

8

Aldosterone blockers: spironolactone and eplerenone



What will I learn?

In this section you will learn:

- When aldosterone blockers should be used in heart failure
- How they improve symptoms and outcomes
- How to start and titrate the dose
- What the possible side effects are and what to do about them

Aldosterone plays an important role in the RAAS. Aldosterone production occurs in the adrenal gland and is stimulated by the increased circulating levels of angiotensin II. It is responsible for increasing sodium and water levels in the blood and it also stimulates the excretion of potassium. Blocking the action of aldosterone will reduce these effects and will therefore reduce fluid overload (Fig. 1).

What impact do aldosterone blockers have on symptoms of heart failure?

Oedema can often be demonstrated by pressing firmly on the skin with a finger. If oedema is present, a hollow may be left that will take some time to disappear. This is called pitting oedema.

Reducing the fluid overload will diminish the unpleasant congestive symptoms associated with heart failure, such as peripheral oedema, and pulmonary oedema leading to breathlessness.

What about outcomes?

The RALES trial¹ in 1999 showed conclusively how useful spironolactone could be in improving outcomes for people with heart failure. The study demonstrated a 30% risk reduction in mortality when low-dose spironolactone was added to an ACE inhibitor, diuretic and digoxin (Fig. 2).

Figure 1. The role of aldosterone in the RAAS.

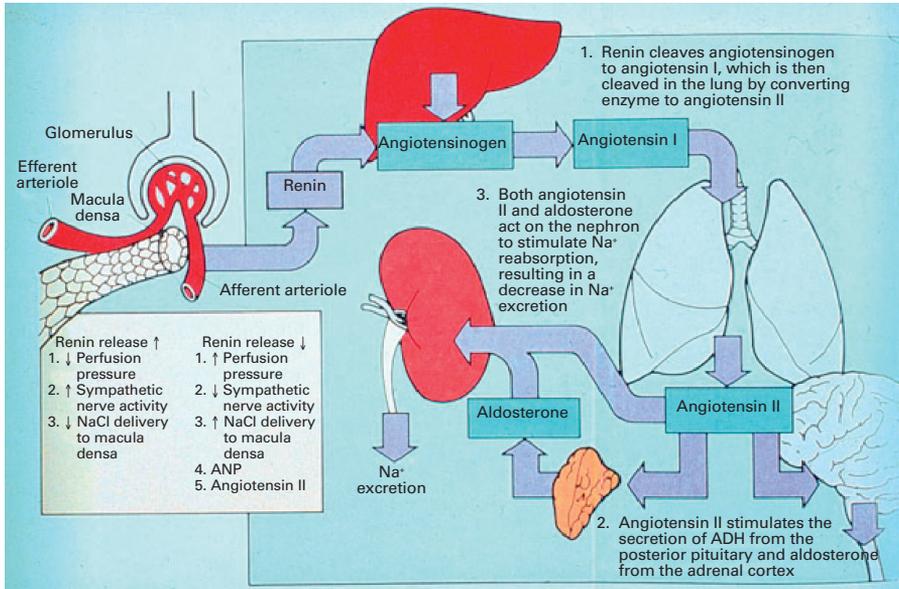
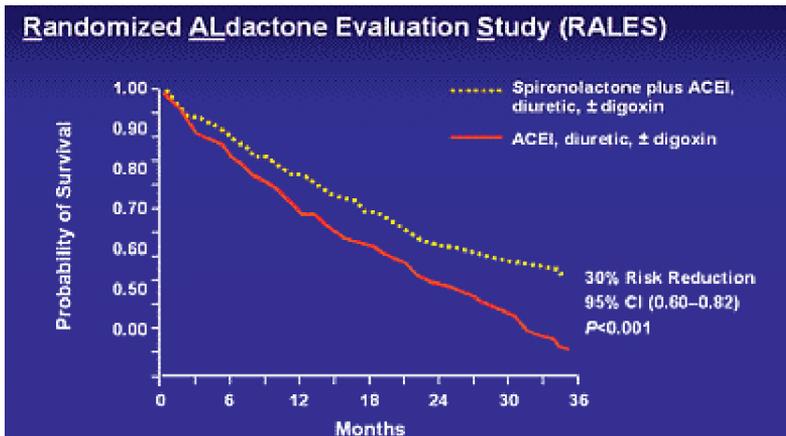


Figure 2. Aldosterone blockade reduces mortality in patients with severe heart failure.



