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ALDOSTERONE ANTAGONIST THERAPY AND MORTALITY IN MYOCARDIAL INFARCTION PATIENTS WITHOUT HEART FAILURE

Aldosterone antagonist therapy is beneficial in patients with ST-segment elevation myocardial infarction with left ventricular ejection fraction (LVEF) <40%. Little evidence is available for aldosterone antagonists with patients with preserved ejection fraction or those without congestive heart failure. This issue of *CLIPs* briefly summarizes a systematic review and meta-analysis that evaluates the mortality associated with aldosterone antagonist therapy in patients with ST-segment elevation myocardial infarction without heart failure. If you need further information, please contact the Center for Healthcare Innovation and Patient Outcomes Research (CHIPOR) at chipor@samford.edu.

Dahal K, Hendrani A, Sharma SP. Aldosterone antagonist therapy and mortality in patients with ST-segment elevation myocardial infarction without heart failure. A systematic review and meta-analysis. *JAMA Intern Med*. 2018; doi:10.1001/jamainternmed.2018.0850

Introduction

- ST-segment elevation myocardial infarction (STEMI) is associated with significant morbidity and mortality (e.g., up to 23% within 5 years after percutaneous coronary intervention (PCI).
- Many of these deaths occur within the first 30 days.
- Ventricular remodeling that occurs after STEMI is associated with higher mortality and morbidity.
- Aldosterone is associated with ventricular remodeling, presumably due to tissue fibrosis. Increased aldosterone levels are associated with worsened clinical outcomes (e.g., mortality).
- Due to the paucity of information associated with the use of aldosterone antagonists after STEMI in patients with a LVEF > 40%, a systematic review and meta-analysis was conducted.

Methods

- A systematic search in PubMed, Embase, CINAHL, and Cochrane Central Register of Clinical trials was searched.
- Search terms included aldosterone antagonists OR AA or spironolactone OR epleronone OR canrenoate AND ST elevation myocardial infarction or acute myocardial infarction or STEMI.
- Randomized controlled trials (RCTs) were included if they evaluated the effects of treatment with AAs in patients with STEMI without heart failure or LVEF >40% in adult patients.
- Outcomes evaluated were mortality, MI, new congestive heart failure (CHF), ventricular arrhythmia, and change in LVEF, serum creatinine level, and potassium.

Results

- A total of 319 citations were retrieved and 10 publications were evaluated in the meta-analysis.
- A total of 4,147 patients were enrolled in the 10 studies; 2093 patints were in the angiotensin antagonist (AA) arm and 2054 were in the control arm.
- Many of the studies were conducted in foreign countries and AAs were used in combination with spironolactone, eplerenone, canrenoate and canrenoate + spironolactone.
- Duration of follow up ranted from 6-12 months for the majority of the studies; however, one study evaluated therapy for 1 month and 10 days, respectively.

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Results (continued)

- Table 1 provides clinical outcomes associated with AA therapy.
- AAs were associated with a reduction in mortality and increased LVEF; however, no significant differences between AA and control were observed for the other outcomes.
- A subgroup analysis revealed that individual agents confirned no mortality benefit.
- Additional analyses were conducted for larger studies, with similar results.
- The study quality was moderate to high. No evidence of publication bias was observed.
- No patient-level data was included with this analysis and various AA agents were included in the study.

Table 1: Clinical outcomes associated with aldosterone antagonists

Clinical outcome	Risk of outcome between AA and control group
Mortality	2.4% vs. 3.9%; OR 0.62 (95% CI, 0.42-0.91);*P*=0.01
Myocardial infarction (MI)	1.6% vs. 1.5%; OR, 1.03 (95% CI, 0.57 – 1.86); *P*=0.91
Congestive heart failure (CHF)	4.3% vs. 5.4%; OR, 0.82 (95% CI, 0.56-1.20); *P*=0.31
Ventricular arrhythmia	4.1% vs. 5.1%; OR, 0.76 (95% CI, 0.45 – 1.31); *P*=0.33
Increased LVEF	MD, 1.58% (95% CI, 0.18% - 2.97%); *P*=0.03.
Serum potassium	MD, 0.07 mEq/L [95% CI, 0.01-0.13mEq/L]; *P* = .02
Serum creatinine level	MD, 106.75 [95% CI, −32.79 to 247.05]
Subgroup analyses of >100 patients	
Mortality	OR, 0.57 [95% CI, 0.35-0.94]; *P* = .03
MI	OR,0.96 [95% CI, 0.52-1.77]; *P* = .89
CHF	OR, 0.90 [95% CI, 0.60-1.37]; *P* = .63
Ventricular arrhythmia	OR,0.65 [95% CI,0.16-2.68]; *P* = .55

Summary

- AAs appear to confer a mortality benefit in patients with STEMI with LVEF > 40% or without heart failure.
- Additional studies are needed to confirm the results of the meta-analysis.

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Aldosterone antagonist therapy and mortality in myocardial infarction in patients without heart failure. *CLIPs - Current Literature and Information for Pharmacists.* 2018 June 4;22(6):1-2.