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Research Article

Evaluating the Role of Intravenous Antihypertensive Agents in Falls of Hopitalized Patients

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Abstract

Purpose: To determine if falls in the hospital occur more frequently in patients receiving intravenous (IV) antihypertensive therapy compared to patients that are not receiving any such treatment.

Methods: Using data retrospectively collected from the institution's electronic records, we filtered dispensing records for select IV antihypertensive medications from January 2018 through December 2019. We then compared the patient identifying numbers from the dispensing records with the patient identifying numbers from the reported inpatient fall records during the same time frame.

Results: There was a total of 617 inpatient falls at the hospital between January 2018 and December 2019. One hundred twenty-three patients out of the 617 (20%) fell while receiving IV antihypertensive agents. During the same time there were a total of 9,226 orders for IV metoprolol, labetalol, and hydralazine. This indicates that out of the 9,226 orders for IV antihypertensives, 1.3% of patients fell while in the hospital because of those medications. Of the 617 falls, 124 of those were associated with an injury report. There were 22 patients (18%) receiving IV antihypertensives that fell and were injured.

Conclusions & Recommendations: Our findings support the need for additional research to determine what factors are contributing to patients falling while on IV antihypertensive therapy. IV antihypertensive medications should be discontinued at the earliest time to prevent falls especially when patients are restarted on oral antihypertensive medications and blood pressure is controlled. Patients should be monitored closely for orthostasis in all settings when antihypertensive therapy is started or changed. Patients and caregivers should be educated particularly on this point especially in frail, elderly patients.

INTRODUCTION

The use of antihypertensive medication in hospitalized patients is a common and necessary practice to keep blood pressure at appropriate levels. A common issue in patients that have come into the hospital with hypertension is being given intravenous (IV) antihypertensive agents when they are not indicated, and/or being left on IV antihypertensive agents after blood pressure control has been achieved on oral medications. Besides not following guideline recommendations on how to treat hypertension in the hospital setting, this practice is potentially dangerous and may potentiate the risk of falling therefore increasing the odds of patient harm and additional healthcare costs. It is well studied that falls may account for up to 70% of accidents in hospitals and that 30% of these falls may lead to physical harm [1]. In developed places such as the United States, Europe, and Australia 0.85 to 1.5% of healthcare costs are related to the treatment of falls [2].

There are several studies that document the associated risk of falls and antihypertensive therapy [2-16]. To our knowledge, there are no studies that evaluate the use of intravenous antihypertensive therapy and falls. A recent consultant audit at the hospital found an increase in reported falls as well as an increase in the use of IV hydralazine. This study aims to provide evidence that patients who are inappropriately receiving IV antihypertensive therapy are more prone to falling in the hospital. Furthermore, this study will attempt to evaluate if there are concomitant medications that may have an additive risk of contributing to falls, and if the duration or type of antihypertensive medication have a particularly increased risk of falls.

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MATERIALS AND METHODS

Objectives

The primary objective in this study was to determine if the number of patients who fell in the hospital receiving intravenous (IV) antihypertensive therapy was greater than the number of patients that fell who were not receiving IV antihypertensive therapy. Secondary objectives included determining if the patients who fell while receiving IV antihypertensive medication were being treated appropriately with IV medications, determine if the length of time on IV antihypertensive medication correlated to total number of falls, evaluate if there is a trend between falls and specific IV antihypertensive medication and class of medication, and determine if falls were more prevalent in patients receiving IV antihypertensive medication and concomitant central nervous system (CNS) depressant medications (i.e. benzodiazepines, opioids, antidepressants), insulin, diuretics, or other cardiovascular medications.

Patients

Our study included patients admitted to the hospital between January 1, 2018 and December 31, 2019, were 18-100 years of age, received at least one dose of an IV antihypertensive medication, and had an accurate medication administration record. Those excluded were less than 18 or over 100 years of age and patients that had an order for IV antihypertensives but never received a dose.

