The risks and benefits of spironolactone use in heart failure with a reduced left ventricular ejection fraction and chronic kidney disease

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Purpose: Mineralocorticoid receptor antagonists (MRAs) remain underused in cases of heart failure with a reduced left ventricular ejection fraction (HFrEF) and chronic kidney disease (CKD), largely due to the fear of inducing worsening of renal function (RF) and hyperkalemia (HK), particularly in combination with renin angiotensin inhibitors.

The aim was to investigate the safety use of spironolactone (SP) in patients with HFrEF (ejection fraction <40%) and CKD and determine predictors of worsening of RF and developing HK.

Methods: 208 patients with HFrEF (on top of standard therapy including ACE-I or an ARB) and CKD (baseline eGFR between 30 and 60 ml/min) were included in the study. The potassium (K) and creatinine (C) levels, plasma aldosterone (AS) and NT-proBNP were estimated at baseline and at week 12. After biochemical evaluation, 101 patients started on SP treatment with a median dose of 23 mg daily (titrated). K and RF were checked at weeks 1, 2, 4, 6, 8, 12.

Results: K and C levels increased significantly after start of SP: mean K levels increased from 4.47±0.59 to 5.23±0.57 mEq/l, ($P<0.01$) and was dose dependent. After 12 weeks of treatment the incidence of severe HK (K+ ≥6.0 mmol/L) was <5%, K 5.5–5.9 mmol/L occurred in 13 patients (13%) and it was predicted by baseline eGFR≤35 ml/min/1.73 m^2. and K ≥5.0 mmol/L/. Subsequently, these patients required a prescription of K binders. Mean eGFR on SP decreased from 48.34±2.23 to 42.19±2.65 ml/min/1.73 m^2 ($P<0.01$) and a significant decrease in GFR was observed only during the first month ($P<0.01$) with not significant increasing to 6 and 12 weeks after the start of SP. Five patients (5%) on SP experienced significant decline of RF result in withdrew SP. Age, NT-proBNP concentration >1550 ng/L and eGFR ≤35 ml/min/1.73 m^2 at baseline had modest discriminative powers for predicting decline of RF (0.456, $P<0.01$; 0.542, $P<0.001$; 0.712, $P<0.001$; respectively). At baseline in patients with HFrEF was an inverse correlation between GFR and NT-proBNP level ($r=-0.298$, $p<0.001$). The SP treatment resulted in significantly reduced NT-proBNP and AS ($P<0.01$; $P<0.05$ respectively). By linear regression analysis in SP group the eGFR was associated with NT-proBNP change (0.362, $P<0.05$).

Conclusion: In patient with HFrEF and CKD the risk-benefit ratio of spironolactone with respect to renal failure appears favourable due to improvement of the neurohumoral profile. Although the renal disfunction and hyperkalemia on spironolactone are common: approximately 18% patients required the prescription of K binders and 5% required the withdrew SP duo to decline RF, the occurrence of hyperkalemia was predicted by baseline potassium level and eGFR. Age, higher level of NT-proBNP and eGFR were identified as potential predictors of worsening of RF. So, caution should be advised when using spironolactone in HFrEF with CKD and potassium of ≥5.0 mmol/L and eGFR ≤35 ml/min/1.73 m^2 and NT-proBNP concentration >1550 ng/L for safety reasons.