759 |
| Male patients with inappropriate medications | 204 (42.6%) | 109 (43.6%) | 0.777 |
| Number of medications in each prescription | 4.9±0.2 | 4.8±0.7 | 0.278 |
| Number of inappropriate medications in each prescription | 1.4±0.6 | 1.2±0.4 | 0.001 |

Table 3. The number of inappropriate medication in each prescription.

| Number of inappropriate medication | Number of prescriptions | P value |
|------------------------------------|-------------------------|---------|
| Before education | After education | |
| One inappropriate medication | 302 (23.6%) | 191 (18.1%) | <0.0001 |
| Two inappropriate medication | 156(12.2) | 56(5.3%) | <0.0001 |
| Three inappropriate medication | 20(1.6%) | 2(0.2%) | <0.0001 |
| All prescriptions with inappropriate medication | 478 (37.3%) | 250(23.6%) | <0.0001 |
| All prescriptions without inappropriate medication | 803(62.7%) | 805(76.4%) | <0.0001 |

The most frequently prescribed inappropriate medications are categorized in 12 pharmacological group and listed in Table 4. According to the results, gastrointestinal drugs and anxiolytics are the most inappropriately prescribed pharmacological categories in both steps of study, however, it is reduced significantly after education.

Table 4. The number of inappropriately prescribed medications in each pharmacological category before and after education.

| Pharmacological category | Before education | After education |
|--------------------------|-----------------|----------------|
| GI drugs | 230 (34%) | 82(26%) |
| Anxiolytics | 146(21%) | 60(19%) |
| Antidepressants | 84(12%) | 49(15%) |
| Antihistamine | 80(11%) | 36(11%) |
| NSAIDS | 40(5%) | 21(6%) |
| Respiratory drugs | 32(4%) | 21(6%) |
| Antihypertensive | 21(3%) | 21(6%) |
| Muscle Relaxants | 21(3%) | 12(3%) |
| Antiplatelet Drugs | 8(1%) | 3(0.95%) |
| Urinary Drugs | 4(0.5%) | 5(1.5%) |
| Analgesics | 4(0.5%) | 0(0%) |
| Cardiac Drugs | 3(0.44%) | 3(0.95%) |
| Total | 673 | 313 |

The most frequently prescribed inappropriate medications were Bisacodyl (53), alprazolam (52), Diphenhydramine (46), Hyoscyamine (45) before education and alprazolam (25), Amitriptyline (20), Hyoscyamine (19), Imipramine (19) after education. So it illustrates that, in spite of a significant reduction in total number of inappropriately prescribed medications, there isn’t a significant change in the types of medications (Table 5).
Table 5. Detailed information about inappropriately prescribed medications before and after education.

