Clinical Investigations

Utilization Pattern of Mineralocorticoid Receptor Antagonists in Contemporary Patients Hospitalized With Acute Decompensated Heart Failure: A Single-Center Experience

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ABSTRACT

Background: Recent studies have broadened the potential use of mineralocorticoid receptor antagonist (MRA) in patients with systolic heart failure after cardiovascular hospitalization. Real-world data on safety and tolerability of MRA initiation during hospitalization for acute decompensated heart failure (ADHF) are lacking. We examined the patterns of utilization of MRAs in patients admitted for ADHF in contemporary clinical practice.

Methods and Results: We reviewed consecutive hospitalized patients admitted with a primary diagnosis of ADHF from March to June 2011. The treatment patterns of MRA use or discontinuation before, during, and after hospitalization were reviewed and analyzed retrospectively. In the study cohort of 500 patients, 106 patients (21%) were on MRAs before admission. During hospitalization, preadmission and newly started MRAs were discontinued in 64 out of 177 (36%), with worsening renal function being the most common identifiable reason. In a multivariate analysis, high admission creatinine was the only significant predictor of MRA discontinuation during hospitalization ($P = .01$). Of the 394 patients who did not receive MRA before admission, 81 were eligible for MRAs, but only 17 (21%) were initiated. After a median follow up of 57 days, 21 additional patients discontinued MRAs; of 72 eligible patients for MRA, 55 patients (76%) were still appropriately taking it.

Conclusions: Despite recent data, MRAs are still underutilized in patients admitted with ADHF who are otherwise eligible for it. Elevated serum creatinine and worsening of renal function are the most common cause of in-hospital discontinuation, which highlights the importance of meticulous follow-up after MRA initiation. (*J Cardiac Fail 2014;20:229−235*)

Key Words: Mineralocorticoid receptor antagonists, acute decompensated heart failure, renal insufficiency.

Beneficial effects of mineralocorticoid receptor antagonists (MRAs) on morbidity and mortality have consistently been demonstrated in patients with systolic HF and advanced symptoms,[1] with postinfarction systolic dysfunction,[2] and most recently with systolic HF and mild symptoms.[3] These benefits are now translating into clinical practice, yet there are ongoing concerns and challenges regarding drug-related adverse effects, especially related to

hyperkalemia and renal insufficiency. Indeed, observational data showed a temporal relationship between increased prescription rate of spironolactone and hyperkalemia-related hospitalizations.[4] Patients with HF receiving MRAs are also more vulnerable to complications in the setting of unsettling intravascular volume and electrolyte shifts which are commonly encountered in the acute decompensated setting. Therefore, only one-third of potentially eligible patients

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may be receiving MRAs at the time of discharge from HF hospitalization from the latest reports.[5]

With increasing recognition regarding the importance in initiation and up-titration of guideline-recommended drug therapy, in-hospital initiation of angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs) and beta-blockers has been strongly recommended by the latest clinical guidelines in patients stabilized from their acute exacerbations before their discharge from the hospital.[6] However, in-hospital initiation of MRAs is less well established, and there are limited real-world data on safety and tolerability of MRA maintenance and/or de novo initiation during hospitalization for acute decompensated heart failure (ADHF). This may be particularly relevant after the recent demonstration of their broad clinical benefits in the EMPHASIS-HF trial (Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure) with the occurrence of cardiovascular hospitalization being an inclusion criterion.[3] The objective of the present study was to determine the prevalence and safety of MRA initiation for potentially eligible patients admitted with ADHF

Methods

Study Population

This was a retrospective study from a tertiary referral center that was performed in compliance with the Declaration of Helsinski and approved by our Institutional Review Board. We identified consecutive patients admitted to a cardiology service with ADHF from March to June of 2011, after the publication of EMPHASIS-HF. The cohort was identified via computerized search of electronic medical records (Epiccare; Epic Systems, Madison, Wisconsin) as primary admission diagnosis of acute systolic and/or diastolic HF by their treating physicians. Patients who developed new-onset HF or HF after cardiac surgery were excluded. Also, patients without reported left ventricular ejection fraction (LVEF) in precise measurements owing to poor image quality were excluded. Eligibility for MRA therapy was defined as patients with LVEF $\leq$30%, admission potassium level $\leq$5.0 mEq/L, and estimated glomerular filtration rate (eGFR) $\geq$30 mL/min/1.73 m^{-2}, largely based on the major inclusion criteria of EMPHASIS-HF.[3]

