



Feature Article

The impact of combined use of fall-risk medications and antithrombotics on injury severity and intracranial hemorrhage among older trauma patients

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ABSTRACT

Purpose: Use of fall-risk medications (medications that increase risk of falling in the elderly as defined by Beers criteria, STOPP/START criteria, and other literature) or antithrombotics is common in the elderly, and the impact of their concomitant use should be assessed in regards to fall injuries. The primary objective of this study is to assess the simultaneous outpatient use of fall-risk medications and antithrombotics in elderly fall-patients, and secondarily to analyze the injury severity score and occurrence of intracranial hemorrhage.

Methods: Consecutive chart review at a level 2 trauma center in California, USA from August 01, 2009 to October 31, 2010. Records included 112 patients at least 65 years of age admitted with an outpatient fall. Fisher's exact and Student's *t*-tests were used (alpha 0.05, two-tailed) to examine prescribing patterns, intracranial hemorrhage occurrence, and injury severity score. Regression adjusted for antithrombotic and fall-risk medication type and number, opiate use, co-morbidities, age, and gender.

Results: Thirty-nine percent (44/112) of outpatients were prescribed antithrombotics plus fall-risk medications. The mean injury severity score (ISS) was 13.3 (range 1–26, standard deviation 7.2) for patients taking both medication classes versus 9.7 (range 1–25, standard deviation 7.5) for patients taking antithrombotics alone ($p = 0.027$). Additionally, in patients over 80 years of age, intracranial hemorrhage occurred more frequently with the use of antithrombotics plus fall-risk medications versus antithrombotics alone (18/29 = 62.1% versus 7/24 = 29.2%, $p = 0.027$, odds ratio = 3.974, 95% confidence interval = 1.094–15.010). Multivariate analyses showed an independent relationship between intracranial hemorrhage occurrence and type of therapy, as well as injury severity score and simultaneous therapy with fall-risk medications and antithrombotics.

Conclusion: Simultaneous prescribing of antithrombotics and fall-risk medications is common. For outpatients over 80 years of age, the odds of experiencing a post-fall intracranial hemorrhage are 4 times higher when prescribed antithrombotics plus fall-risk medications compared to antithrombotics alone, and injury severity is higher with combined use of these medication classes.

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Introduction

More than one-third of ambulatory patients 65 years of age and older and half of those 80 years and older fall annually.^{1,2} The mortality rate from unintentional falls increased each year between 2000 and 2006, from 29.5 to 41.9 per 100,000 Americans aged 65 years and older.³

Of concern is the prescribing of potentially inappropriate medications (PIMs) in the elderly that may contribute to falls. A

recent study reviewed the use of PIMs in 600 elderly hospitalized patients, detecting 219 adverse drug events (ADEs) that were considered causal or contributory to admission.⁴ Of note, falls or symptomatic orthostasis accounted for 67 of these ADEs.

A second concern is the concomitant growth in antithrombotic use, including anticoagulants and antiplatelets. Anticoagulants are often prescribed for prevention of stroke secondary to atrial fibrillation, while antiplatelets are used widely for ischemic heart disease and stroke prevention. Between 2002 and 2006, warfarin usage increased from 7.3% to 12.8% in patients over 65 years.⁵ With the approval of new agents such as prasugrel, ticagrelor, rivaroxaban, apixaban, and dabigatran, previous barriers to prescribing may be lowered. It is also becoming more common to prescribe

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patients multiple antithrombotics at a time, as outlined in the CHEST guidelines.⁶ This is important to consider given studies suggesting a positive correlation between incidence and severity of intracranial hemorrhage (ICH) and warfarin use,^{7,8} and as high as double the post-ICH mortality rate,^{5,9,10} with one 436-patient prospective study reporting a 3-month post-ICH mortality of 25.8% in non-warfarin users and 52.0% in warfarin users.¹⁰

Studies of adverse events in the elderly often focus on fall-risk medications (FRMs, drugs that increase risk of falling due to a sedative effect, alteration of cognitive function or balance, etc.), with little regard for antithrombotics.⁴ Similarly, studies of trauma patients often focus on whether antithrombotics worsen outcomes without consideration of FRMs.^{9–13} Studying the combined impact of these medication classes on elderly patients is important considering the prevalence of polypharmacy in this patient population. With more antithrombotics being marketed, health care providers may have more concerns about the risks of injury and intracranial bleeding in their elderly patients susceptible to falling. Identifying which medication combinations are likely to increase these risks can help health care providers to choose alternative, potentially safer drug regimens for their elderly patients.

