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Original article

Mineralocorticoid receptor antagonism in acutely decompensated chronic heart failure

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ABSTRACT

Background/objectives: Mineralocorticoid receptor antagonist (MRA) use in acutely decompensated chronic heart failure (ADCHF) may improve congestion through diuretic effect and prevent neurohormonal activation. We aimed to evaluate the clinical effect and safety of spironolactone in ADCHF.
Methods: Prospective, experimental, single-center, and single-blinded trial. Patients were treated with: standard ADCHF therapy or oral spironolactone 50–100 mg/d plus standard ADCHF therapy.
Results: During a 1 year period, 100 patients were enrolled, 50 included in the treatment group. Mean (SD) spironolactone dose (mg) at day 1 was 94.5 ± 23.3 and at day 3 was 62.7 ± 24.3. Worsening renal function (increase in pCr ≥ 0.3 mg/dL from day 1 to day 3) was more likely to occur in control group (20% vs. 4%; $p = 0.038$), serum potassium did not differ between groups, and plasma NTproBNP had a significant decrease in spironolactone group at day 3 (median [IQR], 2488 [4579] vs. 1555 [1832]; $p = 0.05$). Furthermore, a greater proportion of patients in the treatment group were free of congestion at day 3: less edema, rales, jugular venous pressure (JVP) and orthopnea (all, $p < 0.05$). In addition, a significantly higher proportion of patients were on oral furosemide at day 3 (44% vs. 82%; $p < 0.001$).
Conclusions: Our study supports the safety of high dose spironolactone in ADCHF and suggests a positive impact in the resolution of congestion. The important findings of our pilot study need to be confirmed in larger trials.

1. Introduction

The recognition of the importance of chronic neurohormonal activation in heart failure (HF) pathophysiology was crucial to the development of new therapies beyond diuretics and digoxin. Pharmacological inhibition of renin–angiotensin–aldosterone system (RAAS) had a remarkable impact on morbidity and mortality of HF patients [1]. Likewise, mineralocorticoid receptor antagonists (MRAs) showed to be effective in reducing hospitalizations and mortality in systolic HF [2,3].

The natural history of HF is characterized by recurrent episodes of acute HF (AHF). AHF defines a new onset HF or acutely decompensated chronic HF (ADCHF). Patients present with signs and symptoms needing urgent therapy [4]. Despite the prominent therapeutic advances in ambulatory HF patient, little progress has been made in the improvement of ADCHF patient treatment [5].

Aldosterone levels are elevated in patients with ADCHF despite the use of angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), and beta-blockers (BB) [6]. In this setting, aldosterone elevation may contribute to cardiorenal dysfunction, increasing the risk of death and ventricular arrhythmias [6–8]. Therefore, MRA use in ADCHF treatment has two major putative advantages: improve congestion and hypervolemia through its diuretic effect and prevent the neurohormonal activation that characterizes ADCHF, and that is enhanced by loop diuretics [5,9,10].

The impact of MRAs in ADCHF patients has not been well-studied. We aimed to evaluate the short-term clinical effect and safety of the MRA antagonist spironolactone in worsening chronic HF patients.

2. Methods

2.1. Study design

Prospective, experimental, single-center, and single-blinded trial conducted in a Portuguese tertiary hospital enrolling participants between February 2012 and February 2013.

2.2. Study participants

Patients were eligible for enrollment if they presented with decompensation of chronic HF with symptoms leading to hospitalization. HF was diagnosed on the basis of the presence of history of chronic heart failure and at least one symptom (dyspnea, orthopnea, or edema) and one sign (rales, peripheral edema, ascites, or pulmonary vascular congestion

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on chest radiography). Exclusion criteria were: chronic use of MRAs, cardiac surgery within 60 days of enrollment, cardiac mechanical support, cardiac resynchronization-therapy within the last 60 days, co-morbid conditions with an expected survival of less than 6 months, acute myocardial infarction at time of hospitalization, hemodynamically significant uncorrected primary cardiac valvular disease, patients requiring intravenous vasodilators or inotropic agents, supine systolic arterial blood pressure <90 mmHg, serum creatinine level >1.5 mg/dL, serum potassium level >5.0 mmol/L, hemoglobin level <9 g/dL, and sepsis.