Clinical Data

We collected demographic information (age, sex, and weight), comorbidities, home medications, standard laboratory data (including B-type natriuretic peptide, serum glucose, sodium, potassium, blood urea nitrogen [BUN], and creatinine) at admission, discharge, and follow-up. ADHF was defined as sudden onset of clinical signs and symptoms of HF requiring hospitalization. Hypertension was defined as systolic blood pressure $\geq$140 mm Hg or diastolic blood pressure $\geq$90 mm Hg at the time of outpatient clinical encounter(s), self-reported history of a diagnosis of hypertension, or the use of antihypertensive medications. Diabetes mellitus was defined as fasting glucose $\geq$126 mg/dL at the time of outpatient encounter, self-reported history of a diagnosis of diabetes mellitus, or the use of hypoglycemic medications. Chronic kidney disease was defined as eGFR <60 mL min^{-1} 1.73 m^{-2} according to the

Modification of Diet in Renal Disease formula. We arbitrarily defined worsening renal function and hyperkalemia as cause of MRA discontinuation as serum creatinine of >2 mg/dl and serum potassium >5.5 mEq/L at the time of discontinuation, respectively. Coronary artery disease was defined by at least moderate (>50%) luminal obstruction on previous diagnostic angiogram, self-reported history of coronary artery disease, and/or past percutaneous or surgical revascularization. Detailed chart review was performed to extrapolate treatment plans of MRA during hospitalization and after discharge by a single extractor, including new initiation and discontinuation (and their causes). In patients with clear documentation for discontinuation reason, such reason was taken into consideration. In patients with lack of documentation, careful chart review at the time of discontinuation was made with arbitrary cutoff points for worsening renal function and hyperkalemia made (serum creatinine of >2 mg/dl and serum potassium >5.5 mEql/L).

Statistical Analysis

Descriptive statistics in the tables are presented as means and standard deviations for continuous variables, and as proportions for categorical variables. Comparisons were made by means of unpaired or paired t test for continuous variables when appropriate, and Fisher exact test or chi-square test for categorical variables. A stepwise nominal logistic regression model was constructed to predict MRA discontinuation. We used a nominal logistic regression model, with clinical parameters including age, sex, serum potassium and creatinine on admission, and history of treatment with thiazide or thiazide-like diuretic. All analysis was performed using JMP software (version 9.0.0; SAS Institute, Cary, North Carolina). A 2-sided P value of $\leq$.05 was considered statistically significant.

Results

Baseline Characteristics

Figure 1 depicts a flow diagram of the total patient cohort (n = 500) stratified according to those with or without MRAs before admission. Approximately 1 in 5 (106 patients, 21%) were receiving MRAs at the time of admission (91% spironolactone, 9% eplerenone). Ninety-six patients (19% of total patient cohort) were on spironolactone, whereas 10 (0.2% of total patient cohort) were on eplerenone. The mean doses of spironolactone and eplerenone were 35 mg and 26 mg, respectively. Baseline characteristics of the study population are presented in Table 1. Compared with those not on MRAs before admission, patients on MRAs before admission were more likely to be younger and less likely to have hypertension and hyperlipidemia, but as likely to have coronary artery disease or chronic kidney disease (even though with lower serum creatinine and sodium). More patients with underlying systolic dysfunction (LVEF $\leq$40%) were on MRAs before admission. In addition, patients with MRA before admission were more likely to have left ventricular dysfunction and biventricular pacemaker device therapy than those not on MRA before admission (P < .0001). Both groups showed no difference in ACE inhibitors, ARBs, and beta-blocker utilization at the time of admission, yet those on