Methods

To identify patients, we evaluated all patients that fell during the study period reported to RL solutions®. We then completed a chart review of all the patients that fell to determine which ones received an IV antihypertensive medication. While completing the chart review, the timing of antihypertensive medication was referenced against the time of the fall, if the antihypertensive was appropriately used, and if the patient was receiving other medications that could increase the risk of a fall. We also evaluated how many patients received IV antihypertensive therapy during the same time, and did not fall, to establish if there was a relationship between inappropriate IV antihypertensive use and falling as well as if there was a relationship between specific IV antihypertensives and falling. Data was collected through a computerized retrospective chart review. Data collected included basic demographics, patients that fell who received an IV antihypertensive medication, patients that did not fall after receiving IV antihypertensive medication, if the administration and duration of the IV antihypertensive use was appropriate, which agent was used, the location of the fall, comorbid conditions that could have predisposed a patient to falling, and concomitant administration of medications that could have precipitated a fall.

Data Analysis

The study was approved by the Quality Improvement Review Board of the Institution. Data was analyzed by Analyse-it for Microsoft Excel v.6.15.4, Copyright©: 1998-2023, Analyse-it Software Ltd., Leeds, England. Descriptive statistics were used to compare patient demographics, odds ratios, and relative risk ratios. Nominal data were compared using X^2 or Fisher's exact test. Continuous data were evaluated with the Shapiro-Wilk test for normality, and all were determined to be non-parametric. Central tendency is expressed as the median with interquartile range for dispersion. Mann-Whitney U, Kruskal Wallis, and Spearman Correlation were utilized as appropriate. Statistical significance was defined at an a-priori alpha < 0.05.

Results

Out of 617 inpatient falls at the hospital between January 2018 and December 2019, 123 (20%) patients fell while prescribed IV antihypertensive agents. Table 1 summarizes the demographics of the 123 patients who fell while prescribed IV antihypertensive agents. As can be seen from Table 1, the patients who fell were predominantly white, middle-aged men who were slightly overweight. During the same time there were a total of 9,226 orders for IV metoprolol, labetalol, and hydralazine. This indicates that out of the 9,226 orders for IV antihypertensives, 123/9226 (1.3)% of patients fell while in the hospital because of those medications. Of the 617 falls, 124 of those were associated with an injury report. There were 22/123 (18%) patients receiving IV antihypertensives that fell and were injured. Most patients that fell and were injured (73%) received IV hydralazine (Table 2). Outcomes are reported in Table 3. Of the 123 falls reported in patients prescribed IV antihypertensive agents, 26 reported an injury due to the fall with six of those resulting in a bleed. Median BMI (IQR) was significantly higher in patients who fell and were injured [32.4 (25.2-37.3) vs. [26.6 (22.1-32.7)], (p =0.0027) and significantly more patients who were obese (BMI>30) were injured [14/26 (53.8%)] vs. [31/97 (32.0%), (p = 0.0396). Of the 123 patients who fell, 25 (20%) had multiple falls. It appears that once someone fell, action was taken as patients with multiple falls had significantly lower BMI [median BMI (IQR) = 22.6 (22-27.3) vs. 28.1 (23.7-35.4), p = 0.0027] and fewer were on subsequent IV antihypertensive agents [2/25, (8.0%) vs. 37/98 (37.8%), p = 0.0043]. Patients who had multiple falls had significantly longer hospital length of stay (LOS) [median LOS (IQR) = 11 (3.7-25 days vs. 4 (2-9) days, p = 0.0014). Out of the 123 patients that fell, 122 patients did receive some type of medication that could have precipitated a fall when used concomitantly with IV antihypertensive therapy. The most common contributing medication were other antihypertensives (73.7%), insulin (6.5%), anticonvulsants (4.1%), and antipsychotics (4.1%), (Figure 1). Figure 2 summarizes the frequency with which the IV antihypertensive agents were administered and the drug combinations.

Table 1. Demographics of 123 patients who fell while prescribed an IV antihypertensive agent

Sex	M	81
	F	42
Age in Years	Median (IQR)	59 (48-71)
BMI in Kg/m²	Median (IQR)	27.1 (22.6-33.7)
BMI >30 Kg/m²		45/123 (36.6%)
BMI >40 Kg/m²		13/123 (10.6%)
Race	White	61
	Black/African American	18
	Hispanic	41
	Asian	2
	Unidentified	1