Institutional review board or ethics committee approval was obtained. All patients provided written informed consent to participate in the study.

2.3. Treatment assignments

Patients were non-randomly assigned in a sequential 1:1 ratio to the intervention or standard treatment. Chief investigator was responsible to assess the eligibility criteria and to allocate the intervention after being contacted by the patient assistant physician. Patients were blinded to the intervention allocation. Assistant physicians were not blinded to intervention allocation. Assistant physicians were Attending Physicians or Fellows of Internal Medicine or Cardiology depending on the ward where each patient was admitted. The assistant physicians evaluated the clinical signs and symptoms and registered their evaluation in the clinical diaries and then transcribed to our database by the authors.

2.4. Trial Intervention

Patients were assigned to either oral spironolactone (minimum and maximum initial dose of 50–100 mg/d, according to assistant physician) plus standard AHF therapy or standard AHF therapy alone. Standard AHF therapy included intra-venous (i.v.) furosemide (bolus or continuous infusion), digoxin, ACEi, ARB, nitrates, and/or non-invasive ventilation (NIV), according to attending physician. At day 2, the attending physician had the option of adjusting spironolactone dose on the basis of the clinical judgment and laboratory results. At this time, the physician could decrease the dose by 50%, to a minimum of 50 mg/d, or maintain the same strategy.

2.5. Study assessments

Patient's clinical status was prospectively recorded, by the assistant physicians, according to previous defined parameters.

An assessment of biomarkers, including plasma creatinine (pCr), ions, N-terminal pro-brain natriuretic peptide (NTproBNP), high sensitivity troponin T (hsTnT) and microalbuminuria was performed at a central core laboratory at admission day (day 1) and day 3. Clinical assessment and routine analyses were performed daily during hospital stay. All patients performed a transthoracic echocardiography within 72 h upon admission. Ejection fraction was calculated according to biplane Simpson method.

2.6. End points

The primary end point was the proportion of patients who were free of congestion at day 3 (defined as jugular venous pressure of <8 cm, no orthopnea and no peripheral edema).

Two safety outcomes (pCr change between day 1 and day 3 plus potassium change between day 1 and day 3) were considered.

Secondary end points included changes in: body weight; NTproBNP levels; microalbuminuria; serum sodium; ionized calcium; serum magnesium; hsTnT; urinary sodium, potassium, urea; and the proportion of patients: taking oral furosemide at day 3; with increase in pCr ≥ 0.3 mg/dL from day 1 to day 3; and with hyper or hypokalemia during the study period.

2.7. Statistical analysis

Comparison between groups was performed using parametric or non-parametric tests, as appropriate. Continuous variables are expressed as mean (standard deviation, SD) or median (inter-quartile range, IQR). Categorical variables are expressed in absolute numbers (no.) and proportions.

Association between different variables was tested by univariate analysis.

Significant association was defined by a p value ≤ 0.05.

Statistical analysis was performed using SPSS software (version 19, Chicago, IL, USA).

3. Results

The pre-specified duration of the enrolment period was one year and during that time we enrolled a total of 100 patients. Fifty patients were allocated to the treatment group. Despite the study protocol referred a range spironolactone dose of 50 to 100 mg/d, one patient had 200 mg at day 1. The mean ± (SD) spironolactone dose at day 1 was 94.5 ± 23.3 mg and at day 3 was 62.7 ± 24.3 mg.