Accordingly, this study aimed to (1) assess the number of patients at least 65 years of age prescribed outpatient FRMs and antithrombotics prior to hospitalization for a fall, and (2) analyze the influence of combined use of antithrombotics and FRMs on intracranial hemorrhage occurrence and injury severity score in these patients.

Methods

Study patients

This study was approved with waiver of informed consent by the authors' associated academic and medical Institutional Review Boards. A trauma center database was used to identify an inclusion group of patients at least 65 years of age admitted to a 319-bed, level 2 trauma center in California, USA between August 1, 2009 to October 31, 2010 and classified with an outpatient "fall from the

same level." Falls in the trauma database were classified as either from the "same level" or "a height." Falls from the "same level" refers to falls taking place on the ground, as opposed to "a height" such as stairs or a ladder. Falls from "a height" were excluded due to the more situational nature of these falls as described in the trauma database, such as a faulty ladder, which could confound the study results. Patients under 65 years of age, missing outpatient medication records, or with a blood alcohol level above the California legal limit of 80 mg/dL were also excluded. Admission to the trauma center was within 12 hours of the outpatient fall.

Study design

In an electronic health record review, the following data were recorded consecutively in accordance with HIPAA regulations: outpatient medications, medical history, outcome, age, gender, race/ethnicity, ICH occurrence based on computed tomography scan, and injury severity score (ISS, based on aggregation of the abbreviated injury scale created by the Association for the Advancement of Automotive Medicine for classification of individual injury severity; an ISS over 15 denotes major trauma).¹⁴ Outpatient medications were recorded if they were mentioned anywhere within the health record as being current and in use (for any period of time) prior to the patient's fall and hospital admission. Simultaneous medication use was judged by dates recorded in the medication reconciliation documents or on-file outpatient prescription records, as well as health care provider notes.

Antithrombotics were chosen for study inclusion based on potential for outpatient use during the study period: dipyridamole and aspirin (Aggrenox), fondaparinux (Arixtra), aspirin, warfarin (Coumadin), dalteparin (Fragmin), heparin, tinzaparin (Innohep), enoxaparin (Lovenox), dipyridamole (Persantine), clopidogrel (Plavix), cilostazol (Pletal), ticlopidine (Ticlid), prasugrel (Effient), or combinations of the aforementioned. FRMs were identified from the STOPP criteria, START criteria, the 2003 and 2012 Beers criteria (Table 1), and other related literature if listed as contributing to falls, sedation, gait imbalance, or mental confusion in elderly patients.^{4,15–26} FRMs included for consideration were:

Table 1
Description of guidelines for potentially inappropriate medications in the elderly.

Guidelines	Published/updated	Description	Methods
Beers criteria ^a	1991, 1997, 2003, 2012	Guidelines to identify potentially inappropriate medications in elderly patients at least 65 years of age, including fall-risk medications. Potentially inappropriate drugs are grouped according to: 1)Diagnosis independent (generally likely to have low efficacy, cause side effects, or have a better alternative in the elderly). 2)Diagnosis dependent (poor choice when combined with certain disease states in the elderly). 3)Caution and individualized dosage stressed. Identifies 53 drug or drug class issues. May use in any health care setting.	Created by a consensus panel of experts. Modified Delphi method in 2012. Evidence-based.
STOPP criteria ^b	2008	Screening Tool of Older People's potentially inappropriate Prescriptions. Guidelines to identify potentially inappropriate medications in elderly patients at least 65 years of age, including fall-risk medications. Groups inappropriate drugs by physiological system. Also includes drug duplication, drug–drug and drug–disease interaction issues. Identifies 65 drug or drug class issues. May use in any health care setting.	Created by a consensus panel of experts. Delphi method. Evidence-based.
START criteria ^c	2008	Screening Tool to Alert doctors to the Right Treatment. Guidelines to identify appropriate medications in elderly patients at least 65 years of age. Often referenced in conjunction with the STOPP criteria. Groups inappropriate drugs by physiological system. Focuses on under-treatment or treatment omission. Identifies 22 drug or drug class issues. May use in any health care setting.	Created by a consensus panel of experts. Delphi method. Evidence-based.

^a Beers criteria.^{15,16,22,26,35}

^b STOPP criteria.^{4,21,24,26}

^c START criteria.^{21,24}

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