

Adverse drug events leading to emergency department visits in elderly: the role of inappropriate prescription

Visitas à emergência relacionadas a efeitos adversos a drogas: o papel da prescrição inapropriada

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ABSTRACT

Objective: Adverse drug reactions are more incident among the elderly and are frequently associated to inappropriate prescription for this group. The objective of the current study was to investigate the incidence and the characteristics of emergency department visits, related to inappropriate prescription, at the Hospital Israelita Albert Einstein. **Methods:** Patients aged 60 years or older, admitted to the emergency department at Unidade Avançada Ibirapuera of Hospital Israelita Albert Einstein, were included in the study. Potentially inappropriate medication for the elderly was evaluated using updated 2003 Beers criteria. **Results:** Over a period of 6 months, 214 individuals were included in the study, being 53.7% male. The mean age was 70.8 years (60-107). A total of 48 registries of inappropriate prescription were recorded in 42 patients (19.6% of sample). An emergency visit related to adverse drug event was verified in 27 individuals (12.5% of the sample). From these patients, 34.5% were admitted to the emergency department because of an adverse event caused by an inappropriate medication. **Conclusion:** Inappropriate prescription is frequent among elderly patients admitted to emergency department. A surveillance system and a program to educate physicians on the most recent criteria of appropriate prescription may help reducing emergency visits and adverse drug events in the elderly population.

Keywords: Pharmaceutical preparations/adverse effects; Pharmaceutical preparations/administration & dosage; Drug prescriptions; Emergency service, hospital; Aged

RESUMO

Objetivo: As reações adversas a medicação são mais incidentes entre idosos e são frequentemente associadas à prescrição inapropriada

para essa população. O objetivo deste estudo foi investigar a incidência e as características das visitas à emergência do Hospital Israelita Albert Einstein, associadas à prescrição inapropriada. **Métodos:** Pacientes com 60 anos ou mais, admitidos na emergência da Unidade Ibirapuera do Hospital Israelita Albert Einstein, foram incluídos no estudo. Fármacos potencialmente inapropriados para a população idosa foram avaliados por meio da versão atualizada do critério de Beers, de 2003. **Resultados:** Durante o período de 6 meses, 214 indivíduos foram incluídos no estudo, sendo 53,7% do sexo masculino. A idade média foi de 70,8 anos (variação de 60-107 anos). Quarenta e oito registros de uso de medicação inapropriada foram verificados em 42 indivíduos (19,6% da amostra). A visita à emergência foi associada a uma reação adversa a fármacos em 27 indivíduos (12,5% da amostra). Destes, 34,5% foram admitidos na emergência por uma reação adversa associada a prescrição inapropriada. **Conclusão:** A prescrição inapropriada é frequente entre idosos admitidos no departamento de emergência. Um sistema de vigilância, associado a um programa de educação médica sobre os critérios recentes de prescrição apropriada, pode reduzir o número de visitas à emergência e de reações adversas a droga na população idosa.

Descritores: Preparações farmacêuticas/efeitos adversos; Preparações farmacêuticas/administração & dosagem; Prescrições de medicamentos; Serviço hospitalar de emergência; Idoso

INTRODUCTION

The outpatient use of drug therapies is common among older adults. More than 80% of elderly take, at least, one over-the-counter medication or dietary supplement, and

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30% report using five or more of these drugs regularly⁽¹⁾. As the world population ages, more patients are treated for acute and chronic diseases, exposing themselves to a higher morbidity and mortality related to adverse drug events⁽²⁻⁹⁾.

A National Surveillance performed in an outpatient setting by the Center for Disease Control and Prevention (CDC), in the United States, reported that adverse drug events accounted for 2.5% of estimated emergency department visits for all unintentional injuries, and 6.7% of these individuals required hospitalization. Adverse drug reactions were more incident among older adults who were more likely to require hospitalization⁽¹⁰⁾.