| Medication  | Before education |          |          | Medication  | Before education |          |          |
|-------------|------------------|----------|----------|-------------|------------------|----------|----------|
|             | Number           | Percent  | Number   | Percent     | Number           | Percent  | Number   | Percent  |
| 1 Bisacodyl | 53               | 7.78%    | 13       | 4.15%       | 19 Belladonna    | 14       | 2.08%    | 5        | 1.59%    |
| 2 Alprazolam| 52               | 7.72%    | 25       | 7.98%       | 20 Prazosin      | 14       | 2.08%    | 14       | 4.47%    |
| 3 Hyoscyamine| 45               | 6.68%    | 19       | 6.07%       | 21 Cimetidine    | 13       | 1.93%    | 0        | 0%       |
| 4 Diphenhydramine| 46               | 6.83%    | 15       | 4.79%       | 22 Clidinium-c   | 12       | 1.78%    | 10       | 3.19%    |
| 5 Dicyclomine| 38               | 5.64%    | 9        | 2.87%       | 23 Hydroxyzine   | 12       | 1.78%    | 6        | 1.91%    |
| 6 Chlor Diazoxide| 32               | 4.75%    | 18       | 5.75%       | 24 Theophylline  | 12       | 1.78%    | 8        | 2.55%    |
| 7 Methoclopramid| 31               | 4.6%     | 15       | 4.79%       | 25 Lorazepam     | 12       | 1.78%    | 3        | 0.95%    |
| 8 Imipramine | 31               | 4.6%     | 19       | 6.07%       | 26 Cyproheptadine| 12       | 1.78%    | 8        | 2.55%    |
| 9 Amitriptyline| 30               | 4.45%    | 20       | 6.38%       | 27 Piroxicam     | 8        | 1.18%    | 3        | 0.95%    |
| 10 Fluoxetine| 23               | 3.41%    | 10       | 3.19%       | 28 Promethazine  | 8        | 1.18%    | 3        | 0.95%    |
| 11 Diazepam  | 22               | 3.26%    | 6        | 1.91%       | 29 Dipyriramole  | 8        | 1.18%    | 3        | 0.95%    |
| 12 Methocarbamol| 21               | 3.12%    | 12       | 3.83%       | 30 Terazosin    | 7        | 1.04%    | 7        | 2.23%    |
| 13 Pseudoephedrine| 20               | 2.97%    | 13       | 4.15%       | 31 Diphenoxylate| 5        | 0.74     | 3        | 0.95%    |
| 14 C-lax     | 19               | 2.82%    | 8        | 2.55%       | 32 Oxybutynin   | 4        | 0.59     | 5        | 1.59%    |
| 15 Naproxen  | 17               | 2.52%    | 9        | 2.87%       | 33 Ketorolac    | 4        | 0.59     | 0        | 0%       |
| 16 Indomethacin| 15               | 2.22%    | 9        | 2.87%       | 34 Amiodarone   | 3        | 0.44     | 3        | 1.59%    |
| 17 Oxazepam  | 14               | 2.08%    | 4        | 1.27%       | 35 Chlorpheniramine| 2        | 0.29     | 4        | 1.27%    |
| 18 Clonazepam| 14               | 2.08%    | 4        | 1.27%       |                  |          |          |          |

As it is obvious in Figure 1, approximately 20-40% of all prescriptions for each physician consist of inappropriate medications before education. This proportion is reduced significantly after education (P<0.05) and it ranged 15-30% of all prescription with the exception of two cases.
Table 6. Detailed information about the most frequently prescribed inappropriate medication for geriatrics in several studies.

| First author's name | Year | Country | The most frequently prescribed inappropriate medication for elderly |
|---------------------|------|---------|---------------------------------------------------------------|
| Azoulay (7)         | 2005 | Iran    | Antihistamines (29%), NSAIDs (23%), Benzodiazepines (16%)    |
| Ghadimi (17)        | 2011 | Iran    | Indomethacin (17%), Diphenhydramine (12%), Methocarbamol (11%) |
| Zargarzadeh (14)    | 2008 | Iran    | Naproxen (18.4%), Fluoxetine (8.3%), Clidinium-C (7.2%) |
| Vali (13)           | 2011 | Iran    | Alprazolam (16.6%), Chlordiazepoxide (14.28%), Fluoxetine (11.9%), Oxazepam (11.9%) |
| Heidari (15)        | 2014 | Iran    | Digoxin (7.9%), Alprazolam (6.1%), Bisacodyl (6.1%), Chlordiazepoxide (4.6%) |
| Raji (18)           | 2003 | United States of America | Chlorpropamide, Propoxyphene, Amitriptyline, Dipyridamole |
| Onder (19)          | 2003 | Italy   | Ticlopidine (6%), Digoxin (3%), Amitriptyline (2%) |
| Chang (20)          | 2004 | Taiwan  | Sedative-hypnotics (18.6%), Muscle relaxants (17.5%) |
| Cannon (21)         | 2006 | United States of America | Lisinopril (32%), Furosemide (31%), Hydrocodone/acetaminophen (29%) |
| Koyama (22)         | 2013 | United States of America | Anticholinergics (15.2%), Benzodiazepines (8.6%), Antispasmodics (8%) |
| Olivera (23)        | 2012 | Brazil  | Diclofenac (20.3%), Dexchlorpheniramine (9.6%), Fluoxetine (9.1%), Diazepam (7.6%), Amitriptyline (7.3%), Clonazepam (6.1%) (according to Beers 2012 criteria) |
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Figure 1. The potentially inappropriate medications as percentage of total prescribed drugs for each physician.

