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New loop diuretic prescriptions may be an acute risk factor for falls in the nursing home

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Abstract

Purpose—Although chronic use of diuretics has been implicated as a risk factor for falls, it is unknown whether changes in diuretic drugs are associated with an acutely elevated risk of falls. We evaluated the relationship between change in a diuretic prescription (new prescription or increased dose) and the occurrence of documented falls among nursing home residents.

Methods—Participants of the cohort were 1,785 long term care residents of two, large nursing homes (2005–2010; Boston, MA). A self-matched, case-crossover analysis was used to examine whether there is an acutely increased risk of falling in the day following a diuretic drug change compared to days without a diuretic drug change. Odds ratios with 95% confidence intervals were calculated using conditional logistic regression models.

Results—During a mean follow-up of 8.4 months, 1,181 participants experienced an incident fall. Nine participants experienced a diuretic change on the day before the fall. The odds of falling one day following a change in a diuretic was elevated (OR: 2.08, 95% CI 0.89, 4.86). The association was stronger and reached nominal statistical significance when loop diuretics were examined separately (OR: 2.46, 95% CI 1.02, 5.92). We estimated that for every 271 loop diuretic drug changes, one excess fall occurred.

Conclusions—Nursing home residents are at an increased risk of falls in the day following a new prescription or increased dose of a loop diuretic drug. Extra precautions should be taken immediately following a loop diuretic drug change in an effort to prevent falls.

Keywords

diuretic; fall; nursing home

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Introduction

Diuretic drugs are commonly prescribed to nursing home residents in an effort to manage congestive heart failure, edema, and hypertension. Studies have suggested chronic diuretic drug use may be associated with a small increased risk of falls.¹ Less is known about whether changes in diuretic drugs are associated with an acutely elevated risk of falls. Since nursing home residents are highly vulnerable to fall (1.5 falls/person-years),² it is important to identify periods of heightened risk, such as a medication change, when precautions may be helpful in preventing falls and injury. We therefore conducted a cohort study of 1,785 long-term care residents from two large nursing homes, and performed a nested case-crossover analysis to examine the association between changes in diuretic drug use (i.e., new prescriptions or increased dose) and the risk of falls in the day following a diuretic drug change.

Methods

Subjects

Participants of the cohort included all long term care residents of two facilities (Hebrew SeniorLife; Boston, MA USA). During the sampling period (January 2005–May 2010), 1,191 residents experienced an incident fall ≥ 15 days from admission. We excluded residents < 60 years ($n=10$) resulting in a final sample of 1,181 cases for the nested case-crossover analysis. Details of the study including ascertainment of participant characteristics have been previously described.³

Study Design

The case-crossover analysis was developed to assess the effects of a transient exposure on an acute event.⁴ Exposure during a selected period of time preceding the event (hazard period) is compared with usual exposure (control period) in the same individual. Self-matching eliminates confounding by risk factors that are constant within an individual over the sampling period but would differ between study subjects.

For each incident fall, we compared the occurrence of diuretic drug changes on the day before the fall to the occurrence 4, 8, and 12 days before the fall (Figure 1). This is analogous to a 3:1 matched case-control study.

Falls

Falls were defined as accidentally coming to rest on the ground or lower surface. Falls were ascertained prospectively by nursing staff using the facility's federally mandated, computerized incident reports. Although many participants experienced recurrent falls during their admission, only the first fall was included in this analysis.

Changes in Diuretic Drug Use

Based on the American Hospital Formulary Services,⁵ diuretics were categorized as loop, potassium sparing, or thiazide and related. All changes in diuretics (new prescription or increased dose) were ascertained using the facility's computerized order entry system. A *new prescription* was defined as an order for any diuretic that the resident was not using up to 15 days before the fall. A *dose increase* was defined as either an increase in the dose or frequency of a diuretic that the resident was using up to 15 days before the fall. We did not consider drug changes that occurred on the day of the fall because we were unable to determine whether the drug was administered prior to the fall.

Statistical analysis

We used conditional logistic regression to estimate the odds ratio and 95% confidence interval for a fall in the day following a diuretic drug change compared to periods with no diuretic drug changes. We planned a priori to examine loop diuretics separately given their unique mechanism and potency of diuresis.