Inappropriate prescription occurs when the risks of an adverse event outweigh the potential benefits of the medication. The prescription to elderly individuals is often given by non-geriatricians who are frequently unfamiliar with the most commonly adopted criteria for medication appropriateness in these patients.

The Beers criteria are a consensus-based list of medications identified as potentially inappropriate for use in elderly patients⁽¹¹⁻¹³⁾. The criteria have become a standard measure of quality of prescribing in research studies⁽¹⁴⁻¹⁹⁾ and were adopted by the Medicare and Medicaid services, in the United States, as a measure of quality of healthcare and safety for older adults in nursing homes⁽²⁰⁾.

The current study intended to investigate the rate of emergency department visits resulting from adverse drug events related to inappropriate medication in an elderly sample admitted to Hospital Israelita Albert Einstein.

METHODS

This retrospective observational study was conducted from December 19, 2006 to June 30, 2007, at the emergency department of Unidade Avançada Ibirapuera of Hospital Israelita Albert Einstein. The emergency department was established in November 2006 and offers primary support for clinical, surgical and orthopedic emergencies. The sample of the study was defined as the elderly population aged 60 years or over, according to international criteria settled to define an elderly population on a developing country. The local Ethics Committee approved this study and, due to its observational nature, informed consent was not required.

All data was obtained by the means of a systematic review of clinical records. The medications taken by the patients were obtained in a predefined form fulfilled by a skilled nurse upon admission to the emergency department. This form included a complete inventory for all over-the-counter medications and dietary

supplements used by the patient, as well as the doses and the frequencies used. If the patient was not on use of any medication, this information was also registered. The individual was excluded from the study whenever the inventory of medications was not completely fulfilled. The medications prescribed at the emergency department as well as those prescribed for home on discharge were also recorded. Age, gender, need for hospitalization and the final diagnosis determined by the emergency physician on discharge were registered. If a patient was readmitted to the emergency department with the same diagnosis, only data from the first admission were analyzed. If a patient was readmitted due to a different diagnosis, both admissions were analyzed.

The most recent version of Beers criteria, updated in 2003, was used to define potentially inappropriate medications⁽¹³⁾. The current version categorizes 41 medications or classes of medication, classified as “always potentially inappropriate”, and other 7 medications or medication classes classified as “potentially inappropriate under certain circumstances”, when drugs are used only in certain doses, frequencies or durations. For example, digoxin prescription is considered inappropriate only when used on a dose higher than 0.125 mg/d, excepting for the treatment of atrial arrhythmias. The medications and classes of medications included on the Beers criteria are listed on chart 1.

The emergency department visit related to adverse drug event was defined when the cause of the visit was clearly related to a drug-specific effect. Adverse events included allergic reactions, undesirable effects of a medication at recommended doses, toxic effects linked to overdoses and secondary effects, such as falls. The emergency visit related to inappropriate medication was considered when the cause of the visit was related to a drug-related effect and the considered medication was included in the list of Beers criteria. The review of the medical records and the report of an emergency visit related to inappropriate medication were performed by a geriatrician. The groups of patients having or not having adverse drug events were compared as to age, gender and specific classes of medication.

The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS), version 13.0. The continuous variables were compared between groups using the Student's *t*-test for equality of means, whereas categorical variables were analyzed using the χ^2 test. The level of significance used was 0.05.

RESULTS

During the period of investigation, 231 emergency visits were registered in 214 patients aged 60 years or older.

Chart 1. Potentially inappropriate medications for individuals aged 65 years or older*