Discussion
Prescribing appropriate medications for elder patients is a worldwide concern because of underlying complications and physiological changes that alter the effects of drugs in this population. Several studies have been conducted all around the world to evaluate the pattern of using medications in older adults. In this study, we evaluated the pattern of inappropriate medication prescriptions for older adults among GPs and also assessed the effect of “Beers Criteria” education on their prescribing pattern. According to the findings, the prevalence of prescribing potentially inappropriate medications for older adults is high among GPs (Tables 2 and 3) and educating “Beers Criteria” significantly reduces the prescription of inappropriate medications (Tables 2-5 and Figure 1).

Detailed information about the most frequently prescribed inappropriate medication for the elderly population in several studies are listed in Table 6. In the study of Azolay et al., the number of medications in each prescription was reported as the only factor that significantly increases inappropriate prescription of medications (7). In the study of Vali et al., the patient’s income and education level had a statically significant relationship with the use of inappropriate medications (13).
Furthermore, Table 6 indicates that the prevalence of using inappropriate medications varies in different countries. It may be due to the differences in pharmaceutical policies and the health status of each country. According to the different studies, anxiolytics and sedative-hypnotics can be considered as the most commonly used inappropriate medications in many countries. In our study, benzodiazepines, three cyclic antidepressants, and gastrointestinal drugs are the most inappropriately prescribed medications. Three cyclic antidepressants are inappropriate for older adults because of anticholinergic effects such as glaucoma, blurred vision, dry mouth, constipation, urinary retention, and confusion. They also increase the risk of syncope and falling which are major problems in the elderly (9). We speculate that the unawareness of GPs about rapid tolerance to the sedative effects of benzodiazepines leads to inappropriate prescription of anxiolytics in insomnia. The physical dependence on benzodiazepines makes medication discontinuation difficult due to withdrawal syndrome. Furthermore, the long term use of these medications increases the risk of falling and fracture (16).

Due to decreased physical activity and improper nutrition patterns, the incidence of constipation is high in older adults. Symptomatic therapy of constipation with stimulant laxatives leads to bowel dependency on these agents and it increases the inappropriate use of bisacodyl and C-lax in older adults. It seems that the lack of appropriate medications as alternatives for stimulant laxatives is an important reason for the increased use of these medications.

Finally, we found that educating “Beers criteria” to GPs reduces inappropriate medication prescription significantly, in most of the pharmacological categories. However, there isn’t a significant variation in the type of inappropriately prescribed medications. The only exception is bisacodyl, which has prescribed significantly less after education. We think that higher costs or unavailability of alternative therapies in Iran may be a rational reason for the continuation of prescribing some potentially inappropriate medications such as terazosin, prazosin, and amiodarone after education. Our study has some limitations which can affect the reliability of the results. The most important one is inadequate information about the patient’s general condition and the exact purpose of prescribing medications. This is a disadvantage in all retrospective studies because of the researcher’s absence in prescribing sessions. Another limitation is the small number of included prescriptions that lead to errors in the generalization of results to larger populations. So we suggest prospective studies with a higher sample size for future researches. Also, the comparison of the effects of different educational tools on prescribing appropriateness may be another concept for future studies.

We concluded that one of the most important reasons for the high prevalence of inappropriate prescription of medication in the elderly population is inadequate knowledge of general practitioners about geriatric’s pharmacotherapy and the severe side effects of medications in this population. It's necessary for the committee of rational use of drugs to take serious strategies to reduce the prevalence of inappropriate medication use. Publishing pamphlets, booklets, and guidelines for pharmacotherapy considerations in older adults, holding geriatric pharmacotherapy courses, training health care providers and patient education can be some of these strategies.

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