We conducted two sensitivity analyses. First, we examined the effect of a diuretic drug change on the acute risk of falls over a longer hazard period (1–7 days following a diuretic drug change). Second, we calculated the odds ratio between fall risk and change in a comparator medication (i.e., ACE-inhibitors, Beta-blockers). We selected comparator medications that are used to manage similar clinical conditions as diuretics but are not associated with urinary urgency. This allowed us to explore the hypothesis that urinary symptoms, rather than changes in blood pressure or associated co-morbidities, were responsible for the acute increased risk of falls.

For ease of interpretation, we estimated the absolute risk of a fall one day following a diuretic drug change. The baseline rate of incident fall was calculated as the number of first falls divided by total person time over the observation period, where person-time was defined as the number of days from the beginning of the sampling period or nursing home admission until the time of incident fall, death, discharge, or study end. The absolute risk was calculated as the difference between the baseline rate multiplied by our estimated odds ratio and the baseline rate of incident falls. We used SAS version 9.2 for all analyses.

Results

Among 1,785 residents, 1,181 experienced an incident fall during a mean 8.4 months follow-up. Mean age of participants with a fall was 88 years ($\pm$ SD 8 years), and 71% were female (Table 1). One-third of participants with a fall used one or more diuretic drugs, and loop diuretics were more commonly used in comparison with other diuretic types.

Of the 1,181 residents with a fall included in the case-crossover analysis, 4 participants received a new prescription for a diuretic and 5 participants received a dose increase of a diuretic on the day preceding the fall. When new prescriptions and dose increases were combined, the odds of a fall were 2.08 times greater in the day following a diuretic drug change compared to periods with no diuretic drug changes (Table 2; 95% CI 0.89, 4.86). The association was stronger and reached nominal statistical significance when we restricted the analysis to changes in loop diuretic drugs (OR=2.46, 95% CI 1.02, 5.92).

In sensitivity analyses, there was no evidence of an increased risk of falls when the hazard period was extended beyond one day following a loop diuretic drug change (OR for days 2–7 range from 1.13–1.57; p-values >0.26). There was no increased risk of falls within one day of a comparator drug change (OR=0.30, 95% CI, 0.04, 2.34).

The absolute risk of falls in the day following a loop diuretic change was 3.7/1,000 loop diuretic changes. Thus, we estimate that for every 271 loop diuretic drug changes in the nursing home, one excess fall occurred.

Discussion

Our findings suggest there is a two-fold increased relative risk of falling within one day of receiving a new prescription or increased dose of a loop diuretic drug in nursing home residents. Despite this moderately increased relative risk, the absolute risk of falls associated with a loop diuretic change was small: approximately 4 excess falls/ 1,000 loop diuretic changes. This absolute risk may still be greater than the risk of falls afforded by chronic

diuretic use. A meta-analysis of nine studies concluded that diuretic drug use was associated with only a slight increased risk of falls in community dwellers (OR=1.08, 95% CI 1.01, 1.16), and there was no statistically significant association between diuretic drug use and falls in nursing home residents (OR=1.02, 95% CI 0.84, 1.25).¹

Our results suggest that the effect of diuretics on falls may be greatest immediately following drug initiation or an increased dose. This is important because in contrast with chronic diuretic use, it may be possible to intervene during this acute window of time in an effort to prevent falls. We speculate that our findings may relate to the drug side effects of urinary urgency and frequency that are prominent with diuretic initiation and could result in a fall while hurrying to the toilet. Prior research suggests that falls occur commonly while toileting in the nursing home.⁶ There is also some evidence to suggest that toileting strategies may be effective in reducing falls among continent nursing home residents.⁷ Alternatively changes in diuretic drugs decrease blood pressure and may lead to dizziness and subsequent falls. Shannon et al. found that systolic blood pressure decreased in response to tilt testing among older, but not younger, volunteers exposed to two days of a thiazide diuretic.⁸ We did not have detailed information on the circumstances of the fall or blood pressure changes before the fall in order to test either hypothesis. Future studies should prospectively consider the mechanism through which diuretic use affects risk of falls as this may lead to important insights in the development of fall prevention strategies.

