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In patients presenting to the emergency department with atrial fibrillation with rapid ventricular response, are calcium channel blockers more effective than beta-blockers for acute management of rate control?

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In patients presenting to the emergency department with atrial fibrillation with rapid ventricular response, are calcium channel blockers more effective than beta-blockers for acute management of rate control?

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Abstract

The evidence on the efficacy of nondihydropyridine calcium channel blockers (CCBs) compared to beta-blockers (BBs) for acute atrial fibrillation (AF) rate control in the emergency department setting was examined. Twelve studies were relevant and revealed that CCBs, specifically diltiazem, were superior to BBs because of their rapid onset of action and the lower number of doses they required to sustain ventricular rate control compared to BBs. However, given the small sample sizes in these studies and the limited number of randomized, double-blinded trials, more research is needed to increase the generalizability and to confirm the significance of these findings.

INTRODUCTION

Atrial fibrillation with a rapid ventricular response (AF with RVR) is one of the most commonly encountered dysrhythmias in the emergency department (ED) and is responsible for over 750,000 hospitalizations each year.¹ Left uncontrolled, AF with RVR often results in complications such as hemodynamic instability, worsening or new onset cardiomyopathy and heart failure, stroke, and increased mortality rates and hospital costs. Therefore, properly recognizing and understanding how to treat AF with RVR is crucial to patient care and management. AF is traditionally defined as an irregularly irregular rhythm with no discernible p-waves and a ventricular conduction rate greater than 120 bpm. The American Cardiology Association (ACA) released guidelines in 2014 with recommendations to treat AF with RVR with either nondihydropyridine calcium channel blockers (CCB) or beta-blockers (BB). Beta-blockers are administered intravenously in the acute ED setting. The most commonly used agents are metoprolol, propranolol, and esmolol. Beta-blockers work by blocking sympathetic

tone, thereby decreasing the ventricular rate. Nondihydropyridine CCBs are also administered intravenously in acute settings. The most commonly used agents are diltiazem and verapamil. Nondihydropyridine CCBs have direct AV nodal effects, blocking L-type calcium channels, and are used to control the ventricular rate.² While both BBs and CCBs are approved for clinical practice, considerable variation and minimal guidance are available for their use in the ED setting. Furthermore, variability in patients who present with AF with RVR, including their demographics and co-morbidities, may affect the effectiveness of CCBs or BBs. To date, a limited number of studies compare the effectiveness of CCBs versus BBs in the ED setting; even fewer examine how comorbidities affect the efficacy of CCBs or BBs. Whether CCBs are more effective than BBs for the acute management of A-fib with RVR in ED patients is examined for the purpose of determining not only which medications are more effective but also in which patients these drugs are more beneficial. A better understanding of the efficacies overall and the benefits in specific populations can lead to improved mortality rates, reduced complications and decreased costs for both patients and hospitals.

DISCUSSION

In order to ascertain which class of drugs is better, studies that addressed the efficacy of rate-control agents, specifically CCBs and BBs, for the acute management of AF with RVR were reviewed. Search engines included PubMed, ScienceDirect, and Google Scholar. Keywords used were “AF with RVR”, “rate-control”, “CCB”, and “BB”. Studies were included if the authors discussed the efficacy of acute rate control of AF with RVR using either CCBs or BBs. Studies were excluded if they were older than 2014, as the ACA guidelines for the treatment of AF with RVR were different prior to 2014. A total of 12 articles were found that met these criteria. High-quality studies, particularly meta-analyses and blinded randomized controlled trials when available, were preferred.

Current ACA guidelines recommend treatment for acute rate control of AF with RVR using a nondihydropyridine CCB or a BB. However, neither adequate guidance nor standardized practice recommendations are currently available for choosing a given drug in specific situations. The focus on patients in the ED setting was chosen for this inquiry because patients in AF with RVR tend to present to the ED initially for acute management and stabilization. A systematic review by Martindale et al included two randomized controlled trials (Demircan et al and Fromm et al), and compared the efficacy of IV diltiazem versus IV metoprolol for rate control in the ED setting. The evidence in both studies showed that IV diltiazem was superior for ventricular rate control in terms of onset of action, sustained rate control, and number of doses required. Diltiazem worked more rapidly with fewer doses for longer durations than metoprolol. In both studies, sustained rate control was defined as a ventricular rate less than 110 bpm persisting without the need for additional doses. Of note, no statistically significant differences in adverse reactions, defined as bradycardia or hypotension, were found between IV diltiazem and IV metoprolol.^{3,4,5}

While the Martindale et al's study has high-quality evidence, some limitations need to be addressed. First and most noteworthy was the small sample size; only two studies were analyzed. Secondly, Martindale et al excluded patients with concomitant conditions such as heart failure, lung diseases, and diabetes mellitus. These encumbrances greatly decrease the power (internal validity) and generalizability (external validity) for effectively interpreting the results. Larger and more diverse populations examined in randomized, double-blinded studies are needed for more useful conclusions. Furthermore, these limitations are troublesome as many patients who present with AF with RVR often have long-standing comorbidities such as coronary artery disease, hypertension, hypothyroidism, diabetes, and obesity. Many of these conditions have relative contraindications to either CCBs, BBs, or both, which would bias the choice of drug used to treat the AF with RVR. In fact, evidence from a retrospective cohort

study by Hines et al. showed that most ED clinicians based their initial drug therapy for acute rate control of AF with RVR on patient's home medications.⁶ For example, in this study, ED clinicians treated patients on home-therapy BB with IV metoprolol and likewise those on CCB at home with IV diltiazem. Therefore, it is important to consider how a patient's home medications can influence the choice of whether a CCB or a BB is used in the acute setting.

