Mineralocorticoid receptor antagonism in chronic kidney disease

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Introduction & aims

The use of mineralocorticoid antagonists (MRA) in chronic kidney disease (CKD) remains controversial. As well as being effective at lowering blood pressure, aldosterone antagonism has pleiotropic effects and may be beneficial in CKD where the renin angiotensin system (RAS) is highly activated[1]. The long-term benefits and harms of MRA have not been fully elucidated in CKD

Methods

A retrospective cohort study of patients with CKD was carried out.

Patients were grouped by use of MRA, and subgrouped by type of MRA and dosage (high dose defined as greater than 50mg).

Blood pressure and CKD EPI eGFR were measured at baseline and at most recent clinic, or prior to commencement of renal replacement therapy.

Hyperkalaemic events were defined as a K > 6.5 mmol/L.

Non-parametric data were compared by Kruskal-Wallis test and multiple variate stepwise linear regression analysis was used to determine independent predictors of progression of CKD.

Results - Baseline

Parameter	Control	MRA	p
n	7364	402	
Female (%)	49.6	49.0	0.81
SIMD quintile	2 (3)	2 (3)	0.83
*Baseline eGFR (ml/min/1.73m^2)	38.9 (26.3)	42.7 (29.3)	0.01
*BP (mmHg)	143/75 (32/17)	140/72 (36/19)	0.03
*Heart failure (%)	7.6	21.9	<0.001
*Diabetes (%)	19.8	28.6	<0.001
*ACE/ARB (%)	62.4	67.7	0.03

Results – Multivariate analysis

Parameter	Beta	p
*Baseline eGFR	-0.12	<0.001
Baseline sBP	-.010	0.40
ACE/ARB	-.008	0.50
MRA	-.005	0.68
Coronary artery disease	.007	0.58
Heart failure	.006	0.62
Diabetes	.012	0.32

On multivariate linear regression analysis, use of MRA was not an independent predictor of change in eGFR over the follow up period, with initial eGFR remaining the only independently predictive variable (R^2 = 0.15, p < 0.001)

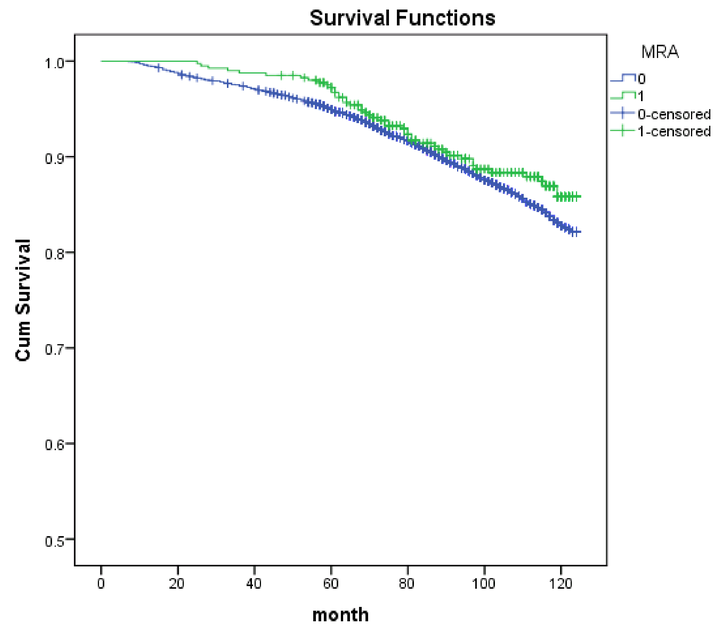
Results – Outcome

Parameter	Control	MRA	p
Change in BP (mmHg)	3/1 (33/17)	5/1 (38/20)	0.86
*Reduction in eGFR (ml/min/1.73m2)	2.3 (4.3)	3.0 (5.3)	0.001
Hyperkalaemia (%)	16.9	15.5	0.60
ESRD (%)	14.9	11.4	0.06

There was no difference in the proportion of patients progressing to end stage renal disease. At the end of follow up, there was no difference in the reduction in blood pressure but there was greater reduction in eGFR per year in the MRA group. There was no difference in the proportion of patients experiencing a hyperkalaemic event in either the MRA group or non MRA group.

Results – survival analysis

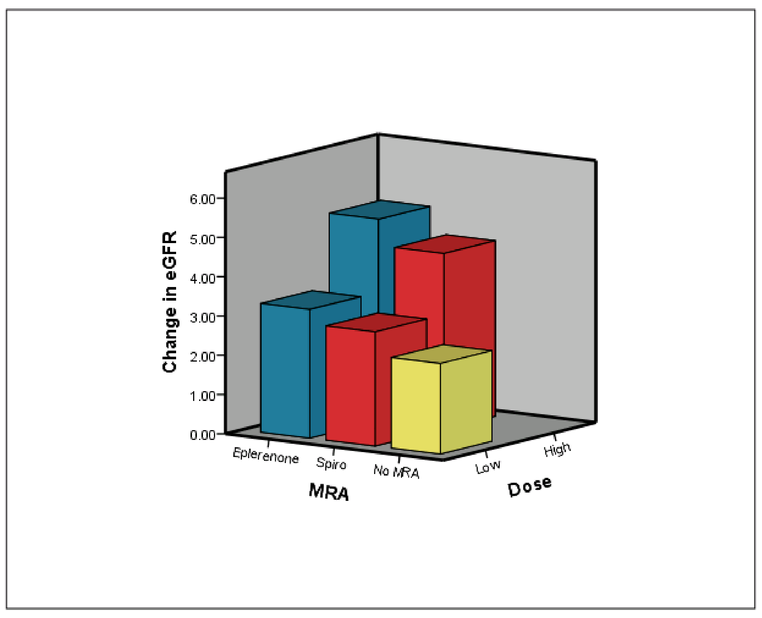
In a Kaplan Meier survival analysis, there was no difference in progression to end stage renal disease in those taking MRA compared to those not taking MRA (Mantel-Cox Log Rank p = 0.15)



Results – subgroup analysis

Change in eGFR per year was greatest in the eplerenone group, and lowest in the group not treated with MRA (3.3 vs 2.9 vs 2.3 ml/min/1.73m2; p=0.001

Change in eGFR per year was highest in the high dose MRA group compared to the low dose and no MRA group (4.5 vs 2.9 vs 2.3 ml/min/1.73m2; p=0.001)



Conclusions

MRA are being used in a high-risk population with high rates of heart failure and diabetes, who are at inherent risk of progressive CKD and other adverse outcomes.

It is reassuring that although the use of MRA appeared to be associated with a higher rate of eGFR decline, on multivariate analysis these medications were not independently associated with progressive CKD and there was no increased incidence of ESRD. Incidence of hyperkalaemic events was not elevated in the MRA group despite a greater use of other renin angiotensin inhibitors.

MRA remain useful medications in high-risk groups for control of blood pressure and cardiovascular risk, and are not associated with an increased rate of adverse renal events.

References

1. Effect of mineralocorticoid receptor antagonists on proteinuria and progression of chronic kidney disease: a systematic review and meta-analysis. Taylor et al, BMC Nephrology 2016

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Clinical hypertension
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