Here are two fundamental facts of modern medicine: first, observational data cannot be used to reliably ascertain the effects of a treatment and, second, only randomised, blinded placebo- (or active-) controlled trials provide a robust estimate of the effects of treatment.

The recent history of cardiovascular medicine is littered with examples of how observational data mislead. One of the best of these was the supposed ‘benefit’ of hormone replacement therapy (HRT) in reducing MI and stroke.\(^1\) When eventually conducted, the prospective randomised trials showed the opposite: HRT actually increased the risk of atherothrombotic events.\(^1\)

Observational ‘benefits’ of vitamins C and E, folic acid and beta-carotene have been similarly discredited by randomised trials.\(^1\)

More recently, observational studies have reported findings contrary to the randomised trials for statins, angiotensin-II receptor blockers (ARBs) and mineralocorticoid receptor antagonists in heart failure.\(^5\)–\(^6\)

The REACH registry results

Consequently, I believe that the findings of the report by Bangalore \(\text{et al}\) (see page 34 of this issue) showing no association between nonrandomised beta-blocker treatment and clinical outcomes in patients with coronary heart disease (including prior MI) should be given little, if any, credence.\(^7\) Moreover other, much larger observational studies have reported findings contrary to this new study.\(^8\)–\(^9\)

The study of Bangalore \(\text{et al}\) does, however, raise a legitimate question of whether the undoubted benefits of beta-blockers after MI, demonstrated in trials conducted in the late 1970s and early 1980s, can still be anticipated in patients treated in 2013.

Clearly, things have moved on and such patients now receive antiplatelet agents, statins and ACE inhibitors and usually undergo early percutaneous coronary intervention, treatments that were not used or not available at the time of the original beta-blocker trials.

Benefits of beta-blockers

As a reminder, collectively the placebo-controlled beta-blocker trials showed a relative risk reduction of 23 per cent in all-cause mortality with long-term oral beta-blockade, with a number needed to treat (NNT) at two years to prevent one death of 42 (compared with 94 for a statin and 153 for antiplatelet therapy).\(^10\),\(^11\)

Beta-blockers also reduce the risk of reinfarction (by 27 per cent) and the risk of ventricular arrhythmias and sudden death (by 32 per cent).\(^10\),\(^11\) Importantly, no other treatment has been shown to reduce the risk of sudden death after infarction so convincingly.

Smaller benefits were also seen if early intravenous beta-blocker treatment was given, although this strategy (or the strategy of early intravenous followed by oral therapy) was never widely adopted partly because of concerns about harming haemodynamically unstable patients.

A recent study confirmed these concerns, showing that early intravenous followed by oral metoprolol (for a median of 15 days) caused an increase in risk of fatal cardiogenic shock (and heart failure) that completely cancelled out a reduction in the risk of arrhythmic death (and ventricular fibrillation) in patients with acute MI.\(^12\)

As shown in the older trials metoprolol reduced the risk of reinfarction from 2.5 to 2.0 per cent, a relative risk reduction of 18 per cent (8–28 per cent) or five fewer patients with reinfarction per 1000 treated (\(p=0.001\)).\(^12\)

An earlier study testing a similar question also showed a reduction in reinfarction (and recurrent chest pain) with early vs late initiation of beta-blockade in patients receiving thrombolytic therapy.\(^13\)

Although these recent findings do not support routine use of early intravenous beta-blockade, they do suggest that beta-blockers still exert their antiarrhythmic and anti-infarction benefits in patients receiving contemporary therapy including coronary reperfusion, antiplatelet and antithrombotic treatment and ACE inhibitors.

Conclusion

Consequently, I know of no good evidence to reject the continued use of beta-blockers as a secondary preventive therapy in patients with acute MI.
For other patients with coronary heart disease there has never been strong evidence that beta-blockers have a protective effect. Undoubtedly, beta-blockers are effective antianginal drugs but there is no evidence that they are more effective than other antianginal agents in reducing the risk of infarction or death.

While many cardiologists feel that beta-blockers may reduce the risk of sudden death should a patient experience infarction, this hypothesis is unproven, although the prevention of sudden death with beta-blockers in patients surviving MI and in those with heart failure lends support to it.

Beta-blockers remain a key treatment in cardiovascular medicine: as antianginal and antiarrhythmic agents, as a first-line treatment for rate control in patients with atrial fibrillation and as drugs that reduce morbidity and mortality after MI and in heart failure.

References

Declaration of interests
None to declare.

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