Baseline characteristics of patients in each of the treatment groups are shown in Table 1. Patients in the control group were significantly older (mean ± (SD), 78.8 ± 9.3 vs. 73.2 ± 11.7 years; p = 0.01). The study groups were well balanced in most clinical characteristics, namely: gender, ejection fraction, baseline HF medications (except for beta-blockers, more common in control group — no. (%): 26 (52) vs. 10 (20); p = 0.001), comorbidities [11], and risk stratification for in-hospital mortality [12,13]. All patients were in New York Heart Association (NYHA) class IV upon admission.

Analyzed end-points are shown in Table 2. Patients in the treatment group had a significant respiratory rate (cycles/minute) reduction at day 3 (median [IQR], 20 [2] vs. 18 [3]; p < 0.001). No differences were observed in weight reduction, heart rate and systolic blood pressure (SBP). No patient developed hypotension (SBP < 90 mmHg).

A greater proportion of patients in the treatment group was free of congestion at day 3: no edema (32% vs. 66%; p = 0.001), no rales (24% vs. 66%; p < 0.001), jugular venous pressure (JVP) ≤ 8 cm (90% vs. 100%; p = 0.02) and no orthopnea (76% vs. 96%; p = 0.004). In addition, a significantly higher proportion of patients were switched to oral furosemide at day 3 (44% vs. 82%; p < 0.001) — Graph 1. Furosemide dose was not significantly different in patients who remained on i.v. administration. ACEi and BB doses did not differ between study groups.

Worsening renal function (increase in pCr ≥ 0.3 mg/dL from day 1 to day 3) was more frequent in control group (20% vs. 4%; p = 0.038).

Indirect markers of glomerular damage were not significantly different between groups, but the treatment group appeared to have less glomerular damage after 3 days of treatment i.e. greater albuminuria reduction (median [IQR], − 7.3 [45.8] vs. 10.1 [71.2]; p = 0.32), and lower albuminuria ratio (median [IQR], 0.9 [0.8] vs. 0.7 [0.7]; p = 0.19).

Fractional excretion of sodium (FENa) and urea (FEUr) did not differ between groups, however urine sodium to potassium (UNa/K) ratio significantly increased at day 3 in the spironolactone group (median [IQR], 2.1 [3.1] vs. 4.0 [3.9]; p = 0.007).

Serum potassium (K^+) levels did not differ significantly between groups — Graph 2. No patients developed hyperkalemia (serum potassium ≥ 5.5 mmol/L). More patients in the control group developed hypokalemia (serum potassium ≤ 3.5 mmol/L) but no significant differences were found (26% vs. 14%; p = 0.13).

Plasma NTproBNP had a significant decrease in spironolactone group at day 3 (median [IQR], 2488 [4579] vs. 1555 [1832]; p = 0.05) — Graph 3.

No significant differences were observed in hsTnT (median [IQR], − 0.0005 [0.01] vs. 0.001 [0.01]; p = 0.57).

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Table 1
Baseline characteristics of the study population.