Our study has limitations. First, we had small numbers of participants with a diuretic drug change, in particular thiazide drug changes. Although we were unable to examine this drug class separately, Gribbin et al. found that new users of thiazide diuretics were at more than a two-fold increased risk of falls during the 21 days following drug initiation.⁹ Further, we did not have an adequate sample size to consider subgroup analyses. Certain subgroups, such as residents with renal impairment or occasional incontinence, may have been differentially affected by a diuretic change. Second, we are unable to separate the effects of the diuretic from the effects of the associated medical condition on risk of falls. This limitation is not specific to the case-crossover approach, but rather it applies to all observational studies of pharmacoepidemiology. Congestive heart failure itself has not been implicated in the etiology of falls, but it is possible that worsening edema or dyspnea could increase the risk of falls. Our finding that changes in comparator medications used to manage heart failure were not associated with an acutely elevated fall risk suggests that our results may not be entirely explained by the underlying medical illness.

Falls result from interactions between chronic risk factors, such as dementia and gait abnormalities, and acute environmental or situational hazards. Our results suggest that changes in loop diuretic prescriptions are an example of an acute situational hazard associated with an elevated risk of falls. We suggest that future fall prevention trials in the nursing home consider not only interventions aimed at ameliorating chronic risk factors for falls, but also consider whether acute environmental or situational hazards, such as a medication change, might lend themselves to successful interventions. Efforts to prevent falls through scheduled toileting and/ or bedside commodes may be useful for continent residents immediately following a diuretic change. Future studies should confirm the association between loop diuretic initiation and the acute risk of falls and to determine whether these strategies are successful in reducing falls in the nursing home.

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Take home points

- Nursing home residents are at more than a two-fold increased relative risk of falls in the day following the initiation or increased dose of a loop diuretic drug.
- We estimate that for every 271 changes to a loop diuretic prescription in nursing home residents, one excess fall will occur. Although this absolute risk is modest, it may be greater than the absolute risk of falls associated with chronic diuretic use, and it identifies a narrow window of time when interventions might be feasible.
- Precautions such as scheduled toileting for continent residents may be effective in reducing falls in the day following a loop diuretic drug change.

Figure 1.
Case-crossover analysis to determine the effect of a diuretic drug change on the acute risk of falls in the nursing home

Table 1

Characteristics* of 1,181 nursing home residents with a fall in a case-crossover study (% , unless otherwise specified)

Age in years, mean (standard deviation)	88 (8)
Female	842 (71.3)
Cognitive status [†]	
Intact or mild impairment	221 (18.7)
Moderate impairment	709 (60.0)
Severe impairment	244 (20.7)
Functional status [‡]	
Intact or mild impairment	155 (13.2)
Moderate impairment	631 (53.9)
Severe impairment	385 (32.9)
Co-morbidities	
Congestive Heart Failure	131 (11.1)
Hypertension	742 (63.2)
Stroke	121 (10.3)
Urinary continence [§]	
Always or usually continent	544 (46.3)
Occasionally or frequently incontinent	348 (29.6)
Never continent	282 (24.0)
Diuretic use	
Any diuretic	392 (33.2)
Loop diuretic	318 (26.9)
Potassium sparing diuretic	25 (2.1)
Thiazide and related diuretic	84 (7.1)
Medication Count	
1–4	146 (12.4)
5–8	527 (44.6)
>8	508 (43.0)

* Ascertained in the 3 months before the incident study fall

[†] Categorized using the Cognitive Performance Scale. Intact (score 0–1), mild-moderate impairment (score 2–4), or severe impairment (score 5–6)

[‡] Categorized using the ADL-short scale. Intact or mild impairment (scores 0–1), moderate impairment (scores 2–3), or severe impairment (scores 4–7)

[§] Categorized using the MDS in the 3 months before the incident study fall as always or usually continent (incontinent $\leq 1 \times$ /week), occasionally or frequently incontinent $\geq$ (incontinent $2 \times$ /week, but with some bladder control), or never continent

Table 2

Odds ratios* of an incident fall one day after a diuretic drug or comparator drug change in a self-controlled case-crossover analysis of 1,181 nursing home residents with a fall

	Number of prescription changes in hazard period (1 day before fall)	Number of prescription changes in control periods (4, 8, and 12 days before fall) [†]	Odds Ratio	95% CI
All diuretics drug changes	9	13	2.08	0.89, 4.86
Loop diuretic drug changes	9	11	2.46	1.02, 5.92
ACE-Inhibitors and Beta blockers drug changes	1	10	0.30	0.04, 2.34

* Odds ratios in this self-controlled case-crossover analysis represent the odds of falling in the day following a drug change compared to periods with no drug change. All models included an indicator term for day of the week on which the fall occurred.

[†] Total number of medication changes observed summed over the three control periods