INPLASY PROTOCOL

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Conflicts of interest:
None.

Efficacy and Safety of Mineralocorticoid Receptor Antagonists for Chronic Dialysis Patients: a Meta-Analysis of Randomized Controlled Studies

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Review question / Objective: **Efficacy and Safety of Mineralocorticoid Receptor Antagonists for Chronic Dialysis Patients**
Condition being studied: **Mineralocorticoid receptor antagonists (MRAs) are widely used in the treatment of heart failure, but the risk/benefit ratio of MRAs in dialysis patients remains unclear because the benefits of MRAs may be counteracted by an excess risk of hyperkalemia. Thus, we conducted this study to precisely estimate the efficacy and safety of MRAs in dialysis patients.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 December 2020 and was last updated on 30 December 2020 (registration number INPLASY2020120143).

INTRODUCTION

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an excess risk of hyperkalemia. Thus, we conducted this study to precisely estimate the efficacy and safety of MRAs in dialysis patients.

METHODS

Participant or population: Chronic Dialysis Patients.

Intervention: Mineralocorticoid Receptor Antagonists.

Comparator: Placebo or none.

Study designs to be included: RCTs.

Eligibility criteria: (1) Only randomized controlled trials (RCTs) were included in the meta-analysis. (2) Participants were on hemodialysis or peritoneal dialysis for at least 1 month, and patients with a history of kidney transplantation were excluded. (3) Oral MRAs (spironolactone or eplerenone) were taken for more than 2 weeks. (4) One of the following outcomes must have been included: serum potassium (SP), left ventricular mass index (LVMI), left ventricular ejection fraction (LVEF), cardiovascular and cerebrovascular mortality (CCVM), all-cause mortality (ACM), systolic blood pressure (SBP) or diastolic blood pressure (DBP).

Information sources: The PubMed, Embase and CNKI databases.

Main outcome(s): Sixteen relevant studies involving 1630 patients were included in the meta-analysis. In terms of safety, the meta-analysis revealed that serum potassium levels were higher in the spironolactone group than in the control group (MD=0.06, P=0.22); however, this difference was not significant. In terms of protective cardiovascular effects, patients receiving low-dose spironolactone presented improved left ventricular mass index (LVMI) (MD=10.33, P<0.0001) and left ventricular ejection fraction (LVEF) (MD=-2.49, P=0.03) and decreased systolic blood pressure (SBP) (MD=-8.16, P<0.00001) and diastolic blood pressure (DBP) (MD=0.04, P<0.00001). Moreover, patients receiving low-dose spironolactone had a significantly reduced all-cause mortality (ACM) (OR=0.41, P<0.0001) and cardiovascular and cerebrovascular mortality (CCVM) (OR=0.44, P=0.002).

Quality assessment / Risk of bias analysis: The quality of all trials was evaluated independently by two authors (TYH and WAJ) according to the Cochrane quality criteria. Any disagreement between the authors (TYH and ZH) was settled by discussion with a third author (ZH). Ethical approval was not required because this protocol did not involve any direct contact with patients.

Strategy of data synthesis: Cochrane RevMan 5.3 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark) was used to perform statistical analyses. Odds ratios (ORs) with 95% confidence intervals (CIs) were used as the effect size measures of dichotomous data. Mean differences (MDs) with 95% CIs were computed for continuous data. The weighted fixed effects model was used if there was no significant heterogeneity. Otherwise, the random effects model was used. Heterogeneity was analyzed statistically by I2 and $\chi 2$ statistics. The critical value for homogeneity was a P value less than 0.05. If there was significant heterogeneity, a sensitivity analysis was conducted to evaluate the consistency and quality of the results. Publication bias was evaluated using Begg's and Egger's tests by STATA 12.0 (Stata Corp LP, College Station, TX, USA). Heterogeneity was categorized as follows: low, I2 =0%-25%; medium, I2 =25%-50%; high, I2 =50%-75%; and powerful, I2 =75%-100%; and I2 less than 50% was considered to represent tolerable heterogeneity[27]. P values were determined using the $\chi 2$ test; results were considered statistically significant at $P < 0.05$ for all included studies.

Subgroup analysis: None.

Sensibility analysis: If there was significant heterogeneity, a sensitivity analysis was conducted to evaluate the consistency and

quality of the results. Publication bias was evaluated using Begg's and Egger's tests by STATA 12.0 (Stata Corp LP, College Station, TX, USA).

Country(ies) involved: China.

Keywords: hemodialysis; meta-analysis; mineralocorticoid receptor antagonists; safety; efficacy; spironolactone; eplerenone.

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