Important New Evidence Service

In Partnership with The Centre for Medicines Optimisation at Keele University

ScriptSwitch™ Rapid Update 2 – February 2018

Biochemical monitoring: UK observational study in people taking an aldosterone antagonist finds many are not monitored in line with guidelines

A large UK cohort study has investigated whether patients already taking an angiotensin converting enzyme inhibitor (ACEi) or an angiotensin receptor blocker (ARB) who were started on an aldosterone antagonist had biochemical monitoring in line with recommendations made in the NICE guideline on heart failure. Less than one-third of patients were monitored within two weeks of starting treatment. More frequent monitoring may reduce the risk of adverse events.

Reference: Sinnott S, Mansfield KE, Schmidt M *et al.* Biochemical monitoring after initiation of aldosterone antagonist therapy in users of renin–angiotensin system blockers: a UK primary care cohort study. BMJ Open 2017;**7**:e018153. doi: 10.1136/bmjopen-2017-018153

What do we know already?

- People prescribed an ACEi or an ARB in combination with an aldosterone antagonist (e.g. spironolactone) are at increased risk of severe hyperkalaemia, particularly people with renal impairment. A 2016 MHRA Drug Safety Update highlighted the risk of potentially fatal hyperkalaemia when spironolactone and renin-angiotensin system drugs were used together.
- The 'practical notes' accompanying the 2010 NICE guideline on chronic heart failure in adults advise that urea, creatinine, eGFR and electrolytes should be measured before starting aldosterone antagonists, 1 week after initiation, and then at 1, 2, 3, and 6 months and 6 monthly thereafter. The notes also state that the aldosterone antagonist should be stopped if potassium rises above 6 mmol/L or the creatinine above 220 µmol/L.

What does this evidence add?

- This latest UK cohort study (Sinnott et al, 2017) found that from a population of over 10,000 people taking an ACEi or an ARB who were started on an aldosterone antagonist, less than one-third had a record of biochemical monitoring within two weeks of starting therapy.
- Of people tested within two months (n = 6,520), 2.0% had hyperkalaemia, 2.7% had raised creatinine (≥ 220 µmol/L), and 13.5% had an increase in creatinine of 30% or more from baseline. Aldosterone antagonist treatment was discontinued in approximately half of those with hyperkalaemia or creatinine ≥ 220 µmol/L.
- The study used linked primary and secondary care data, although the investigators could only assess adverse biochemical results for patients who had their blood tested in primary care. Secondary care data on biochemical monitoring was not available and the authors suggested this may have led to missing data from the sickest patients, and potentially an overall underestimation of the rate of adverse biochemical results.
- Although only a small proportion of patients would appear to have received blood monitoring in line with NICE guidance on heart failure, it should be remembered that aldosterone antagonists are also used for other conditions, and not all people in the study population will have had heart failure.

Study details

Participants:

- This UK primary care cohort study drew linked data from the Clinical Practice Research Datalink (CPRD) and Hospital Episodes Statistics (HES).
- The cohort included 10,546 adults (aged 18 years and over) who were started on an ACEi or an ARB between April 1997 and March 2014. Within this cohort the researchers identified people who had also been started on an aldosterone antagonist between 2004 and 2014. The year 2004 was chosen as this was when the Quality and Outcomes Framework (QOF) was introduced.
- Within the study population, the mean age was 71.8 years, and 41% of participants were women. At baseline the mean serum potassium level was 4.4 mmol/L, and around 20% of participants had an eGFR < 30 ml/min/1.73m^2.

Intervention and comparison:

- The mostly commonly prescribed aldosterone antagonist was spironolactone (94%), with the remaining participants prescribed eplerenone.
- The authors did not report which specific ACEi or ARB drugs were prescribed.

Outcomes and results:

- Within two weeks of starting on an aldosterone antagonist, 31.2% of the cohort had blood testing. Blood tests were carried out within two months of starting an aldosterone antagonist for 63.5% of the cohort, with 84.2% having a blood test within 6 months, and nearly all people (94.9%) tested within a year.
- The proportion of people having six tests within a year of starting therapy (representing the NICE guideline recommended testing schedule of 7 days, 1, 2, 3, 6 and 12 months) was approximately 1%.
- For those people who had follow-up monitoring within two months of starting treatment (n = 6,520), 128 (2.0%) had hyperkalaemia, of whom 68 (53%) stopped their aldosterone antagonist treatment. In total, 177 people (2.7%) had raised creatinine (≥ 220 µmol/L) within two months, with 76 people (43%) stopping treatment. Finally, 877 people (13.5%) had an increase in creatinine of 30% or more, of whom 251 (28.6%) stopped the aldosterone antagonist.
- The authors found that women and younger patients were less likely to have had blood testing within two weeks of starting treatment, and patients who started an aldosterone antagonist after 2007 were more likely have blood tests compared to patients who started earlier.

Level of evidence:
Level 3 (other evidence) according to the SORT criteria

Study funding:
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