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Title **A Systematic Review and Economic Evaluation of the Clinical Effectiveness and Cost Effectiveness of Aldosterone Antagonists for Postmyocardial Infarction Heart Failure**

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Aim

Two aldosterone inhibitors (spironolactone and eplerenone) are licensed for heart failure (HF) in the UK. Recent clinical guidelines recommend eplerenone after acute myocardial infarction (MI) for patients with symptoms and/or signs of HF and left ventricular dysfunction (LVSD).

Conclusions and results

Only two large randomized control trials (RCTs) of aldosterone inhibitors in patients with HF and LVSD were found: EPHESUS (Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study), which examined the effectiveness of eplerenone in patients with HF within 3 to 14 days of an acute MI, and RALES (Randomized Aldactone Evaluation Study), which examined the effectiveness of spironolactone in the HF population. Structural similarity of spironolactone and eplerenone suggests that they may be interchangeable, but trial differences limited formal indirect comparison between the trials. A network of evidence from smaller trials was used to facilitate indirect comparison of eplerenone and spironolactone.

Relative safety data were limited from RCTs and observational sources. Hyperkalemia rates varied, but were generally higher than for placebo; data were insufficient to assess discontinuation because of hyperkalemia. Gynecomastia rates were higher with spironolactone. The decision analytic model indicated that, compared with usual care, use of an aldosterone antagonist appears to be a highly cost-effective strategy in managing postMI HF in the NHS. Eplerenone was the most cost-effective strategy for postMI HF; ICER of eplerenone compared with standard care was 4457 pounds sterling (GBP) per QALY, increasing to GBP 7893 per QALY if treatment continued over the patient's lifetime. In neither scenario did spironolactone appear cost effective. The ICER of eplerenone was consistently under the GBP 20 000 to GBP 30 000 per QALY threshold used to establish value for money in the NHS.

Recommendations

See Executive Summary link www.hta.ac.uk/project/1817.asp.

Methods

See Executive Summary link www.hta.ac.uk/project/1817.asp.

Further research/reviews required

An adequately powered, well-conducted RCT that directly compares spironolactone and eplerenone is required to provide more robust evidence on the optimal management of postMI HF patients. Differences in mortality appear to be the major source of current uncertainty. Hence, design and follow-up should reflect this. Given the lack of evidence for either drug in terms of hospitalizations, additional data on nonfatal events requiring hospitalization and side effects would be important outcomes. Estimates of the expected value of perfect information appear sufficiently high to conclude that a head-to-head RCT is likely to provide value for money. Should a future RCT be considered, then a more formal assessment of the costs and benefits should be conducted using the cost-effectiveness model presented here to ensure that this is done efficiently and to assess the feasibility of conducting such a trial.

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