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Meta-regression to estimate treatment effects in cost-effectiveness models: Aldosterone blockers in recent myocardial infarction complicated by heart failure

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Objectivos (Objectives):

Aldosterone blockers in conjunction with other neurohormonal modulators are recommended for use in heart failure (HF) and acute myocardial infarction (MI) in patients with left ventricular dysfunction (including heart failure and post-MI). A recent synthesis of individual trials confirmed that aldosterone blockade improves patient prognosis, demonstrating a 20% reduction in all-cause mortality. This analysis did not address differences between treatments. Existing trials are clinically heterogeneous, and typically these include either patients with recent MI complicated by HF (e.g. EPHESUS trial) or a wider population of patients with HF (e.g. RALES trial). Although only EPL is licensed for post-MI treatment, SPI could be used in some clinical settings. Understanding potential differences is important when aiming at informing decision making based on the cost effectiveness of these treatments.

The objective of this study is to estimate the expected clinical benefits of individual aldosterone blockers, in patients with recent MI complicated by HF. The results of this analysis will inform a decision model estimating the value for money of using eplerenone (EPL) when compared to spironolactone (SPI) for this patient population.

Metodologia (Methodology):

The evidence for the efficacy of spironolactone, eplerenone, or canrenoate (CAN) compared to placebo or active control was identified in a recent systematic review of randomised controlled trials [Ezekowitz and McAlister, 2008]. We adopted a meta-regression approach to aggregate the efficacy results from these trials. This methodology allows all existing evidence to be incorporated and, further, allows explicit characterisation of clinical heterogeneity among the respective the trial populations. We then estimated the treatment effects of EPL and SPI on all cause mortality for patients with MI complicated by HF. We have also evaluated the inclusion of individual patient data (IPD) instead of aggregate data on the two larger trials (RALES and EPHESUS). This was accomplished through Bayesian inference. Evidence on CAN was used only to inform differences between populations, although this treatment is not currently licensed across Europe.

Resultados (Results):

Seventeen randomized controlled trials (evaluating a total of 10448 patients) were included. Of these trials, 13 were conducted in patients with HF (3036 patients) and four

trials (7412 patients) specifically tested aldosterone blockade after MI. SPI was used in 12 trials (2464 patients), CAN in three trials (1200 patients) and EPL in two trials (6784 patients). Results from the meta-regression indicate that, in MI patients, SPI is expected to have a relative risk (RR) of 0.96 [95% confidence interval (CI95%) of 0.26 to 3.62] while EPL is expected to have a relative risk of 0.86 (CI95% of 0.73 to 1.01) and CAN of 0.67 (CI95% of 0.33 to 1.35). Also, results were slightly more precise when data from the two larger trials were included as IPD (EPL: RR of 0.86, CI95% of 0.77 to 0.95; SPI: RR of 0.97, CI95% of 0.45 to 2.94). Using both methods the results for SPI and EPL were robust to a sensitivity analysis where evidence on CAN was excluded.

Conclusões (Conclusions):

The benefits of EPL in MI patients estimated through the meta-regression model are concordant with the results established in the larger clinical trial (EPHESUS). These are estimated to exceed the benefits from SPI use in the same population, but there is great uncertainty concerning the estimates for SPI due to the lack of large clinical trials in this population. By complying with the standards for an accurate assessment of uncertainty in decision models, these results are appropriate to inform cost effectiveness of eplerenone and spironolactone in patients with recent MI complicated by HF.