How should these drugs be used?

There are two aldosterone blockers licensed for use: spironolactone and eplerenone. Spironolactone 25 mg daily can be used for patients with symptoms suggestive of moderate to severe heart failure, or NYHA class

III–IV, assuming that they are already being maintained on an ACE inhibitor and diuretic. Blood samples should be taken at weeks one, four, eight and 12 and every three months after that for the first year. Afterwards they should be monitored at least every six months. This is because of the significant risk of hyperkalaemia. If potassium levels rise to 5.5–5.9 mmol/l and creatinine levels to 200 µmol/l, then the dose should be reduced to 25 mg every other day. The drug should be stopped if levels go higher than this.

Eplerenone is for use in post-myocardial infarction; the starting dose is 25 mg, which may be increased to 50 mg within four weeks if the patient can tolerate it. Once again, care should be taken to monitor renal function with these drugs as electrolyte disturbances may occur (Table 1).

It is important to remember that the benefit from aldosterone blockers may not be felt for weeks or even months after starting on them.

Table 1. Administration and dosing considerations with aldosterone antagonists (spironolactone, eplerenone).*

- Consider whether a patient is in severe heart failure (NYHA class III–IV) despite ACE inhibition/diuretics.
- Check serum potassium (< 5.0 mmol/l) and creatinine (< 250 µmol/l).
- Add a low-dose aldosterone blocker (spironolactone 12.5–25 mg, eplerenone 25 mg) daily.
- Check serum potassium and creatinine levels after four to six days.
- If at any time serum potassium level is 5–5.5 mmol/l, reduce dose by 50%. Stop if serum potassium level is < 5.5 mmol/l.
- If after one month, symptoms persist and normokalaemia occurs, increase to 50 mg daily. Check serum potassium/creatinine levels after one week.

*Extracted from ESC guidelines, 2005.



Mary is currently taking perindopril 8 mg and furosemide 20 mg bd. She cannot tolerate beta-blocker therapy. She is currently breathless when she gets dressed in the morning and is unable to go shopping or do her housework. Describe a management plan for the first year of treatment with spironolactone, including follow up and blood tests required.

Which side effects should I be aware of?

We have already described the importance of monitoring renal function and electrolytes. Another important side effect is breast and nipple tenderness and swelling. This can be unbearable for some people and they may have to stop treatment because of it. Eplerenone does not cause this side effect. Gastrointestinal side effects such as nausea and diarrhoea may also occur and the drug should be temporarily stopped if patients are badly affected.



For more information about spironolactone and the RALES trial or eplerenone and the EPHEsus trial go to www.medscape.com or try www.gpnotebook.co.uk



What you need to know

- Aldosterone blockers should be used for people who remain symptomatic, with heart failure symptoms at NYHA level III–IV despite treatment with an ACE inhibitor and diuretic.
- Both RALES and EPHEsus have shown that mortality can be reduced by a third when aldosterone-blocking drugs are used.
- Spironolactone is used at a dose of 25 mg daily; eplerenone, which is licensed for post-MI use, is used at 25–50 mg. Reduced doses and/or frequency may be necessary if side effects occur.
- Side effects include hyperkalaemia and renal dysfunction; breast tenderness may occur although this is less likely with eplerenone.



Self-assessment questions

Take a minute to test your knowledge:

1. What role does aldosterone play in the RAAS?
2. How do aldosterone blockers help alleviate symptoms?
3. Describe the important side effects of aldosterone blockers.

Reference

1. Schwinger RH. The aldosterone antagonist spironolactone prolongs the survival of chronic heart failure patients. The results of the RALES study. *Dtsch Med Wochenschr* 1999; **124**(34–35): 987–988.