Table 2. IV Antihypertensive use resulting in falls leading to injuries

Hydralazine	16	22%
Labetalol	5	23%
Metoprolol	1	5%
	22	

Table 3. Outcomes.		
Fall with Injury		26/123 (20%)
BMI with Injury	Median (IQR) Kg/M^2	32.4 (25.2-37.30
BMI without Injury	Median (IQR) Kg/M^2	26.6 (22.1-32.7), p = 0.0187
BMI >30 Kg/M^2 with Injury		14/26 (53.8%)
BMI >30 Kg/M^2 without Injury		31/97 (32.0%) p = 0.0396
Fall with Bleed		6/123 (4.9%)
Multiple Falls		25/123 (20%)
Length of Hospital Stay in Days with Multiple Falls	Median LOS (IQR)	11 (3.7-25)
Length of Hospital Stay in Days without Multiple Falls	Median LOS (IQR)	4 (2-9), p = 0.0014
BMI with Multiple Falls	Median (IQR) Kg/M^2	22.6 (22-27.3)
BMI without Multiple Falls	Median (IQR) Kg/M^2	28.1 (23.7-35.4), p = 0.0027
BMI >30 Kg/M^2 with Multiple Falls		5/45 (11.1%)
BMI >30 Kg/M^2 without Multiple Falls		20/78 (25.6%), p = 0.0538
Continued IV Antihypertensive Agents with Multiple Falls		2/39 (5.1%)
Continued IV Antihypertensive Agents without Multiple Falls		23/84 (27.4%), p = 0.0043

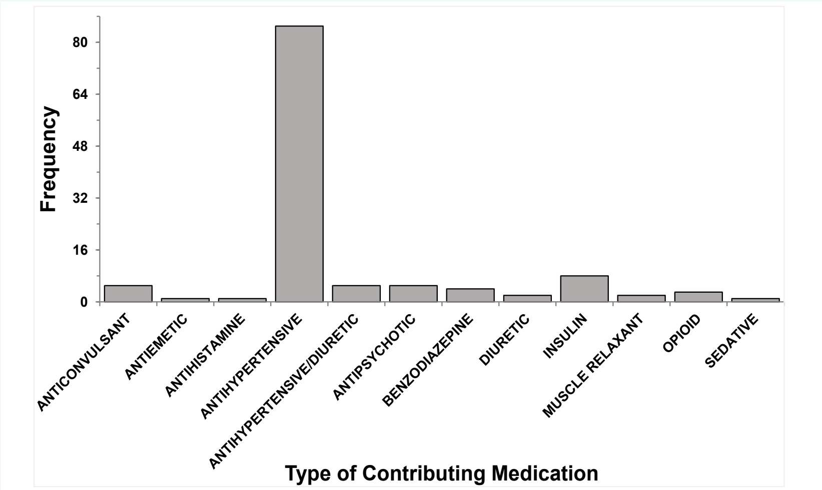

Figure 1 Frequency of other Classes of Contributing Medications to Falls in Patients prescribed Antihypertensive Medication.

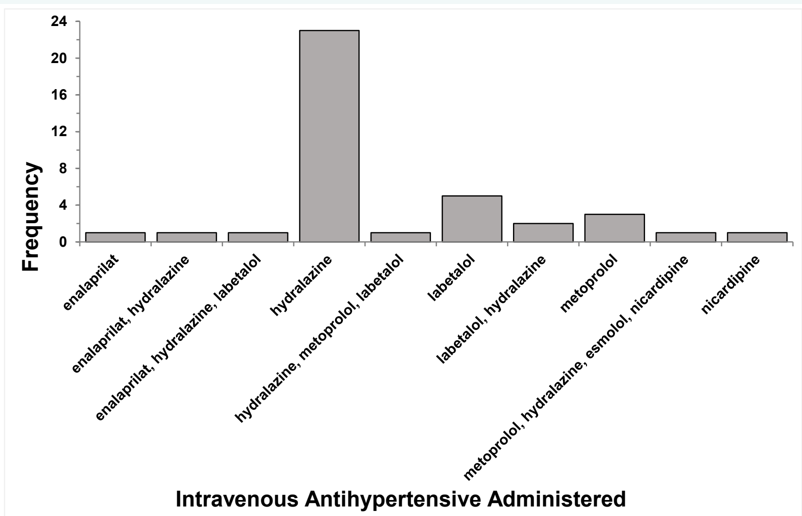

Figure 2 Frequency of different types of IV Antipertensives Administered.