	Control group	Spironolactone group	p value
Age (yrs)	78.8 ± 9.3	73.2 ± 11.7	**0.01**
Male sex — no. (%)	17 (34)	22 (44)	0.31**
Ejection Fraction (%)	45.5 ± 10.7	41.4 ± 12.4	0.08
Left Atrial Size (mm)	47.4 ± 5.3	46.3 ± 7.1	0.40
Charlson Index (pts)	6, 1 ± 1.1	5.9 ± 0.9	0.38
HgB (g/dL)	12.2 ± 1.8	12.7 ± 2.3	0.22
Albumin (mg/dL)	3.7 ± 0.4	3.6 ± 0.4	0.63
TSH (mUI/L)	2.8 ± 3.0	2.6 ± 2.8	0.79
Etiology of Heart Failure — no. (%)			
Ischemic	24 (48)	26 (52)	0.69**
Non-Ischemic	26 (52)	24 (48)	0.84**
Basal NYHA class — no. (%)			
II	41 (82)	44 (88)	0.40**
III	9 (18)	6 (12)	0.40**
History of Atrial Fibrillation or Flutter — no. (%)	34 (68)	25 (50)	0.07**
Outpatients Medications — no. (%)			
Furosemide	37 (74)	35 (70)	0.65**
ACE Inhibitors	24 (48)	18 (36)	0.22**
Beta-Blockers	26 (52)	10 (20)	**0.001****
Outpatients Oral Dose (mg)			
Furosemide	69.2 ± 37.8	68 ± 30	0.89
ACE Inhibitors	5 ± 3	4.3 ± 2.5	0.43
Beta-Blockers	4.4 ± 2.7	4.5 ± 1.1	0.90
Adhere: in-hospital mortality risk – no. (%)			
Low	44 (88)	40 (80)	0.27**
Intermediate 2	2 (4)	3 (6)	0.65**
Intermediate 3	4 (8)	7 (14)	0.34**
Effect: heart failure mortality risk prediction – no. (%)			
Low	4 (8)	8 (16)	0.22**
Intermediate	27 (54)	25 (50)	0.69**
High	18 (36)	17 (34)	0.83**
BMI ≥ 30 (kg/m^2) — no. (%)	14 (28)	19 (38)	0.29**
Diabetes mellitus — no. (%)	25 (50)	20 (40)	0.31**
Glycated hemoglobin (%)	6.9 ± 0.7	7.1 ± 1.2	0.43
Obstructive sleep apnea Syndrome — no. (%)	5 (10)	13 (26)	0.32**
Non-Invasive ventilation — no. (%)	7 (14)	10 (20)	0.42**
AHF precipitant (n)			
Undertreatment	34 (68)	29 (58)	0.30**
Dysrythmia	10 (20)	9 (18)	0.80**
Non-compliance	6 (12)	8 (16)	0.56**
NSAIDs	0	4 (8)	**0.04****

Continuous variables are presented as mean value ± standard deviation [SD], p value. Categorical variables are presented as absolute number (%), p value. **Chi-square test. HgB = hemoglobin; ACE = angiotensin-converting enzyme; BMI = Body Mass Index; NYHA = New York Heart Association; AHF = Acute Heart Failure; NSAID = Non-Steroidal Anti-Inflammatory Drug.

Hospital length of stay did not differ between the two groups [median [IQR], 9 [5] vs. 8 [5]; p = 0.8).

4. Discussion

Our study strongly suggests that the use of spironolactone in ADCHF patients is safe. Furthermore, spironolactone treatment was also associated with an earlier resolution of symptoms and signs of congestion, as well as a more pronounced NTproBNP reduction.

Baseline clinical characteristics were well balanced between the two groups. Although control participants were older than those in the treatment group, that difference did not significantly change the mortality risk prediction scores. The control group had also higher proportion of baseline beta-blockers prescription. However, during hospitalization the beta-blocker treatment did not differ between groups.

The concern about hyperkalemia erroneously precludes the judicious prescription of MRAs in many clinical settings. Our study findings show that this therapy is safe in ADCHF as the use of spironolactone in

Table 2
Study End-Points.

