EFFECT OF SPIRONOLACTONE ON LEFT VENTRICULAR HYPERTROPHY IN PATIENTS UNDERGOING CHRONIC HEMODIALYSIS

FINAL REPORT

Aims of the study:

The main purpose of the study is to evaluate the effects of mineralocorticoid receptor blockade on left ventricular mass in patients undergoing chronic hemodialysis.

Hypothesis:

Our hypothesis is that the spironolactone will cause regression of left ventricular hypertrophy or prevent cardiac fibrosis in chronic hemodialysis patients.

Recruitment Efforts

We screened 80 patients meeting the inclusion criteria from Barnes-Jewish, Chromalloy American, Gambro DeBaliviere and Gambro West dialysis centers. Of those, 62 patients consented for the study. However, some of them either did not qualify for the study by echocardiographic criteria, and a much larger number failed to obtain echocardiograms because of transportation and other social issues. In the end, 30 randomized patients followed through the study. 16 patients received the drug spironolactone 50 mg po QD and 14 were in a control group.

Side effects/adverse reactions. One patient in the spironolactone treated group developed an episode of chest pain taking a study drug and requested to be withdrawn from the study. The side effect was deemed to be not study medicine related. One male patient in the drug treatment group developed gynecomastia after 6 months of drug therapy. This side effect was thought to be drug related. Mammogram confirmed the diagnosis of gynecomastia, which resolved after discontinuation of the drug. One female patient in the drug treatment arm developed deep venous thrombosis in the lower extremity. This side effect was deemed to not to be related to the study drug, but the patient decided to stop the study drug.

Lost to follow-up: The patient who developed chest pain in the drug treatment group withdrew from the study and later transferred to another hemodialysis unit. He was the only patient who was lost to follow-up. Two patients receiving the drug were transplanted during the 12-month study period.

Study Results:

Table 1 shows patient characteristics at the start of the study in both spironolactone treated and control groups. There was no statistical difference between the groups at the start of the study.

Primary endpoint: Table 2 shows the effect of the treatment with spironolactone on left ventricular mass and other echocardiographic parameters. Treatment with spironolactone did not lower left ventricular mass. Left ventricular mass index (LVMI) remained unchanged from baseline at 6 and 12 months. At all time points, LVMI did not differ statistically from the control group. Other parameters, left ventricular end-systolic, end-diastolic dimensions and ejection fraction also remained unchanged (Table 2).

Secondary endpoints:

Effect of spironolactone on pre-dialysis plasma potassium concentration. We observed no significant changes to plasma pre-dialysis potassium concentration. Figure 1 depicts the monthly average pre-dialysis plasma potassium concentration in spironolactone treated and control groups.

Effect of spironolactone on morbidity and mortality. Spironolactone treated group had zero cardiovascular events and zero mortality during the study. There were 2 deaths in the control group giving it a 14 ± 40% annual mortality rate (Table 3). There were 3 myocardial infarctions (MI) in the control group (annual MI rate 21 ± 40%) and none in the drug treatment group (Table 3). The differences in annual mortality and myocardial infarction rates were not statistically significant due to low number of patients and events, but the trend was noticeable. Annual all hospitalization rate per patient also was lower in the drug group, but did not reach statistical significance (Table 3). Cardiovascular hospitalization rate was significantly lower in the drug treatment group.

Conclusions

The treatment with spironolactone did not lower left ventricular mass, i.e. did not cause a regression of left ventricular hypertrophy in hemodialysis patients. However the spironolactone treated group had a lower cardiovascular hospitalization rate and showed a trend towards lower cardiovascular events and lower overall mortality. Because the hospitalization rates, morbidity and mortality were only secondary end points and number of patients and events in the study were relatively small, one should interpret the results with caution.

Table 1. Baseline Patient Characteristics at the Start of Study

	Spironolactone	No Spironolactone
n	16	14
Age (years)	52 ± 16	58 ± 13
Sex		
Men n (%)	10 (62%)	5 (36%)
Women n (%)	6 (38%)	9 (64%)
Race		
African-American n (%)	13 (81%)	12 (86%)
Caucasian n (%)	3 (19%)	2 (14%)
Age (years)	52 ± 16	58 ± 13
Months on hemodialysis	32 ± 20	37 ± 34
Cause of ESRD		
Diabetes Mellitus n (%)	3 (19%)	5 (36%)
Hypertension n (%)	9 (56%)	8 (57%)
Glomerulonephritis n (%)	2 (13%)	1 (7%)
Other n (%)	2 (13%)	0 (0%)
Baseline Laboratory Data		
Plasma Potassium (mmol/L)	4.6 ± 0.5	4.4 ± 0.5
Hemoglobin (mg/dl)	11.4 ± 1	11.9 ± 0.9

All p values for variables between the two groups are > 0.05

Table 2. The Effect of Spironolactone on the Primary Endpoint: Left Ventricular Mass

	Baseline		6 Months		12 Months	
Parameter	Drug	No drug	Drug	No drug	Drug	No drug
Left Ventricular Mass Index (g/m2)	153 ± 38	159 ± 22	153 ± 41	141 ± 41	161 ± 41	127 ± 28
End Diastolic (cm)	5.2 ± 0.7	5.1 ± 0.5	5.1 ± 0.7	5.0 ± 0.6	5.3 ± 0.7	5.1 ± 1.0
End Systolic (cm)	3.5 ± 0.8	3.2 ± 0.6	3.7 ± 0.9	3.1 ± 0.7	3.9 ± 1.2	3.2 ± 1.1
Ejection Fraction (%)	59 ± 10	60 ± 6	56 ± 11	57 ± 15	55 ± 20	59 ± 13

All p values between drug and no drug groups are > 0.05

Table 3. Effect of Spironolactone on Hospitalizations and Cardiovascular Morbidity and Mortality

Outcome	Spironolactone	No Spironolactone	P Value
Deaths			
Number of patients deceased	0	2	
Annual mortality	0%	14 ± 40%	0.14
Acute myocardial infarction (MI)			
Number of acute MI's	0	3	
Annual MI rate	0	21 ± 40%	0.06
Cardiovascular (CV) Hospitalizations			
n	0	14	
Annual CV hospitalizations per patient	0	1.0 ± 1.6	0.02
All cause annual hospitalizations per patient	1.1 ± 1.8	2.3 ± 1.9	0.09

Figure 1. Average Pre-dialysis Plasma Potassium Concentration