DISCUSSION

There are several classes of medications that may predispose a patient to falling such as benzodiazepines, antidepressants, antipsychotics, antihypertensives, antiarrhythmics, and opioids [1]. Numerous studies suggest that there is an association between the use of antihypertensives and falls, and that the risk of falling is highest with antihypertensive medications compared to other classes of medications [1-16]. Several studies have shown that the chronic use of various antihypertensive regimens are not associated with an increased risk of falls, however, the initiation of a new regimen or a change in regimen [2,4,7,13,15,17-18]. These changes vary from 0-24 hours [2,18] to 30 days[4], up to 180 days prior to a fall [15]. Shimbo et al. evaluated Medicare patients and had similar findings to other studies mentioned here [18]. This study evaluating Medicare patients found that the odds of falling were elevated in the first 15 days after starting or intensifying antihypertensive medications [18]. An Irish community pharmacy found that for each 5-day gap in refill adherence for antihypertensive medications, the risk of self-reported injurious falls increased by 18% [17]. This is very similar to initiating IV antihypertensive therapy given in the hospital as one or two additional doses with simultaneous adjustments being made in other oral antihypertensive therapy. Several classes of antihypertensive agents have been associated with an increase in falls in the community or long-term care setting. These include alpha-blockers [12,15,19], beta-blockers [3,14], Central acting agents [19], diuretics [9,10], amlodipine [11] and ≥2 antihypertensive agents [9,15-16]. In a pharmacokinetic study by Ploegmakers, et al., patients with a fall had more metoprolol concentrations above the median (cardioselective) compared with several nonselective beta-blocking agents (sotalol, timolol, propranolol, and carvedilol) [3]. Patients taking thiazide diuretics had significantly more episodes of syncope and falls, hyponatremia, and hypokalemia [9]. In our study, >70% of patients were on other antihypertensive agents. This was shown to increase the risk of falls in three other studies [9, 15-16].

In a study by Rivasi, et al., benzodiazepines proved to be an independent predictor of lower baseline SBP (149 vs. 161 mm Hg) [20]. Benzodiazepines significantly affected 10s post standing SBP and was maximum at 21 mm Hg. SBP continued to decrease after the test while control patients recovered. We know that benzodiazepines increase the risk of falls due to their CNS effects, however, this new information sheds light on their additional effects on orthostatic hypotension and falls when combined with intravenous antihypertensive medications. Serious falls/syncope were significantly higher for minimum SBP ≤110 mm Hg (OR = 2.18) and mean SBP <100 mm Hg (OR = 1.54) [21].

Archer et al., has developed a predictive model of falls consisting of 24 predictors including age, alcohol consumption, a history of falls, and prescriptions of antihypertensives, antidepressants, hypnotics, and anxiolytics [6]. Sheppard et al., showed an increased risk of falls particularly in older patients (80-89 years) and in those with severe frailty [5]. Amongst frail or prefrail patients using antihypertensive medications, each 5 mm Hg increase in long-term variability in MAP increased the risk of falls by 16% (OR = 1.16) [7]. Hospitalized patients are potentially weaker and less stable and, therefore, would be at an increased risk of having antihypertensive medications changed to what the hospital has on formulary as well as having doses increased or even started on IV formulations [2]. All of the aforementioned factors could place hospitalized individuals at an increased risk of falling. As demonstrated in these studies there is an established relationship between the use of antihypertensives and falls. However, the studies cited evaluated antihypertensives in older adults who were mostly 60 years of age or older. These studies did not specify if the antihypertensives being used were oral or IV which lends itself to the need for this study. The use of IV antihypertensive agents was associated with patient falls in this study. Based on the data collected at our facility, hydralazine was the most common agent associated with patient falls. What is not clear and requires further investigation is if there is a significant comorbid condition that contributes to falling while on IV antihypertensive agents. Patients with a larger BMI were more associated with falling and being injured. Our findings are consistent with several studies showing increases in both falls and injuries from falls in obese patients [22-24]. Once a patient fell, intervention was taken as patients with multiple falls had lower BMI and were on less subsequent IV antihypertensive agents. This is in contrast to an outpatient study by Omer et al., who showed that antihypertensive regimens were frequently unchanged after a serious fall [25].

Conclusions and Recommendations

Our findings support the need for additional research to determine what factors are contributing to patients falling while on IV antihypertensive therapy. IV antihypertensive medications should be discontinued at the earliest time to prevent falls especially when patients are restarted on oral antihypertensive medications and blood pressure is controlled. Patients should be monitored closely for orthostasis in all settings when antihypertensive therapy is started or changed. Patients and caregivers should be educated particularly on this point especially in frail, elderly patients.

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