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COMPARISON OF WEIGHT-BASED DOSE VS. STANDARD DOSE DILTIAZEM IN PATIENTS WITH ATRIAL FIBRILLATION PRESENTING TO THE EMERGENCY DEPARTMENT

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□ **Abstract—Background: Despite evidence-based recommended weight-based (WB) dosing of diltiazem for the initial treatment of atrial fibrillation (AF) with rapid ventricular response (RVR), many providers utilize lower initial doses of diltiazem. Objective: We sought to determine whether a low, standard dose of diltiazem is noninferior to WB diltiazem as an initial bolus dose in the treatment of AF with RVR. Methods: This retrospective review included patients who presented to the emergency department (ED) of an urban, academic tertiary medical center experiencing AF with RVR from November 2010 to August 2014. Adult patients were categorized by the dose of diltiazem received; 10 mg standard dose or 0.2−0.3 mg/kg WB dose. The primary outcome of successful treatment was defined as a composite of the following parameters 15 min after the initial bolus dose: heart rate (HR) < 100 beats/min, reduction of HR ≥ 20%, or a conversion to normal sinus rhythm. Results: Four hundred and fifty-six patients who received diltiazem were included for study evaluation (standard dose: n = 255 patients, WB: n = 201 patients). Baseline characteristics, medical history, and medication use before ED presentation were similar between the groups. Significant differences at baseline between the groups included weight and HR at presentation. The primary outcome of successful treatment was attained in 60.8% of the standard dose patients and 68.7% of the WB patients (p = 0.082). Conclusions: In patients presenting to the ED, we found that standard dose diltiazem was noninferior to WB dosing in the initial treatment of AF with RVR.**

□ **Keywords—diltiazem; cardizem; atrial fibrillation; rapid ventricular response; afib; heart rate; pharmacology; clinical pharmacy**

INTRODUCTION

Atrial fibrillation (AF) is a common cardiac dysrhythmia that requires many patients to seek emergency treatment each year (1). Currently, the American Heart Association estimates the prevalence of AF in the United States to be 3−6 million and is expected to double by 2050 (2). Approximately 60%−70% of patients with AF present to the emergency department (ED) with rapid ventricular response (RVR) (3). AF with RVR occurs when the heart rate (HR) increases in response to inappropriate ventricular rate control, such as β-adrenergic stimulation or the absence of vagal stimulation (4,5). AF with RVR can lead to significant morbidity and mortality if not treated promptly (4). Complications of untreated AF with RVR can include hemodynamic instability,

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tachycardia-induced cardiomyopathy, arterial thromboembolism, cerebrovascular accidents, and death (4,6,7).

The 2014 American Heart Association/American College of Cardiology/Heart Rhythm Society (AHA/ACC/HRS) guideline for the acute management of patients with rapid AF suggest using an intravenous (IV) β-receptor antagonist (BB) or a non-dihydropyridine calcium channel antagonist (CCB) to slow RVR in the absence of hemodynamic instability or pre-excitation syndromes (4). One of the most common medications used clinically to slow RVR is diltiazem (8). There are data showing that CCB may be more effective at treating RVR than BB (9−11). The AHA/ACC/HRS guidelines recommend an initial diltiazem bolus dose that is weight-based (WB) (0.25 mg/kg) given over 2 min, followed by a continuous-rate infusion of diltiazem at 5−15 mg/h (4). Furthermore, they advise an additional, higher WB bolus of diltiazem (0.35 mg/kg) after 15 min if the patient does not demonstrate an adequate response to the initial bolus (4,12,13).

Importance

Despite the long-standing WB guideline recommended dosing, recent research has investigated whether this dosing strategy is necessary for reduction of a rapid ventricular rate (14). A non-WB or lower WB strategy has been utilized by providers at our institution and others (14). This strategy carries the thought of "start low, and go slow" in lieu of a single, larger WB dose, despite the well-studied safety of WB diltiazem dosing (3,9−13,15−18). A previously published retrospective study proposed that low-dose diltiazem (<0.2 mg/kg) might be as effective as guideline recommended WB diltiazem in treating RVR, and result in less hypotension (14).

Goal of This Investigation

We hypothesize that diltiazem may not require WB dosing to emergently and adequately treat patients presenting to the ED in AF with RVR. The aim of this study was to determine whether a low, standard dose of diltiazem is noninferior to WB diltiazem as an initial IV bolus dose in the treatment of AF with RVR.

MATERIALS AND METHODS

Study Design

This was a single-site, retrospective, electronic medical record review conducted at a large, academic, tertiary medical center. Demographic and clinical data collected included age, weight, sex, ethnicity, comorbid conditions, concomitant medications, onset of AF, HR, and blood pressure (BP) at baseline and 15 min after diltiazem administration, dose of diltiazem administered, and whether a patient received additional doses of diltiazem. In the event that a patient had no recorded weight from the ED, a weight from a previous hospital visit within 1 year of the encounter date was utilized.

Selection of Participants

This study included records of patients at least 18 years old who presented to the ED between November 2010 and August 2014, inclusive, experiencing acute AF with RVR, with a HR $\geq$ 120 beats/min and received an initial IV bolus dose of diltiazem. Patients were excluded if there was no recorded weight within 1 year of encounter, insufficient recording of vital sign data, or concurrent administration of any rhythm modifying or rate-controlling agent by a first responder or at the ED 30 min before the initial diltiazem bolus (with the exception of adenosine, due to an extremely rapid half-life).

Interventions

Records were divided into two groups, standard dose vs. WB dose. For the purpose of this study, standard dose was defined as 10 mg diltiazem, as this was recognized as the most commonly ordered dose in the ED. WB dosing was defined in this study as a diltiazem dose of 0.2−0.3 mg/kg. All individuals receiving 10 mg diltiazem were first evaluated to determine whether the patient was receiving a WB dose and, if not, was placed in the standard dose group. The WB range for this study reflects the inclusion of the guideline recommended dosing and rounded doses (5-mg increments), as was practically given at the bedside.

Outcome Measures

The primary outcome measured was successful treatment, defined a priori as a composite of any one of the following: HR < 100 beats/min, HR reduction of > 20% from initial presentation within 15 min after the bolus dose was given, or a spontaneous conversion to normal sinus rhythm. Secondary outcomes evaluated included HR and BP 15 min after diltiazem administration and conversion to normal sinus rhythm. Hypotension was evaluated as a side effect of the dosing regimens.

Statistical Analysis

Based on previous studies, we assumed the success rate of a single bolus dose of diltiazem would be 75% (12,14−16,19). A sample size of 292 patients in both