

Abstract

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| Charles University, Faculty of Pharmacy in Hradec Králové | |
| Training Workplace | Department of Social and Clinical Pharmacy |
| Doctoral Degree Program | Clinical and Social Pharmacy |
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| Title of Doctoral Thesis | Drug-related problems as a potential cause of hospitalizations |

Introduction and objectives:

A drug-related problem is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes. Manifested drug-related problems may contribute to hospital admissions of patients. Such hospital admissions, known as drug-related hospital admissions (DRA), represent a significant and potentially preventable burden on health systems. DRA often arise from the combination of multiple medications, making it important to pay increased attention to drug interactions, particularly in older patients who are taking a larger number of medications. DRA can result from inappropriate medication dosing or the selection of medications in the presence of chronic kidney disease. The main objectives of this thesis are:

- 1)** to determine the prevalence and preventability of DRA and to identify medications and clinical manifestations associated with DRA in patients admitted to hospital via the department of emergency medicine;
- 2)** to determine the prevalence and characteristics of potentially clinically significant drug-drug interactions in the subgroup of older patients;
- 3)** to determine the prevalence and characteristics of medications dosed in disagreement with the dosing recommendations in renal impairment of the Summary of Product Characteristics in the subgroup of patients with chronic kidney disease;
- 4)** to determine the prevalence and preventability of hospitalizations associated with adverse drug events in older patients admitted to the geriatric ward.

Methods:

- 1)** A cross-sectional study was conducted to examine unplanned hospitalizations at the University Hospital Hradec Králové through the department of emergency medicine between August and November 2018. Data were collected from the electronic health records and entered into a Microsoft Access database. The methodology of DRA identification was based on the European OPERAM adjudication guide.
- 2)** A substudy focused on drug-drug interactions was conducted in a subgroup of patients aged ≥ 65 years. Drug-drug interactions were identified using the international consensus list of potentially clinically significant drug-drug interactions in older patients.
- 3)** A substudy focused on medication dosing in renal impairment was conducted in a subgroup of patients with an estimated glomerular filtration rate below 60 ml/min. Prescribed medication dosing was compared with the recommendations for dosing in renal impairment of the Summary of Product Characteristics.
- 4)** A cross-sectional study was conducted to examine the associations of hospitalizations with adverse drug events in older patients admitted to the geriatric ward of the University Hospital Hradec Králové from April to December 2017.

Results:

1) Out of 1252 hospitalizations analyzed, 195 DRA were identified, with 145 DRA related to treatment safety and 50 DRA related to treatment effectiveness. The prevalence of DRA was 15.6% (95% CI 13.6–17.6). In 55% of cases, medications represented only a contributory reason for hospitalization.

Antithrombotic agents, cytostatics, diuretics, corticosteroids for systemic use, and beta blockers were the most common medication classes implicated in DRA related to treatment safety. Diuretics, antithrombotic agents, drugs used in diabetes, drugs acting on the renin-angiotensin system, and lipid-modifying agents were the most common classes of drugs involved in DRA related to treatment effectiveness. Gastrointestinal disorders were the main causes of DRA related to treatment safety, while cardiac disorders were the main causes of DRA related to treatment effectiveness. The potential preventability of DRA was 51% (95% CI 44–58). The highest proportion of potential preventability among medication classes that are repeatedly involved in safety-related DRA was observed for anti-inflammatory and anti-rheumatic agents, psycholeptics, and drugs used in diabetes.

2) Among the 812 older patients admitted to the hospital, 46% (95% CI 43–50) were exposed to potentially clinically significant drug-drug interactions. Drug combinations affecting potassium concentrations accounted for 47% of all potentially caused clinically significant drug-drug interactions. In 27 (3.3%) cases, potentially clinically significant drug-drug interactions were implicated in DRA. The drug-drug interactions most often included combinations of antithrombotic agents (anticoagulants and antiplatelet agents).

3) Among the 375 included patients with chronic kidney disease, 30% (95% CI 25–34) were prescribed at least one medication dosed in disagreement with the recommendations for the dosing in renal impairment of the Summary of Product Characteristics. The most common medications were perindopril, fenofibrate, metformin and ramipril. The prevalence of hospital admissions related to adverse drug events in patients with chronic kidney disease was 20 % (95% CI 16–24).

4) The prevalence of hospitalizations related to adverse drug events in older patients admitted to the geriatric ward was 12% (95% CI 8–15). Antithrombotic agents and diuretics represented the most common medication groups associated with adverse drug events.

Conclusion:

DRA remain prevalent, with medications often acting as contributing factors rather than the sole cause of hospitalization. The results emphasize the need to carefully balance benefits and risks, as demonstrated by the involvement of antithrombotic agents and diuretics in both treatment DRA related to treatment safety and DRA related to treatment effectiveness. The findings regarding drug-drug interactions highlight that even potentially clinically significant drug-drug interactions are very common in older patients. Manifest drug-drug interactions, which were involved in DRA, most frequently concern bleeding events and most frequently involve the combinations of antithrombotic agents. The findings regarding drug dosing in renal impairment showed that almost one-third of included patients with an estimated glomerular filtration rate below 60 ml/min admitted to the hospital were prescribed at least one medication dosed in disagreement with the recommendations for dosing in renal impairment of the Summary of Product Characteristics. In older patients, a higher prevalence and preventability of adverse drug events is observed compared to the younger population. Apart from the drug-related problems associated with drug-drug interactions or inappropriate renal dosing, drug-related problems associated with lifestyle measures (such as fluid and food intake), monitoring and medication nonadherence deserve further attention.