Always potentially inappropriate
High Severity
Amiodarone
Amitriptyline
Chlorpropamide
Dessicated thyroid
Disopyramide
Doxepin
Guanadrel
Guanethidine
Indomethacin
Ketorolac
Meperidine
Meprobamate
Mesoridazine
Methyldopa
Methyltestosterone
Mineral oil
Nitrofurantoin
Nifedipine (short-acting)
Orphenadrine
Oxybutynin (short-acting)
Pentazocine
Thioridazine
Ticlopidine
Trimethobenzamide
Amphetamines (except methylphenidate)
Anorexic agents
Anticholinergic and antihistamine agents (chlorpheniramine, diphenhydramine, hydroxyzine, cyproheptadine, promethazine, tripeleminamine and dexchlorpheniramine)
Barbiturates (except phenobarbital)
Gastrointestinal antispasmodics (dicyclomine, hyoscyamine, propantheline, belladonna alkaloids and clidinium-chlordiazepoxide)
Long-acting benzodiazepines (chlordiazepoxide, diazepam, flurazepam, quazepam, halazepam and clorazepate)
Muscle relaxants and antispasmodics (methocarbamol, carisoprodol, chlorzoxazone, metaxalone and cyclobenzaprine)
Low severity
Cimetidine
Clonidine
Cyclandelate
Dipyridamole (short-acting)
Doxazosin
Ergot mesyloids
Estrogens (oral)
Ethacrynic acid
Isoxsuprine
Propoxyphene
Potentially inappropriate in certain circumstances
High severity
Fluoxetine
Longer half-life nonsteroidal anti-inflammatory agents (long-term use of full-dosage naproxen, oxaprozin, piroxicam)
Short-acting benzodiazepines (lorazepam - 3 mg, oxazepam - 60 mg, alprazolam - 2 mg, temazepam - 15 mg, triazolam - 0.25 mg)
Stimulant laxatives (long-term use of bisacodyl, hamnus, castor oil except in presence of opiate analgesic use)
Low severity
Digoxin (0.125 mg/d, except when treating atrial arrhythmias)
Ferrous sulfate (325 mg/d)
Reserpine (0.25 mg)

* Medications identified as potentially inappropriate on the basis of the updated Beers criteria, 2003¹³.

The mean age of the sample was 70.8 years (range of 60-107 years) and 53.7% were male.

A total of 48 registries of inappropriate prescriptions, according to Beers criteria, were recorded in 42 patients (19.6% of the sample included in the study). Table 1 shows the frequency of inappropriate prescriptions according to medications and classes of medications. Twelve patients (5.6%) received an inappropriate prescription during their stay at the emergency department (8 received anticholinergic or antihistamine agents, 2 received long-acting benzodiazepines and 2 received muscle relaxants) and other 19 patients (8.9%) were discharged home with an inappropriate prescription (14 had muscle relaxants prescription and other 5 had longer half-life non-steroidal anti-inflammatory agents).

Table 1. Inappropriate prescriptions according to medications and classes of medications

Class of medication	Number of events (Total = 48)
Short-acting benzodiazepines	11
Long-acting benzodiazepines	8
Amiodarone	7
Fluoxetine	5
Anticholinergics and antihistamines	3
Anorexic agents	3
Muscle relaxants	3
Non-steroidal anti-inflammatory agents	3
Doxazosin	2
Estrogens	1
Chlorpropamide	1
Ticlopidine	1

There were 29 visits to the emergency department related to adverse drug events (12.5% of the emergency visits in this sample). The most common events were falls, which occurred in 15 patients, dizziness in 5 and bleeding in 3 patients. Ten emergency visits were directly related to an inappropriate medication (4.3% of the total of registered visits). Chart 2 describes the event and the medication related to these visits.

Chart 2. Event and class of medication in emergency visits related to inappropriate prescription

Event	Class of medication
Fall – hip fracture	Long-acting Benzodiazepine
Fall – hip fracture	Short-acting Benzodiazepine
Fall – foot fracture	Long-acting Benzodiazepine
Fall – head trauma	Long-acting Benzodiazepine
Fall – back trauma	Short-acting Benzodiazepine
Fall – hand contusion	Short-acting Benzodiazepine
Anxiety	Fluoxetine abstinence
Dizziness	Fluoxetine
Dizziness	Muscle relaxants
Dizziness	Antihistamines

Three of the 17 hospitalizations required in the sample (17.6%) were related to adverse drug events. Two of the hospitalizations were directly related to inappropriate medications. Both of them were caused by falls leading to hip fracture.

