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Evidence Updated: None
Bottom Line: Unchanged
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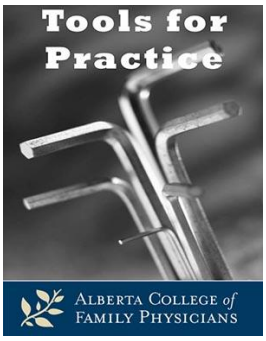

Aldosterone Antagonists in Heart Failure with Reduced Ejection Fraction (HFrEF)—No longer an afterthought

Clinical Question: What is the role of aldosterone antagonists in patients with chronic HFrEF?

Bottom Line: Aldosterone antagonists reduce mortality and hospitalizations in patients with HFrEF (NYHA class II–IV). The benefit appears similar to β-blockers or ACE inhibitors. Close monitoring is required for those at risk of hyperkalemia.

Evidence:

- Two randomized controlled trials:
  - RALES:[1] 1,663 patients with NYHA class 3-4 HF with HFrEF on ACE inhibitors and diuretics. Given spironolactone or placebo. At 24 months:
    - Statistically significant reduction in:
      - Mortality: Spironolactone 35%, placebo 46%, Number Needed to Treat (NNT)=10.
      - Cardiovascular hospitalization: 32% versus 40%, NNT=12.
    - Adverse events:
      - Gynecomastia/breast pain in men: Spironolactone 10%, placebo 1%, Number Needed to Harm (NNH)=11.
      - Serious hyperkalemia (potassium ≥6 mmol/L): not statistically different.
  - EMPHASIS-HF:[2] 2,737 patients with NYHA class II HFrEF with majority on ACE inhibitors and β-blockers. Given eplerenone or placebo. At 21 months:
    - Statistically significant reduction in:
      - Mortality: Eplerenone 13%, placebo 16%, NNT=34.
      - Cardiovascular hospitalization: 22% versus 29%, NNT=15.
    - Adverse events:
      - Hyperkalemia (>5.5 mmol/L) increased with eplerenone 12%, placebo 7%, NNH=22.
      - No difference in gynecomastia or renal failure.
- Two meta-analyses found similar results.[3,4]

Context:

- Aldosterone antagonists compare favourably to other agents used in HFrEF whose relative risk reductions for mortality are:
  - Aldosterone antagonists[1,2] ~25%.
  - β-blockers[5] ~29%.
  - ACE inhibitors[6,7] ~23%.
- Aldosterone antagonists are prescribed at less than half the rate of β-blockers and ACE inhibitors, and therefore represent the greatest potential for increased HFrEF survival.[8]
- Titration to target doses of ACE inhibitors and β-blockers before adding aldosterone antagonists has been advocated,[9] however the usage/doses of these medications were quite different in RALES and EMPHASIS-HF, yet they had similar outcomes.
- There is no head-to-head trial of spironolactone versus eplerenone. Spironolactone ($12/month) could be used first and, if gynecomastia/breast pain develop, switch to eplereonone ($100/month).

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Tools for Practice is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practising family physicians who are joined occasionally by a health professional from another medical specialty or health discipline. Each article is peer-reviewed, ensuring it maintains a high standard of quality, accuracy, and academic integrity. If you are not a member of the ACFP and would like to receive the TFP emails, please sign up for the distribution list at http://bit.ly/signupfortfps. Archived articles are available on the ACFP website.