Spironolactone in Patients with Heart Failure: Friend or Foe?

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22nd SHA International Symposium, 2011/Riyadh

Disclosure: None
Background

- ALDOSTERONE promotes the retention of sodium, the loss of magnesium and potassium, sympathetic activation, parasympathetic inhibition, myocardial and vascular fibrosis....

- It has a significant mortality and morbidity benefit in the placebo-controlled trials 1

(1) RALES 7 February 2001
Guidelines recommend using Spironolactone in moderate to severe heart failure (HF) and reduced left ventricular systolic function, if there is no contraindication.
Objectives

- To study the frequency and causes of discontinuing spironolactone in adult HF patients following with nurse-led clinic over 10 years

- To define the predictors of intolerance to spironolactone
Methodology

- A Retrospective study
- Inclusion criteria
  - Age > 18 years
  - All patients with EF<40%
  - Enrolled in nurse led clinic KACC from 1/1/2000 - 30/11/2010
  - Received spironolactone at any period and stopped in the follow-up
What is Disease Management?

A system of:
- **Coordinated** healthcare interventions and communications for populations with conditions in which patient **self-care efforts** are significant

- Nurse lead, physician supervised
- Target oriented
- Multidisciplinary Team
CVDMP Goals

- Improve clients & family members quality of life
- Reduce hospital admissions, ER visits & time in hospital
- Enhance knowledge, self-management, optimize medical therapy & improve health related outcomes
- Provide continuous improvement of services
- Ensure care is evidence based
Statistical Methods

- Continuous data is presented as mean ± standard deviation and were compared using Student’s t-test.

- Categorical data was presented as frequencies and compared using Fischer Exact test.
Outcomes

- 1376 patients were enrolled in HF clinic between 1/1/2000 - 30/11/2011
- 585 patients met the guideline criteria to start spironolactone
- 306 patients continue receiving spironolactone at last follow up
- Spironolactone was stopped for 279 patients
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total (n=279)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (years)</td>
<td>56 ± 13</td>
</tr>
<tr>
<td>Male Gender</td>
<td>86 %</td>
</tr>
<tr>
<td>Mean SBP (mmHg)</td>
<td>113 ± 18</td>
</tr>
<tr>
<td>Mean HR (b/min)</td>
<td>76 ± 13</td>
</tr>
<tr>
<td>Mean Potassium Level (MMOL/L)</td>
<td>4.4 ± 0.4</td>
</tr>
<tr>
<td>Mean Creatinine (UMOL/L)</td>
<td>93 ± 24</td>
</tr>
<tr>
<td>Mean Base Line EF</td>
<td>30 ± 9</td>
</tr>
</tbody>
</table>
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total (n=279)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Failure stage D</td>
<td>7%</td>
</tr>
<tr>
<td>MI</td>
<td>30 %</td>
</tr>
<tr>
<td>CABG</td>
<td>18 %</td>
</tr>
<tr>
<td>PCI</td>
<td>17 %</td>
</tr>
<tr>
<td>Diastolic Dysfunction</td>
<td>79 %</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>25 %</td>
</tr>
<tr>
<td>Hypertension</td>
<td>58 %</td>
</tr>
<tr>
<td>History of Renal Disease</td>
<td>2 %</td>
</tr>
</tbody>
</table>
Rationale of stopping spironolactone
(279 patients)

- Improved EF/NYHA: 69%
- Hyperkalemia: 16%
- High creatinine: 16%
- Others: 1%
- Others: 16%
Ejection Fraction (n=279)

- **Enrollment**: 30%
- **Follow up**: 37%

P < 0.001
NYHA (n= 279)

- NYHA I: Enrollment 71%, Follow up 85%
- NYHA II: Enrollment 25%, Follow up 14%
- NYHA >II: Enrollment 4%, Follow up 1%

Significance levels:
- P<0.0001
- P<0.001
- P<0.05
Definition

- **Group one**: Patients who stopped spironolactone due to improvement NYHA or EF