	Control group	Spironolactone group	p Value
Heart rate (beats/min)			
Day 1	91.2 ± 24.7	96.1 ± 23.9	0.30
Day 3	74.9 ± 12.4	77.9 ± 11.4	0.20
SBP (mm Hg)			
Day 1	140.5 ± 23.9	139 ± 27.9	0.80
Day 3	122 ± 15.6	121.9 ± 16.8	0.97
RR (cycles/min)			
Day 1	35 [5]	33.5 [6]	0.90*
Day 3	20 [2]	18 [3]	< **0.001***
BMI (kg/m^2)			
Day 1	29.3 ± 5.7	29.5 ± 6.6	0.90
Day 3	28.1 ± 5.4	27.7 ± 6.6	0.76
Peripheral edema – no. (%)			
Day 1	50 (100)	50 (100)	
Day 3	34 (68)	17 (34)	**0.001****
Rales — no. (%)			
Day 1	50 (100)	50 (100)	
Day 3	38 (76)	17 (34)	<**0.001****
JVP ≥ 8 cm — no. (%)			
Day 1	32 (64)	28 (56)	0.41**
Day 3	5 (10)	0	**0.02****
Orthopnea — no. (%)			
Day 1	50 (100)	50 (100)	–
Day 3	12 (24)	2 (4)	**0.004****
pCr (mg/dL)	1.15 ± 0.27	1.03 ± 0.29	**0.026**
Day 1	1.23 ± 0.43	1.06 ± 0.33	**0.035**
Day 3			
pCr change (mg/dL)			
Day 3 — day 1	0.075 ± 0.3	0.038 ± 0.17	0.47
Increase in pCr ≥ 0.3 mg/dL from Day 1 to day 3 — no. (%)	10 (20)	2 (4)	**0.038****
pUrea	59.32 ± 22.27	51.10 ± 18.63	**0.048**
Day 1	67.08 ±	57.54 ± 23.03	0.061
Day 3	27.09		
pUrea change (mg/dL)			
Day 3 — day 1	7.7 ± 22.9	6.4 ± 17.9	0.75
Albuminuria (mg/g)	73.50 [196.5]	54.05 [203.7]	0.521*
Day 1	60.16 [203]	27.9 [80.2]	0.118*
Day 3			
Albuminuria change (mg/g)			
Day 3 — day 1	−7.3 [45.8]	−10.1 [71.2]	0.32*
Albuminuria ratio	0.9 [0.8]	0.7 [0.7]	0.19*
Day 3/day 1			
FENa (%)			
Day 1	1.4 [2]	2.4 [3.5]	0.24*
Day 3	1.2 [2]	1.6 [2.5]	0.27*
FEUr (%)			
Day 1	38.9 ± 12.7	38.2 ± 11.1	0.47
Day 3	39.5 ± 13.2	37.1 ± 10.5	0.31
UNa/K Ratio			
Day 1	2.7 [3.7]	3.6 [4.7]	0.18*
Day 3	2.1 [3.1]	4.0 [3.9]	**0.007***
Serum potassium (mmol/L)			
Day 1	4.1 ± 0.4	4.0 ± 0.6	0.33
Day 3	3.9 ± 0.5	4.1 ± 0.5	0.15
Hypokalemia (mmol/L) at day 3 — no. (%)	13 (26)	7 (14)	0.13**
Serum sodium (mmol/L)			
Day 1	140 [7]	141 [4]	0.9*
Day 3	141.2 ± 4.3	140.2 ± 3.5	0.2
Serum Ionized calcium (mmol/L)			
Day 1	1.2 [0.1]	1.2 [0.1]	0.6*
Day 3	1.2 [0.1]	1.2 [0.1]	0.1*

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Table 2 (*continued*)

	Control group	Spironolactone group	p Value
Serum Magnesium (mmol/L)			
Day 1	0.84 [0.1]	0.8 [0.1]	0.2*
Day 3	0.87 [0.1]	0.85 [0.1]	0.6*
ProBNP (pg/ml)			
Day 1	3102 [6408]	2701 [3541]	0.17*
Day 3	2488 [4579]	1555 [1832]	**0.05***
TnT (ng/mL)			
Day 1	0.034 [0.035]	0.03 [0.032]	0.5*
Day 3	0.032 [0.036]	0.029 [0.028]	0.3*
TnT reduction (ng/mL)			
Day 3–day 1	−0.0005 [0.01]	−0.001 [0.01]	0.57*
CkMB (UI/L)			
Day 1	15.5 [9]	14 [9]	0.14*
Day 3	14 [8]	12 [8]	0.13*
CkMB reduction (UI/mL)			
Day 3–day 1	−1.7 ± 6.2	−2.3 ± 4.3	0.63
IV furosemide dose (mg)			
Day 1	80 [20]	80 [30]	0.86*
Day 3	60 [20]	60 [30]	0.22*
Oral furosemide at day 3 — no. (%)	22 (44)	41 (82)	< **0.001****
ACE Inhibitors dose (mg)			
Day 1	2.5 [3.8]	2.5 [2.5]	0.75*
Day 3	2.5 [3.8]	2.5 [3.8]	0.72*
ACE Inhibitors — no. (%)			
Day 1	19 (38)	25 (50)	0.20**
Day 3	30 (60)	31 (62)	0.80**
Beta-blockers dose (mg)			
Day 1	2.5 [0]	2.5 [2.5]	0.95*
Day 3	2.5 [2.5]	2.5 [1.25]	0.46*
Beta-blockers — no. (%)			
Day 1	21 (42)	16 (32)	0.30**
Day 3	27 (54)	30 (60)	0.50**
Length of stay (days)	9 [5]	8 [5]	0.8*