Two studies examined the effect of home medications on acute treatment of AF with RvR. The first was a single-center retrospective cohort study conducted by Kuang et al on the effectiveness of IV metoprolol for the treatment of AF with RVR in BB-naïve patients versus BB-chronic use patients. Beta-blocker naïve patients were defined as individuals who had not used any BB within the past 5 days. Beta-blocker chronic patients were defined as those who had used a BB within the past 5 days of admission. Compared to the BB chronic use patients, the BB naïve patients had a greater response to IV metoprolol in achieving control of the ventricular rate of AF with RVR in the ED setting.⁷ The second investigation was also a single-center retrospective cohort study by Feeney et al that examined whether chronic BB users had better rate control with IV diltiazem versus IV metoprolol in the ED setting. The authors found that IV diltiazem had a faster onset of action but produced a higher rate of hypotension in chronic BB patients. Otherwise, there was no statistical difference between IV diltiazem versus IV metoprolol for rate control.⁸ From these two studies, it can be deduced that BB naïve patients responded better to IV metoprolol compared to IV diltiazem for acute management of AF with RVR in the ED setting. However, in chronic BB users, efficacy and adverse reactions were similar for IV diltiazem and IV metoprolol. Even though efficacies may differ, both drugs can be used safely with the exception of IV diltiazem in chronic BB patients.

A second consideration is whether heart failure with reduced ejection fraction (HFrEF) can affect the efficacy or limit the safety of CCBs and BBs. In HFrEF patients, CCBs are relatively contraindicated due to their negative inotropic effects. However, as noted previously,

IV diltiazem is the preferred and more commonly used agent for AF with RVR in the ED setting. Thus, with this comorbidity, it is necessary to determine whether CCBs, especially IV diltiazem, are equally effective and safe compared to BBs such as IV metoprolol. A single-center retrospective cohort study in HFrEF patients by Hirschy et al addressed this issue and revealed that IV diltiazem achieved similar rate control with no increase in adverse events when compared to IV metoprolol for AF with RVR.⁹ Interestingly, ACA recommendations contrast with the Hirschey et al findings and suggest using BBs for HFrEF. Thus, clinicians should proceed with caution when treating HFrEF patients presenting with AF with RVR.

The other common presenting comorbidity found AF with RVR patients is obstructive lung disease (OLD), which includes asthma and emphysema or chronic obstructive pulmonary disease (COPD). In OLD, BBs are relatively contraindicated because they can induce or exacerbate bronchospasm. To date, studies on the treatment of AF with RVR in ED patients with OLD are lacking. However, one nation-wide study conducted in Korea by You et al did address AF and OLD treatment in the outpatient setting. Evidence from this study showed that patients with OLD and concomitant AF had decreased mortality rates and better symptom control on BBs compared to CCBs.¹⁰ Additional studies in ED patients with OLD and with concomitant rapid AF are necessary to corroborate these findings.

A few studies examined rate control of AF with RVR in other situations, but their outcomes were different from those found in EDs. Several of these small studies performed in outpatient and intensive care unit (ICU) settings revealed that IV metoprolol was the most commonly used drug for AF with RVR. Furthermore, in a study by Moskowitz, et al conducted in the ICU setting, IV metoprolol had lower failure rates and required fewer doses to achieve rate control compared to either IV diltiazem or IV amiodarone.¹¹ However, the different conditions in the ICU in this trial, including aggressive intravenous fluid resuscitation and

electrolyte replacement, may have influenced the results. The small sample sizes and disparate conditions of these investigations make any comparisons with the ED studies inequitable.

In summary, these articles point to IV diltiazem, rather than IV metoprolol, as the more commonly used agent in the ED setting. While evidence from the Martindale study showed that IV diltiazem was superior for rate control of AF with RVR in ED patients, additional randomized controlled trials (RCTs) with larger sample sizes and more diverse comorbidities among participants are needed to confirm this finding. However, the evidence did confirm that both IV diltiazem and IV metoprolol had a similar onset of action and were safe for treatment of AF with RVR regardless of a patient's home medication use and other comorbidities. For more conclusive recommendations, future research should include double-blinded RCTs and patients with HFrEF and OLD.

CONCLUSION

In conclusion, the current evidence suggests that controlling atrial fibrillation with a rapid ventricular response in the emergency department setting with a CCB may be superior to using a BB because of the CCBs faster onset of action and its ability to control the ventricular rate with fewer doses. Furthermore, few statistically significant differences were found for adverse reactions due to CCBs compared to those associated with BBs. Calcium channel blockers also seemed either equal or superior to BBs for treating AF with RVR in patients with HFrEF on chronic BB therapy. One exception to CCBs superiority may be that BBs showed better outcomes in OLD patients. However, except for one study conducted by Fromm et al, most of these studies had smaller sample sizes or were not double-blinded randomized controlled trials. Therefore, additional research using larger sample sizes and better study designs is needed to conclude that CCB's are superior to BBs for controlling AF with RVR in acute settings. What can be derived from the current evidence is that CCBs and BBs are both

effective for treatment of AF with RVR; thus, ED medical providers can safely use either class of drugs, even in the setting of co-morbidities.

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