- **Group two**: Patients who stopped spironolactone secondary to side effects
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group 1 (n=197)</th>
<th>Group 2 (n=83)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Gender</td>
<td>72%</td>
<td>83%</td>
<td>0.06</td>
</tr>
<tr>
<td>Mean Age (Years)</td>
<td>54 ± 13</td>
<td>59 ± 12</td>
<td>0.005</td>
</tr>
<tr>
<td>Mean DBP (mmHg)</td>
<td>74 ± 9</td>
<td>71 ± 13</td>
<td>0.006</td>
</tr>
<tr>
<td>Mean SBP (mmHg)</td>
<td>114 ± 20</td>
<td>122 ± 17</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean HR (b/min)</td>
<td>72 ± 9</td>
<td>71 ± 13</td>
<td>0.9</td>
</tr>
<tr>
<td>Mean Potassium (MMOL/L)</td>
<td>4.4 ± 4</td>
<td>4.4 ± 4</td>
<td>0.3</td>
</tr>
<tr>
<td>Mean Creatinine (UMOL/L)</td>
<td>91 ± 24</td>
<td>97 ± 22</td>
<td>0.04</td>
</tr>
<tr>
<td>Mean Base Line EF</td>
<td>31%</td>
<td>29%</td>
<td>0.03</td>
</tr>
</tbody>
</table>
## Baseline Characteristics

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<th>Group 1 (n=196)</th>
<th>Group 2 (n=83)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Failure stage C</td>
<td>92%</td>
<td>99%</td>
<td>0.12</td>
</tr>
<tr>
<td>Heart Failure stage D</td>
<td>8%</td>
<td>1%</td>
<td>0.0001</td>
</tr>
<tr>
<td>MI</td>
<td>36%</td>
<td>41%</td>
<td>0.5</td>
</tr>
<tr>
<td>CABG</td>
<td>15%</td>
<td>24%</td>
<td>0.05</td>
</tr>
<tr>
<td>PCI</td>
<td>19.3</td>
<td>14%</td>
<td>0.3</td>
</tr>
<tr>
<td>Diastolic Dysfunction</td>
<td>77%</td>
<td>69%</td>
<td>0.1</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>57 %</td>
<td>71 %</td>
<td>0.02</td>
</tr>
<tr>
<td>Hypertension</td>
<td>64 %</td>
<td>69 %</td>
<td>0.4</td>
</tr>
<tr>
<td>Hx of Renal Disease</td>
<td>3%</td>
<td>13.3%</td>
<td>0.001</td>
</tr>
</tbody>
</table>
Medication

<table>
<thead>
<tr>
<th>Medication</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE/ARBs</td>
<td>100%</td>
<td>96%</td>
</tr>
<tr>
<td>Beta Blockers</td>
<td>100%</td>
<td>94%</td>
</tr>
<tr>
<td>Statin</td>
<td>94%</td>
<td>90%</td>
</tr>
<tr>
<td>Duiretics</td>
<td>65%</td>
<td>92%</td>
</tr>
</tbody>
</table>

P-values:
- P=1.0
- P=0.5
- P=0.3
- P<0.0001
Heart Failure Etiology

- **Ischemic**: 48% (Group 1), 57% (Group 2), $P=0.19$
- **Idiopathic**: 32% (Group 1), 30% (Group 2), $P=0.7$
- **Hypertensive**: 12% (Group 1), 6% (Group 2), $P=0.19$
- **Others**: 8% (Group 1), 7% (Group 2), $P=0.8$

- **P=0.8**
Heart Failure Stage

- Group 1: 92% (Stage C), 8% (Stage D)
- Group 2: 99% (Stage C), 1% (Stage D)

P = 0.02
NYHA

Group 1

Group 2

P<0.0001

P<0.001

P=0.2

NYHA I

NYHA II

NYHA III

NYHA IV
Ejection fraction

- Group 1: Enrollment 31%, Follow up 40%
- Group 2: Enrollment 29%, Follow up 30%

P<0.0001
Mortality

P<0.0001

Group 1: stopped spironolactone due to Improved NYHA or EF
Group 2: stopped spironolactone secondary to side effect
Mortality

Group 1: stopped spironolactone due to Improved NYHA or EF
Group 2: stopped spironolactone secondary to side effect
Conclusion

- In this study, spironolactone was discontinued in 49% of Saudi patients with HF

- Two thirds of this discontinuation was due to improved ejection fraction and/or functional class; the remainder was secondary to side effects (hyperkalemia/worsening renal function)

- There was significantly higher mortality in the group that stopped spironolactone due to side effects.
Implications

- In patients with HF, Spironlactone may have a significant impact on mortality.

- Intolerance to spironlactone may be an indicator (biomarker) of poor prognosis in patients with HF.
THANK YOU
Chronic Disease Challenge

“The United States cannot effectively address escalating health care costs without addressing the problem of chronic diseases”

Centers for Disease Control & Prevention 2003
Heart Failure Etiology

Group 1
- Ischemic: 30%
- Idiopathic: 58%
- others: 7%

Group 2
- Ischemic: 48%
- Idiopathic: 31%
- Hypertension: 23%
- Others: 7%