Beta-blockers in people with and without coronary artery disease

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A large observational study was conducted in people who had a history of myocardial infarction (MI), coronary artery disease (CAD) without MI, or CAD risk factors without established CAD. It compared outcomes among people taking and not taking beta-blockers at baseline over a median of 44 months. The study found no significant difference in the rate of a composite of cardiovascular death, nonfatal MI, or nonfatal stroke among people with CAD or a history of MI, but an increased risk in people who had risk factors for CAD but no established disease. The limitations of this study within the context of existing NICE guidance (due to be updated in November 2013) are discussed in the commentary at the end of this document.

Overview and current advice

Beta-blockers are widely used in the care of people with coronary artery disease (CAD) especially those who have had a myocardial infarction (MI)\(^1\). The evidence to support this use is derived from relatively old post-MI studies, most of which were carried out before modern reperfusion or medical therapy, and from heart failure trials. It is not known if extrapolation of the evidence to people with CAD and even to people at high risk for but without established CAD is justified. Moreover, the long-term efficacy of beta-blockers in people treated with contemporary medical therapies is not known, even in people with prior MI.

NICE has published guidance on secondary prevention following an MI (due to be updated in November 2013). The current guidance advises that all patients should be offered treatment with a beta-blocker early after an acute MI, whether or not they have left ventricular systolic dysfunction, and that the beta-blocker should be continued indefinitely. After a proven MI in the past, the guidance advises that all patients with left ventricular systolic dysfunction should be offered treatment with a beta-blocker whether or not they have symptoms, and care of those with heart failure should be in line with NICE guidance on chronic heart failure. However, people with an MI in the past who have preserved left ventricular function and are asymptomatic should not be routinely offered treatment with a beta-blocker, unless they are identified to be at increased risk of further cardiovascular events, or there are other compelling indications for beta-blocker treatment.
New evidence

This longitudinal, observational study recruited patients between December 2003 and June 2004 from the international REACH registry across 7 geographical regions. It assessed the association of beta-blocker use with cardiovascular events in 3 groups of people 1:

- clinically stable patients with a prior history of MI
- those with CAD but no history of MI
- those with risk factors for CAD only.

Within each group, patients were divided into 2 subgroups based on beta-blocker use at study entry. Propensity scoring was used to adjust for differences in baseline characteristics. The results discussed below are those for the propensity-matched population. The analysis was based on the intention-to-treat principle regardless of subsequent beta-blocker use and the overall median follow-up was 44 months. The primary outcome of the study was a composite of cardiovascular mortality, nonfatal MI, or nonfatal stroke.

The risk of the primary outcome was not statistically significantly different in patients using beta-blockers at study entry compared with non-users in people with a prior MI event (n=6,758; 14.47% versus 15.74%, respectively; hazard ratio [HR] 0.90 [95% confidence interval [CI] 0.79 to 1.03; p=0.14). The risk was also not statistically significantly different in people with CAD but no previous MI (n=7,198; 10.86% versus 11.25%; HR 0.92 [95% CI 0.79 to 1.08]; p=0.31).

However, in the group of people with CAD risk factors but no established disease (n=7,904), the risk of the primary outcome was statistically significantly higher in those who took beta-blockers at baseline (11.82%) compared with those who did not (10.20%): HR 1.18 (95% CI 1.02 to 1.36; p=0.02).

The main analysis was based on beta-blocker use at baseline and did not look at whether or not people stopped or started beta-blockers after study entry. However, the authors also carried out sensitivity analysis that incorporated changes in beta-blocker use over time (but not the type of beta-blocker used). Another sensitivity analysis excluded people with known heart failure, (because of the proven benefits of beta-blockers in people with heart failure). These sensitivity analyses produced results similar to the main analysis.

It should be noted that observational studies, such as this one, are prone to confounding. Unlike in the setting of a randomised controlled trial, in ‘real life’, treatment plans are chosen, changed, or actively not chosen in the light of individual patients’ risk factors, preferences and tolerability or response to other drugs. Thus observed differences in outcomes may be due to differences among the patients, not only the different treatments. In this study the authors adjusted for a number of such possible confounders. However, residual confounding cannot be ruled out. In addition, the study did not access data on the type of beta-blocker the participants were taking, or the dosage, or the reasons why participants were without a beta-blocker.

Commentary

Commentary provided by Dr. Robert Henderson, Consultant Cardiologist, Trent Cardiac Centre, Nottingham University Hospitals:

Current NICE guidance and the existing evidence base have established that beta-blockers confer benefit in people with heart failure, and acute coronary syndrome. Long-term beta-blockade reduces mortality after acute MI, but the evidence base for this benefit appears to have been obtained before the advent of contemporary re-perfusion and medical therapies and only extends for up to four years2. The relevance of this evidence to current management of people with acute coronary syndrome is therefore uncertain and the optimal duration of beta-blocker therapy in unselected people
with acute MI is not known. Nevertheless beta-blockers are an established part of secondary prevention therapy and NICE currently recommends indefinite treatment after acute MI (NICE clinical guideline 48 – currently under review).

Beta-blockers have also been used in other clinical circumstances in the belief that these drugs have a ‘cardio-protective’ effect, but in a recent meta-analysis of beta-blockers in people with stable angina concluded that they ‘do not have statistically significant impact on mortality versus placebo or versus other active comparators’ 3. The longer-term effect of beta-blockade on survival in people with stable CAD has not been examined in appropriately designed prospective clinical trials, but is relevant because treatment with beta-blockers may be complicated by adverse effects on glucose and lipid metabolism.

The data from the current study 1 have limitations as discussed above. If supported by other evidence, then this may challenge the concept that beta-blocker therapy has a ‘cardio-protective’ effect in patients with stable CAD with or without previous MI, or in patients with risk factors for CAD. These observations suggest that symptom control should remain the main indication for beta-blockade in patients with stable CAD and are consistent with current NICE guidance for the management of stable angina, which recommends that beta-blockers or calcium channel blockers can both be used as a first-line treatment for control of symptoms of stable angina (NICE clinical guideline 126). This study does raise a question about how long patients should remain on a beta-blocker treatment after acute coronary syndrome. Further evidence on the long term effects of conjunctive beta-blockade with contemporary interventional and medical therapy is required to clarify this issue.

References

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