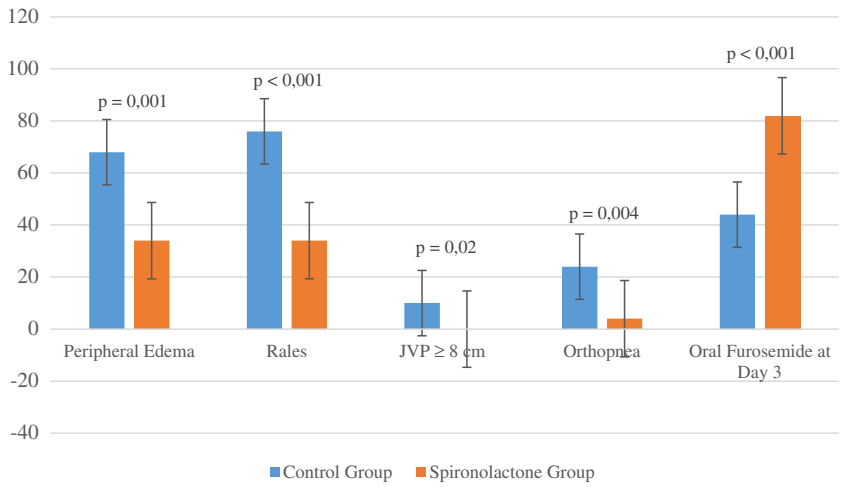
Continuous variables are presented as mean value ± standard deviation [SD], p value or median [inter-quartile range, IQR], p value. Categorical variables are presented as absolute number (%), p value. *Non-parametric test; **Chi-square test.
SBP = systolic blood pressure; RR = respiratory rate; JVP = jugular venous pressure; BMI = Body Mass Index; PaO_2/FiO_2 = partial pressure arterial oxygen/fraction inspired oxygen; pCr = plasma creatinine; FENa = spot urine fractional excretion of sodium; FEUr = spot urine fractional excretion of urea; UNa/K = urinary sodium to potassium ratio; proBNP = N-terminal pro brain natriuretic peptide; TnT = high-sensitivity troponin T; CkMB = creatine kinase-MB; ACE = angiotensin-converting enzyme.

this setting was not associated with renal dysfunction or hyperkalemia. The concomitant use of i.v. diuretics with kaliuretic properties could contributed to the absence of hyperkalemia [19]. In clinical trials enrolling chronic HF patients, MRAs were well tolerated when patients with pCr > 2.5 mg/dL and serum potassium > 5 mmol/L were excluded [2,20]. Still regarding the potassium levels, we observed a trend to hypokalemia in the control group compared to the treatment group. This result is concordant with a previous study where the risk of hypokalemia was significantly reduced among patients receiving MRAs [3]. Reducing the risk of hypokalemia is a significant issue due to the fact that a potassium level below 4.0 mmol/L has been associated with an increased risk of death from any cause among patients with systolic heart failure [21].