There was no association between the occurrence of adverse drug event and age (70.4 years for the group not having adverse drug event and 73.1 years for the group presenting an adverse event, $p = 0.15$) or gender ($p = 0.56$). A statistically significant association was found between the use of benzodiazepines and emergency visits related to adverse drug event (13.9% of the visits in non-users of benzodiazepines and 41.4% of the visits in users of benzodiazepines, $p < 0.001$). Statistically significant associations between emergency visits related to adverse drug events and other medications or classes of medication were not found.

DISCUSSION

The present study demonstrated that more than a third of the emergency department visits related to adverse drug events among older adults were caused by medications listed on the Beers criteria. This finding is different from the study performed by Budnitz et al., in a national surveillance survey in the United States which reported that only 3.6% of the emergency visits for adverse events were caused by inappropriate medications⁽¹⁰⁾.

This difference could be explained by the higher number of inappropriate prescriptions found in our sample. In Budnitz sample, inappropriate medications were prescribed in 10.5% of outpatient care visits. In our sample, approximately one fifth of the patients were regularly taking at least one medication listed in the Beers criteria. Brazilian physicians are probably not completely aware of the most recent criteria used for appropriate prescription in older adults. Another fact that could explain this difference is the existence of a national surveillance system in the United States and its inexistence in Brazil. The surveillance system existence can itself prevent the use of inappropriate medications. Physicians could be more careful with their prescriptions knowing that a surveillance system is under effect.

Hospitalization for adverse drug event was not frequent. However, one fifth of the emergency care visits related to inappropriate prescriptions resulted in hospitalization and in serious disability of the patient. Inappropriate prescription to older adults frequently results in low complexity visits to the emergency department, but sometimes can lead to serious and irreversible damage.

Our results are in agreement with those of Budnitz et al.⁽¹⁰⁾, showing that most of the emergency visits related

to adverse drug events are caused by medications that are not labeled as inappropriate for older adults. However, there are differences between the Budnitz study and the current study regarding the class of medication that leads to the adverse drug events. Budnitz et al. reported that warfarin, insulin and digoxin accounted for one third of all emergency department visits for adverse drug events among older adults in the United States⁽¹⁰⁾. We had two visits related with warfarin, but always in association with acetylsalicylic acid. There were no visits associated with adverse events caused by insulin or digoxin. In our study, the association of two or more anti-hypertensive medications was frequently related to emergency visits caused by falls, dizziness or syncope. A special attention should be given to this association, even if these medications are not referred as inappropriate in any doses, regimens or frequencies.

The benzodiazepines were the only class of medication statistically associated with emergency visits for an adverse drug event. Most of the visits related to benzodiazepine use were related to falls, an association that is clearly demonstrated by previous literature⁽²¹⁾.

Fall was the most common drug-related adverse event, and fractures in consequence of a fall were the main cause of the most of hospitalization cases in patients admitted to the emergency department due to a drug-related adverse event. Elderly patients presenting risk of falling require continuous review of their prescriptions and are the main target of any program attempting to decrease the number of emergency visits related to adverse drug events.

Some limitation of this study must be addressed. First, it was conducted in a single center and may not reflect the situation of adverse drug event or inappropriate prescription in other institutions in Brazil. Second, the study was performed soon after the establishment of the emergency department, when most of patients were admitted for low complexity events. The profile of the patients admitted to the unit, as well as the incidence of adverse drug events and its consequences, could have changed over time, as the number of admissions and complexity rise. Third, the retrospective nature of this study could interfere in its results if medical records were not properly fulfilled.

Adverse drug events among elderly outpatients are a frequent cause of visit to the emergency department and may lead to serious complications and hospitalization⁽¹⁴⁻²⁰⁾.

CONCLUSIONS

A significant percentage of emergency visits are associated with the prescription of an inappropriate medication. A surveillance system, searching for adverse drug events, as well as a program to educate physicians

on most recent criteria of appropriate prescription may help, reducing the occurrence of emergency visits and adverse drug events in the elderly.

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