Moreover, worsening renal function occurred more frequently in control group. Previous studies suggest that high i.v. diuretic dose is associated with worsening renal function in the short term [17,18]. The frequent congestion status of ADHF and the diuretic therapy activate the RAAS and SNS, which induce renal arteriolar vasoconstriction, endothelial dysfunction and increased tubular reabsorption of sodium and urea [18]. The spironolactone diuretic and renoprotective potential can contribute to these clinical important findings.

We found that patients submitted to high dose spironolactone as add-on to standard AHF therapy had a faster resolution of congestive signs and an earlier switch to oral furosemide. The diuretic effect of spironolactone and possibly the attenuation of the pathological effects of mineralocorticoid receptor (MR) activation [14,15] could explain these findings. In a previous study including 21 AHF patients with insufficient response to loop diuretics, 16 patients (76%) were submitted to 100 mg spironolactone once a day for 7 days in addition to high-dose loop diuretic (10 mg oral bumetanide) in combination with the maximum tolerable dose of an ACEi. Spironolactone coadministration was highly effective in 13 of 16 patients (81%). Marked natriuresis and diuresis were achieved within the next week of treatment, and HF symptoms decreased or disappeared [16]. Despite the earlier resolution of congestive signs found in the treatment group, no significant differences were observed in body weight change; this finding can be explained by the multiple patterns of congestion found i.e., many patients had *left heart* predominance with little weight change, and patients with *right heart* predominance presented with different levels of congestion. These differences (not discriminated in the study) may contribute for this apparent mismatch.

Consistent with the faster resolution of congestive signs and with the preservation of the renal function discussed above, we documented a significant reduction in NTproBNP within the spironolactone group. This is a notable finding since natriuretic peptides have shown to



Graph 1. Changes in congestive signs and patients taking oral furosemide at day 3 (%) in the control and spironolactone groups.

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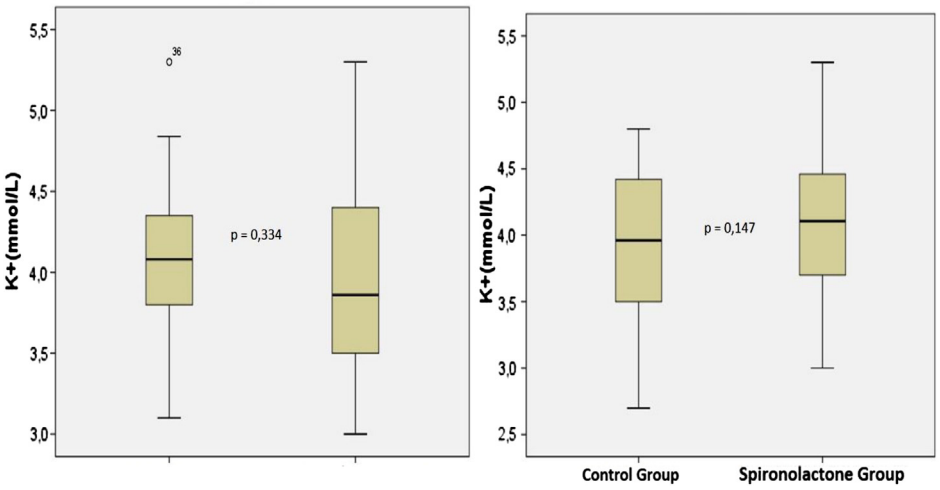


Graph 2. Changes in serum potassium (K+) from day 1 to day 3 in the control and spironolactone groups.

correlate with changes in ventricular wall stress, are inversely related to the severity of left ventricular dysfunction, and are robust prognostic predictors in HF [22–26].

Despite no significant differences were found, patients in the treatment group had greater albuminuria reduction during the treatment period. Albuminuria is an important predictor of adverse cardiovascular events in various populations and MRAs have been shown to attenuate vascular hypertrophy and reduce albuminuria [27,28]. The improvement of this surrogate endpoint gives additional insight on possible benefits of MRA in ADCHF.

Mineralocorticoid receptor antagonists have been observed to stimulate natriuresis and improve diuretic responsiveness in patients with HF [29]. Although FENa did not differ between groups, urine sodium to potassium (UNa/K) ratio significantly increased at day 3 in the spironolactone group. Elevation of UNa/K ratio has been demonstrated to be a translatable biomarker of MRA effect [30]. These findings were reproducible in our study. Future research should be conducted to validate this promising neurohormonal biomarker in the ADHF setting.

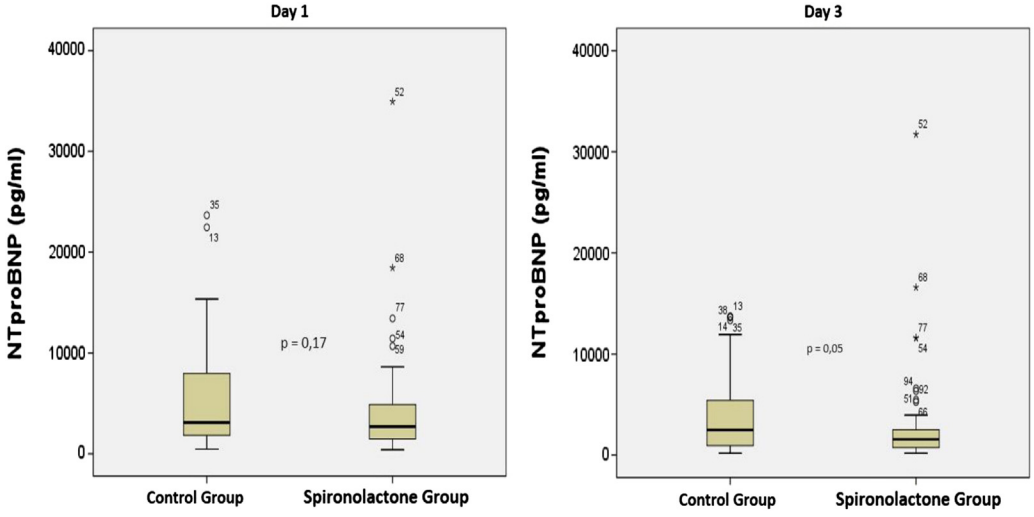
Several limitations in this study should be noted. Firstly, given that no randomization or concealed allocation was performed, we cannot exclude a selection bias, which can impact on our conclusions' external validity. Secondly, the assistant physicians performed the congestive signs assessment, therefore, we cannot exclude an ascertainment bias. This can affect the internal validity of the comparison of subjective outcomes such as congestive signs or symptoms. Though, we had included an important internal control such as plasma NTproBNP that is unaffected by this bias and appear to be consistent with the earlier resolution of the congestive signs in the treatment group. Lastly, our study was underpowered to detect the differences of the expected low rate of adverse events between groups. Thus, our safety data should be viewed as exploratory.

5. Conclusion

Our study shows that treating ADHF patients with spironolactone was safe. It was also associated with an earlier resolution of the congestive signs and with a more pronounced NTproBNP reduction. Despite its exploratory nature, our study highlights the need to improve the treatment of ADHF and points out the direction of future investigation towards MRAs.

Learning points

- Mineralocorticoid receptor antagonists (MRAs) used in acutely decompensated chronic heart failure (ADCHF) may improve congestion through diuretic effect and prevention of neurohormonal activation.
- High dose MRAs (±100 mg Spironolactone) used in ADCHF is safe: is not associated with renal injury and/or hyperkalemia, but may prevent loop diuretic induced hypokalemia.
- Congestion relief is translated into a more pronounced natriuretic peptide reduction.



Graph 3. Changes in mean plasma levels of NT pro-brain natriuretic peptide (NTproBNP) from day 1 to day 3 in the control and spironolactone groups.

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Conflict of interest

The authors have no conflicts to disclose.

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